Shared Care Guidelines

Contents

Introduction to Shared Care Guidelines

Developed: November 2005
Updated : April 2008

IMPORTANT	In its guidance on responsibility for prescribing between hospital and general practitioners, the Department of Health has advised that the legal responsibility for prescribing lies with the doctor who signs the prescription. See Shared Care, Prescription Writing. BNF

Background
Shared Care Guidelines are intended to provide GPs with sufficient information to undertake prescribing responsibility for specialist therapies where:

- Treatment is complex
- Monitoring is required
- Communication between primary and secondary care is vital
- GPs are unfamiliar with the therapy, particularly new treatments.
- GPs will usually be asked to assume prescribing responsibility by an appropriate specialist

Treatment with these drugs will be initiated by the specialist, who is responsible for prescribing until shared care is agreed. Any GP who does not wish to undertake the clinical and legal responsibility for a shared care drug is not obliged to undertake the prescribing.

These Shared Care Guidelines are clinical guidelines only. Please contact your PCT GP contract lead to discuss funding issues.

Initiating Therapy
Having assessed the patient and discussed with them the benefits, side effects, frequency of dosing and monitoring requirements of the drug the specialist team will send a letter to the GP asking whether the GP will agree to share care for the patient. The GP will notify the specialist, in writing, whether or not he/she agrees to share care and prescribe for the patient.

A Shared Care Agreement Letter is included in Appendix 1 to facilitate this process.

The Guidelines
The information is derived from relevant references and expert advice and is intended to be sufficient to empower a non-specialist prescriber to undertake the prescribing responsibility for the drug. However, in order to keep the guidelines concise there may be occasions when prescribers need to contact the specialist team for further information.

Each guideline contains the following information:

- Indications
- Dosage, including target/maintenance range and titration details, if any
- GP Monitoring required, including appropriate actions to abnormal results
- References and sources of additional information.
- Side effects
- Drug interactions
- Other relevant clinical information may be included, such as usage in pregnancy, additional vaccination requirements etc.
- Specialist team responsibilities, including those required to initiate therapy as well as ongoing responsibilities.
- GP responsibilities
- Patient's responsibilities
- Contact details of the specialist teams concerned

Please note, new guidelines will only be written when it has been agreed that shared care is an appropriate option.

Individualised Management Plan for Exceptional Prescribing by GPs

There may be occasions where a specialist, following discussion with and agreement by the GP, feels that an individualised management plan for an exceptional drug should be produced. An individualised management plan may be appropriate where

- The therapy being proposed is used exceptionally and it would not be appropriate to agree a formal shared care guideline. There should be no reason why a GP cannot prescribe the drug.
- A GP would need further information about the drug in order to prescribe it.
- The South Devon Joint Formulary does not specify that the drug should only be prescribed by a hospital specialist.

- The GP is happy to prescribe the drug, under an individualised management plan, but needs information to support him / her to take the legal responsibility for the prescribing.

Where a hospital specialist wishes the GP to prescribe a drug under an individualised management plan arrangement he / she should make personal contact with the GP to discuss whether such an arrangement would be appropriate.

If the GP is in agreement then the hospital specialist should write to the GP using the agreement letter (Appendix 2) and should produce an individualised management plan for exceptional prescribing, including sufficient information to enable the GP to prescribe the drug. A template for an individualised management plan is included as Appendix 2.

Where a GP is not happy to prescribe under an individualised management plan for exceptional prescribing then prescribing responsibility will remain with the hospital specialist.

Appendix 1 Shared Care Agreement Letter

Consultant Request

To Dr ……..

Practice Address:

Patient Name
Hospital number
Date of birth
Address

Diagnosed condition:……..

I recommend treatment with the following drug: …….

I am requesting your agreement to sharing the care of this patient according to the South Devon Shared Care Guideline for this drug. If you agree, I will send you, in writing, any additional information required for you to undertake prescribing responsibility, as laid down in the Shared Care Guideline.

Signed:…….. Date……

Consultant name:……..

Department:……..……

Contact telephone number: …….

GP Response

I agree / do not agree* to share the care of this patient in accordance with the Shared Care Guideline.

Signed:…….. Date……

GP name:……...
*Delete as appropriate

Appendix 2 Individualised Management Plan for Exceptional Prescribing

a) Request letter

Consultant Request

To Dr ……..

Practice Address:

Patient Name
Hospital number
Date of birth
Address

Diagnosed condition:…….

I recommend treatment with the following drug: …….

Following our telephone conversation, I am writing to request your agreement to sharing the care of this patient according to the enclosed individualised management plan. If you agree, I will send you, in writing, any patient specific information required for you to undertake prescribing responsibility as laid down in the management plan, for example, results of blood tests.

Signed:…….. Date……

Consultant name:…….. Contact number: …….

Department:……..……..……

Enclosed: Completed Individualised Management Plan for Exceptional Prescribing

GP Response

I agree / do not agree* to share the care of this patient in accordance with the Individualised management plan.

Signed:…….. Date……

GP name:……...
*Delete as appropriate

b) Template Individualised Management Plan for Exceptional Prescribing

Drug		**Patient**	
Hospital Specialist		**GP**	

This is an individualised management plan specific for the above named drug and patient. Please refer to South Devon Joint Formulary (chapter 20 p3 for information on when an individualised management plan for exceptional prescribing is appropriate).

Indication(s)	
Dose	
Likely duration of treatment	
Formulation and strengths available	
Is the drug licensed for this indication?	
Side effects	
Drug interactions	
Other relevant clinical information, such as Special precautions / warnings Use in pregnancy Renal / hepatic impairment Additional vaccination requirements	
GP Monitoring required, including appropriate actions to abnormal results	
Specialist team responsibilities (initial and ongoing)	
GP responsibilities	
Patient's responsibilities	
Contact details of the specialist teams concerned	
References and sources of additional information.	

Appendix 3 List of Shared Care Guidelines with indications

Guideline	Speciality	Indications
Atomoxetine	Paediatrics	Attention deficit hyperactivity disorder.
Azathioprine	Dermatology	Psoriasis, eczema, pyoderma gangrenosum (all unlicensed).
	Gastroenterology	Ulcerative colitis (unlicensed), Crohn's disease (unlicensed) and autoimmune hepatitis
	Ophthalmology	Thyroid eye diseases, corneal melt, cicatrizing conjunctivitis, corneal graft rejection, scleritis and uveitis (all unlicensed).
	Respiratory	Interstitial lung disease (including cryptogenic fibrosing alveolitis) and pulmonary vasculitis (all unlicensed).
	Rheumatology	Rheumatoid arthritis, other inflammatory arthritis, connective tissue disease, vasculitis, and as a steroid sparing agent.
Ciclosporin	Dermatology	Psoriasis, atopic eczema.
	Gastroenterology	Ulcerative colitis and autoimmune hepatitis (all unlicensed).
	Ophthalmology	Corneal melt, cicatrizing conjunctivitis, corneal graft rejection, and scleritis and uveitis (all unlicensed).
	Respiratory	Interstitial lung disease (including cryptogenic fibrosing alveolitis) and pulmonary vasculitis (all unlicensed).
	Rheumatology	Connective tissue disease (unlicensed) and rheumatoid arthritis.
Colistin nebulised	Respiratory	Ps. Aeruginosa in patients with Cystic Fibrosis.
Gentamicin nebulised	Respiratory	Ps. Aeruginosa in patients with Cystic Fibrosis. (unlicensed)
Hydroxy-chloroquine	Dermatology	Dermatological conditions caused or aggravated by sunlight e.g. cutaneous lupus erythematosus.
	Rheumatology	Rheumatoid arthritis, other inflammatory arthritis and connective tissue disease.
Leflunomide	Rheumatology	Rheumatoid arthritis, psoriatic arthritis and other inflammatory arthritis.
Lisdexamfetamine	Paediatrics	Attention deficit hyperactivity disorder.
Lithium	Psychiatry	Management of acute mania or hypomanic episodes; episodes of recurrent depressive disorders where treatment with other antidepressants has been unsuccessful; prophylaxis against bipolar affective disorders; control of aggressive behaviour or intentional self-harm.
Methotrexate	Dermatology	Severe, uncontrolled psoriasis, unresponsive to other therapy.
	Gastroenterology	Crohn's disease and ulcerative colitis unresponsive to other therapy (unlicensed).
	Ophthalmology	Uveitis (unlicensed).
	Respiratory	Severe steroid-resistant asthma (unlicensed).
	Rheumatology	Rheumatoid arthritis and other types of inflammatory arthritis, myositis, vasculitis, other connective tissue diseases and as a steroid sparing agent.
Methylphenidate	Paediatrics	Attention deficit hyperactivity disorder.
Penicillamine	Rheumatology	Rheumatoid arthritis
Riluzole	Neurology	To extend life or the time to mechanical ventilation for patients with amyotrophic lateral sclerosis
Sodium aurothiomalate	Rheumatology	Rheumatoid arthritis and other inflammatory arthritis.
Sulfasalazine	Gastroenterology	Ulcerative colitis and Crohn's disease
	Rheumatology	Rheumatoid arthritis and other inflammatory arthritis.
Tobramycin nebulised	Respiratory	Ps. Aeruginosa in patients with Cystic Fibrosis.

Appendix 4 Quick reference guide to ongoing monitoring requirements

Drug	FBC	U&Es/serum creatinine	LFTs	Other
Azathioprine	Weekly for 8 weeks, then monthly		Weekly for 8 weeks, then monthly*	
Ciclosporin	Monthly until dose stable for 3 months, then 3 monthly	Fortnightly until dose stable for 3 months, then monthly	Monthly until dose stable for 3 months, then 3 monthly*	Blood pressure: Fortnightly until dose stable for 3 months, then monthly. Serum lipids: 6 monthly
Hydroxy-chloroquine				Visual acuity: Annual
Leflunomide	Fortnightly for 6 months, then monthly	6 – 12 monthly	Fortnightly for 6 months, then monthly*	Blood pressure: Fortnightly for 6 months, then monthly
Lithium (Priadel®)		6 monthly		Lithium levels: Monthly until dose stable for 3 months, then 3 monthly Thyroid: 6 monthly ECG: Annually
Methotrexate	Fortnightly for 3 months, then monthly	6 – 12 monthly (unless deteriorating renal function suspected)	Fortnightly for 3 months, then monthly*	
Penicillamine	Fortnightly until dose stable, then monthly			Protein Urinalysis: Fortnightly until dose stable, then monthly
Riluzole	Every 3 months for first 9 months**		Every 3 months for first 9 months**	**Not including initial 3 months monitored by specialist team
Sodium aurothiomalate	At each injection			Protein Urinalysis: At each injection
Sulfasalazine	Fortnightly for 3 months, then every 3 months		Fortnightly for 3 months, then every 3 months*	

*Please include CRP with LFTs for Rheumatology.

Indications for this guideline

Hypocalcaemia due to hypoparathyroidism (most commonly after Thyroid or Parathyroid surgery) in Adults and Children.
Alpha calcidol is also used in patients with CKD with secondary hyperparathyroidism. This guideline should not be used for this indication. The renal teams will provide guidance on monitoring for those patients.
Alpha calcidol is a very potent short-acting vitamin D analogue with high risk of side effects (see below). Other less potent Vitamin D preparations should be used for prevention and treatment of osteoporosis in those with normal renal function.

Dosage

Maintenance doses generally range between 0.25 to 1 microgram daily

IMPORTANT	Higher doses may occasionally be required in acute hypocalcaemia in specialist care. If doses higher than 2.0 micrograms seem to be required in the non-acute setting seek specialist advice. Patients with normal renal function with significant hypoparathyroidism will usually require calcium supplements as well as Alpha Calcidol. Patients should be receiving supplemental calcium 1-2g per day. In patients who have normal serum calcium without calcium supplementation consideration should be given to whether the alpha calcidol treatment can be stopped (seek advice).

GP Monitoring

Alpha calcidol must not be prescribed without monitoring of serum calcium and renal function. If monitoring is not possible, specialist advice should be sought and consideration given to the use of alternative therapies.

GPs will only be asked to monitor alpha calcidol treatment once the need for long-term therapy has been established (in surgical hypoparathyroidism 3-6 months post-operatively) and the patient is on a stable dose of therapy.

Once on stable dose of Alpha Calcidol, serum calcium (corrected for protein binding) magnesium, phosphate and renal function should be checked every 3 months (more frequently if symptoms of possible over or under-treatment). Monitoring will need to be continued indefinitely while taking the therapy.

The aim of treatment in general is to achieve serum corrected calcium 2.0 – 2.2 mmol/l (higher levels even within the normal range may increase the risk of nephrocalcinosis.).

If Calcium <2.0 but >1.7 increase alpha calcidol by 0.25 – 0.5 micrograms daily. Check patient is still taking Calcium supplements (see above 'important notes') Repeat serum calcium within one week if dose changed.
If Calcium >2.2 but less than 2.6, repeat serum calcium within one week.

If persistently raised, reduce dose of alpha calcidol by 0.25 – 0.5 micrograms daily.
Repeat serum calcium after one week on new dose.

If Calcium >2.6 mmol/l reduce alpha calcidol by 0.5 micrograms daily and repeat serum calcium in 2-3 days.
If serum calcium <1.7 mmol/l or >3.0 mmol/l or patient markedly symptomatic (malaise, thirst, perioral tingling, cramps or tetany, seek specialist advice urgently or consider admission.
If serum calcium results persistently outside target range, check serum Magnesium and seek specialist advice (see below).

Please copy results to secondary care team if under active specialist follow up.

Corrected serum Calcium Level	Dose adjustment micrograms	Action
1.7 to 2.0	Increase by 0.25-0.5 daily	Check serum levels in 1 week
2.2 to 2.6	Decrease by 0.25-0.5 daily	Check serum levels in 1 week
>2.6	Decrease by 0.5 daily	Repeat serum levels in 2-3 days
<1.7		Seek Specialist advice
>3.0		Seek Specialist advice

Side effects (not covered by specific monitoring requirements)

Over-treatment causing hypercalcaemia may cause thirst, malaise, polyuria.
Severe hypercalcaemia can cause cardiac dysrythmias.

Persistent hypercalcaemia due to over-treatment with Alpha Calcidol can cause irreversible nephrocalcinosis and end-stage renal failure.

Hypocalcaemia due to under-treatment can cause marked symptoms (muscle weakness, perioral tingling, cramps and tetany) and when severe can cause convulsions or cardiac arrythmias.

Drug interactions: (refer to BNF, Appendix 1 for full list of interactions)

Alpha calcidol should be used with caution for:
Patients being treated with cardioactive glycosides or digitalis as hypercalcaemia may lead to arrhythmia in such patients
Patients taking barbiturates or anticonvulsants may require larger doses of Alpha calcidol to produce the desired effect due to the induction of hepatic detoxification enzymes.
Concomitant administration of colestyramine may interfere with the intestinal absorption of alfacalcidol.
Use with caution in patients being treated with thiazide diuretics as they may have an increased risk of developing hypercalcaemia.

Concomitant Drug Therapy

Many patients will be taking levothyroxine as well as alpha calcidol and the dose of levothyroxine should be increased in line with separate guidelines 0582.
Some patients may be Vitamin D deficient as well as hypoparathyroid. In that circumstance it may be appropriate to co-prescribe alpha calcidol and other Vitamin D3 supplements. The specialist will advise.

Pregnancy and breastfeeding.

Patients planning pregnancy or found to be pregnant should have serum calcium and renal function measured at the earliest opportunity. Alpha calcidol is unlikely to be harmful in pregnancy as long as serum calcium in target range (2.0 – 2.2 mmol/l). Risk to the foetus is likely to be greater if the therapy is discontinued through risk of maternal hypocalcaemia. Hypercalcaemia during pregnancy may produce congenital disorders in the offspring.
Although it has not been established, it is likely that increased amounts of 1,25-dihydroxyvitamin D will be found in the milk of lactating mothers treated with Alpha calcidol. This may influence calcium metSabolism in the infant.Please seek specialist advice (see below).

Initiating therapy – Specialist Team

Having assessed the patient and discussed with them the benefits, side effects, frequency of dosing and monitoring requirements of Alpha Calcidol treatment the specialist team will:-

- **Communicate with the patient's GP, in writing, and confirm that the GP agrees to share care, as described in the Introduction to Shared Care Guidelines.**
- Record the patient's confirmation of understanding of the risks, benefits and consent.
- Undertake baseline investigations and initiation and stabilisation of therapy.
- Specify target doses, monitoring and review dates at clinically relevant time intervals for both the GP and specialist team and any other patient specific information.
- Ensure that full information is sent to the GP without undue delay and recommend that the GP continues treatment in accordance with this shared care guideline.

Information given to patient

Web Link (Hypoparathyroidism UK)

- The need for long-term Alpha calcidol treatment has been established.
- On-going monitoring of serum calcium and renal function is required indefinitely. Once a stable dose of alpha calcidol is achieved the GP will arrange blood tests every 3 months. If the patient has persistent symptoms he/she should contact the GP and have another blood test.
- Alpha calcidol treatment is usually accompanied by calcium supplementation.

GP Responsibilities

The GP will notify the specialist, in writing, whether or not he/she agrees to share care and prescribe for the patient, according to this guideline.

- Monitor for adverse effects and drug interactions and report adverse events to the CSM and specialist team.
- Conduct blood tests, review results and any necessary action is undertaken as specified in GP Monitoring section above.
- Report to and seek advice from the specialist team on any aspect of patient care which is of concern to the GP and may affect treatment.
- Prescribe further supplies of Alpha Calcidol according to the regimes specified in this guideline.

Ongoing Specialist Team Responsibilities

- Review the patient at agreed intervals when appropriate. Long term follow up may not be required by the specialist team (e.g. post-operatively after surgery for benign thyroid disease). Follow up arrangements will be agreed prior to discharge.
- Provide advice as requested by the GP.
- Assess patients referred back by GPs as soon as is practical.

Patient's Responsibilities

- Report any adverse effects to their GP and / or specialist team.
- Ensure that they have a clear understanding of their treatment.
- Ensure they attend for monitoring requirements as specified in this shared care guideline.
- Be aware that treatment will be stopped it they do not attend for monitoring.

Contact details for the Specialist Teams

9am to 5pm weekdays
Contact Consultant Endocrinologist who initiated treatment.
Or
Endocrine Specialty mobile phone (via Torbay Hospital switchboard 01803 614567
Or
Sue Cox, Endocrine Specialist Nurse 01803 656019
Out of Hours:
Medical SpR on-call via SDHCT switchboard (01803 614 567).

Full Prescribing Information

For full prescribing information please consult summaries of product characteristics and the current BNF.

References

- eSPC for One-alpha capsules®
- BNF 63 March 2012

The information contained in these shared care guidelines is issued on the understanding that it is the best available from the resources at our disposal at the time of issue. Please see Chapter 20 – Introduction to Shared Care Guidelines for more information.

For attention deficit hyperactivity disorder in children and adolescents (6 years to under 18 years)

This guideline highlights significant prescribing issues. Not all prescribing information and potential adverse effects are listed. Please refer to SPC/data sheet for full prescribing data.

Specialist:

Please complete letter at the end of this document and send together with the shared care guideline to the GP.

GP:

Please indicate whether you wish to share patient's care by completing letter at the end of this document and return to specialist.
GPs are invited to participate. If a GP is not confident to undertake these roles, then they are under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist
Aim of treatment

Aim of treatment

The degree of impairment experienced by individual people with attention deficit hyperactivity disorder (ADHD) varies depending on personal circumstances, and individuals can also respond differently to treatment. A person-centered approach is essential to identify the needs of the patient and family, agree treatment goals, develop a tailored treatment plan, re-assess and evaluate treatment response, and ensure goals are regularly updated to reflect changed circumstances and needs.
Medication may be indicated as part of a comprehensive treatment programme for confirmed ADHD when remedial measures alone prove insufficient. Stimulants (e.g. methylphenidate, dexamfetamine and lisdexamfetamine dimesylate) and non-stimulants (e.g. atomoxetine) are the two types of medication available for the treatment of ADHD.

Specialist responsibilities

Complete initial assessment and establish diagnosis of ADHD
Where appropriate- offer and initiate medication for management of ADHD (including appropriate pre-treatment screening and required baseline monitoring)
Provide the person and/ or the person's parents/guardians/carers with suitable written and verbal information about the medication prior to starting treatment and discuss the benefits and side effects of treatment including the monitoring of therapy.
Information should include advice about over the counter (OTC) drugs that can interact with atomoxetine and a recommendation to consult a pharmacist before using OTC remedies.
Ensure a comprehensive care plan is developed and agreed- setting out the required level of care and support needed as well as clear guidance about how response to treatment will be reviewed (to include all health and social care professionals involved in delivery of care).
Ensure formal communication is sent to the child/ young person's school regarding the use of atomoxetine where indicated.
Prescribing the medication for the first 3 months of treatment or until the person's condition/dose is stabilised, and the GP agrees to take over responsibility for prescribing.
Specify review dates at clinically relevant time intervals (for both the GP and the consultant/ specialist provider)
Ensure prompt communication with GP (and other service providers as appropriate) of any changes in treatment, results of monitoring undertaken and assessment of adverse events.
On-going monitoring for effectiveness of treatment (based on clinician's assessment and feedback/ observations from individual and/or parents.
Reporting adverse events to the Commission on Human Medicines (CHM)
Ask the GP whether they are willing to participate in shared care.
Provide the GP with relevant contact information with clear arrangements for back-up advice and support should further assistance be required relating to this medication.
Where indicated- advice to GPs on when and how to stop treatment:
e.g. Medication free periods may be recommended to allow catch up growth (rarely growth retardation may occur during prolonged treatment) and the consultant overseeing treatment should liaise with the individual, their parents/ guardians and the individual's GP to advise on the timing of this.
Liaise with Adult ADHD services (Currently DANA service) to facilitate safe transition from children's to adult's services when necessary.

General practitioner responsibilities

- Ensure a timely reply is sent to specialist in response to request for shared care.
- Where agreed, continue to prescribe atomoxetine in accordance with shared care guidelines.

- Ensure that monitoring (height, weight, blood pressure and pulse) is completed in accordance with shared care guidelines (see monitoring section)
- Prompt referral to a specialist if there is a change in the person's physical or mental health status.
- Report to and seek advice from a specialist on any aspect of patient care which is of concern to the GP and may affect treatment.
- Reporting adverse events to specialist and Commission on Human Medicines (CHM)
- Stop treatment/ amend dose in the case of a severe adverse event or as per shared care guideline.

Monitoring

Baseline assessment & monitoring (to be completed by the specialist service provider):

- Full history and physical examination to include:
    - assessment for the presence of cardiac disease (including history of exercise syncope, undue breathlessness and other cardiovascular symptoms)
    - heart rate and blood pressure (plotted on a centile chart)
    - height and weight (plotted on a growth chart)
    - family history of cardiac disease and examination of the cardiovascular system
- An electrocardiogram (ECG) if there is past medical or family history of serious cardiac disease, a history of sudden death in young family members or abnormal findings on cardiac examination

Where findings suggest a history or presence of cardiac disease, individuals should be referred for a specialist cardiac evaluation prior to initiating drug treatment.

Before initiating treatment for young women of child-bearing potential it is essential to consider and discuss contraception and/ or, where appropriate, the risks of pregnancy (including relapse, risk to the foetus and risks associated with stopping or changing medication). If there is any possibility that the individual may be pregnant it is important to confirm this prior to starting treatment.

Following an adequate treatment response, drug treatment for ADHD should be reviewed annually and continued for as long as it is clinically effective.
The specialist will plot results received from the GP on a centile chart (for heart rate and blood pressure) and growth chart (for height and weight).

Where abnormal results or presence of side effects are identified, the specialist will contact the individual and/ or GP to advise on action required (e.g. need for additional specialist treatment review/ stop treatment).

As part of transition service planning, young people should receive a timely review by a specialist to discuss drug treatment and consider whether continuation into adulthood will continue to provide therapeutic benefit.

Monitoring during treatment (to be completed by the GP in accordance with shared care):

The following monitoring should be carried out as follows (and before and after each dose change):

- Height & weight, at least every 6 months
- Blood pressure & pulse, every 3 months

Monitoring undertaken by the GP must be copied to the Consultant to ensure accurate monitoring and review of treatment. Where abnormal results or presence of side effects are identified (which could indicate need to review/ stop treatment) the GP should seek advice from a specialist.

Where an individual presents to the GP with any of the following symptoms (which may be associated with ADHD medication) or if the GP has any concerns about possible diversion, misuse or abuse of medication, specialist advice must be sought:

- Development or worsening of psychiatric disorders (e.g. anxiety, psychotic or manic symptoms).
- Development of symptoms such as palpitations, exertional chest pain, unexplained syncope, dyspnoea or other symptoms suggestive of cardiac disease (prompt specialist cardiac evaluation indicated)
- Onset or exacerbation of motor and verbal tics.
- Hepatic impairment:

Very rarely, spontaneous reports of liver injury, manifested by elevated hepatic enzymes and bilirubin with jaundice, have been reported. Also very rarely, severe liver injury, including acute liver failure, have been reported. Atomoxetine should be discontinued in patients with jaundice or laboratory evidence of liver injury, and should not be restarted.

Patient responsibilities

- Take (or support administration of) medication as directed by the prescriber.
- Report any adverse effects to the GP and/or specialist regarding their treatment.
- Ensure prescribed medication is stored safely and securely

- Ensure that they or their carers have a clear understanding of the treatment, expected benefits and potential side effects.
- Ensure they understand the importance of monitoring treatment and attend specialist appointments and/ or GP appointments to ensure timely monitoring can be completed (in accordance with the shared care guideline).
- Understand that treatment will be stopped if patient does not attend for monitoring and treatment reviews

Supporting Information

The aim of these guidelines, applicable to children (aged 11 years or under) and young people (12-18 years), is to support adherence to:
NICE CG 72: Attention deficit hyperactivity disorder. Diagnosis and management of ADHD in children, young people and adults
NICE TAG 98: Methylphenidate, atomoxetine and dexamfetamine for attention deficit hyperactivity disorder (ADHD) in children and adolescents
Advise and regularly reiterate importance of safe and secure storage of medication at home (and at school where necessary).

Product information: refer to local formulary

Doses: refer to SPC or BNF

- Children and young people up to 70 kg Body Weight:
  - Initiate treatment with a total daily dose of approximately 0.5mg/kg.
  - The initial dose should be maintained for a minimum of 7 days prior to upward dose titration according to clinical response and tolerability. The recommended maintenance dose is approximately 1.2mg/kg/day (depending on the patient's weight and available dosage strengths of atomoxetine).
- Children and young people over 70 kg Body Weight:
  - Initiate treatment with a dose 40mg once daily.
  - The initial dose should be maintained for a minimum of 7 days prior to upward dose titration according to clinical response and tolerability. The recommended maintenance dose is 80mg.

Contraindications and precautions: refer to SPC

Side effects: refer to SPC

Interactions: refer to SPC

Pregnancy and lactation

There is limited information available regarding the use of atomoxetine during pregnancy and lactation. Young women of child-bearing potential should be provided with appropriate advice (e.g. contraception).
Atomoxetine should not be used during pregnancy and avoided during breast-feeding, unless the potential benefit justifies the potential risk to the foetus. Additional advice from specialist medicine information department and, where appropriate, perinatal mental health service should be sought if needed.

Refer to Summary of Product Characteristics for full information.

Contact details	
Virgincare (CAMHS)	email: vcl.devonspa@nhs.net telephone : 0330 0245 321 Website
RD&E Foundation Trust	rde-tr.exeterchildhealth@nhs.net
Livewell Southwest	www.livewellsouthwest.co.uk/services/child-adolescent-mental-health-services-camhs
Torbay and South Devon NHS Foundation Trust	www.torbayandsouthdevon.nhs.uk/services/camhs/

Guideline updated by Devon Partnership NHS Trust in consultation with local specialists and GPs
For non-clinical enquiries: D-CCG.DevonFormularies@nhs.net

Date ratified: 9th March 2016

References:
National Institute for Health and Care Excellence. 2006. Technology Appraisal Guidance 98: Lisdexamfetamine, atomoxetine and dexamfetamine for attention deficit hyperactivity disorder (ADHD) in children and adolescents. Available from: http://www.nice.org.uk/guidance/ta98/resources/guidance-lisdexamfetamine-atomoxetine-and-dexamfetamine-for-attention-deficit-hyperactivity-disorder-adhd-in-children-and-adolescents-pdf [Accessed 2Mar2015]
National Institute for Health and Care Excellence. 2008 (Modified 2013) Clinical Guidance 72- Attention deficit hyperactivity disorder. Diagnosis and management of ADHD in children, young people and adults. Available from: http://www.nice.org.uk/guidance/cg72/resources/guidance-attention-deficit-hyperactivity-disorder-pdf [Accessed 2Mar2015]
Bolea-Alamanac B, Nutt D, Fone K, et al (2014) Evidence-based guidelines for management of attention-deficit hyperactivity disorder: Update on recommendations from the British Association for Psychopharmacology. Available from: http://www.bap.org.uk/pdfs/ADHD_Guidelines.pdf [Accessed 26 Mar 2014]
British National Formulary for Children (2014-2015) British Medical Association/ Royal Pharmaceutical Society/ Royal College of Paediatrics and Child Health/ Neonatal and Paediatric Pharmacists Group
Strattera® Summary of Product Characteristics

Shared Care Agreement Letter - Consultant Request

To: Dr…….

Practice Address: ……

……

……

Patient Name:	
NHS number:	
Date of birth:	
Address:	Diagnosed condition: Attention Deficit Hyperactivity Disorder (ADHD)

I recommend treatment with the following drug: Atomoxetine
I request your agreement to sharing the care of this patient according to the North and East Devon Health Community Shared Care Prescribing Guidelines for this drug.
GPs are invited to participate. If GP is not confident to undertake these roles, then they are under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If a specialist asks the GP to prescribe this drug the GP should reply to this request as soon as practical. Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient and accepted by them.
The doctor who prescribes the medication has the clinical and legal responsibility for the drug and the consequences of its use.

Signed:		Date:
Consultant name:		
Contact telephone number:		

GP RESPONSE
I agree/ do not agree* to share the care of this patient in accordance with the Shared Care Guideline.
Signed: …… Date: ……
GP name: …… *Delete as appropriate

Indications for this guideline

As an immunosuppressant antimetabolite either alone or, more commonly, in combination with other agents (usually corticosteroids) often having a steroid-sparing effect.

Dermatology
Psoriasis, eczema, pyoderma gangrenosum (all unlicensed).

Gastroenterology
Ulcerative colitis (unlicensed), Crohn's disease (unlicensed) and autoimmune hepatitis.

Ophthalmology
Thyroid eye diseases, corneal melt, cicatrizing conjunctivitis, corneal graft rejection, scleritis and uveitis (all unlicensed).

Respiratory
Interstitial lung disease (including cryptogenic fibrosing alveolitis) and pulmonary vasculitis (all unlicensed).

Rheumatology
Rheumatoid arthritis, other inflammatory arthritis, connective tissue disease, vasculitis, and as a steroid sparing agent.

Dosage

- The normal dosage is 1mg – 2.5mg per kg (giving a dose range of 50mg to 200mg daily).
- The regime and target dose will be clearly specified in the clinic letter. ***Gastroenterology patients will be stabilised by the specialist team.***
- Available as 25mg and 50mg tablets. 10mg tablets are unlicensed, but are available on a named patient basis.
- Taking tablets after meals or in divided doses may relieve nausea.

GP Monitoring

Infection (e.g. persistent sore throat, fever) or easy bruising should be reported to specialist team.

Please copy all results to secondary care team.
LFTs and FBC every week for 8 weeks then monthly.
Please include CRP with LFT for Rheumatology.
Seek advice from specialist team and consider stopping if any of the following occur:

- WCC or platelet count falls on 3 successive occasions.
- Total WCC < 4.0 or neutrophils < 1.8 (isolated lymphopaenia is not usually an indication for cessation of azathioprine therapy).
- Platelet count < 150
- ALT or AST > 120
- Alk Phos > 300

MCV may rise. If > 110 consider checking B12 & folate if patient is anaemic. If continues to rise above 110, discuss with specialist team.
A rising LDH may herald adverse reactions to azathioprine. Discuss with specialist team.

Gastroenterology has a monitoring system in place, but only for their Crohn's disease and ulcerative colitis patients. Requests for blood samples are made by the specialist team but patients may have samples taken in community or hospital.
GPs are responsible for monitoring autoimmune hepatitis patients as for all other indications covered by this guideline.

Side effects (not covered by specific monitoring requirements)

Patients must report mouth ulcers, sore throat, fever, epistaxis, unexplained bruising or bleeding, and any unexplained illness/infection and should be seen urgently for full blood count and liver function tests.

Very common/ Common:

- Nausea – often relieved by administering tablets after meals or by dividing dose.
- Diarrhoea.

Uncommon:

- Hypersensitivity reactions including general malaise, dizziness, vomiting, diarrhoea, fever, rigors, exanthema, rash, vasculitis, myalgia, arthralgia, hypotension, renal dysfunction, hepatic dysfunction and cholestasis. Following a hypersensitivity reaction to azathioprine, the necessity for continued administration of azathioprine should be carefully considered on an individual basis.

- Bone marrow depression manifested as leucopenia, thrombocytopenia, anaemia (rarely aplastic anaemia or pancytopenia) or infection. Occurs particularly in patients with TPMT (thiopurine methyltransferase) deficiency, hepatic or renal failure or concurrent allopurinol therapy.
- Hepatotoxicity-see hypersensitivity reactions, hepatic damage (usually reversible on withdrawal of treatment) has also been associated with chronic administration of azathioprine.
- Pancreatitis.

Rare:

- Hair loss.

Drug interactions: (refer to BNF, Appendix 1 for full list of interactions)

- **Co-trimoxazole** – Increased risk of haematological toxicity if renal function impaired. Discuss with specialist team.
- **Allopurinol** – Reduce azathioprine to 25% of original dose. Increased risk of toxicity.
- **Warfarin** – anticoagulant effect possibly reduced.

Pregnancy and breast feeding

May sometimes be used in pregnancy. Discuss with specialist team.
Contraindicated in breastfeeding women.

Vaccinations and infectious illness

- Live attenuated vaccines are contraindicated in patients taking immunosuppressants unless stopped at least 3 months beforehand. Live vaccines include MMR, BCG, varicella-zoster and yellow fever vaccines.
- Where a patient has received a live vaccine allow at least 2, preferably 4, weeks before starting immunosuppressive therapy.
- Patients should be advised to avoid contact with anyone with active chickenpox and shingles.
- If a patient is vaccinated (with 'killed' vaccines) while taking immunosuppressants they may not mount the appropriate immune response. Consider repeating 3 months after therapy has ceased if antibody titres are low.
- If contact risk is significant (e.g. Varicella, Measles) discuss with specialist team and consider using specific immunoglobulin.
- Vaccinate against influenza annually and with Pneumovax® II every five years.

For additional information refer to the British Society of Rheumatology guidance on vaccinations for immunosuppressed patients at www.rheumatology.org.uk

Initiating therapy

Having assessed the patient and discussed with them the benefits, side effects, frequency of dosing and monitoring requirements of azathioprine treatment the specialist team will:-

- **Communicate with the patient's GP, in writing, and confirm that the GP agrees to share care, as described in the Introduction to Shared Care Guidelines.**
- Record the patient's confirmation of understanding of the risks, benefits and consent.
- Undertake baseline investigations* and initiate therapy.
- Specify target doses, monitoring and review dates at clinically relevant time intervals for both the GP and specialist team and any other patient specific information.
- Ensure that full information is sent to the GP without undue delay and recommend that the GP continues treatment in accordance with this shared care guideline.

Gastroenterology will stabilise the dose for their patients. They have a monitoring system in place, but only for their Crohn's disease and ulcerative colitis patients. Requests for blood samples are made by the specialist team for these patients, but they may have samples taken in community or hospital. GPs are responsible for monitoring autoimmune hepatitis patients as for all other indications covered by this guideline.

*Specialist team will measure baseline TPMT (thiopurine methyltransferase) level before initiating azathioprine. Patients with reduced TPMT activity are at an increased risk of azathioprine toxicity. Patients with increased TPMT activity may not have a good clinical response to normal doses.

Information given to patient

- The specialist team will provide a patient information leaflet.

GP Responsibilities

The GP will notify the specialist, in writing, whether or not he/she agrees to share care and prescribe for the patient, according to this guideline.

- Monitor for adverse effects and drug interactions and report adverse events to the CSM and specialist team.
- Conduct blood tests, review results and undertake any necessary action as specified in GP Monitoring section above.
- Report to and seek advice from the specialist team on any aspect of patient care which is of concern to the GP and

may affect treatment.
- Prescribe further supplies of azathioprine according to the recommendations specified in this guideline.
- Inform the specialist team if treatment is stopped for any reason.

NB **Gastroenterology** has a monitoring system in place, but only for their **Crohn's disease** and **ulcerative colitis** patients. Requests for blood samples are made by the specialist team but patients may have samples taken in community or hospital.

GPs are responsible for monitoring autoimmune hepatitis patients as in the GP Monitoring section above as for all other indications covered by this guideline.

Ongoing Specialist Team Responsibilities

- Review the patient at agreed intervals.
- Provide advice as requested by the GP.
- Assess patients referred back by GPs as soon as is practical.
- Gastroenterology specialist team organise regular blood monitoring and advise GPs of dosage adjustments for their Crohn's disease and ulcerative colitis patients. GPs are responsible for routine monitoring of autoimmune hepatitis patients.

Patient's Responsibilities

- Report any adverse effects to their GP and / or specialist team.
- Ensure that they have a clear understanding of their treatment.
- Ensure they attend for monitoring requirements as specified in this shared care guideline.
- Be aware that treatment will be stopped it they do not attend for monitoring.

Contact details for the Specialist Teams

Dermatology
Dr J. Adams, secretary: 01803 654 837, e-mail: jill.adams@nhs.net
Dr T. Frost, secretary: 01803 654 869, e-mail: tessa.frost@nhs.net

Gastroenterology
Crohn's disease and ulcerative colitis
IBD Nurse Specialist: 01803 654 951, bleep: 07666 548 580
Dr C. Edwards, secretary: 01803 654 796

Autoimmune hepatitis
Dr J. Lowes, secretary: 01803 654 865
Dr K. George, secretary: 01803 654 984

Ophthalmology:
Ophthalmic Nurse Specialist, Eye Clinic: 01803 655 123

Respiratory:
Respiratory Nurse Specialist: 01803 655 147, bleep: #6 733 via SDHCT switchboard.

Rheumatology:
Rheumatology Nurse: 01803 654 939
Rheumatology secretary: 01803 654 832
e-mail: rheumatology.sdhct@nhs.net

Out of Hours:
Medical SHO on-call via SDHCT switchboard (01803 614 567) for all indications except Ophthalmology when the Ophthalmic SHO on-call should be contacted.

Full Prescribing Information

For full prescribing information please consult summaries of product characteristics and the current BNF.

References

- eSPC for Imuran® 25mg, July 2003, 50mg August 2003
- BNF 50, September 2005
- British Society for Rheumatology. National Guidelines for the Monitoring of Second Line Drugs, July 2000

The information contained in these shared care guidelines is issued on the understanding that it is the best available from the resources at our disposal at the time of issue. Please see Chapter 20 – Introduction to Shared Care Guidelines for more information.

Indications for this guideline

Dermatology
Psoriasis, atopic eczema.

Gastroenterology
Ulcerative colitis and autoimmune hepatitis (all unlicensed).

Ophthalmology
Corneal melt, cicatrizing conjunctivitis, corneal graft rejection, and scleritis and uveitis (all unlicensed).

Respiratory
Interstitial lung disease (including cryptogenic fibrosing alveolitis) and pulmonary vasculitis (all unlicensed).

Rheumatology
Connective tissue disease (unlicensed) and rheumatoid arthritis.

Dosage

- Patients will be stabilized by the specialist team before GPs will be asked to prescribe under this shared care agreement.
- Usual dosage is 1.25mg – 2.5mg per kg BD
- Preparations
  - Capsules 10mg, 25mg, 50mg, 100mg.
  - Oral solution 100mg per ml

IMPORTANT	Prescribe as Neoral®. Different brands are not bioequivalent.

GP Monitoring

Infection (e.g. persistent sore throat, fever) or easy bruising should be reported to specialist team.

- Please copy all results to secondary care team.
- **Blood pressure and U&E every fortnight until dose stable for 3 months then every month.**
- **LFT & FBC monthly until dose stable for 3 months, then every 3 months.**
- **Please include CRP with LFT for Rheumatology.**
- **Serum lipids every 6 months.**

Seek advice from specialist team and consider stopping ciclosporin if any of the following occur:
- Creatinine rises by 30% of baseline.
- Potassium rises above normal range.
- Significant rise in lipids.
- Platelet count < 150
- ALT or AST > 120
- Alk Phos > 300

If blood pressure rises above normal range discuss with specialist team.

Gastroenterology has a monitoring system in place for their **ulcerative colitis** patients. Requests for blood samples are made by the specialist team but patients may have samples taken in community or hospital.
GPs are responsible for monitoring autoimmune hepatitis patients as for all other indications covered by this guideline.

Side effects (not covered by specific monitoring requirements)

- Some patients feel a burning sensation in their hands and feet during the first weeks of therapy. This may disappear with continued therapy, if not discuss this with specialist team.
- All patients put on this medication will be warned of the theoretical but as yet unquantifiable risk of lymphoproliferative disorders and other malignancies.

Very common / common:
- Hyperlipidaemia, hyperuricaemia, hyperkalaemia, hypomagnesaemia
- Tremor, headache, fatigue
- Paraesthesia, muscle cramps, myalgia
- Hypertension
- Gingival hypertrophy, gastro-intestinal disturbance
- Hepatic dysfunction
- Hypertrichosis

Uncommon:

- Anaemia, thrombocytopenia
- Rashes, oedema, weight gain

Drug interactions: (refer to BNF, Appendix 1 for full list of interactions)
Drugs that activate or inhibit the hepatic microsomal p450 oxidation system will alter the elimination of ciclosporin. Concurrent administration of ciclosporin and interacting drugs is not precluded but requires close monitoring (e.g. when starting or stopping the interacting drug).

The following is a **GUIDE** to some of the interactions that may occur with ciclosporin therapy

Drugs that may Reduce blood levels	**Drugs that may Increase blood levels**
Rifampicin	Erythromycin and other macrolides
Carbamazepine	Ketoconazole, fluconazole and itraconazole
Phenobarbitone/Primidone	Allopurinol
Phenytoin	Danazol
Octreotide	Doxycycline
Orlistat	Diltiazem, nicardipine, verapamil Methylprednisolone (high doses)
St John's Wort	Oral contraceptives and progestogens
	Propafenone
	Chloroquine
	Metoclopramide
	Amiodarone
	Ursodeoxycholic acid
	Protease inhibitors
	Grapefruit juice

Care should also be taken using ciclosporin with:
- **Nephrotoxic drugs: NSAIDS** (including adjusting dosage), aminoglycoside antibiotics, ciprofloxacin (and other quinolones), aciclovir, trimethoprim, co-trimoxazole, amphotericin, melphalan and colchicine
- **Potassium-sparing agents**: Amiloride, spironolactone, ACE inhibitors.
- **Digoxin**: May increase digoxin levels. Monitor for digoxin toxicity.
- **Statins**: Increased risk of myopathy. Max. dose of Simvastatin

Pregnancy and breastfeeding
May sometimes be used in pregnancy. Discuss with specialist team.
Breastfeeding is contraindicated. Ciclosporin passes into breast milk.

Vaccinations and infectious illness
- Live attenuated vaccines are contraindicated in patients taking immunosuppressants unless stopped at least 3 months beforehand. Live vaccines include MMR, BCG, varicella-zoster and yellow fever vaccines.
- Where a patient has received a live vaccine allow at least 2, preferably 4, weeks before starting immunosuppressive therapy.
- Patients should be advised to avoid contact with anyone with active chickenpox and shingles.
- If a patient is vaccinated (with 'killed' vaccines) while taking immunosuppressants they may not mount the appropriate immune response. Consider repeating 3 months after therapy has ceased if antibody titres are low.
- If contact risk is significant (e.g. Varicella, Measles) discuss with specialist team and consider using specific immunoglobulin.
- Vaccinate against influenza annually and with Pneumovax® II every five years.

For additional information refer to the British Society of Rheumatology guidance on vaccinations for immunosuppressed patients at www.rheumatology.org.uk

Initiating therapy
Having assessed the patient and discussed with them the benefits, side effects, frequency of dosing and monitoring requirements of ciclosporin treatment the specialist team will:-
- **Communicate with the patient's GP, in writing, and confirm that the GP agrees to share care, as described in the Introduction to Shared Care Guidelines.**
- Record the patient's confirmation of understanding of the risks, benefits and consent.
- Undertake baseline investigations, initiate and stabilise therapy.
- Specify dose, monitoring and review dates at clinically relevant time intervals for both the GP and specialist team and any other patient specific information.
- Ensure that full information is sent to the GP without undue delay and recommend that the GP continues treatment in accordance with this shared care guideline.

Baseline investigations
Prior to therapy, FBC, LFT serum lipids and repeated measurements of U&Es including serum creatinine and blood

pressure to establish baseline.

Information given to patient

- Patient information leaflets may be available from some specialities.

GP Responsibilities

The GP will notify the specialist, in writing, whether or not he/she agrees to share care and prescribe for the patient, according to this guideline.

- Monitor for adverse effects and drug interactions and report adverse events to the CSM and specialist team.
- Conduct blood tests, review results and undertake any necessary action as specified in GP Monitoring section above.
- Report to and seek advice from the specialist team on any aspect of patient care which is of concern to the GP and may affect treatment.
- Prescribe further supplies of ciclosporin according to the recomendations specified in this guideline.
- Inform specialist team if treatment is stopped for any reason.

NB Gastroenterology has a monitoring system in place only for their ulcerative colitis patients. Requests for blood samples are made by the specialist team but patients may have samples taken in community or hospital.

GPs are responsible for monitoring autoimmune hepatitis patients as in the GP Monitoring section above as for all other indications covered by this guideline.

Ongoing Specialist Team Responsibilities

- Review the patient at agreed intervals.
- **Gastroenterology** specialist team organise regular blood monitoring and advise GPs of dosage adjustments for their ulcerative colitis patients. **GPs are responsible for routine monitoring of autoimmune hepatitis patients**.
- Provide advice as requested by the GP.
- Assess patients referred back by GPs as soon as is practical.

Patient's Responsibilities

- Report any adverse effects to their GP and / or specialist team.
- Ensure that they have a clear understanding of their treatment.
- Ensure they attend for monitoring requirements as specified in this shared care guideline.
- Be aware that treatment will be stopped it they do not attend for monitoring.

Contact details for the Specialist Teams

Dermatology
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Rheumatology:
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Rheumatology secretary: 01803 654 832
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Medical SHO on-call via SDHCT switchboard (01803 614 567) for all indications except Ophthalmology when the Ophthalmic SHO on-call should be contacted.

Full Prescribing Information
For full prescribing information please consult summaries of product characteristics and the current BNF.

References

- eSPC for Neoral®, February 2005
- BNF 50, September 2005
- British Society for Rheumatology. National Guidelines for the Monitoring of Second Line Drugs, July 2000

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Introduction

Nebulised colistin forms only part of the treatment for Cystic Fybrosis (CF) patients. Details on the treatment of CF can be found in the two Cystic Fibrosis Trust documents:

- Standards of care of children and adults with cystic fibrosis in the UK 2001 and
- Antibiotic treatment for Cystic Fibrosis, 2002.

Details of the current prescribing practice relating to the use of nebulised antibiotics for infection with Pseudomonas aeruginosa within South Devon can be seen in the treatment pathway in Appendix 1.

In the absence of appropriate antibiotic treatment, the abnormal respiratory secretions of the infant with CF soon become sequentially infected with S. aureus, H. influenzae and Ps. aeruginosa leading ultimately to death from progressive respiratory failure.

During childhood and adolescence the majority of patients with CF will become first colonised, then chronically infected, with Ps. aeruginosa. Early eradication of Ps. aeruginosa is important because, once the infection is well established, it forms a mucoidal biofilm which is difficult to penetrate. Chronic infection with this organism is associated with deterioration in lung function and a higher mortality rate. Chronic infection is defined as the regular culture of Ps. aeruginosa from the sputum or respiratory secretions, on two or more occasions extending over 6 months or a shorter period if accompanied by a sustained rise in anti-pseudomonas antibodies.

Regular courses of intravenous antibiotics have improved survival by reducing sputum bacterial load and maintaining pulmonary function. However, the addition of nebulised antibiotics to existing treatment have been shown to reduce the rate of deterioration of respiratory function and the number of intravenous antibiotics needed to treat exacerbations. Nebulised anti-pseudamonal antibiotics commonly used include gentamicin, colistin and tobramycin. Introduction of nebulised colistin (combined with oral ciprofloxacin) or the aminoglycosides (gentamicin and tobramycin) at the time of initial colonisation with Ps. aeruginosa has been shown to eradicate Ps. aeruginosa in 80% of newly infected patients and delay chronic infection for 18 months. The decision on which drug to choose is based on evidence, cost, toxicity and current UK licensing of the product. Colistin is generally used 1st line because it has reliable activity against Ps. aeruginosa and the development of resistance is not common. Tobramycin is reserved for patients who are unable to tolerate colistin or continue to decline despite its use. Gentamicin injection can also be nebulised although tobramycin has greater activity against Ps. aeruginosa. The treatment pathway seen in Appendix 1 shows the current treatment options within South Devon.

Colistin (Colomycin®) is a polymixin antibiotic active against Gram-negative organisms and is licensed to be used by inhalation for treatment of CF patients. It has excellent ant-pseudomonal activity and, although resistance has been reported, it is very rare and is usually less of a problem than with aminoglycosides.

Nebulised antibiotics can also be used in patients with Bronchiectasis in the absence of CF. The scope of this guideline encompasses treatment for this patient group.

Indications for this guideline

Delay or prevention of chronic infection with Ps. aeruginosa

- Management after the first respiratory culture is reported positive for Ps. aeruginosa
- Management of subsequent positive cultures for Ps. Aeruginosa or
- Prevention of clinical deterioration in patients chronically infected with Ps. aeruginosa.

Chronic infection is defined as the regular culture of P. aeruginosa from the sputum or respiratory secretions, on two or more occasions extending over 6 months or a shorter period if accompanied by a sustained rise in anti-pseudomonas antibodies.

Patient Criteria

1. Have one of the above indications.
2. Complying with standard treatment e.g. physiotherapy, pancreatic supplements etc.
3. Sputum cultures show susceptibility to colistin (may start treatment pending culture results).
4. Use nebuliser regularly as prescribed***. Irregular use is a reason for stopping treatment.***

Dosage

The dose and treatment plan for each patient will be decided by the specialist team and will be communicated in the clinical letter to the GP.

Child < 2 years:	500,000 to 1 million units twice daily
Child > 2 years and adults:	1 million to 2 million units twice daily
	(some centres use 1 million units for child < 10yrs)

Initial dose is chosen according to clinical condition and the size of child. Further dose adjustments are made

according to patient response and patient tolerability of the drug.

Preparations:
Powder for reconstitution as 500,000 unit, 1,000,000 unit and 2,000,000 unit vials.

Administration:
- Each patient should be given an initial hospital-supervised dose after chest physiotherapy
- Bronchodilators (usually beta2-agonists) should be given before the antibiotic
- A mouthpiece is preferable to a facemask to maximise pulmonary disposition. Small children below 3 years old will usually require a mask held firmly on the face
- Relaxed tidal volume breathing through the mouth and not the nose is ideal. A nose clip will increase the efficiency of delivery to the lungs in some patients but is not popular in practice and is not used by the majority
- The contents of a vial containing the appropriate dose is dissolved preferably in 2-4ml 0.9% sodium chloride solution
- Alternatively, an isotonic solution should be used to reduce the risk of bronchoconstriction consisting of:

Vial size	Water for Injections	Sodium chloride 0.9%	Final Volume
2 million units	1.5ml	1ml	2.5ml
2 million units	2ml	1ml	3ml
2 million units	2ml	2ml	4ml*
1 million units	1ml	1ml	2ml
1 million units	1ml	2ml	3ml*

* is the optimal final volume to minimise percentage of dose remaining in residual volume.
- The resultant solution is poured into the nebuliser
- The solution will be slightly hazy and may froth if shaken
- The solution is for single use only and any remaining solution should be discarded

NB there is some data on stability up to 24hrs if stored in fridge but patients should be encouraged to discard any remaining solution after use.

CF /Respiratory specialist nurses organise and monitor the following:

Nebuliser-compressor systems for antibiotics:
- Use an active venture nebuliser (breath-assisted) e.g. Pari LC Plus® or E Flow Rapid®, with a compressor producing a flow rate of 6 litres per minute. E Flow Rapid nebulisers are paid for by the patient but deliver a higher percentage of the dose.
- If unacceptably long, the nebulisation time can be reduced for patients with low inspiratory flow.
- A Ventistream® may also be used rarely.

All disposable plastics required for the nebuliser system will be provided through secondary care.
- Environmental safety:
- The output from the above nebulisers is automatically filtered. Output from nebulisers without inbuilt filters should be vented to the open air.
- It is advisable for patients to receive nebulised antibiotics in a separate area from other patients. Hospital patients should be routinely placed in a side room.
- Nebulisation should take place in a well ventilated room e.g. with a window open.

GP Monitoring
There are no specific GP monitoring requirements beyond normal clinical care.

Side effects
(for a full list of systemic side effects, see the summary of product characteristics (SPC) for colistin)
Bronchospasm may occur on inhalation of antibiotics. This may be prevented by, or treated with, the appropriate use of beta2-agonists. If troublesome, treatment should be withdrawn.

Important	There is potential for systemic absorption, with reported serum levels from nil to potentially therapeutic concentrations. Therefore, the possibility of systemic absorption, although rare, should always be borne in mind when treating patients by inhalation.

Nebulisation:
- Inhalation may induce coughing or bronchospasm.
- Sore throat or mouth has been reported and may be due to Candida albicans infection or hypersensitivity .
- Skin rash may also indicate hypersensitivity, if this occurs treatment should be withdrawn.
- Transient sensory disturbances have been reported.

Systemic: (unlikely but possible)
- Neurological effects may include apnoea, transient sensory disturbances, and rarely, vasomotor instability, slurred speech, visual disturbances, confusion or psychosis. Generally mild and resolve during or shortly after treatment
- Neurotoxicity if doses used are too high. Usually reversible on discontinuation of therapy

Toxicity:

- **Nephrotoxicity and Neurotoxicity**: No toxicity of this type has been reported for nebulised colistin therapy. However it would be prudent to be aware that although systemic absorption is unlikely the potential is there. Therefore, patients at risk of nephrotoxicity or neurotoxicity should be monitored accordingly.

Drug interactions: *refer to BNF, Appendix 1 and SPC for full list of interactions*

Although rare, the possibility of systemic absorption, and hence the possibility of interactions should always be borne in mind when treating patients by inhalation.

Drugs commonly seen in primary care:

- Antibiotics: seek specialist advice before prescribing any antibiotics for CF patients.

Drugs not commonly seen in primary care:

- Concomitant use of colistin with other medical products of neurotoxic and/or nephrotoxic potential should be avoided. These include the aminoglycosides antibiotics such as gentamicin, amikacin, netilmicin and tobramycin. There may be an increased risk of nephrotoxicity if given concomitantly with cephalosporin antibiotics. However, due to the aggressive treatment required in CF patients, two nephrotoxic drugs are commonly used together with the appropriate close monitoring by the specialist secondary care team. The risk of toxicity is deemed to be low as one drug will usually have minimal systemic absorbtion when given by the nebulised route.
- Neuromuscular blocking drugs and ether should be used with extreme caution in patients receiving colistin.

Contra-indications

- Hypersensitivity to colistin or to polymixin b.
- Myasthenia gravis

Initiating therapy

Having assessed the patient at a six or eight weekly review and suspecting or confirming infection with Ps. aeruginosa the ***specialist consultant*** will:

- Discuss with the patient and/or the parent(s)/carer(s), the benefits, side effects, frequency of dosing, the importance of compliance, monitoring requirements of nebulised colistin treatment and long term treatment options.
- Give the first dose in hospital after a physiotherapy session.
- Baseline monitoring including sputum/throat swabs, renal function, liver function, lung function, weight.
- Prescribe the first month's therapy for the patient.
- **Communicate with the patient's GP, in writing, and confirm that the GP agrees to share care, as described in the Introduction to Shared Care Guidelines.**
- Record the patient's confirmation of understanding of the risks, benefits and consent.
- Ensure that full information, including dose and duration of therapy, is sent to the GP without undue delay and recommend that the GP continues treatment in accordance with this shared care guideline.
- Ensure that the patient/parent(s)/carer(s) are aware that they need to inform the community pharmacy to order colistin in advance of presenting a script from the GP.
- Once the patient has been prescribed nebulised colistin, the ***CF specialist nurse*** will:
- Provide and train the patient/parent/carer in the use and administration of nebulised colistin
- Remind the patient/parent(s)/carer(s) that they need to inform the community pharmacy to order colistin in advance of presenting a script from the GP.

GP Responsibilities

The GP will notify the specialist, in writing, whether or not he/she agrees to share care and prescribe for the patient, according to this guideline.

- Prescribe subsequent courses of nebulised colistin according to the treatment plan provided by the specialist.
- Communicate with the specialist consultant/nurse if the patient presents with any problems associated with the nebulised colistin or deterioration in CF related health.
- Be aware of the monitoring parameters for patients prescribed nebulised colistin.
- Report to and seek advice from the specialist team on any aspect of patient care which is of concern to the GP and may affect treatment.
- Inform the specialist team if treatment is stopped for any reason.

Ongoing Specialist Team Responsibilities

- Review and monitor the patient at agreed intervals (see Appendices 1 and 2) and advise GP of any changes to the treatment plan.
- Provide advice as requested by the GP.
- Assess patients referred back by GPs as soon as is practical.

Patient's Responsibilities including parents and or carers

- Report any adverse effects to their GP and / or specialist team.
- Ensure that they have a clear understanding of their treatment.
- Ensure they attend for monitoring requirements as specified in this shared care guideline.
- Be aware that treatment will be stopped it they do not attend for monitoring.
- Correct storage and administration of the nebuliser solution

Contact details for the Specialist Teams

Specialist CF nurse
Rachel Crimmins, Specialist CF nurse: 01803 655 586, e-mail: rachelcrimmins@nhs.net

Consultant Paediatrician
Dr C. Sainsbury, secretary: 01803 654 824, e-mail: clive.sainsbury@nhs.net

Respiratory Consultant
Dr L. Dobson, secretary: 01803 654 014, e-mail: lee.dobson@nhs.net

Microbiology Consultants:
Dr P. Turner, secretary: 01803 654 990, e-mail: paul.turner@nhs.net
Dr T. Maggs, secretary: 01803 654 990, e-mail: tony.maggs@nhs.net
Dr S. Hoque, secretary :01803 654 990, e-mail: selina.hoque@nhs.net

Out of Hours:
Paediatric or **Respiratory** SHO on-call via SDHCT switchboard (01803 614 567).

Full Prescribing Information
For full prescribing information please consult summaries of product characteristics (emc.medicines.org.uk) and the current BNF.

References

1. eSPC Colomycin® Injection (Forest Laboratories UK), January 2006
2. Standards of care of children and adults with cystic fibrosis in the UK. Cystic Fibrosis Trust, 2001
3. Antibiotic treatment for Cystic Fibrosis. Cystic Fibrosis Trust, 2002

The information contained in these shared care guidelines is issued on the understanding that it is the best available from the resources at our disposal at the time of issue. Please see Chapter 20 – Introduction to Shared Care Guidelines for more information.

Appendix 1 Treatment pathway for CF patients with Ps. aeruginosa

	Routine Outpatient	Routine Home visit	As required if patient unwell
MDT care input	**Specialist CF consultant** Paeds and adults every 3 months	**Specialist CF nurse** Paeds and adults at least every 3 months	• Phone CF nurse • Home visit by CF nurse • GP visit • Urgent paed. hospital appointment
Tests	**Every 6 – 8 weeks** • Sputum cultures, cough swab • Lung function tests **When required** • FBC, U&Es, Serum creatinine, LFTs, others		Tests conducted according to necessity. GPs liase as necessary with specialist team
Drug treatment	If culture positive for Ps. aeruginosa: **Paeds** • Nebulised colistin • Oral ciprofloxacin for 3 weeks **Adults** • Nebulised colistin for 3 months • Oral ciprofloxacin	Continue thereafter according to patient response. Continuous nebulisers may be required. Nebulised gentamicin or tobramiycin may be substituted according to patient progress.	
Prescribing and supply	**First month** Prescribed by specialist team Dispensed by hospital pharmacy **Remainder of treatment course** GP prescribes in accordance with Shared Care. Dispensed by community pharmacy.		
Monitoring	All routine monitoring by secondary care every 6 – 8 weeks during routine visits or as frequently as necessary: • Sputum cultures including susceptibility and resistance • Lung function • U&Es, serum creatinine, LFTs • Compliance and technique • Clinical assessment and others as necessary.		

Notes:

1. All relevant findings and results will be communicated by specialist team to GP
2. GP should communicate any relevant tests conducted to specialist team.

Appendix 2 Patient monitoring relating to Ps. Aeruginosa infection

Adults and children are seen every:

- 6-8 weeks by the specialist CF nurse, usually in the form of a home visit
- three months by the local specialist consultant at Torbay Hospital
- year at the specialist CF centre in Exeter.

Infants are seen more frequently until thriving.

6-8 week CF specialist nurse visit and three monthly specialist consultant appointment the following will be monitored :

- Review of respiratory function including:
  - spirometery
  - oximetery
  - peak flow (FEV1)

  } every visit
- Sputum cultures and sensitivities or cough swabs, nasopharyngeal aspirates or deep throat swabs
- Chest X-ray: condition dependent/if significant fall in lung function
- Weight and height: three monthly unless antibiotics need dosing
- Physiotherapy review including nebuliser techniques: every clinic visit. At home only if concerns

Annual review at Specialist CF centre will monitor the following:

- Detailed assessment of progress, review of results and planning for future therapy. Copy sent to GP, and possibly patient
- Weight and height
- Sputum culture (summary of cultures and antibiotics used is produced by specialist nurse prior to visit)
- Oximetry
- Spirometry
- Chest X-ray
- Blood gas in adults if indicated (i.e. if very ill)
- Full blood count, urea and electrolytes, liver function tests including serum albumin, clotting studies, aspergillus species RAST, serum HbA1c, vitamin levels
- Pseudamonal antibody levels

Other monitoring that may be required between CF clinic visits:

- Colds and exacerbations of chest symptoms
- Pre and post antibiotic sputum cultures
- Patient tolerability of antibiotic therapy
- Compliance with antibiotic therapy
- Nebuliser technique
- Equipment safety and maintenance
- Renal function if on potentially nephrotoxic medication
- Sputum culture resistance to current antibiotic treatment

Response to therapy: The main parameters used to monitor response to nebulised drugs in CF are:

- Stability and/or lack of deterioration in spirometry, particularly
  - forced expiratory volume in one second (FEV1), as a percentage of that which is predicted and
  - forced vital capacity (FVC), as a percentage of that which is predicted.
- It is important to remember that 4-5 percent variability can exist in spirometric readings due to patient effort and also operator variability.
- In children, resolution of a wet cough is also indicative of treatment success.
- In adults, the cough may not dry up completely but changes in volume and appearance of sputum should be evident.

Introduction

Nebulised gentamicin may form only part of the treatment for cystic fibrosis (CF) patients. Details on the treatment of CF can be found in the two Cystic Fibrosis Trust documents:

- Standards of care of children and adults with cystic fibrosis in the UK, 2001 and
- Antibiotic treatment for Cystic Fibrosis, 2002.

Details of the current prescribing practice relating to the use of nebulised antibiotics for infection with Pseudomonas aeruginosa within South Devon can be seen in the treatment pathway in Appendix 1.

In the absence of appropriate antibiotic treatment, the abnormal respiratory secretions of the infant with CF soon become sequentially infected with S. aureus, H. influenzae and Ps. aeruginosa leading ultimately to death from progressive respiratory failure.

During childhood and adolescence the majority of patients with CF will become first colonised, then chronically infected, with Ps. aeruginosa. Early eradication of Ps. aeruginosa is important because, once the infection is well established, it forms a mucoidal biofilm which is difficult to penetrate. Chronic infection with this organism is associated with deterioration in lung function and a higher mortality rate. Chronic infection is defined as the regular culture of Ps. aeruginosa from the sputum or respiratory secretions, on two or more occasions extending over 6 months or a shorter period if accompanied by a sustained rise in anti-pseudomonas antibodies.

Regular courses of intravenous antibiotics have improved survival by reducing sputum bacterial load and maintaining pulmonary function. However, the addition of nebulised antibiotics to existing treatment have been shown to reduce the rate of deterioration of respiratory function and the number of intravenous antibiotics needed to treat exacerbations. Nebulised anti-pseudamonal antibiotics commonly used include colistin, gentamicin and tobramycin. Introduction of nebulised colistin (combined with oral ciprofloxacin) or the aminoglycosides (gentamicin or tobramycin) at the time of initial colonisation with Ps. aeruginosa has been shown to eradicate Ps. aeruginosa in 80% of newly infected patients and delay chronic infection for 18 months. The decision on which drug to choose is based on evidence, cost, toxicity and current UK licensing of the product. Colistin is generally used 1st line because it has reliable activity against Ps. aeruginosa and the development of resistance is not common. Tobramycin is reserved for patients who are unable to tolerate colomycin or continue to decline despite its use. Gentamicin injection can also be nebulised although tobramycin has greater activity against Ps. aeruginosa. The treatment pathway seen in Appendix I shows the current treatment options within South Devon.

Gentamicin and tobramycin are aminoglycoside antibiotics active against Gram-negative organisms. Although both being two of the most commonly used antibiotics for nebulisation, neither of the intravenous formulations are licensed to be used by inhalation for treatment of CF patients. Gentamicin is less active against Ps .aeruginosa than tobramycin but resistance has been reported to be more common than with tobramycin and colistin.

Nebulised antibiotics can also be used in patients with Bronchiectasis in the absence of CF. The scope of this guideline encompasses treatment for this patient group.

Indications for this guideline

Delay or prevention of chronic infection with Ps. aeruginosa where:

- Colistin or tobramycin have not produced a satisfactory clinical result
- patient has been unable to tolerate colistin or tobramycin
- cultures show resistance to colistin or tobramycin and sensitivity to gentamicin (may start pending culture results)

or

Prevention of clinical deterioration in patients chronically infected with Ps. aeruginosa where other nebulised antibiotics are unsuitable. Chronic infection is defined as the regular culture of Ps. aeruginosa from the sputum or respiratory secretions, on two or more occasions extending over 6 months or a shorter period if accompanied by a sustained rise in anti-pseudomonas antibodies.

Patient Criteria

1. Have one of the above indications.
2. Complying with standard treatment e.g. physiotherapy, pancreatic supplements etc.
3. Sputum cultures show susceptibility to gentamicin (may start treatment pending culture results).
4. Use nebuliser regularly as prescribed. Irregular use is a reason for stopping treatment.

Dosage

The dose and treatment plan for each patient will be decided by the specialist team and will be communicated in the clinical letter to the GP.

Child < 5 years nebulised 40mg twice a day

5-10 years nebulised 80mg twice a day
>10 years & adult nebulised 160mg twice a day

Preparations: Intravenous preparations to be used via the nebulised route (unlicensed).
40mg in 1ml and 80mg in 2ml vials. Use phenol-free formulations.

Administration:
- Dilute the appropriate volume of the above solutions to 4ml with 0.9% sodium chloride
- The resultant solution is poured into the nebuliser
- The solution is for single use only and any remaining solution should be discarded
- Each patient should be given an initial hospital-supervised dose after chest physiotherapy
- Measure respiratory function before and after initial dosage
- Bronchodilators (usually beta2-agonists) should be given before the antibiotic
- A mouthpiece is preferable to a facemask to maximise pulmonary disposition. Small children below 3 years old will usually require a mask held firmly on the face
- Relaxed tidal volume breathing through the mouth and not the nose is ideal. A nose clip will increase the efficiency of delivery to the lungs in some patients but is not popular in practice and is not used by the majority

CF /Respiratory specialist nurses organise and monitor the following:

Nebuliser-compressor systems for antibiotics:
- Use an active venture nebuliser (breath-assisted) e.g. Pari LC Plus® or E Flow Rapid®, with a compressor producing a flow rate of 6 litres per minute. E Flow Rapid nebulisers are paid for by the patient but deliver a higher percentage of the dose.
- If unacceptably long, the nebulisation time can be reduced for patients with low inspiratory flow.
- A Ventistream® may also be used rarely.

All disposable plastics required for the nebuliser system will be provided through secondary care.
Environmental safety:
- The output from the above nebulisers is automatically filtered. Output from nebulisers without inbuilt filters should be vented to the open air.
- It is advisable for patients to receive nebulised antibiotics in a separate area from other patients. Hospital patients should be routinely placed in a side room.
- Nebulisation should take place in a well ventilated room e.g. with a window open.

GP Monitoring

There are no specific GP monitoring requirements beyond normal clinical care (see appendix 2).

Side effects (for a full list of systemic side effects, see the summary of product characteristics (SPC) for gentamicin or tobramycin respectively)
Bronchospasm may occur on inhalation of antibiotics. This may be prevented by, or treated with, the appropriate use of beta2-agonists. If troublesome, treatment should be withdrawn.

Important	**There is potential for systemic absorption**, with reported serum levels from nil to potentially therapeutic concentrations. Therefore, the possibility of systemic absorption, although rare, should always be borne in mind when treating patients by inhalation.

Nebulisation:
- Mainly local effects
- Inhalation may induce coughing or bronchospasm, although less likely than with colistin

Systemic:
- Ototoxicity and nephrotoxicity.
- Rarely: hypomagnesaemia, hypocalcaemia and hypokalaemia caused by renal tubular dysfunction.
- Possibility of endotoxin-like reactions following higher doses of gentamicin therapy.
- Associated with pseudomembranous colitis (although concomitant use of other antimicrobials is common).
- Central neurotoxicity (extremely rare).

Toxicity:
- **Nephrotoxicity and Audiotoxicity**: In people with CF repeated courses of high dose IV aminoglycosides have been associated with deafness and renal damage but these have not been reported with nebulised therapy.

Drug interactions: refer to BNF, Appendix 1 and SPC for full list of interactions

Although rare, the possibility of systemic absorption, and hence the possibility of interactions should always be borne in mind when treating patients by inhalation.

Drugs commonly seen in primary care:

- Bisphosphonates: Increased risk of hypocalcaemia.
- Cephalosporins: Increased risk of nephrotoxicity.
- Warfarin and phenidione: Anticoagulant effect enhanced.
- Amphotericin: increased risk of nephrotoxicity.
- Loop diuretics: increased risk of ototoxicity.

Drugs not commonly seen in primary care:

- Cholinergics: antagonism of effect of neostigmine and pyridostigmine.
- Ciclosporin: increased risk of nephrotoxicity.
- Cisplatin: increased risk of nephrotoxicity and possible ototoxicity.
- Muscle relaxants: effect of non-depolarising muscle relaxants such as tubocurare enhanced. Use with great caution in patients receiving curare-type muscle relaxants.
- Botulinum toxin: Enhanced neuromuscular block.

Contra-indications

- Hypersensitivity to any aminoglycoside
- Myasthenia gravis

Initiating therapy

Having assessed the patient at a six or eight weekly review and suspecting or confirming infection with Ps. aeruginosa the **specialist consultant** will:

- Discuss with the patient and/or the parent(s)/carer(s), the benefits, side effects, frequency of dosing, the importance of compliance, monitoring requirements of nebulised gentamicin treatment and long term treatment options.
- Give the first dose in hospital after a physiotherapy session
- Baseline monitoring including sputum/throat swabs, renal function, liver function, lung function, weight.
- Prescribe the first month's therapy for the patient.
- **Communicate with the patient's GP, in writing, and confirm that the GP agrees to share care, as described in the Introduction to Shared Care Guidelines.**
- Record the patient's confirmation of understanding of the risks benefits and consent.
- Ensure that full information, including dose and duration of therapy, is sent to the GP without undue delay and recommend that the GP continues treatment in accordance with this shared care guideline.
- Ensure that the patient/parent(s)/carer(s) are aware that they need to inform the community pharmacy to order gentamicin in advance of presenting a script from the GP.

Once the patient has been prescribed nebulised gentamicin, the **CF specialist nurse** will:

- Provide and train the patient/parent/carer in the use and administration of nebulised gentamicin
- Remind the patient/parent(s)/carer(s) that they need to inform the community pharmacy to order gentamicin in advance of presenting a script from the GP.

GP Responsibilities

The GP will notify the specialist, in writing, whether or not he/she agrees to share care and prescribe for the patient, according to this guideline.

- Prescribe subsequent courses of nebulised gentamicin according to the treatment plan provided by the specialist.
- Communicate with the specialist consultant/nurse if the patient presents with any problems associated with the nebulised gentamicin or deterioration in CF related health.
- Be aware of the monitoring parameters for patients prescribed nebulised gentamicin (see appendix 2).
- Report to and seek advice from the specialist team on any aspect of patient care which is of concern to the GP and may affect treatment.
- Inform the specialist team if treatment is stopped for any reason.

Ongoing Specialist Team Responsibilities

- Review and monitor the patient at agreed intervals (see Appendix 1 and 2) and advise GP of any changes to the treatment plan.
- Provide advice as requested by the GP.
- Assess patients referred back by GPs as soon as is practical.

Patient's Responsibilities including parents and or carers

- Report any adverse effects to their GP and / or specialist team.
- Ensure that they have a clear understanding of their treatment.
- Ensure they attend for monitoring requirements as specified in this shared care guideline.
- Be aware that treatment will be stopped it they do not attend for monitoring.

Contact details for the Specialist Teams

Specialist CF nurse
Rachel Crimmins, Specialist CF nurse: 01803 655 586, e-mail: rachelcrimmins@nhs.net

Consultant Paediatrician
Dr C. Sainsbury, secretary: 01803 654 824, e-mail: clive.sainsbury@nhs.net

Respiratory Consultant
Dr L. Dobson, secretary: 01803 654 014, e-mail: lee.dobson@nhs.net

Microbiology Consultants:
Dr P. Turner, secretary: 01803 654 990, e-mail: paul.turner@nhs.net
Dr T. Maggs, secretary: 01803 654 990, e-mail: tony.maggs@nhs.net
Dr S. Hoque, secretary :01803 654 990, e-mail: selina.hoque@nhs.net

Out of Hours:
Paediatric or Respiratory SHO on-call via SDHCT switchboard (01803 614 567).

Full Prescribing Information

For full prescribing information please consult summaries of product characteristics (emc.medicines.org.uk) and the current BNF.

References

4. eSPC Cidomycin® Adult Injectable 80mg/2ml (Sanofi-Aventis), July 2005
5. Standards of care of children and adults with cystic fibrosis in the UK. Cystic Fibrosis Trust, 2001

- Antibiotic treatment for Cystic Fibrosis. Cystic Fibrosis Trust, 2002

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Appendix 1 Treatment pathway for CF patients with Ps. aeruginosa

	Routine Outpatient	Routine Home visit	As required if patient unwell
MDT care input	**Specialist CF consultant** Paeds and adults every 3 months	**Specialist CF nurse** Paeds and adults at least every 3 months	• Phone CF nurse • Home visit by CF nurse • GP visit • Urgent paed. hospital appointment
Tests	**Every 6 – 8 weeks** • Sputum cultures, cough swab • Lung function tests **When required** • FBC, U&Es, Serum creatinine, LFTs, others		• Tests conducted according to necessity. • GPs liase as necessary with specialist team
Drug treatment	If culture positive for Ps. aeruginosa: **Paeds** • Nebulised colistin • Oral ciprofloxacin for 3 weeks **Adults** • Nebulised colistin for 3 months • Oral ciprofloxacin Continue thereafter according to patient response. Continuous nebulisers may be required. Nebulised gentamicin or tobramiycin may be substituted according to patient progress.		
Prescribing and supply	**First month** Prescribed by specialist team Dispensed by hospital pharmacy **Remainder of treatment course** GP prescribes in accordance with Shared Care. Dispensed by community pharmacy.		
Monitoring	All routine monitoring by secondary care every 6 – 8 weeks during routine visits or as frequently as necessary: • Sputum cultures including susceptibility and resistance • Lung function • U&Es, serum creatinine, LFTs • Compliance and technique • Clinical assessment and others as necessary.		

Notes:

3. All relevant findings and results will be communicated by specialist team to GP
4. GP should communicate any relevant tests conducted to specialist team.

Appendix 2 Patient monitoring relating to Ps. Aeruginosa infection

Adults and children are seen every:

- 6-8 weeks by the specialist CF nurse, usually in the form of a home visit
- three months by the local specialist consultant at Torbay Hospital
- year at the specialist CF centre in Exeter.

I**nfants** are seen more frequently until thriving.

6-8 week CF specialist nurse visit and three monthly specialist consultant appointment the following will be monitored :

- Review of respiratory function including:
  - spirometery
  - oximetery
  - peak flow (FEV1)

  } every visit
- Sputum cultures and sensitivities or cough swabs, nasopharyngeal aspirates or deep throat swabs
- Chest X-ray: condition dependent/if significant fall in lung function
- Weight and height: three monthly unless antibiotics need dosing
- Physiotherapy review including nebuliser techniques: every clinic visit. At home only if concerns

Annual review at Specialist CF centre will monitor the following:

- Detailed assessment of progress, review of results and planning for future therapy. Copy sent to GP, and possibly patient
- Weight and height
- Sputum culture (summary of cultures and antibiotics used is produced by specialist nurse prior to visit)
- Oximetry
- Spirometry
- Chest X-ray
- Blood gas in adults if indicated (i.e. if very ill)
- Full blood count, urea and electrolytes, liver function tests including serum albumin, clotting studies, aspergillus species RAST, serum HbA1c, vitamin levels
- Pseudamonal antibody levels

Other monitoring that may be required between CF clinic visits:

- Colds and exacerbations of chest symptoms
- Pre and post antibiotic sputum cultures
- Patient tolerability of antibiotic therapy
- Compliance with antibiotic therapy
- Nebuliser technique
- Equipment safety and maintenance
- Renal function if on potentially nephrotoxic medication
- Sputum culture resistance to current antibiotic treatment

Response to therapy: The main parameters used to monitor response to nebulised drugs in CF are:

- Stability and/or lack of deterioration in spirometry, particularly
  - forced expiratory volume in one second (FEV1), as a percentage of that which is predicted and
  - forced vital capacity (FVC), as a percentage of that which is predicted.

It is important to remember that 4-5 percent variability can exist in spirometric readings due to patient effort and also operator variability.

- In children, resolution of a wet cough is also indicative of treatment success.
- In adults, the cough may not dry up completely but changes in volume and appearance of sputum should be evident.

Hydroxychloroquine

Developed: November 2005
For Review: November 2009

Indications for this guideline

Dermatology
Dermatological conditions caused or aggravated by sunlight *e.g.* cutaneous lupus erythematosus.

Rheumatology
Rheumatoid arthritis, other inflammatory arthritis and connective tissue disease.

Dosage

- Normal dosage is 200mg BD for 3 months and then 200mg OD thereafter.
- Available as 200mg tablets.

Hydroxychoroquine may take several weeks to have a beneficial effect whereas minor side effects may occur relatively early. Treatment should be discontinued if there is no improvement after 6 months.

Dermatology patients may be able to stop taking hydroxychloroquine during winter months. Discuss with specialist team.

Very toxic in overdose, particularly in young children. Symptoms of overdose may include headache, visual disturbance, cardiovascular collapse and convulsions followed by sudden and early respiratory and cardiac arrest.
*****Urgent hospital treatment is needed*****

GP Monitoring

- **Annual visual acuity test by an optician**. The patient should explain to the optician that they are taking hydroxychloroquine so that appropriate tests will be performed.
  Full advice on visual monitoring is contained in Ocular toxicity and hydroxychloroquine: Guidelines for screening 2004 at:
http://www.rcophth.ac.uk/core/core_picker/download.asp?id=165&filetitle=Ocular+Toxicity+and+Hydroxychloroquine%3A+Guidelines+for+Screening+2009

Side effects

Very common / common:

- Nausea and diarrhoea, abdominal pain

Uncommon:

- Pigmentary changes in skin and mucous membranes
- Retinopathy, corneal changes
- Alopecia, exfoliative dermatitis
- Precipitate or exacerbate porphyria
- Vertigo, tinnitus, headache, nervousness, skeletal muscle myopathy

Rare:

- Bone marrow depression, cardiomyopathy, convulsions, hepatic failure

Drug interactions: (refer to BNF, Appendix 1 for full list of interactions)

- **Amiodarone** – avoid concomitant use as increases risk of ventricular arrhythmias.
- **Digoxin** – digoxin levels may be increased.
- **Antimalarials** – interaction depends on agent used.
- **Antiepileptics** – can reduce convulsion threshold.
- Use with caution in patients taking medicines which may cause ocular or skin reactions or drugs known to affect liver or kidney function.
- **Cimetidine –** plasma concentration of hydroxychloroquine increased due to inhibition of metabolism.
- **Antacids** – avoid use within 4 hours of hydroxychloroquine dose.

Pregnancy and breastfeeding

Hydroxychloroquine is contraindicated in pregnancy and breastfeeding.

Vaccinations and infectious illness

- Vaccinate against influenza annually.
- No additional specific precautions required.

Initiating therapy

Having assessed the patient and discussed with them the benefits, side effects, frequency of dosing and monitoring requirements of hydroxychloroquine treatment the specialist team will:-

- **Communicate with the patient's GP, in writing, and confirm that the GP agrees to share care, as described in the Introduction to Shared Care Guidelines.**
- Record the patient's confirmation of understanding of the risks, benefits and consent.

- Undertake baseline investigations and initiate therapy. All patients should have an ophthalmological examination before initiating treatment.
- Specify target doses, monitoring and review dates at clinically relevant time intervals for both the GP and specialist team and any other patient specific information.
- Ensure that full information is sent to the GP without undue delay and recommend that the GP continues treatment in accordance with this shared care guideline.

Information given to patient

A patient information leaflet from the specialist team.

GP Responsibilities

The GP will notify the specialist, in writing, whether or not he/she agrees to share care and prescribe for the patient, according to this guideline.

- Monitor for adverse effects and drug interactions and report adverse events to the CSM and specialist team.
- Report to and seek advice from the specialist team on any aspect of patient care which is of concern to the GP and may affect treatment.
- Prescribe further supplies of hydroxychloroquine according to the recommendations specified in this guideline.
- Inform the specialist team if treatment is stopped for any reason.

Ongoing Specialist Team Responsibilities

- Review the patient at agreed intervals.
- Provide advice as requested by the GP.
- Assess patients referred back by GPs as soon as is practical.

Patient's Responsibilities

- Report any adverse effects to their GP and / or specialist team.
- Ensure that they have a clear understanding of their treatment.
- Ensure they attend for monitoring requirements as specified in this shared care guideline.
- Be aware that treatment will be stopped it they do not attend for monitoring.

Contact details for the Specialist Teams

Dermatology
Dr J. Adams, secretary: 01803 654 837, e-mail: jill.adams@nhs.net
Dr T. Frost, secretary: 01803 654 869, e-mail: tessa.frost@nhs.net

Rheumatology
Rheumatology Nurse Specialist: 01803 654 939
Rheumatology secretary: 01803 654 832
e-mail: rheumatology.sdhct@nhs.net

Out of hours
Medical SHO on-cal via SDHCT switchboard: (01803) 614 567

Full Prescribing Information

For full prescribing information please consult summaries of product characteristics and the current BNF.

References

- eSPC for Plaquenil®, October 2003
- BNF 50, September 2005
- Ocular toxicity and hydroxychloroquine: Guideline for screening 2004. Royal College of Ophthalmologists

The information contained in these shared care guidelines is issued on the understanding that it is the best available from the resources at our disposal at the time of issue. Please see Chapter 20 – Introduction to Shared Care Guidelines for more information.

Indications for this guideline

Rheumatology: Rheumatoid arthritis, psoriatic arthritis and other inflammatory arthritis.

Dosage

- **The first 3 months of treatment will be prescribed from secondary care. GPs will be asked to take over prescribing and monitoring if the patient's clinical situation is stable.**
- Normal range: 10mg – 20mg daily. The loading regime described in the BNF is not used.
- Dose may be increased from 10mg to 20mg OD after 4 – 8 weeks if there is no response and no evidence of toxicity.
- Available as 10mg and 20mg tablets.
- A significant clinical effect may not be observed for 6 – 12 weeks.

Important	**Stopping Leflunomide** Leflunomide has a very long half-life. Where necessary, e.g. severe hepatic reaction or where a patient doesn't want to wait for natural decay prior to starting a family, washouts with either colestyramine or activated powdered charcoal can be prescribed. Full details are available in the BNF, SPC or from the Rheumatology Team.

GP Monitoring

Infection (e.g. persistent sore throat, fever) or easy bruising should be reported to specialist team.

- **FBC, LFT, CRP and blood pressure every 2 weeks for 6 months and then monthly.**
  - Seek advice from specialist team and consider stopping leflunomide if any of the following occur:
  - WCC or platelet count falls on 3 successive occasions.
  - Total WCC < 4.0 or Neuts. < 1.8.
  - Platelet count < 150
  - ALT or AST > 120
  - Alk Phos > 300
  - Uncontrolled hypertension (for mild hypertension, treat with usual antihypertensive drugs and possibly reduce leflunomide dose).
- **U & Es and creatinine every 6 – 12 months.**

Side effects (not covered by specific monitoring requirements)

Patients must report mouth ulcers, sore throat, fever, epistaxis, unexplained bruising or bleeding, and any unexplained illness/infection and should be seen urgently for full blood count and liver function tests.

Common: Mild to moderate diarrhoea.

Less common: Rash, mild reversible alopecia, hypertension, headache, nausea, dyspepsia, mouth ulcers, mild LFT abnormalities, mild leucopaenia.

Uncommon: Bone marrow suppression, severe liver toxicity.

Drug interactions: (refer to BNF, Appendix 1 for full list of interactions)

- **Warfarin**: Anticoagulant effect enhanced.
- **Phenytoin**: Plasma concentration of phenytoin potentially increased.
- **Tolbutamide**: Hypoglycaemic effect enhanced.
- **Colestyramine**: Avoid. Effect of leflunomide significantly decreased.

NB **The active metabolite has a very long half life and a washout procedure (see eSPC) may be required if other DMARDs or haematotoxic agents are required**.

Pregnancy and breastfeeding

Male and female patients should not procreate within 2 years of discontinuing leflunomide. It is also contraindicated in breastfeeding.

Vaccinations and infectious illness

- Live attenuated vaccines are contraindicated. Live vaccines include MMR, BCG, varicella-zoster and yellow fever vaccines.
- Where a patient has received a live vaccine allow at least 2, preferably 4, weeks before starting immunosuppressive therapy.
- Patients should be advised to avoid contact with anyone with active chickenpox and shingles.
- If a patient is vaccinated (with 'killed' vaccines) while taking immunosuppressants they may not mount the appropriate

immune response. Consider repeating 3 months after therapy has ceased if antibody titres are low.
- If contact risk is significant (e.g. Varicella, Measles) discuss with specialist team and consider using specific immunoglobulin.
- Vaccinate against influenza annually and with Pneumovax® II every five years.

For additional information refer to the British Society of Rheumatology guidance on vaccinations for immunosuppressed patients at www.rheumatology.org.uk

Initiating therapy

Having assessed the patient and discussed with them the benefits, side effects, frequency of dosing and monitoring requirements of leflunomide treatment the specialist team will:-

- **Communicate with the patient's GP, in writing, and confirm that the GP agrees to share care, as described in the Introduction to Shared Care Guidelines.**
- Record the patient's confirmation of understanding of the risks, benefits and consent.
- Undertake baseline investigations and initiate therapy.
- Specify target doses, monitoring and review dates at clinically relevant time intervals for both the GP and specialist team and any other patient specific information.
- Ensure that full information is sent to the GP without undue delay and recommend that the GP continues treatment in accordance with this shared care guideline.

Baseline investigations

FBC, LFT and blood pressure monitored before treatment, then as for GP monitoring.

Information given to patient

A patient information leaflet from the specialist team.

GP Responsibilities

The GP will notify the specialist, in writing, whether or not he/she agrees to share care and prescribe for the patient, according to this guideline.

- Monitor for adverse effects and drug interactions and report adverse events to the CSM and specialist team.
- Conduct blood tests, review results and undertake any necessary action as specified in GP Monitoring section above.
- Report to and seek advice from the specialist team on any aspect of patient care which is of concern to the GP and may affect treatment.
- Prescribe further supplies of leflunomide according to the recommendations specified in this guideline.
- Inform specialist team if treatment is stopped for any reason.

Ongoing Specialist Team Responsibilities

- Review the patient at agreed intervals.
- Provide advice as requested by the GP.
- Assess patients referred back by GPs as soon as is practical.

Patient's Responsibilities

- Report any adverse effects to their GP and / or specialist team.
- Ensure that they have a clear understanding of their treatment.
- Ensure they attend for monitoring requirements as specified in this shared care guideline.
- Accept responsibility for using effective contraception.
- Be aware that treatment will be stopped it they do not attend for monitoring.

Contact details for the Specialist Teams

Rheumatology

Rheumatology Nurse Specialist 01803 654 939
Rheumatology secretary 01803 654 832
e-mail: rheumatology.sdhct@nhs.net

Out of hours

Medical SHO on-cal via SDHCT switchboard 01803 614 567

Full Prescribing Information

For full prescribing information please consult summaries of product characteristics and the current BNF.

References

- eSPC for Arava®, December 2004
- BNF 50, September 2005
- British Society for Rheumatology. National Guidelines for the Monitoring of Second Line Drugs, July 2000

The information contained in these shared care guidelines is issued on the understanding that it is the best available from the resources at our disposal at the time of issue. Please see Chapter 20 – Introduction to Shared Care Guidelines for more information.

Shared Care Prescribing Guide

Lisdexamfetamine

For attention deficit hyperactivity disorder in children and adolescents (6 years to under 18 years)
This guideline highlights significant prescribing issues. Not all prescribing information and potential adverse effects are listed. Please refer to SPC/data sheet for full prescribing data.

Specialist:

Please complete letter at the end of this document and send together with the shared care guideline to the GP.

GP:

Please indicate whether you wish to share patient's care by completing letter at the end of this document and return to specialist.
GPs are invited to participate. If a GP is not confident to undertake these roles, then they are under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist

Aim of treatment

The degree of impairment experienced by individual people with attention deficit hyperactivity disorder (ADHD) varies depending on personal circumstances, and individuals can also respond differently to treatment. A person-centered approach is essential to identify the needs of the patient and family, agree treatment goals, develop a tailored treatment plan, re-assess and evaluate treatment response, and ensure goals are regularly updated to reflect changed circumstances and needs.
Medication may be indicated as part of a comprehensive treatment programme for confirmed ADHD when remedial measures alone prove insufficient. Stimulants (e.g. methylphenidate, dexamfetamine and lisdexamfetamine dimesylate) and non-stimulants (e.g. atomoxetine) are the two types of medication available for the treatment of ADHD.

Specialist responsibilities

- Complete initial assessment and establish diagnosis of ADHD
- Where appropriate - offer and initiate medication for management of ADHD (including appropriate pre-treatment screening and required baseline monitoring)
- Provide the person and/ or the person's parents/guardians/carers with suitable written and verbal information about the medication prior to starting treatment and discuss the benefits and side effects of treatment including the monitoring of therapy.
    - Information should include advice about over the counter (OTC) drugs that can interact with lisdexamfetamine and a recommendation to consult a pharmacist before using OTC remedies.
- Ensure a comprehensive care plan is developed and agreed- setting out the required level of care and support needed as well as clear guidance about how response to treatment will be reviewed (to include all health and social care professionals involved in delivery of care).
- Ensure formal communication is sent to the child/ young person's school regarding the use of lisdexamfetamine where indicated.
- Prescribing the medication for the first 3 months of treatment or until the person's condition/dose is stabilised, and the GP agrees to take over responsibility for prescribing.
- Specify review dates at clinically relevant time intervals (for both the GP and the consultant/ specialist provider)
- Ensure prompt communication with GP (and other service providers as appropriate) of any changes in treatment, results of monitoring undertaken and assessment of adverse events.
- On-going monitoring for effectiveness of treatment (based on clinician's assessment and feedback/ observations from individual and/or parents.
- Reporting adverse events to the Commission on Human Medicines (CHM)
    - This medicinal product is still holds black triangle status▼ and is subject to additional monitoring requirements
- Ask the GP whether they are willing to participate in shared care.
- Provide the GP with relevant contact information with clear arrangements for back-up advice and support should further assistance be required relating to this medication.
- Where indicated- advice to GPs on when and how to stop treatment:
- e.g. Medication free periods may be recommended to allow catch up growth (rarely growth retardation may occur during prolonged treatment) and the consultant overseeing treatment should liaise with the individual, their parents/ guardians and the individual's GP to advise on the timing of this.
- Liaise with Adult ADHD services (Currently DANA service) to facilitate safe transition from children's to adult's services when necessary.

General practitioner responsibilities

- Ensure a timely reply is sent to specialist in response to request for shared care.
- Where agreed, continue to prescribe lisdexamfetamine in accordance with shared care guidelines. (Prescriptions should be for 28 days or less in accordance with controlled drug legislation).

- Ensure that monitoring (height, weight, blood pressure and pulse) is completed in accordance with shared care guidelines (see monitoring section)
- Prompt referral to a specialist if there is a change in the person's physical or mental health status.
- Report to and seek advice from a specialist on any aspect of patient care which is of concern to the GP and may affect treatment.
- Reporting adverse events to specialist and Commission on Human Medicines (CHM)
  - This medicinal product is still holds black triangle status ▼ and is subject to additional monitoring requirements
- Stop treatment/ amend dose in the case of a severe adverse event or as per shared care guideline.

Monitoring

Baseline assessment & monitoring (to be completed by the specialist service provider):

- Full history and physical examination to include:
  - assessment for the presence of cardiac disease (including history of exercise syncope, undue breathlessness and other cardiovascular symptoms)
  - heart rate and blood pressure (plotted on a centile chart)
  - height and weight (plotted on a growth chart)
  - family history of cardiac disease and examination of the cardiovascular system
- An electrocardiogram (ECG) if there is past medical or family history of serious cardiac disease, a history of sudden death in young family members or abnormal findings on cardiac examination
- Risk assessment for substance misuse and drug diversion
- Where findings suggest a history or presence of cardiac disease, individuals should be referred for a specialist cardiac evaluation prior to initiating drug treatment.

Before initiating treatment for young women of child-bearing potential it is essential to consider and discuss contraception and/ or, where appropriate, the risks of pregnancy (including relapse, risk to the foetus and risks associated with stopping or changing medication). If there is any possibility that the individual may be pregnant it is important to confirm this prior to starting treatment.

Following an adequate treatment response, drug treatment for ADHD should be reviewed annually and continued for as long as it is clinically effective.

The specialist will plot results received from the GP on a centile chart (for heart rate and blood pressure) and growth chart (for height and weight).

Where abnormal results or presence of side effects are identified, the specialist will contact the individual and/ or GP to advise on action required (e.g. need for additional specialist treatment review/ stop treatment).

As part of transition service planning, young people should receive a timely review by a specialist to discuss drug treatment and consider whether continuation into adulthood will continue to provide therapeutic benefit.

Monitoring during treatment **(to be completed by the GP in accordance with shared care):**

The following monitoring should be carried out as follows (and before and after each dose change):

- Height & weight, at least every 6 months
- Blood pressure & pulse, every 3 months

Monitoring undertaken by the GP must be copied to the Consultant to ensure accurate monitoring and review of treatment. Where abnormal results or presence of side effects are identified (which could indicate need to review/ stop treatment) the GP should seek advice from a specialist.

Where an individual presents to the GP with any of the following symptoms (which may be associated with ADHD medication) or if the GP has any concerns about possible diversion, misuse or abuse of medication, specialist advice must be sought:

- Development or worsening of psychiatric disorders (e.g. anxiety, psychotic or manic symptoms).
- Development of symptoms such as palpitations, exertional chest pain, unexplained syncope, dyspnoea or other symptoms suggestive of cardiac disease (prompt specialist cardiac evaluation indicated)
- Onset or exacerbation of motor and verbal tics.

Patient responsibilities

Take (or support administration of) medication as directed by the prescriber.

- Report any adverse effects to the GP and/ or specialist regarding their treatment.
- Ensure prescribed medication is stored safely and securely
- Ensure that they or their carers have a clear understanding of the treatment, expected benefits and potential side effects.
- Ensure they understand the importance of monitoring treatment and attend specialist appointments and/ or GP appointments to ensure timely monitoring can be completed (in accordance with the shared care guideline).

Understand that treatment will be stopped if patient does not attend for monitoring and treatment reviews.
Supporting Information

The aim of these guidelines, applicable to children (aged 11 years or under) and young people (12-18 years), is to support adherence to:
NICE CG 72: Attention deficit hyperactivity disorder. Diagnosis and management of ADHD in children, young people and adults
NICE TAG 98: Methylphenidate, atomoxetine and dexamfetamine for attention deficit hyperactivity disorder (ADHD) in children and adolescents
Lisdexamfetamine is a Schedule 2 controlled drug (pro-drug of dexamfetamine). Prescriptions must comply with Misuse of Drugs Regulations 2001 (Maximum legal quantity which may be prescribed= 28 days).
Advise and regularly reiterate importance of safe and secure storage of medication at home (and at school where necessary).
To maximise safety, ensure that the patient / patient's parents/carers have been advised to tell the pharmacist that the individual is taking lisdexamfetamine when requesting over the counter medicine (e.g. cough or cold remedies).

Product information: refer to local formulary

Doses: refer to SPC or BNF

The starting dose is 30mg taken once daily in the morning. The dose may be increased by 20mg increments, at approximately weekly intervals. Lisdexamfetamine should be administered orally at the lowest effective dosage. The maximum recommended dose is 70mg/day

Contraindications and precautions: refer to SPC

Side effects: refer to SPC

Interactions: refer to SPC

Pregnancy and lactation
There is no information available regarding the use of lisdexamfetamine during pregnancy and lactation. Young women of child-bearing potential should be provided with appropriate advice (e.g. contraception).
Additional advice from specialist medicine information department and, where appropriate, perinatal mental health service should be sought if needed.
Refer to Summary of Product Characteristics for full information.

Contact details	
Virgincare (CAMHS)	email: vcl.devonspa@nhs.net telephone : 0330 0245 321 Website
RD&E Foundation Trust	rde-tr.exeterchildhealth@nhs.net
Livewell Southwest	www.livewellsouthwest.co.uk/services/child-adolescent-mental-health-services-camhs
Torbay and South Devon NHS Foundation Trust	www.torbayandsouthdevon.nhs.uk/services/camhs/

Guideline updated by Devon Partnership NHS Trust in consultation with local specialists and GPs
For non-clinical enquiries: D-CCG.DevonFormularies@nhs.net
Date ratified: 9th March 2016

References:

National Institute for Health and Care Excellence. 2006. Technology Appraisal Guidance 98: Lisdexamfetamine, atomoxetine and dexamfetamine for attention deficit hyperactivity disorder (ADHD) in children and adolescents. Available from: http://www.nice.org.uk/guidance/ta98/resources/guidance-lisdexamfetamine-atomoxetine-and-dexamfetamine-for-attention-deficit-hyperactivity-disorder-adhd-in-children-and-adolescents-pdf [Accessed 2Mar2015]
National Institute for Health and Care Excellence. 2008 (Modified 2013) Clinical Guidance 72- Attention deficit hyperactivity disorder. Diagnosis and management of ADHD in children, young people and adults. Availabe from: http://www.nice.org.uk/guidance/cg72/resources/guidance-attention-deficit-hyperactivity-disorder-pdf [Accessed 2Mar2015]
NICE (2013) ESNM19: Attention deficit hyperactivity disorder in children and young people: lisdexamfetamine dimesylate. Available at: http://www.nice.org.uk/mpc/evidencesummariesnewmedicines/ESNM19.jsp [Accessed on 5/3/14]

Bolea-Alamanac B, Nutt D, Fone K, et al (2014) Evidence-based guidelines for management of attention-deficit hyperactivity disorder: Update on recommendations from the British Association for Psychopharmacology. Available from: http://www.bap.org.uk/pdfs/ADHD_Guidelines.pdf [Accessed 26 Mar 2014]
British National Formulary for Children (2014-2015) British Medical Association/ Royal Pharmaceutical Society/ Royal College of Paediatrics and Child Health/ Neonatal and Paediatric Pharmacists Group
Elvanse® Summary of Product Characteristics

Shared Care Agreement Letter - Consultant Request

To: Dr…….

Practice Address: ……

……

……

Patient Name:	
NHS number:	
Date of birth:	
Address:	

Diagnosed condition:
Attention Deficit Hyperactivity Disorder (ADHD)

I recommend treatment with the following drug: Lisdexamfetamine

I request your agreement to sharing the care of this patient according to the North and East Devon Health Community Shared Care Prescribing Guidelines for this drug.

GPs are invited to participate. If GP is not confident to undertake these roles, then they are under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If a specialist asks the GP to prescribe this drug the GP should reply to this request as soon as practical. Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient and accepted by them.

The doctor who prescribes the medication has the clinical and legal responsibility for the drug and the consequences of its use.

Signed:		Date:
Consultant name:		
Contact telephone number:		

GP RESPONSE

I agree/ do not agree* to share the care of this patient in accordance with the Shared Care Guideline.

Signed: …… Date: ……

GP name: …… *Delete as appropriate

Note: Shared care is an entirely voluntary agreement between a GP and a specialist. If a GP chooses not to opt in to shared care with lithium the specialist will retain prescribing responsibilities for their patient.

IMPORTANT	**Different brands of lithium are NOT bioequivalent.** **Prescribe by brand.** This guideline is for Priadel®, the lithium brand included in the South Devon Joint Formulary. Treat changing brands as if starting new therapy.

Indications for this guideline

- Management of acute mania or hypomanic episodes.
- Management of episodes of recurrent depressive disorders where treatment with other antidepressants has been unsuccessful.
- Prophylaxis against bipolar affective disorders.
- Control of aggressive behaviour or intentional self harm.

Mode of action: Not fully understood. Lithium modifies the production and turnover of certain neurotransmitters, particularly serotonin, and may also block dopamine receptors. Modifies concentrations of some electrolytes, particularly calcium and magnesium, and it may reduce thyroid activity.

Dosage

The dose will be stabilised for each patient by the specialist team according to clinical response and required plasma concentration of lithium.

Priadel® tablets: NB modified release.

- Normal range: 400mg – 1g daily usually taken as single dose at night.
- Must be swallowed whole (modified release).
- Available as 200mg and 400mg m/r tablets containing lithium carbonate.

Priadel® liquid

- Normal dose range: 520mg – 1.56g BD (5ml to 15ml BD).
- Available as sugar-free liquid containing lithium citrate 520mg in 5ml.

Priadel® formulations are not bioequivalent and should not be interchanged. Seek specialist advice.

Patients should be advised to maintain an adequate fluid intake and avoid dietary changes which might reduce or increase sodium intake.

Lithium should not be stopped abruptly but reduced gradually over a minimum of 4 weeks.

GP Monitoring

Copy all results to specialist team.

Serum lithium concentration: Taken 12 hours after dose.
Specify times of dose and of sample on blood form

- Normal range: 0.4 – 1.0mmol/l, unless specified by consultant.
- Monthly for 3 months when stabilised, then every 3 months thereafter.
- Contact specialist team for advice if results outside normal range.

More frequent testing is required after dose changes, development of intercurrent disease, signs of manic or depressive relapse, following significant change in sodium or fluid intake, during illness involving fluid loss or if signs of lithium toxicity occur..

U&Es and serum creatinine and thyroid function test every 6 months.
ECG annually. Seek specialist advice if results are abnormal.

Side effects (not covered by specific monitoring requirements)

Common: Nausea and diarrhoea (usually settles after first few weeks), metallic taste, weight gain, difficulty concentrating (usually mild), increased thirst.

Less common: oedema which should not be treated with diuretics), aggravation of skin conditions, tremor, hypothyroidism, hypercalcaemia, hypermagnesaemia, hyperparathyroidism, sexual dysfunction, cardiac abnormalities including arrhythmias, sinus node dysfunction, premature ventricular contractions, AV block, T-wave depression and myocarditis.

Nephrotoxicity: Up to one third of patients may develop polyuria and polydipsia which is usually reversible on withdrawal. Long term treatment may result in permanent changes and renal impairment.

Lithium toxicity symptoms include anorexia, diarrhoea and vomiting. CNS effects include blurred vision, drowsiness, giddiness, ataxia, coarse tremor, muscle twitching.
Severe overdosage: hyperreflexia and hyperextension of limbs, convulsions, toxic psychosis, syncope, oliguria, circulatory failure, coma.

The excretion of lithium is dependent on blood sodium concentration. Anything which affects blood sodium concentration will affect blood levels of lithium to an extent which may become toxic e.g. vomiting, febrile illness or sweating due to hot weather.

Drug interactions: (refer to BNF, Appendix 1 for full list of interactions)

- **Diuretics** - Lithium excretion reduced.
- **ACE inhibitors and Angiotesin-II Antagonists** - Lithium excretion reduced.
- **Metronidazole**: Inreased risk of lithium toxicity.
- **NSAIDs** - Lithium excretion reduced. Aspirin may be the safest for occasional use.
- **SSRI antidepressants** - increased risk of CNS toxicity.
- **Methyldopa-** Neurotoxicity.
- **Sumatriptan** - Increased risk of CNS toxicity.
- **Theophylline** – Lithium excretion increased.
- **Antipsychotics** - Rare cases of increased toxicity of either agent. Consult specialist.
- **Amiodarone**- Risk of ventricular arrhythmias

Pregnancy and breastfeeding

Women treated with lithium should use a reliable method of contraception. Discuss with specialist team for further advice. Contraindicated in breastfeeding women.

Initiating therapy

Having assessed the patient and discussed with them the benefits, side effects, frequency of dosing and monitoring requirements of lithium treatment the specialist team will:-

- **Communicate with the patient's GP, in writing, and confirm that the GP agrees to share care, as described in the Introduction to Shared Care Guidelines.**
- Record the patient's confirmation of understanding of the risks, benefits and consent.
- Provide the patient with a purple patient information pack which includes a lithium therapy record book.
- Undertake baseline investigations, initiate and stabilise therapy.
- Specify treatment doses, target plasma range, monitoring and review dates at clinically relevant time intervals for both the GP and specialist team and any other patient specific information.
- Ensure that full information, including results from baseline investigations, is sent to the GP without undue delay and recommend that the GP continues treatment in accordance with this shared care guideline.

Baseline investigations
U&Es including serum creatinine, thyroid function test and ECG.

Information given to patient

- A purple lithium patient information pack containing patient information booklet, lithium alert card and record book for tracking blood tests should be given to the patient by the specialist team.

GP Responsibilities

The GP will notify the specialist, in writing, whether or not he/she agrees to share care and prescribe for the patient, according to this guideline.

- Be aware of potential for adverse effects and drug interactions and report adverse events to the CSM and specialist team.
- Conduct blood tests, review results and undertake any necessary action as specified in GP Monitoring section above.
- Report to and seek advice from the specialist team on any aspect of patient care which is of concern to the GP and may affect treatment.
- Prescribe further supplies of lithium according to the recommendations specified in this guideline.
- Ensure results of blood tests and doses are recorded in the patient held record.
- Inform the specialist team if treatment is stopped for any reason.
- Provide additional lithium record books as required. Lithium packs may be ordered from PCSS stationery by email to d-pc.PCSSstationery@nhs.net or by fax to 01392 445431

Ongoing Specialist Team Responsibilities

- Review the patient at agreed intervals.
- Provide advice as requested by the GP.
- Assess patients referred back by GPs as soon as is practical.

Patient's Responsibilities

- Report any adverse effects to their GP and / or specialist team.
- Ensure that they have a clear understanding of their treatment.
- Ensure they attend for monitoring requirements as specified in this shared care guideline.
- Be aware that treatment will be stopped it they do not attend for monitoring.

Contact details for the Specialist Teams

Consultants

Dr M Al-Gahry	01626 357 335
Dr M Das	01803 526 808
Dr T Dickinson	01803 526 808
Dr J Dunn	01626 362 179
Dr R Horvath	01803 214 597
Dr D Somerfield	01803 528 100
Dr F Watt	01803 214 597
Dr J Wildgoose	01803 528 100
Chadwell (Older person's mental health, Torbay)	01803 546470
Waverley (Recovery and Independent Living South Bay and Well being and Access Torbay, Torbay Assertive Outreach)	01803 214597
Culverhay (North Bay RAIL)	01803 526808

Out of Hours

Psychiatric SHO on-call via SDHCT switchboard 01803 614 567

Full Prescribing Information

For full prescribing information please consult summaries of product characteristics and the current BNF.

References

- eSPC for Priadel® tablets, September 2010
- eSPC for Priadel® liquid, September 2010
- BNF 60, September 2010
- Taylor D, Paton C and Kapur s. 2009 The South London & Maudsley NHS Trust Prescribing Guidelines 10th Ed.
- Mood stabilisers - lithium carbonate, www.NeLMH.org, July 2003
- Lithium Patient Advice Leaflet, UKPPG, 2001
- NPSA Patient Safety Alert. Safer Lithium Therapy. NPSA/2009/PSA005 1st December 2009

The information contained in these shared care guidelines is issued on the understanding that it is the best available from the resources at our disposal at the time of issue. Please see Chapter 20 – Introduction to Shared Care Guidelines for more information.

Note: Shared care is an entirely voluntary agreement between a GP and a specialist. If a GP chooses not to opt in to shared care with melatonin the specialist will retain prescribing responsibilities for their patient.

Indications for this guideline

Melatonin should only be prescribed under this Shared Care Guideline and only for the following indications:

- Sleep and circadian rhythm disorders in children over the age of 3 with significant neurodevelopmental disability, including autistic spectrum disorders, attention deficit hyperactivity disorder (ADHD), or sensory impairment.
- Treatment of side effects from medication for attention deficit hyperactivity disorder (ADHD) in children over the age of 3.

Normal sleep hygiene

Melatonin should only be used in conjunction with good, normal sleep hygiene. Patients should be encouraged to adopt a regular, relaxing bedtime routine avoiding stimulating TV programmes and computer games.

Background

Melatonin is a pineal hormone produced from the amino acid tryptophan. There appears to be a diurnal rhythm of melatonin secretion; it is secreted during hours of darkness and may therefore have a role in influencing circadian rhythm. It is involved in the inhibition of gonadal development, the control of oestrus and in protective changes in skin colouration.

Important **Melatonin is unlicensed in the UK for these indications**

Dosage for patients over 3 years old

Patients will be stabilised by the specialist team over a period of 8 months (see Initiating Therapy section) before GPs will be asked to prescribe under this shared care agreement.

There is at present very limited trial data for the use of melatonin in children, and in those trials that have been done doses have varied. The dosages used are therefore based on the clinical experience of the specialists.

The MHRA has issued guidance stating that the licensed product of melatonin available in the UK is used wherever possible (www.mhra.gov.uk). This includes off licence use of the licensed product, if deemed suitable by the clinician. As a result of this guidance, patients will be initiated on the UK licensed product Circadin® (licensed for adults over 55 years) if they are able to take tablets and if a modified release preparation is considered appropriate.

The usual dosage of Circadin® prescribed is **2mg ON taken 1-2 hours before the desired sleep time.**
For children unable to swallow tablets or for whom a modified release product is not suitable, the usual dosage of melatonin is **3mg OD taken 45 minutes before the desired sleep time**.
All dose adjustments will be led by the specialist team.
A protocol for dose titration is included at the end of this guideline for information only.

Preparations

- Modified release tablets 2mg (Circadin®), cost per 28 days at 2mg OD = £14.36.
- Melatonin capsules or orodispersible tablets 3mg (Penn Pharmaceuticals Specials Manufacturing 01495 711 222). £100 per 100 caps/tabs, cost per 28 days at 3mg OD = £28
- Capsules 3mg (LifeExtension® imported by Idis, 01932 824 000). £13 per 60 capsules, cost per 28 days at 3mg OD = £6.07. Contents may be mixed with food or drink.
- Sugar free oral liquid, 1mg in 1ml (Kidnaps® produced by Special Products Ltd, 01483 736 950). £16.74 per 200ml, cost per 28 days at 3mg OD= £7.03. Strawberry flavoured. The prescribed dose may be mixed with warm milk or cold water and swallowed immediately or retained in the mouth for about 3 minutes before being swallowed for a more rapid response. Liquid should be reserved for patients who are unable to tolerate capsules or where a rapid response is required.

N.B Carriage costs may be added to the costs quoted above for imported products

If any product other than Circadin® is prescribed, MHRA guidance specifies that prescribers will need to provide written details of the special clinical need to the importer for submission to the MHRA. Details have to be provided with every order and not just the first occasion. A template letter is included in Appendix 1.

GP Monitoring

No specific requirements above normal clinical care. However, GPs are encouraged to remind patients and parents / carers of the importance of maintaining normal sleep hygiene whenever possible. The Specialist team will continue to review the patient (see Ongoing Specialist Team Responsibilities).

Side effects (not covered by specific monitoring requirements)

- May cause irregular sleep patterns.
- Drowsiness upon waking and somnolence.

- Headache
- Increase in seizure activity in patients with neurological deficits.
- Possible effects on gonadal development. **Additional monitoring at times of growth and pubertal / sexual development will be undertaken by the specialist team.**

Drug interactions:

- No interactions have been identified from published literature. However, clinicians should be aware that published evidence is derived from small-scale studies. Suspected interactions should be discussed with the specialist team and a Yellow Card completed and sent to the MHRA.

Precautions and contraindications

- Not recommended in pregnancy.
- Not recommended in patients with a history of seizures.
- Should be avoided in endocrine disorders.

Initiating therapy (by Specialist Team)

Having assessed the patient and discussed with them the benefits, side effects, frequency of dosing and monitoring requirements of melatonin treatment the specialist team will initiate therapy in the following way:

For patients who are able to swallow tablets: 2mg m/r (Circadin®) OD for 3 month trial, then stop for 2 weeks. If the disorder resolves, no further treatment is given. If the problem recurs when the melatonin is stopped, a second trial with 2mg m/r OD for 3 months is made. Treatment is stopped for a further 2 weeks to see if the problem has resolved. If the sleep disorder recurs when melatonin is stopped, treatment is restarted by the specialist and continued. GPs will only be asked to assume prescribing responsibilities when stabilised (i.e. after 8 months).

If unable to swallow tablets or if next day drowsiness is a problem with the modified release preparation: 3mg OD for 3 month trial. Proceed as described above.

Once the patient is stabilised the specialist will:

- **Communicate with the patient's GP, in writing, and confirm that the GP is happy to share care, as described in the Introduction to Shared Care Guidelines (see Appendix 2- Request to share care letter). Where a GP is not happy to share care the specialist will continue to prescribe.**
- Record and communicate to the GP the patient's and/or carer's confirmation of understanding of the risks, benefits and consent.
- Record and communicate to the GP the patient's and/or carer's confirmation of understanding of the implications of the medicine being unlicensed.
- Specify dose, monitoring and review dates at clinically relevant time intervals for both the GP and specialist team and any other patient specific information.
- Ensure that full information, including issues resulting from the unlicensed use of this medication, is sent to the GP without undue delay and recommend that the GP continues treatment in accordance with this shared care guideline.
- Inform the GP of any potential drug interactions relevant to the patient.
- Provide a patient information leaflet to the patient.

GP Responsibilities

The GP will notify the specialist, in writing, whether or not he/she agrees to share care and prescribe for the patient, according to this guideline.

- Be aware of drug interactions and report adverse events to the MHRA and specialist team.
- Refer patient back to the specialist where a dose adjustment may be necessary (due to problems with tolerability or efficacy).
- Report to and seek advice from the specialist team on any aspect of patient care which is of concern to the GP and may affect treatment.
- Prescribe further supplies of melatonin at the dose requested by the specialist team.
- Inform the specialist team if treatment is stopped for any reason.

Ongoing Specialist Team Responsibilities

- Review the patient at agreed intervals. Regular reviews will be undertaken as follows:
    - ADHD patients, as per ADHD protocol.
    - Other patients, every 6 – 12 months.
- Review the patient (including for dose adjustments) where necessary as requested by the GP.
- Provide advice as requested by the GP.
- Assess patients referred back by GPs as soon as is practical.
- Plan for transition to adult services at 18 if necessary.

Patient's and Carer's Responsibilities

- Report any adverse effects to their GP and / or specialist team.
- Ensure that they have a clear understanding of their treatment.
- Ensure they attend for monitoring requirements as specified in this shared care guideline.
- Be aware that treatment will be stopped it they do not cooperate with monitoring.

Additional Information

Dose titration:

Most patients are maintained on 2mg m/r tablets or 3mg immediate release daily and require no further dose adjustment for the duration of treatment. However, in some patients tolerance develops and the dosage of melatonin may be increased, by the Specialist, if they are confident that good, normal sleep hygiene is still being practised. Prescribers should remind patients and carers of the importance of practicing normal sleep hygiene in addition to taking melatonin at every dosage increase.

Step 1: Increase to 4mg m/r OD, taken 1-2 hours before the desired sleep time or 6mg OD of immediate release taken 45 minutes before the desired sleep time.

Step 2: The modified release preparation should not be increased beyond 4mg OD. If treatment becomes ineffective, treatment should be stopped for 2 weeks and then restarted at 2mg OD. If 6mg immediate release becomes ineffective, increase the dose to 9mg OD. There is no evidence that any further increase in dose is likely to have any additional benefit.

Step 3: If 9mg becomes ineffective, treatment should be stopped for 2 weeks and then restarted at 3mg OD.

Contact details for the Specialist Teams

Paediatrics:

Dr I Guarino Direct Dial 01803 655 863 or via Torbay hospital switchboard

CAMHS:

Contact Child and Family Guidance, Torbay Hospital Annex, 187 Newton Road, Torquay, TQ2 7BA 01803 655692

Out of Hours:

Paediatric SHO via hospital switchboard 01803 614 567

References

1. Product information leaflet, melatonin oral liquid. Special Products Limited, March 2006
2. BNF for Children, 2010-11
3. Medicines for Children, Royal College of Paediatrics and child health, 2003
4. Guidelines on melatonin, Alder Hey. Personal communication.
5. Martindale 36th Ed. 2009

Appendix 1- Letter of clinical need

Dear Pharmacist,

Re: Paediatric Melatonin Prescription

Name:

D.O.B:

This child has been assessed by a paediatrician who feels they may benefit from treatment with melatonin. For this child the UK licensed preparation Circadin® is not appropriate because (delete as necessary):

- A liquid formulation is necessary
- An immediate release formulation is required.

It is therefore necessary for me to request that you obtain an alternative formulation elsewhere.

Yours sincerely

Dr……

Appendix 2 – Request to share care letter

Dear Dr

Re: (Name of child, DOB)

Shared Care Guidelines: Melatonin
For Children Already on Melatonin

Please find enclosed a copy of the agreed Shared Care Guidelines for Melatonin. Your patient is established on this medication, and is under supervision from the Hospital. The dose, effectiveness and safety has been established as per the Guidelines.

I am therefore writing to ask if you would now consider taking over the prescription of this, mainly because it is so much more convenient for parents to collect their prescriptions from primary care. If I do not hear from you by …….., I will assume that you are willing to take on prescribing.

Yours sincerely

Dr.....
Consultant Paediatrician

I agree/do not agree* to taking over the prescribing of Melatonin as above.

Signed: …….

Date: ……

*Please delete as required, sign and date and return to the above address.

Methotrexate must only be given weekly.
Serious errors have occurred.

Indications for this guideline

- **Dermatology**: Severe, uncontrolled psoriasis, unresponsive to other therapy.
- **Gastroenterology**: Crohn's disease and ulcerative colitis unresponsive to other therapy (unlicensed).
- **Ophthalmology**: Uveitis (unlicensed).
- **Respiratory**: Severe steroid-resistant asthma (unlicensed).
- **Rheumatology**: Rheumatoid arthritis and other types of inflammatory arthritis, myositis, vasculitis, other connective tissue diseases and as a steroid sparing agent.

Dosage

- Prescribe **2.5mg tablets** only to avoid confusion.
- May be taken as a single dose or spread out during the day if preferred by the patient.
- **Folic acid 5mg OD** taken 6 days per week (avoiding the day on which methotrexate is taken) is recommended from the outset to guard against GI side effects.

IMPORTANT	**Methotrexate must be administered as a WEEKLY dose.** Serious errors have occurred as a result of ambiguous instructions. Prescriptions **must state:** • ***dose*** in ***numbers of 2.5mg tablets*** and • "***to be taken once a week"*** rather than "as directed".

- Methotrexate prescribing will be initiated by the hospital consultant.
- This guideline **does not** cover methotrexate injection.
- GPs should prescribe subsequently according to the following regimes:-

Dermatology
Target dose range 5 to 20mg (2 to 8 tablets) **once a week.** Patients will be stabilised on target dose by specialist team.
Gastroenterology
Target dose range 15 to 25mg (6 to 10 tablets) **once a week.** Patients will be stabilised on target dose by specialist team.
Ophthalmology
Target dose range 2.5 to 25mg (1 to 10 tablets) **once a week**. Patients will be stabilised on target dose by specialist team.
Respiratory
Target dose range 10 to 15mg (4 to 6 tablets) **once a week**. Patients will be stabilised on target dose by specialist team.
Rheumatology

- Starting dose and regime for increasing dose will be specified by specialist team.

GP Monitoring

Infection (e.g. persistent sore throat, fever) or easy bruising should be reported to specialist team.

- Please copy all results to secondary care team.
- **FBC & LFT every 2 weeks for 3 months and then monthly.**
- **Please include CRP with LFT for Rheumatology.**
  Seek advice from specialist team and consider stopping methotrexate if any of the following occur:
  - WCC or platelet count falls on 3 successive occasions.
  - Total WCC < 4.0 or neutrophils < 1.8 (isolated lymphopaenia is not usually an indication for cessation of methotrexate therapy).
  - Platelet count < 150
  - ALT or AST > 120
  - Alk Phos > 300
- MCV may rise. If > 110 consider checking B12 & folate if patient is anaemic. If continues to rise above 110, discuss with specialist team.
- **U&Es and serum creatinine every 6 – 12 months**, or more frequently if any reason to suspect renal impairment (methotrexate metabolites renally excreted). Dose reduction may be required.

Gastroenterology has a monitoring system in place for their **Crohn's disease** and **ulcerative colitis** patients. Requests for blood samples are made by the specialist team but patients may have samples taken in community or hospital.

Pneumonitis affects up to 1% of rheumatology patients and can occur at any time during treatment. Presentation is usually "sub-acute" with increasing dyspnoea, dry cough +/- fever. Patients should be aware of the need to report these symptoms. Seek advice from Rheumatology Department, request chest x-ray urgently and consider stopping methotrexate. (If referred to Respiratory physicians instead, please send copy to Rheumatologists.)

Side effects (not covered by specific monitoring requirements)

Patients must report mouth ulcers, sore throat, fever, epistaxis, unexplained bruising or bleeding, and any unexplained illness/infection and should be seen urgently for full blood count and liver function tests.

Common: Nausea*, stomatitis / mouth ulcers*
Less common: Bone marrow suppression, LFT abnormalities, diarrhoea*, reversible alopecia, rash, malaise, drowsiness
Uncommon: Pneumonitis, hepatitis.

*Note: GI side effects can be abolished in 80% of affected patients by co-prescription of folic acid (see page 20-32).

Beware of patients attending GP surgeries or pharmacies presenting with other symptoms; signs of methotrexate toxicity may present as, for example, breathlessness, dry persistent cough, vomiting and diarrhoea.

Drug interactions: (refer to BNF, Appendix 1 for full list of interactions)

- **NSAIDs** / aspirin – May be co-prescribed, but best taken in steady dose as can reduce excretion of methotrexate – Beware of over the counter analgesia.
- **Trimethoprim** – Avoid because increased anti-folate effect (also co-trimoxazole)
- **Phenytoin** – Care required because increased anti-folate effect
- **Others** - Ciclosporin, acetretin, probenecid - See BNF

Alcohol

Patients taking methotrexate should ideally abstain from alcohol as this can theoretically increase the chances of liver toxicity. However, the consensus amongst specialist fields is that modest amounts (up to 5 units per week) are unlikely to cause problems, except in Dermatology patients. Dermatology patients are advised to abstain from alcohol.
Patients should avoid alcohol on the day on which methotrexate is taken.

Pregnancy, breastfeeding and fertility

- **Methotrexate is teratogenic.** Patients (**both men and women**) of child-rearing age should be advised to use a reliable method of contraception during treatment and for 6 months afterwards. When planning a pregnancy it is important that **both men and women** discuss the potential risks from medication with the specialist team (at least six months before conception).
- Methotrexate is contraindicated in breastfeeding mothers.

Vaccinations and infectious illness

- Live attenuated vaccines are **contraindicated** in patients taking immunosuppressants unless stopped at least 3 months beforehand. Live vaccines include MMR, BCG, varicella-zoster and yellow fever vaccines.
- Where a patient has received a live vaccine allow at least 2, preferably 4, weeks before starting immunosuppressive therapy.
- Patients should be advised to avoid contact with anyone with active chickenpox and shingles.
- If a patient is vaccinated (with 'killed' vaccines) while taking immunosuppressants they may not mount the appropriate immune response. Consider repeating 3 months after therapy has ceased if antibody titres are low.
- If contact risk is significant (e.g. Varicella, Measles) discuss with specialist team and consider using specific immunoglobulin.
- Vaccinate against influenza annually and with Pneumovax® II every five years.

For additional information refer to the British Society of Rheumatology guidance on vaccinations for immunosuppressed patients at www.rheumatology.org.uk

Initiating therapy

Having assessed the patient and discussed with them the benefits, side effects, frequency of dosing and monitoring requirements of methotrexate treatment the specialist team will:-

- **Communicate with the patient's GP, in writing, and confirm that the GP agrees to share care, as described in the Introduction to Shared Care Guidelines.**
- Record the patient's confirmation of understanding of the risks, benefits and consent.
- Issue a booklet to the patient ("patient-held record") for recording test results and explain its use.
- Undertake baseline investigations and initiate therapy.
- Explain to appropriate patients the importance to use an effective contraceptive during treatment and for 6 months after.

- Specify target doses, monitoring and review dates at clinically relevant time intervals for both the GP and specialist team and any other patient specific information and recording them in the patient-held record.
- Ensure that full information, including results from baseline investigations, is sent to the GP without undue delay and recommend that the GP continues treatment in accordance with this shared care guideline.

Gastroenterology will stabilise the dose for their patients. They have a monitoring system in place for their **Crohn's disease** and **ulcerative colitis** patients. Requests for blood samples are made by the specialist team but patients may have samples taken in the community or the hospital.
Dermatology, Ophthalmology and **Respiratory** will stabilise the dose for their patients. GPs are responsible for conducting blood samples and monitoring results as described in GP Monitoring section above.

Baseline Investigations

- FBC, LFT, U&Es and serum creatinine before treatment, then as for GP Monitoring.
- **Dermatology, Ophthalmology, Respiratory** and **Rheumatology** patients will have a baseline chest X-ray and lung function test. Gastroenterology patients do not routinely have baseline chest X-ray or lung function test.

Information given to patient

- The specialist team will supply each patient with an information leaflet and a booklet to record appropriate monitoring ('patient-held record') and provide appropriate information.

GP Responsibilities

The GP will notify the specialist, in writing, whether or not he/she agrees to share care and prescribe for the patient, according to this guideline.

- Monitor for adverse effects and drug interactions and report adverse events to the CSM and specialist team.
- Conduct blood tests, review results and any necessary action is undertaken as specified in GP Monitoring section above, copying results and actions into patient-held record
- Report to and seek advice from the specialist team on any aspect of patient care which is of concern to the GP and may affect treatment.
- Prescribe further supplies of methotrexate according to the recommendations specified in this guideline.
- Regularly discuss the frequency of doses with the patient.
- Inform the specialist team if treatment is stopped for any reason.

Gastroenterology has a monitoring system in place for their Crohn's disease and ulcerative colitis patients. Requests for blood samples are made by the specialist team but patients may have samples taken in community or hospital.

Very Important

- **Practice computer systems must have up to date methotrexate alerts and prompts.**
- **Repeat prescriptions should be removed from the surgery repeats pile and retained separately for prescriber review prior to authorising by signature. Changes to software to shade prescription signature space on FP10 to alert prescriber to high-risk drug might help in this instance.**

Ongoing Specialist Team Responsibilities

- Review the patient at agreed intervals.
- Regularly discuss the frequency of doses with the patient.
- Provide advice as requested by the GP.
- Assess patients referred back by GPs as soon as is practical.
- **Gastroenterology** specialist team conduct regular blood monitoring and advise GPs of dosage adjustments for their patients.
- **Respiratory** will stabilise dose for their patients and advise on dose titration.

Patient's Responsibilities

- Report any adverse effects to their GP and / or Secondary Care Team.
- Ensure that they have a clear understanding of their treatment.
- Ensure they attend for monitoring requirements as specified in this shared care guideline.
- Accept responsibility for using effective contraception.
- Be aware that treatment will be stopped it they do not attend for monitoring.

Contact details for the Specialist Teams

Dermatology
Dr J. Adams, secretary: 01803 654 837, e-mail: jill.adams@nhs.net
Dr T. Frost, secretary: 01803 654 869, e-mail: tessa.frost@nhs.net

Gastroenterology
IBD Nurse Specialist: 01803 654 951, bleep: 07666 548 580

Ophthalmology:
Ophthalmic Nurse Specialist, Eye Clinic: 01803 655 123

Respiratory
Respiratory Nurse Specialist: 01803 655 147, bleep: #6 733 via SDHCT switchboard

Rheumatology
Rheumatology Nurse Specialist: 01803 654 939
Rheumatology secretary: 01803 654 832
e-mail: rheumatology.sdhct@nhs.net

Out of Hours:
Medical SHO on-call via SDHCT switchboard 01803 614 567 for all indications except Ophthalmology when the Ophthalmic SHO on-call should be contacted.

Full Prescribing Information

For full prescribing information please consult summaries of product characteristics and the current BNF.

References

- eSPC for Maxtrex®, March 2004
- BNF 50, September 2005
- National Guidelines for the Monitoring of Second Line Drugs, British Society for Rheumatology July 2000
- Reducing the harm caused by oral methotrexate; Patient safety alert 03, National Patient Safety Agency, July 2004

The information contained in these shared care guidelines is issued on the understanding that it is the best available from the resources at our disposal at the time of issue. Please see Chapter 20 – Introduction to Shared Care Guidelines for more information.

For attention deficit hyperactivity disorder in children (6 years to under 18 years)
This guideline highlights significant prescribing issues. Not all prescribing information and potential adverse effects are listed. Please refer to SPC/data sheet for full prescribing data.

Specialist:
Please complete letter at the end of this document and send together with the shared care guideline to the GP.

GP:
Please indicate whether you wish to share patient's care by completing letter at the end of this document and return to specialist.
GPs are invited to participate. If a GP is not confident to undertake these roles, then they are under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist
Aim of treatment

Aim of treatment

The degree of impairment experienced by individual people with attention deficit hyperactivity disorder (ADHD) varies depending on personal circumstances, and individuals can also respond differently to treatment. A person-centered approach is essential to identify the needs of the patient and family, agree treatment goals, develop a tailored treatment plan, re-assess and evaluate treatment response, and ensure goals are regularly updated to reflect changed circumstances and needs.
Medication may be indicated as part of a comprehensive treatment programme for confirmed ADHD when remedial measures alone prove insufficient. Stimulants (e.g. methylphenidate, dexamfetamine and lisdexamfetamine dimesylate) and non-stimulants (e.g. atomoxetine) are the two types of medication available for the treatment of ADHD.
Specialist responsibilities

Specialist Responsibilities

- Complete initial assessment and establish diagnosis of ADHD
- Where appropriate- offer and initiate medication for management of ADHD (including appropriate pre-treatment screening and required baseline monitoring)
- Provide the person and/ or the person's parents/guardians/carers with suitable written and verbal information about the medication prior to starting treatment and discuss the benefits and side effects of treatment including the monitoring of therapy.
    - Information should include advice about over the counter (OTC) drugs that can interact with methylphenidate and a recommendation to consult a pharmacist before using OTC remedies.
- Ensure a comprehensive care plan is developed and agreed- setting out the required level of care and support needed as well as clear guidance about how response to treatment will be reviewed (to include all health and social care professionals involved in delivery of care).
- Ensure formal communication is sent to the child/ young person's school regarding the use of methylphenidate where indicated.
- Prescribing the medication for the first 3 months of treatment, or until the person's condition/dose is stabilised, and the GP agrees to take over responsibility for prescribing.
- Specify review dates at clinically relevant time intervals (for both the GP and the consultant/ specialist provider)
- Ensure prompt communication with GP (and other service providers as appropriate) of any changes in treatment, results of monitoring undertaken and assessment of adverse events.
- On-going monitoring for effectiveness of treatment (based on clinician's assessment and feedback/ observations from individual and/or parents.
- Reporting adverse events to the Commission on Human Medicines (CHM)
- Ask the GP whether they are willing to participate in shared care.
- Provide the GP with relevant contact information with clear arrangements for back-up advice and support should further assistance be required relating to this medication.
- Where indicated- advice to GPs on when and how to stop treatment:
- e.g. Medication free periods may be recommended to allow catch up growth (rarely growth retardation may occur during prolonged treatment) and the consultant overseeing treatment should liaise with the individual, their parents/ guardians and the individual's GP to advise on the timing of this.
- Liaise with Adult ADHD services (Currently DANA service) to facilitate safe transition from children's to adult's services when necessary.

General practitioner responsibilities

- Ensure a timely reply is sent to specialist in response to request for shared care.
- Where agreed, continue to prescribe **methylphenidate** in accordance with shared care guidelines. (Prescriptions should be for 28 days or less in accordance with controlled drug legislation).
- Ensure that monitoring (height, weight, blood pressure and pulse) is completed in accordance with shared care guidelines (see monitoring section)

- Prompt referral to a specialist if there is a change in the person's physical or mental health status.
- Report to and seek advice from a specialist on any aspect of patient care which is of concern to the GP and may affect treatment.
- Reporting adverse events to specialist and Commission on Human Medicines (CHM)
- Stop treatment/ amend dose in the case of a severe adverse event or as per shared care guideline.

Monitoring

Baseline assessment & monitoring (to be completed by the specialist service provider):

- Full history and physical examination to include:
  - assessment for the presence of cardiac disease (including history of exercise syncope, undue breathlessness and other cardiovascular symptoms)
  - heart rate and blood pressure (plotted on a centile chart)
  - height and weight (plotted on a growth chart)
  - family history of cardiac disease and examination of the cardiovascular system
- An electrocardiogram (ECG) if there is past medical or family history of serious cardiac disease, a history of sudden death in young family members or abnormal findings on cardiac examination
- Risk assessment for substance misuse and drug diversion

Where findings suggest a history or presence of cardiac disease, individuals should be referred for a specialist cardiac evaluation prior to initiating drug treatment.
Before initiating treatment for young women of child-bearing potential it is essential to consider and discuss contraception and/ or, where appropriate, the risks of pregnancy (including relapse, risk to the foetus and risks associated with stopping or changing medication). If there is any possibility that the individual may be pregnant it is important to confirm this prior to starting treatment.
Following an adequate treatment response, drug treatment for ADHD should be reviewed annually and continued for as long as it is clinically effective.
The specialist will plot results received from the GP on a centile chart (for heart rate and blood pressure) and growth chart (for height and weight).
Where abnormal results or presence of side effects are identified, the specialist will contact the individual and/ or GP to advise on action required (e.g. need for additional specialist treatment review/ stop treatment).
As part of transition service planning, young people should receive a timely review by a specialist to discuss drug treatment and consider whether continuation into adulthood will continue to provide therapeutic benefit.

Monitoring during treatment (to be completed by the GP in accordance with shared care):
The following monitoring should be carried out as follows (and before and after each dose change):

- Height & weight, at least every 6 months
- Blood pressure & pulse, every 3 months

Monitoring undertaken by the GP must be copied to the Consultant to ensure accurate monitoring and review of treatment. Where abnormal results or presence of side effects are identified (which could indicate need to review/ stop treatment) the GP should seek advice from a specialist.
Where an individual presents to the GP with any of the following symptoms (which may be associated with ADHD medication) or if the GP has any concerns about possible diversion, misuse or abuse of medication, specialist advice must be sought:

- Development or worsening of psychiatric disorders (e.g. anxiety, psychotic or manic symptoms).
- Development of symptoms such as palpitations, exertional chest pain, unexplained syncope, dyspnoea or other symptoms suggestive of cardiac disease (prompt specialist cardiac evaluation indicated)
- Onset or exacerbation of motor and verbal tics.

Patient responsibilities

- Take (or support administration of) medication as directed by the prescriber.
- Report any adverse effects to the GP and/or specialist regarding their treatment.
- Ensure prescribed medication is stored safely and securely
- Ensure that they or their carers have a clear understanding of the treatment, expected benefits and potential side effects.
- Ensure they understand the importance of monitoring treatment and attend specialist appointments and/ or GP appointments to ensure timely monitoring can be completed (in accordance with the shared care guideline).
- Understand that treatment will be stopped if patient does not attend for monitoring and treatment reviews.
- Supporting Information

Supporting Information

The aim of these guidelines, applicable to children (aged 11 years or under) and young people (12-18 years), is to support adherence to:

- NICE CG 72: Attention deficit hyperactivity disorder. Diagnosis and management of ADHD in children, young people and adults

- NICE TAG 98: Methylphenidate, atomoxetine and dexamfetamine for attention deficit hyperactivity disorder (ADHD) in children and adolescents

Methylphenidate is a Schedule 2 controlled drug. Prescriptions must comply with Misuse of Drugs Regulations 2001 (Maximum legal quantity which may be prescribed = 28 days).
Advise and regularly reiterate importance of safe and secure storage of medication at home (and at school where necessary).
To maximise safety, ensure that the patient / patient's parents/carers have been advised to tell the pharmacist that the individual is taking methylphenidate when requesting over the counter medicine (e.g. cough or cold remedies).

Product information: refer to local formulary

Doses: refer to SPC or BNF
Usual doses of selected preparations are as follows:

Preparation & available strengths	Formulation characteristics	Typical dose duration	Typical dose range
Immediate release			
Methylphenidate tablets 5mg, 10mg, 20mg	100% immediate release	Peak effects occur 1 to 2 hours after ingestion and effects last for 4-6 hours	Initially 5mg 2-3 times a day, increased at weekly intervals to usual maximum of 60mg daily in divided doses
Sustained/ prolonged release			
Concerta® XL tablets: 18mg, 27mg, 36mg, 54mg	22% immediate release; 78% sustained release	Immediate release component provides peak plasma levels after 1- 2 hours. Prolonged release component provides peak plasma concentration after 6- 8 hours Clinical studies showed that the effects of Concerta XL are maintained until 12 hours after dosing when the product was taken once daily in the morning	Initially 18mg once daily in the morning, adjusted at weekly intervals up to a maximum of 54mg daily
Equasym® XL capsules: 10mg, 20mg, 30mg	30% immediate release; 70% sustained release	Designed to deliver therapeutic plasma levels for a period of approximately 8 hours	Initially 10mg each morning before breakfast, increased gradually at weekly intervals, according to response, to a maximum of 60mg daily
Medikinet® XL capsules: 5mg, 10mg, 20mg, 30mg, 40mg, 50mg, 60mg	50% immediate release; 50% sustained release	Designed to deliver therapeutic plasma levels for a period of approximately 8 hours	Initially 10mg each morning before breakfast, increased gradually at weekly intervals, according to response, to a maximum of 60mg daily
Xenidate® XL tablets 18mg, 36mg	21% immediate release; 79% sustained release	Immediate release component provides peak plasma levels after 1.35 hours. Prolonged release component provides peak plasma concentration after 5.30 hours Designed to deliver therapeutic plasma levels for 12 hours.	Initially 18mg once daily in the morning, adjusted at weekly intervals up to a maximum of 54mg daily

Contraindications and precautions: refer to SPC

Side effects: refer to SPC

Interactions: refer to SPC

Pregnancy and lactation

There is limited information available regarding the use of methylphenidate during pregnancy and lactation. Young women of child-bearing potential should be provided with appropriate advice (e.g. contraception).
Additional advice from specialist medicine information department and, where appropriate, perinatal mental health service should be sought if needed.

Refer to Summary of Product Characteristics for full information.

Support

Contact details	
Virgincare (CAMHS)	email: vcl.devonspa@nhs.net telephone : 0330 0245 321 Website
RD&E Foundation Trust	rde-tr.exeterchildhealth@nhs.net
Livewell Southwest	www.livewellsouthwest.co.uk/services/child-adolescent-mental-health-services-camhs
Torbay and South Devon NHS Foundation Trust	www.torbayandsouthdevon.nhs.uk/services/camhs/

Guideline updated by Devon Partnership NHS Trust in consultation with local specialists and GPs
For non-clinical enquiries: D-CCG.DevonFormularies@nhs.net

Date ratified: 9th March 2016

References:

National Institute for Health and Care Excellence. 2006. Technology Appraisal Guidance 98: Methylphenidate, atomoxetine and dexamfetamine for attention deficit hyperactivity disorder (ADHD) in children and adolescents. Available from: http://www.nice.org.uk/guidance/ta98/resources/guidance-methylphenidate-atomoxetine-and-dexamfetamine-for-attention-deficit-hyperactivity-disorder-adhd-in-children-and-adolescents-pdf [Accessed 2Mar2015]
National Institute for Health and Care Excellence. 2008 (Modified 2013) Clinical Guidance 72- Attention deficit hyperactivity disorder. Diagnosis and management of ADHD in children, young people and adults. Availabe from: http://www.nice.org.uk/guidance/cg72/resources/guidance-attention-deficit-hyperactivity-disorder-pdf [Accessed 2Mar2015]
Bolea-Alamanac B, Nutt D, Fone K, et al (2014) Evidence-based guidelines for management of attention-deficit hyperactivity disorder: Update on recommendations from the British Association for Psychopharmacology. Available from: http://www.bap.org.uk/pdfs/ADHD_Guidelines.pdf [Accessed 26 Mar 2014]
British National Formulary for Children (2014-2015) British Medical Association/ Royal Pharmaceutical Society/ Royal College of Paediatrics and Child Health/ Neonatal and Paediatric Pharmacists Group

Indications for this guideline

Rheumatology: Rheumatoid arthritis

Dosage

- **Starting dose**: 125mg OD
- **Target dose range**: 500mg to 750mg OD
- **Dosage increments**: Increase by 125mg every 4 weeks to 500mg. If no response after 3 months, increase to 750mg per day. If no response after 3 months on maximum tolerated dose, stop treatment.
- Available as 125mg and 250mg tablets.

Take as a single daily dose on an empty stomach with a glass of water. Usually taken on waking.
Wait at least half an hour before having a cup of tea and 1 hour before having breakfast.

GP Monitoring

Infection (e.g. persistent sore throat, fever) or easy bruising should be reported to specialist team.

- Please copy all results to secondary care team.
- FBC & urinalysis for protein every 2 weeks until on a stable dose and then monthly.
  Seek advice from specialist team and consider stopping penicillamine if any of the following occur:
  - WCC or platelet count falls on 3 successive occasions.
  - Total WCC < 4.0 or Neuts. < 1.8
  - Platelet count < 150

If 2+ proteinuria on 2 or more occasions then arrange 24 hour protein estimate and discuss with Rheumatology team.

Microscopic haematuria is rarely due to penicillamine and patients with haematuria should be investigated in accordance with normal practice.

Side effects (not covered by specific monitoring requirements)

Very common / common:

- Rash in up to 35% of patients
- Taste loss or metallic taste; may be transient for a few weeks

Uncommon: Myositis, myasthenic syndrome, drug induced SLE
Dyspepsia is most likely to be secondary to NSAID, but reduce dose if severe.
Drug interactions: (refer to BNF, Appendix 1 for full list of interactions)
Digoxin: Plasma concentration of digoxin possibly reduced.
Clozapine: Avoid combination.
Vaccinations and infectious illness

- Vaccinate against influenza annually.
- No additional specific precautions required.

Pregnancy and breastfeeding

Pregnancy and breastfeeding are contraindications.

Initiating therapy

Having assessed the patient and discussed with them the benefits, side effects, frequency of dosing and monitoring requirements of penicillamine treatment the specialist team will:-

- **Communicate with the patient's GP, in writing, and confirm that the GP agrees to share care, as described in the Introduction to Shared Care Guidelines.**
- Record the patient's confirmation of understanding of the risks, benefits and consent.
- Undertake baseline investigations and initiate therapy.
- Specify target doses, monitoring and review dates at clinically relevant time intervals for both the GP and specialist team and any other patient specific information.
- Ensure that full information is sent to the GP without undue delay and recommend that the GP continues treatment in accordance with this shared care guideline.

Baseline investigations

FBC, U&E and serum creatinine prior to treatment, then as for GP Monitoring.

Information given to patient

- Patient information leaflet from specialist team

GP Responsibilities

The GP will notify the specialist, in writing, whether or not he/she agrees to share care and prescribe for the patient, according to this guideline.

- Monitor for adverse effects and drug interactions and report adverse events to the CSM and specialist team.
- Conduct blood tests, review results and undertake any necessary action as specified in GP Monitoring section above.
- Report to and seek advice from the specialist team on any aspect of patient care which is of concern to the GP and may affect treatment.
- Prescribe further supplies of penicillamine according to the recommendations specified in this guideline.
- Inform specialist team if treatment is stopped for any reason.

Ongoing Specialist Team Responsibilities

- Review the patient at agreed intervals.
- Provide advice as requested by the GP.
- Assess patients referred back by GPs as soon as is practical.

Patient's Responsibilities

- Report any adverse effects to their GP and / or specialist team.
- Ensure that they have a clear understanding of their treatment.
- Ensure they attend for monitoring requirements as specified in this shared care guideline.
- Be aware that treatment will be stopped it they do not attend for monitoring.

Contact details for the Specialist Teams

Rheumatology

Rheumatology Nurse Specialist: 01803 654 939
Rheumatology secretary: 01803 654 832
e-mail: rheumatology.sdhct@nhs.net

Out of Hours:

Medical SHO on-call via SDHCT switchboard 01803 614 567

Full Prescribing Information

For full prescribing information please consult summaries of product characteristics and the current BNF.

References

- eSPC for Distamine®, October 2005,
- BNF 50, September 2005
- British Society for Rheumatology. National Guidelines for the Monitoring of Second Line Drugs, July 2000

The information contained in these shared care guidelines is issued on the understanding that it is the best available from the resources at our disposal at the time of issue. Please see Chapter 20 – Introduction to Shared Care Guidelines for more information.

Indications for this guideline

To extend life or the time to mechanical ventilation for patients with amyotrophic lateral sclerosis (ALS), initiated by specialists in the management of motor neurone diseases.
Safety and efficacy of riluzole has only been studied in ALS. Therefore, riluzole should not be used in patients with any other form of motor neurone disease. The current licensed indications limit its use to ALS alone.

Pharmacology

Riluzole is proposed to act by inhibiting glutamate processes. The mode of action is unclear.
Although the pathogenesis of ALS is not completely elucidated, it is suggested that glutamate (the primary excitatory neurotransmitter in the central nervous system) plays a role for cell death in the disease.

Dosage

50mg BD. No significant increased benefit can be experienced from higher daily doses.
The consultant neurologist will be responsible for prescribing and monitoring for the initial three months of treatment. Although requests for blood samples are made by the specialist team in this period, patients may have samples taken in community or hospital.
Available as white, capsule shaped 50mg tablets (film coated).

Patients with swallowing difficulties or who are tube fed
Crush tablets and mix with water, sugar or soft food e.g. puree or yoghurt4,5. NB Unlicensed procedure. The manufacturer advises that riluzole has a local anaesthetic effect, hence the film coating on the tablet.

GP Monitoring

Any febrile illness should be reported to the specialist team and the white blood cell count checked. Riluzole should be discontinued in the case of neutropenia.

Please copy all results to secondary care team.
LFTs and FBC every three months for the first nine months (not including the initial three months monitored by the specialist team). LFTs should be monitored periodically thereafter.
Discontinue riluzole and seek advice if:
- ALT increases to 5 times the upper limit of normal.
- There is evidence of neutropenia.

Side effects (not covered by specific monitoring requirements)

- Patients and their carers should be told how to recognise signs of neutropenia and advised to seek immediate medical attention if symptoms such as fever occur.
- Dizziness or vertigo may affect performance of skilled tasks, e.g. driving.

Very common: Asthenia, nausea, transient elevations in ALT (see below).
Common: Headache, abdominal pain, pain, vomiting, dizziness, tachycardia, somnolence, circumoral paresthesia.
Uncommon/rare: Anaphylactoid reaction, angiodema, pancreatitis and neutropenia.

Elevations of ALT levels to more than 3 times the upper limits of normal (ULN) were observed in about 11% of the patients treated with riluzole compared to 4.2% in the placebo group; levels increased to more than 5 times the ULN in 3.8% of the patients treated with riluzole compared to 1.7% of the placebo treated patients. The increases in ALT usually appeared within 3 months after the start of therapy with riluzole were usually transient and levels returned to below twice the ULN after 2 to 6 months while treatment was continued. These increases were rarely associated with jaundice. In patients with increases in ALT to more than 5 times the ULN, treatment was discontinued and the levels returned to less than 2 times the ULN within 2 to 4 months.

Drug interactions: (refer to the SPC for full list of interactions)

There have been no clinical studies to evaluate the interactions of riluzole with other medicinal products.

In vitro studies using human liver microsomal preparations suggest that CYP 1A2 is the principal isozyme involved in the initial oxidative metabolism of riluzole.
- Inhibitors of the enzyme could potentially decrease the rate of riluzole elimination e.g. caffeine, diclofenac, diazepam, nicergoline, clomipramine, imipramine, fluvoxamine, phenacetin, theophylline, amitriptyline and quinolones
- Inducers could increase the rate of riluzole elimination e.g. cigarette smoke, charcoal-broiled food, rifampicin and omeprazole.

Precautions and contraindications

Riluzole should be prescribed with care in patients with a history of abnormal liver function, or in patients with slightly elevated serum transaminases (ALT, AST) up to 3 times the upper limit of the normal range, bilirubin and/or GGT levels. Baseline elevations of several liver function tests (especially elevated bilirubin) should preclude the use of riluzole.

Pregnancy and breastfeeding are contraindicated in patients taking riluzole.

Initiating therapy

Having assessed the patient and discussed with them the benefits, side effects, frequency of dosing and monitoring requirements of riluzole treatment the specialist team will:-

- **Communicate with the patient's GP, in writing, and confirm that the GP agrees to share care, as described in the Introduction to Shared Care Guidelines.**
- Record the patient's confirmation of understanding of the risks, benefits and consent.
- Undertake baseline investigations and initiate therapy.
- Prescribe riluzole and monitor the patient for at least the first three months of therapy.
- Specify dose, monitoring and review dates at clinically relevant time intervals for both the GP and specialist team and any other patient specific information.
- Ensure that full information is sent to the GP without undue delay and recommend that the GP continues treatment in accordance with this shared care guideline.
- Inform the GP of any potential drug interactions relevant to the patient.

Baseline investigations

LFT and WBC:
Before therapy and monthly during the first three months of treatment.

GP Responsibilities

The GP will notify the specialist, in writing, whether or not he/she agrees to share care and prescribe for the patient, according to this guideline.

- Monitor for adverse effects and drug interactions and report adverse events to the CSM and specialist team.
- Conduct blood tests, review results and any necessary action is undertaken as specified in GP Monitoring section above.
- Report to and seek advice from the specialist team on any aspect of patient care which is of concern to the GP and may affect treatment.
- Prescribe further supplies of riluzole according to the regimes specified in this guideline.

Ongoing Specialist Team Responsibilities

- Review the patient at agreed intervals.
- Provide advice as requested by the GP.
- Assess patients referred back by GPs as soon as is practical.

Patient's Responsibilities

- Report any adverse effects to their GP and / or specialist team.
- Ensure that they have a clear understanding of their treatment.
- Ensure they attend for monitoring requirements as specified in this shared care guideline.
- Be aware that treatment will be stopped it they do not cooperate with monitoring.

Contact details for the Specialist Teams

Dr JD Gibson: secretary 01752 792618
Dr Simon Edwards: secretary 01752 517638
Dr Jeremy Hobart: secretary 01752 517642
Dr Martin J Sadler: secretary 01752 792620

Out of Hours:
Medical SHO on-call via SDHCT switchboard (01803 614 567).

Full Prescribing Information
For full prescribing information please consult summaries of product characteristics and the current BNF.

References

6. eSPC for Rilutek® (Sanofi Aventis), January 2003
7. BNF 49, March 2005
8. NICE TAG20; Guidance on the use of riluzole (Rilutek) for the treatment of motor neurone disease, January 2001
9. Administering medicines through enteral feeding tubes. 2nd Ed. The Royal Hospitals, 2004.
10. Personal communication from Sanofi Aventis, July 2005

The information contained in these shared care guidelines is issued on the understanding that it is the best available from the resources at our disposal at the time of issue. Please see Chapter 20 – Introduction to Shared Care Guidelines for more information.

Indications for this guideline
- Rheumatoid arthritis and other inflammatory arthritis.

Dosage
- Given by deep IM injection.
- Test dose: 10mg given by specialist team.
- Maintenance dose: 50mg weekly for a total of 20 injections.

Patients should be observed for 30 minutes after each injection due to risk of anaphylactoid reaction.
Available as 0.5ml ampoules containing 10mg, 20mg and 50mg.

GP Monitoring
Infection (e.g. persistent sore throat, fever), easy bruising, breathlessness, cough or rash should be reported to specialist team.

- Please copy all results to secondary care team.
- FBC & urinalysis for protein, each time the injection is given. It is permissible to work one set of results in arrears.

Seek advice from specialist team and consider stopping sodium aurothiomalate if any of the following occur:
- WCC or platelet count falls on 3 successive occasions.
- Total WCC < 4.0 or Neuts. < 1.8
- Platelet count < 150

If 2+ proteinuria on 2 or more occasions then arrange 24 hour protein estimate and discuss with Rheumatology team.

Microscopic haematuria is rarely due to gold therapy and patients with haematuria should be investigated in accordance with normal practice.

Side effects (not covered by specific monitoring requirements)
Common: Mouth ulcers, rash – mild scaly rash to severe dermatitis (may not necessitate withdrawal of drug. Significant skin complications are almost always prutitic).
Uncommon: Metallic taste, hypersensitivity reactions
Rare: Hepatotoxity with cholestatic jaundice, severe enterocolitis, pulmonary fibrosis / pneumonitis, alopecia.

Drug interactions (refer to SPC for full list of interactions)
ACE inhibitors: increased risk of anaphylactoid reaction

Vaccinations and infectious illness
- Vaccinate against influenza annually.
- No additional specific precautions required.

Pregnancy and breastfeeding
May sometimes be used in pregnancy. Discuss with specialist team.
Breastfeeding is a contraindication.

Initiating therapy
Having assessed the patient and discussed with them the benefits, side effects, frequency of dosing and monitoring requirements of sodium aurothiomalate treatment the specialist team will:-
- **Communicate with the patient's GP, in writing, and confirm that the GP agrees to share care, as described in the Introduction to Shared Care Guidelines.**
- Record the patient's confirmation of understanding of the risks, benefits and consent.
- Undertake baseline investigations and initiate therapy.
- Specify target doses, monitoring and review dates at clinically relevant time intervals for both the GP and specialist team and any other patient specific information.
- Ensure that full information is sent to the GP without undue delay and recommend that the GP continues treatment in accordance with this shared care guideline.

Baseline investigations
FBC & urinalysis for protein, then as for GP Monitoring.

Information given to patient
Patient information leaflet from the specialist team

GP Responsibilities
The GP will notify the specialist, in writing, whether or not he/she agrees to share care and prescribe for the patient, according to this guideline.

- Monitor for adverse effects and drug interactions and report adverse events to the CSM and specialist team.
- Conduct blood tests, review results and undertake any necessary action as specified in GP Monitoring section above.
- Report to and seek advice from the specialist team on any aspect of patient care which is of concern to the GP and may affect treatment.
- Prescribe further supplies of sodium aurothiomalate according to the recommendations specified in this guideline.
- Inform the specialist team if treatment is stopped for any reason.

Ongoing Specialist Team Responsibilities

- Review the patient at agreed intervals.
- Provide advice as requested by the GP.
- Assess patients referred back by GPs as soon as is practical.

Patient's Responsibilities

- Report any adverse effects to their GP and / or specialist team.
- Ensure that they have a clear understanding of their treatment.
- Ensure they attend for monitoring requirements as specified in this shared care guideline.
- Be aware that treatment will be stopped it they do not attend for monitoring.

Contact details for the Specialist Teams

Rheumatology
Rheumatology Nurse Specialist: 01803 654 939
Rheumatology secretary: 01803 654 832
e-mail: rheumatology.sdhct@nhs.net

Out of Hours:
Medical SHO on-call via SDHCT switchboard 01803 614 567.

Full Prescribing Information
For full prescribing information please consult summaries of product characteristics and the current BNF.

References

- eSPC for Myocrisin®, September 2002
- BNF 50, September 2005
- British Society for Rheumatology. National Guidelines for the Monitoring of Second Line Drugs, July 2000

The information contained in these shared care guidelines is issued on the understanding that it is the best available from the resources at our disposal at the time of issue. Please see Chapter 20 – Introduction to Shared Care Guidelines for more information.

Indications for this guideline

- **Gastroenterology:** Ulcerative colitis and Crohn's disease
- **Rheumatology**: Rheumatoid arthritis and other inflammatory arthritis.

Dosage Take with or after meals.

Gastroenterology

Maintenance therapy: With induction of remission reduce the dose gradually to 500mg QDS.
Preparations: 500mg tablets (uncoated), EC tablets 500mg (Salazopyrin EN®) and suspension 250mg in 5ml.

Rheumatology

Dose: 500mg per day increasing by 500mg every week to a target dose of 1g BD. In some cases up to 1.5g BD may be necessary. May take 6 – 12 weeks before it becomes effective.
Preparation: EC tablets 500mg (Salazopyrin EN®)

GP Monitoring

Infection (e.g. persistent sore throat, fever) or easy bruising should be reported to specialist team.

Nausea, dizziness, headache or malaise may resolve if dose reduced. Consider stopping sulfasalazine if symptoms are severe.

- Please copy all results to secondary care team.
- FBC & LFT every 2 weeks for 3 months and then every 3 months.

Please include CRP with LFT for Rheumatology.
Seek advice from specialist team and consider stopping sulfasalazine and if any of the following occur:

- WCC or platelet count falls on 3 successive occasions.
- Total WCC < 4.0 or Neuts. < 1.8.
- Platelet count < 150
- ALT or AST > 120
- Alk Phos > 300

MCV may rise. If > 110 consider checking B12 & folate if patient is anaemic. If continues to rise above 110, discuss with specialist team.

Side effects (not covered by specific monitoring requirements)

Sulfasalazine may colour urine orange and may stain soft contact lenses orange.

Common: Mild nausea or diarrhoea usually settles if treatment is continued, oligospermia (reversible).

Less common: Severe nausea, malaise, headaches. See advice in GP Monitoring.

Uncommon: Bone marrow suppression, haemolysis, LFT abnormalities, skin rash (may be severe - erythema multiforme), mouth ulceration, hypersensitivity reactions, peripheral neuropathy, crystalluria, haematuria, proteinuria, nephrotic syndrome, hepatitis and pancreatitis.

Drug interactions: (refer to BNF, Appendix 1 for full list of interactions)

- Absorption of digoxin and folic acid may be reduced.

Sulfasalazine is contraindicated in patients hypersensitive to sulfasalazine, sufonamides or salicylates (e.g. aspirin).

Vaccinations and infectious illness

- Vaccinate against influenza annually.
- No additional specific precautions required.

Pregnancy and breastfeeding

Long-term clinical usage and experimental studies have failed to reveal any teratogenic or icteric hazards. Adequate folate supplements should be given to the mother to reduce the theoretical risk of neonatal haemolysis.
Oligospermia, is reversible on discontinuance of drug.
The amounts of drug present in breast milk should not present a risk to a healthy infant.

Initiating therapy

Having assessed the patient and discussed with them the benefits, side effects, frequency of dosing and monitoring requirements of sulfasalazine treatment the specialist team will:-

- **Communicate with the patient's GP, in writing, and confirm that the GP agrees to share care, as described in the Introduction to Shared Care Guidelines.**
- Record the patient's confirmation of understanding of the risks, benefits and consent.
- Undertake baseline investigations and initiate therapy.

- Specify target doses, monitoring and review dates at clinically relevant time intervals for both the GP and specialist team and any other patient specific information.
- Ensure that full information is sent to the GP without undue delay and recommend that the GP continues treatment in accordance with this shared care guideline.

Baseline investigations
FBC, LFT, U&Es and serum creatinine prior to therapy, then as in GP Monitoring.

Information given to patient
The specialist team will supply a patient information leaflet.

GP Responsibilities

The GP will notify the specialist, in writing, whether or not he/she agrees to share care and prescribe for the patient, according to this guideline.

- Monitor for adverse effects and drug interactions and report adverse events to the CSM and specialist team.
- Conduct blood tests, review results and undertake any necessary action as specified in GP Monitoring section above.
- Report to and seek advice from the specialist team on any aspect of patient care which is of concern to the GP and may affect treatment.
- Prescribe further supplies of sulfasalazine according to the recommendations specified in this guideline.
- Inform the specialist team if treatment is stopped for any reason.

Ongoing Specialist Team Responsibilities

- Review the patient at agreed intervals.
- Provide advice as requested by the GP.
- Assess patients referred back by GPs as soon as is practical.

Patient's Responsibilities

- Report any adverse effects to their GP and / or specialist team.
- Ensure that they have a clear understanding of their treatment.
- Ensure they attend for monitoring requirements as specified in this shared care guideline.
- Be aware that treatment will be stopped it they do not attend for monitoring.

Contact details for the Specialist Teams

Gastroenterology
IBD Nurse Specialist: 01803 654 951, Bleep: 07666 548 580

Rheumatology
Rheumatology Nurse Specialist: 01803 654 939
Rheumatology secretary: 01803 654 832
e-mail: rheumatology.sdhct@nhs.net

Out of Hours:
Medical SHO on-call via SDHCT switchboard 01803 614 567 for all indications except Ophthalmology when the Ophthalmic SHO on-call should be contacted.

Full Prescribing Information
For full prescribing information please consult summaries of product characteristics and the current BNF.

References

- eSPCs for Salazopyrin® tablets (April 2002), suspension (July 2001) and EN-tabs® (April 2004).
- BNF 50, September 2005
- British Society for Rheumatology. National Guidelines for the Monitoring of Second Line Drugs, July 2000

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Introduction

Nebulised Tobramycin forms only part of the treatment for cystic fibrosis (CF) patients. Details on the treatment of CF can be found in the two Cystic Fibrosis Trust documents:

- Standards of care of children and adults with cystic fibrosis in the UK, 2001 and
- Antibiotic treatment for Cystic Fibrosis, 2002.

Details of the current prescribing practice relating to the use of nebulised antibiotics for infection with Pseudomonas aeruginosa within South Devon can be seen in the treatment pathway in Appendix 1.

In the absence of appropriate antibiotic treatment, the abnormal respiratory secretions of the infant with CF soon become sequentially infected with S. aureus, H. influenzae and Ps. aeruginosa leading ultimately to death from progressive respiratory failure.

During childhood and adolescence the majority of patients with CF will become first colonised, then chronically infected, with Ps. aeruginosa. Early eradication of Ps. aeruginosa is important because, once the infection is well established; it forms a mucoidal biofilm which is difficult to penetrate. Chronic infection with this organism is associated with deterioration in lung function and a higher mortality rate. Chronic infection is defined as the regular culture of Ps. aeruginosa from the sputum or respiratory secretions, on two or more occasions extending over 6 months or a shorter period if accompanied by a sustained rise in anti-pseudomonas antibodies.

Regular courses of intravenous antibiotics have improved survival by reducing sputum bacterial load and maintaining pulmonary function. However, the addition of nebulised antibiotics to existing treatment have been shown to reduce the rate of deterioration of respiratory function and the number of intravenous antibiotics needed to treat exacerbations. Nebulised anti-pseudamonal antibiotics commonly used include colistin, gentamicin and tobramycin. Introduction of nebulised colistin (combined with oral ciprofloxacin) or the aminoglycosides (gentamicin or tobramycin) at the time of initial colonisation with Ps. aeruginosa has been shown to eradicate Ps. aeruginosa in 80% of newly infected patients and delay chronic infection for 18 months. The decision on which drug to choose is based on evidence, cost, toxicity and current UK licensing of the product. Colistin is generally used 1st line because it has reliable activity against Ps. aeruginosa and the development of resistance is not common. Tobramycin is reserved for patients who are unable to tolerate colomycin or continue to decline despite its use. Gentamicin injection can also be nebulised although tobramycin has greater activity against Ps. aeruginosa. The treatment pathway seen in Appendix I show the current treatment options within South Devon.

Tobramycin is an aminoglycoside antibiotic active against Gram-negative organisms. Although both being one of the most commonly used antibiotics for nebulisation, the intravenous formulation is not licensed to be used by inhalation for treatment of CF patients. BRAMITOB® is a licensed preservative free formulation for nebulisation.
Tobramycin is more active against Ps. aeruginosa than gentamicin and resistance has been reported to be more common than with tobramycin and colistin.

Tobramycin nebuliser solution BRAMITOB® has been evaluated in two 24-week randomised controlled trials. Active treatment was associated with improvements in lung function as measured by FEV1 and reductions in hospitalisations and IV antibiotic use.

Nebulised antibiotics can also be used in patients with Bronchiectasis in the absence of CF. The scope of this guideline encompasses treatment for this patient group.

Indications for this guideline

Delay or prevention of chronic infection with Ps. aeruginosa where either:

- Initially where colistin or gentamicin has not produced a satisfactory result.
- cultures show resistance to colistin and/or gentamicin and sensitivity to tobramycin (may start pending culture results).
- For use of the BRAMITOB® formulation, the unlicensed use of solution for injection has not produced a satisfactory clinical result and/or not tolerated by the patient.

or

Prevention of clinical deterioration in patients chronically infected with Ps. aeruginosa where other nebulised antibiotics are unsuitable. Chronic infection is defined as the regular culture of Ps. aeruginosa from the sputum or respiratory secretions, on two or more occasions extending over 6 months or a shorter period if accompanied by a sustained rise in anti-pseudomonas antibodies.

Patient Criteria for use of intravenous formulation Tobramycin

1. Have one of the above indications.
2. Complying with standard treatment e.g. physiotherapy, pancreatic supplements etc.
3. Sputum cultures show susceptibility to tobramycin (may start treatment pending culture results).
4. Use nebuliser regularly as prescribed. Irregular use is a reason for stopping treatment.

Patient Criteria for use of BRAMITOB®

1. As above but with the added cautions:

2. Patients are > 6 yrs of age.
3. BRAMITOB® should not be used during pregnancy or lactation unless the benefits to the mother outweigh the risks to the foetus or baby.

Dosage

The dose and treatment plan for each patient will be decided by the specialist team and will be communicated in the clinical letter to the GP.

Tobramycin Intravenous formulation for nebulisation.	
Child < 5 years	nebulised 40mg twice a day
5-10 years	nebulised 80mg twice a day
>10 years & adult	nebulised 160mg twice a day

Preparations: Intravenous preparations to be used via the nebulised route (unlicensed).
40mg in 1ml and 80mg in 2ml vials. Use phenol-free formulations.

Administration:

Dilute the appropriate volume of the above solutions to 4ml with 0.9% sodium chloride.
The resultant solution is poured into the nebuliser.
The solution is for single use only and any remaining solution should be discarded.
Each patient should be given an initial hospital-supervised dose after chest physiotherapy.
Measure respiratory function before and after initial dosage.
Bronchodilators (usually beta2-agonists) should be given before the antibiotic.
A mouthpiece is preferable to a facemask to maximise pulmonary disposition. Small children below 3 years old will usually require a mask held firmly on the face.
Relaxed tidal volume breathing through the mouth and not the nose is ideal. A nose clip will increase the efficiency of delivery to the lungs in some patients but is not popular in practice and is not used by the majority.

BRAMITOB®

All patients > 6 yrs	300mg twice a day

After a 28 course of therapy, patients should discontinue nebulised tobtamycin therapy for the next 28 days. A cycle of 28 days active therapy and 28 days off treatment should be maintained for as long as clinical benefit is seen.

Preparations: 300mg/4ml nebuliser solution in 4ml ampoules.

Administration:
The contents of one ampoule should be emptied into the nebuliser and administered over approximately a 15-minute period.
Use a hand-held Pari LC Plus® reusable nebuliser with a suitable compressor.
The solution is for single use only and any remaining solution should be discarded.
Each patient should be given an initial hospital-supervised dose after chest physiotherapy.
Measure respiratory function before and after initial dosage.
Bronchodilators (usually beta2-agonists) should be given before the antibiotic.
A mouthpiece is preferable to a facemask to maximise pulmonary disposition. Relaxed tidal volume breathing through the mouth and not the nose is ideal. A nose clip will increase the efficiency of delivery to the lungs in some patients but is not popular in practice and is not used by the majority.

CF /Respiratory specialist nurses organise and monitor the following:

Nebuliser-compressor systems for BRAMITOB®:
Use a Pari LC Plus reusable nebuliser with a suitable compressor. Suitable compressors are those which, when attached to a Pari LC Plus nebuliser, deliver a flow rate of 4-6 L/min and/or a back pressure of 110-217kPa.
Nebuliser-compressor systems for Tobramycin Intravenous nebulised formulation.
Use an active venture nebuliser (breath-assisted) e.g. Pari LC Plus® or E Flow Rapid®, with a compressor producing a flow rate of 6 litres per minute. E Flow Rapid nebulisers are paid for by the patient but deliver a higher percentage of the dose.
If unacceptably long, the nebulisation time can be reduced for patients with low inspiratory flow.
A Ventistream® may also be used rarely.
All disposable plastics required for the nebuliser system will be provided through secondary care.
Environmental safety:
The output from the above nebulisers is automatically filtered. Output from nebulisers without inbuilt filters should be vented to the open air.
It is advisable for patients to receive nebulised antibiotics in a separate area from other patients. Hospital patients should be routinely placed in a side room.
Nebulisation should take place in a well ventilated room e.g. with a window open.

GP Monitoring

There are no specific GP monitoring requirements beyond normal clinical care.

Side effects (for a full list of systemic side effects, see the summary of product characteristics (SPC) for Tobramycin and BRAMITOB®).

Bronchospasm may occur on inhalation of antibiotics. This may be prevented by or treated with the appropriate use of beta2-agonists. If troublesome, treatment should be withdrawn.

Important

Nebulisation:

- Mainly local effects.
- Inhalation may induce coughing or bronchospasm, although less likely than with colistin.
- May induce further haemorrhage in patients with active, severe haemoptysis.

Systemic:

- Renal function changes have been associated with parenteral aminoglycoside therapy especially in patients with a history of renal impairment. These changes can occur in patients with initially normal renal function.
- There was no evidence of nephrotoxicity during clinical trials with BRAMITOB®. Renal function should be monitored before treatment and urea and creatinine should be reassessed after every 6 complete cycles.
- Ototoxicity: In patients with a predisposing risk due to previous prolonged systemic aminoglycoside therapy it may be necessary to consider audiological assessment before initiating BRAMITOB®. Tinitus is a sentinel symptom of ototoxicity.
- Neurotoxicity: Use BRAMITOB® with great caution in patients with neuromuscular disorders such as parkinsonian or other conditions characterised by myasthenia gravis.

Toxicity:

- **Nephrotoxicity and Audiotoxicity**: In people with CF repeated courses of high dose IV aminoglycosides have been associated with deafness and renal damage but these have not been reported with nebulised therapy.
- If there is evidence of nephrotoxicity, all tobramycin should be discontinued until trough serum concentrations fall below 2 micrograms/ml.

Drug interactions: refer to BNF, Appendix 1 and SPC for full list of interactions

Although rare, the possibility of systemic absorption, and hence the possibility of interactions should always be borne in mind when treating patients by inhalation.

Drugs commonly seen in primary care:

- Cephalosporins: Increased risk of nephrotoxicity.
- Amphotericin B: increased risk of nephrotoxicity.
- Furosemide, urea or mannitol: increased risk of toxicity; Loop diuretics increased risk of ototoxicity.
- Warfarin and phenindione: Anticoagulants enhanced

Drugs not commonly seen in primary care:

- Cholinergics: antagonism of effect of neostigmine and pyridostigmine.
- Ciclosporin: increased risk of nephrotoxicity.
- Platinum compounds: increased risk of nephrotoxicity and possible ototoxicity.
- Anticholinesterases, botulinum toxin: neuromuscular effects.
- Muscle relaxants:effect of non-depolarising muscle relaxants such as tubocurarine enchanced.
- Tacrolimus: increased risk of nephrotoxicity.
- Polymyxins: increased risk of nephrotoxicity.

Contra-indications

- Hypersensitivity to any aminoglycoside.
- Myesthenia gravis.

Initiating therapy

Having assessed the patient at a six or eight weekly review and suspecting or confirming infection with Ps. aeruginosa the ***specialist consultant*** will:

- Discuss with the patient and/or the parent(s)/carer(s), the benefits, side effects, frequency of dosing, the importance of compliance, monitoring requirements of nebulised tobramycin treatment and long term treatment options.
- Give the first dose in hospital after a physiotherapy session.
- Baseline monitoring including sputum/throat swabs, renal function, liver function, lung function, weight.
- Prescribe the first months therapy for the patient.
- **Communicate with the patient's GP, in writing, and confirm that the GP agrees to share care, as described in the Introduction to Shared Care Guidelines**.

- Record the patient's confirmation of understanding of the risks, benefits and consent.
- Ensure that full information, including dose and duration of therapy, is sent to the GP without undue delay and recommend that the GP continues treatment in accordance with this shared care guideline.
- Ensure that the patient/parent(s)/carer(s) are aware that they need to inform the community pharmacy to order tobramycin in advance of presenting a script from the GP.

Once the patient has been prescribed nebulised tobramycin, the CF specialist nurse will:
- Provide and train the patient/parent/carer in the use and administration of nebulised tobramycin.
- Remind the patient/parent(s)/carer(s) that they need to inform the community pharmacy to order tobramycin in advance of presenting a script from the GP.

GP Responsibilities

The GP will notify the specialist, in writing, whether or not he/she agrees to share care and prescribe for the patient, according to this guideline.

- Prescribe subsequent courses of nebulised tobramycin according to the treatment plan provided by the specialist.
- Communicate with the specialist consultant/nurse if the patient presents with any problems associated with the nebulised gentamicin/tobramycin or deterioration in CF related health.
- Be aware of the monitoring parameters for patients prescribed nebulised tobramycin (see appendix 2).
- Report to and seek advice from the specialist team on any aspect of patient care that is of concern to the GP and may affect treatment.
- Inform the specialist team if treatment is stopped for any reason.

Ongoing Specialist Team Responsibilities

- Review and monitor the patient at agreed intervals (see Appendices 1 and 2) and advise GP of any changes to the treatment plan.
- Provide advice as requested by the GP.
- Assess patients referred back by GPs as soon as is practical.

Patient's Responsibilities including parents and or carers

- Report any adverse effects to their GP and / or specialist team.
- Ensure that they have a clear understanding of their treatment.
- Ensure they attend for monitoring requirements as specified in this shared care guideline.
- Be aware that treatment will be stopped it they do not attend for monitoring.
- Correct storage and administration of the nebuliser solution.

Contact details for the Specialist Teams

Specialist CF nurse
Rachel Crimmins, Specialist CF nurse: 01803 655 586, e-mail: rachelcrimmins@nhs.net

Consultant Paediatrician
Dr C. Sainsbury, secretary: 01803 654 824, e-mail: clive.sainsbury@nhs.net

Respiratory Consultant
Dr L. Dobson, secretary: 01803 654 014, e-mail: lee.dobson@nhs.net

Microbiology Consultants:
Dr P. Turner, secretary: 01803 654 990, e-mail: paul.turner@nhs.net
Dr T. Maggs, secretary: 01803 654 990, e-mail: tony.maggs@nhs.net
Dr S. Hoque, secretary :01803 654 990, e-mail: selina.hoque@nhs.net

Out of Hours:
Paediatric or Respiratory SHO on-call via SDHCT switchboard (01803 614 567).

Full Prescribing Information

For full prescribing information please consult summaries of product characteristics (emc.medicines.org.uk) and the current BNF.

References

1. eSPC Bramitob® 300mg in 4ml nebuliser solution (Chiesi UK Ltd) Sept 2006

2. Standards of care of children and adults with cystic fibrosis in the UK. Cystic Fibrosis Trust, 2001
3. Antibiotic treatment for Cystic Fibrosis. Cystic Fibrosis Trust, 2002

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Appendix 1 Treatment pathway for CF patients with Ps. aeruginosa

	Routine Home visit	As required if patient unwell
MDT care input	Specialist CF nurse Paeds and adults at least every 3 months	• Phone CF nurse • Home visit by CF nurse • GP visit • Urgent paed. hospital appointment
Tests	• Tests conducted according to necessity. • GPs liase as necessary with specialist team	
Drug treatment	Continue thereafter according to patient response. Continuous nebulisers may be required. Nebulised gentamicin or tobramiycin may be substituted according to patient progress.	
Prescribing and supply		
Monitoring		

Notes:

1. All relevant findings and results will be communicated by specialist team to GP.
2. GP should communicate any relevant tests conducted to specialist team.

Appendix 2 Patient monitoring relating to Ps. aeruginosa infection

Adults and children are seen every:

- 6-8 weeks by the specialist CF nurse, usually in the form of a home visit
- three months by the local specialist consultant at Torbay Hospital
- year at the specialist CF centre in Exeter.

Infants are seen more frequently until thriving.

6-8 week CF specialist nurse visit and three monthly specialist consultant appointment the following will be monitored :

- Review of respiratory function including:
  - spirometery
  - oximetery
  - peak flow (FEV1)

  } every visit
- Sputum cultures and sensitivities or cough swabs, nasopharyngeal aspirates or deep throat swabs
- Chest X-ray: condition dependent/if significant fall in lung function
- Weight and height: three monthly unless antibiotics need dosing
- Physiotherapy review including nebuliser techniques: every clinic visit. At home only if concerns

Annual review at Specialist CF centre will monitor the following:

- Detailed assessment of progress, review of results and planning for future therapy. Copy sent to GP, and possibly patient
- Weight and height
- Sputum culture (summary of cultures and antibiotics used is produced by specialist nurse prior to visit)
- Oximetry
- Spirometry
- Chest X-ray
- Blood gas in adults if indicated (i.e. if very ill)
- Full blood count, urea and electrolytes, liver function tests including serum albumin, clotting studies, aspergillus species RAST, serum HbA1c, vitamin levels
- Pseudamonal antibody levels

Other monitoring that may be required between CF clinic visits:

- Colds and exacerbations of chest symptoms
- Pre and post antibiotic sputum cultures
- Patient tolerability of antibiotic therapy
- Compliance with antibiotic therapy
- Nebuliser technique
- Equipment safety and maintenance
- Renal function if on potentially nephrotoxic medication
- Sputum culture resistance to current antibiotic treatment

Response to therapy: The main parameters used to monitor response to nebulised drugs in CF are:

- Stability and/or lack of deterioration in spirometry, particularly
  - forced expiratory volume in one second (FEV1), as a percentage of that which is predicted and
  - forced vital capacity (FVC), as a percentage of that which is predicted.
- It is important to remember that 4-5 percent variability can exist in spirometric readings due to patient effort and also operator variability.
- In children, resolution of a wet cough is also indicative of treatment success.
- In adults, the cough may not dry up completely but changes in volume and appearance of sputum should be evident.