

DERBYSHIRE JOINT AREA PRESCRIBING COMMITTEE
SHARED CARE AGREEMENT

VIGABATRIN for children with epilepsy
(for University Hospitals of Derby and Burton NHS Foundation Trust only)

1. REFERRAL CRITERIA

- Shared Care is only appropriate if it provides the optimum solution for the patient
- Prescribing responsibility will only be transferred when it is agreed by the consultant and the patient's GP that the patient's condition is stable or predictable
- Patients will only be referred to the GP once the GP has agreed in each individual case
- The patient will be given a supply of vigabatrin sufficient for 4 weeks maintenance therapy

2. AREAS OF RESPONSIBILITY

GP RESPONSIBILITIES	CONSULTANT RESPONSIBILITIES
1) To agree to prescribe in line with the shared care agreement 2) Adjust the dosage of vigabatrin and if appropriate other therapy on the advice of the specialist. 3) Stop treatment on advice of, or in consultation with, a specialist - treatment should be withdrawn gradually. 4) Ensure that the patient has visual field checks undertaken (see appendix 1). 5) To seek advice from the specialist immediately if a visual field defect is suspected or detected. 6) To report to and seek advice from the specialist on any aspect of patient care which is of concern to the GP and may affect treatment. 7) Referral to a specialist in the event of unsatisfactory control of the patient's epilepsy. 8) To report any adverse effects to the referring specialist and the MHRA yellow card scheme.	1) Initiation and provision of treatment with vigabatrin until patient is stabilised on the optimal dose. 2) Discussion with the patient/carer regarding the benefits, side effects and risks of treatment including the need for regular visual field monitoring. 3) Paediatricians to make appropriate arrangements for visual field checks or where these are not practical, alternative arrangements for visual screening/monitoring. 4) Obtaining agreement of GP to participate in shared-care arrangement for vigabatrin therapy using the transfer letter in appendix 2. 5) Regular follow up of the patient and subsequent adjustment of anti-epileptic therapy, as appropriate. 6) Prompt communication with the GP regarding the patient's progress, any reassessment and changes in treatment. 7) Provide additional information and advice to the GP on actions he/she may need to take e.g. on dosage adjustment, other changes in therapy and management of adverse effects, as required. 8) Review undertaken by a paediatric neurologist and consultant paediatrician on average once every 1-2 years. 9) To report any adverse effects to the MHRA yellow card scheme and GP.
PATIENT RESPONSIBILITIES	
1) Report any adverse reactions (including any new visual symptoms) to the GP or specialist whilst receiving treatment with vigabatrin 2) Share any concerns in relation to treatment with vigabatrin 3) Report to the specialist or GP if they do not have a clear understanding of their treatment	

3. COMMUNICATION AND SUPPORT

i. Hospital contacts: <u>University Hospitals of Derby and Burton NHS Foundation Trust</u> <u>Paediatrics</u> Dr Sally Moss 01332 785103 <u>Ophthalmology</u> Mr Roger Holden – 01332 786886	ii. Out of hours contacts and procedures: Pharmacy, UHDB, ask for on-call pharmacist via switchboard – 01332 340131
iii. Specialist support/resources available to GP including patient information Summary of Product Characteristics (SPC) for vigabatrin: http://www.medicines.org.uk/emc/medicine/26956	

4. CLINICAL INFORMATION

<p>i. Prescribed indications</p>	<p>Treatment in combination with other anti-epileptic drugs for patients with resistant partial epilepsy with or without secondary generalisation; that is, where all other appropriate drug combinations have proved inadequate or have not been tolerated.</p> <p>Mono-therapy in the treatment of infantile/epileptic spasms (West syndrome with and without tuberous sclerosis).</p> <p>The use of vigabatrin has been considered by NICE and its guidance states that:</p> <ul style="list-style-type: none"> • The indications for vigabatrin are limited to adjunctive use only when all other appropriate antiepileptic drug combinations have proved ineffective or poorly tolerated. • Vigabatrin should not be initiated as mono-therapy except in West syndrome, where it remains as one of the first-line treatments. • Vigabatrin should be initiated by a specialist in epilepsy, a neurologist or a paediatric neurologist.
<p>ii. Therapeutic summary</p>	<p>Vigabatrin is an anticonvulsant that has been available in the UK since 1989. It is believed to act by increasing the levels of the inhibitory transmitter Gamma Amino Butyric Acid (GABA) in the central nervous system. It is very effective for partial onset seizures and infantile/epileptic spasms, but use is limited, as it is now known to be associated with irreversible constriction of the visual fields in up to 50% of patients. The visual field defect is usually asymptomatic in the early stages.</p> <p>Vigabatrin may still be used in patients whose epilepsy is refractory to other medication and in whom a risk / benefit assessment has been undertaken. It is now no longer routinely used in adults though it remains a treatment in infantile/epileptic spasms (West Syndrome). Treatment with vigabatrin should be initiated only by a physician or paediatrician with expertise in epilepsy</p>
<p>iii. Dose & Route of administration</p>	<p><u>Epilepsy</u> <u>With current antiepileptic therapy:</u> <u>CHILD:</u> With current anti-epileptic therapy <u>Neonate:</u> Initially 15–20 mg/kg twice daily, to be increased over 2–3 weeks to usual maintenance dose, usual maintenance 30–40 mg/kg twice daily (max. per dose 75 mg/kg). <u>Child 1-23 months</u> Initially 15-20mg/kg twice daily (max. per dose 250mg), to be increased over 2-3 weeks to usual maintenance dose, usual maintenance 30-40mg/kg twice daily (max dose 75mg/kg) <u>Child 2-11 years</u> Initially 15-20mg/kg twice daily (max. per dose 250mg), to be increased over 2-3 weeks usual maintenance dose, usual maintenance 30-40mg/kg twice daily (max. per dose 1.5g) <u>12-18 years</u> Initially 250mg twice daily increase over 2-3 weeks to usual maintenance dose 1-1.5g twice daily</p> <p><i>Infantile/epileptic spasms (West syndrome)</i> Neonate and child Initially 15-25mg/kg twice daily adjusted dose adjusted according to response over 7 days to usual maintenance dose 40-50mg/kg twice daily (max 75mg/kg twice daily as per specialist advice).</p>
<p>iv. Duration of treatment</p>	<p>Indefinite – as long as treatment is considered appropriate by specialist (epilepsy specialist, adult or paediatric neurologist)</p> <p>When used for treatment of Epileptic spasms (West Syndrome) there is a Trust approved guideline which follows regional (CEWT: Children’s Epilepsy Workflow in Trent) guidelines regarding length of treatment (see appendix 3)</p>
<p>v. Adverse effects</p>	<p>Visual field defects (see appendix 1)</p> <p>Drowsiness, fatigue, dizziness, nervousness, irritability, behavioural effects such as excitation and agitation especially in children; depression, abnormal thinking, headache, nystagmus, ataxia, tremor, paraesthesia, impaired concentration; less commonly confusion, aggression, psychosis, mania, memory disturbance, visual disturbance (e.g. diplopia); also weight gain, oedema, gastro-intestinal disturbances, alopecia, rash; less commonly, urticaria, occasional increase in seizure frequency (especially if myoclonic), decrease in liver enzymes, slight decrease in haemoglobin; photophobia and retinal disorders (e.g. peripheral retinal atrophy); optic neuritis, optic atrophy, hallucinations also reported.</p>

vi. Monitoring Requirements	Hospital Specialist Patients above the age of 12 should undergo, where appropriate, systematic screening examination when starting vigabatrin and at regular intervals for detection of visual field defects.	GP Ensure that the patient has visual field check undertaken. Any concerns should be reported to the specialist.
	Manufacturer advises that visual field testing and assessment of visual acuity should continue at 6 month intervals for the whole duration of treatment.	
vii. Action to be taken	Visual Field Defects Encephalopathic symptoms (rare) consisting of marked sedation, stupor, and confusion with non-specific slow wave EEG.	
	Withdrawing treatment Seek advice from specialist regarding reducing dose or withdrawing treatment.	
viii. Clinically relevant drug interactions	Anticonvulsant effect of vigabatrin may be reduced by antidepressants (tricyclics, SSRIs and MAOIs), anti-psychotics and antimalarials (chloroquine, hydroxychloroquine and mefloquine). Use of vigabatrin may gradually lower plasma levels of phenytoin (by 16-33%), but this is not normally clinically important.	
ix. Contra-indications	Renal impairment - Caution should be exercised when administering the vigabatrin to the elderly and more particularly in patients with creatinine clearance less than 60ml/min. Adjustment of dose or frequency of administration should be considered. Such patients may respond to a lower maintenance dose. Patients should be monitored for undesirable effects such as sedation or confusion.	
	Hypersensitivity to vigabatrin or to any excipient in the medicinal product.	
	Any pre-existing significant visual field defect.	
	Vigabatrin should not be used concomitantly with other retinotoxic drugs.	
x. Special precautions/warnings	Available data suggests that visual field defects are irreversible even after discontinuation of vigabatrin. Therefore, vigabatrin should only be used after a careful assessment of the balance of benefits and risk compared with alternatives. Renal impairment (eGFR < 60ml/min), elderly - closely for undesirable effects such as sedation and confusion. Avoid sudden withdrawal (taper off over 2–4 weeks); history of psychosis, depression or behavioural problems; pregnancy and breast-feeding; absence seizures (may be exacerbated).	
xi. Supply of ancillary equipment	Not applicable	
xii. Supply, storage and reconstitution instructions	Not applicable	
xiii. Prepared by	Dr Will Carroll, Consultant Paediatrician, University Hospitals of Derby and Burton NHS Foundation Trust	
Reviewed by	Dr H Faza (Feb 2019) Dr. S Moore (Jan 2021) Derbyshire Medicines Management Shared Care & Guideline Group	

This does not replace the SPC, which should be read in conjunction with this shared care guideline

Date Prepared: January 2017

Reviewed: January 2021

Review Date: December 2023

References

British National formulary for Children, accessed via www.medicinescomplete.com 1/3/2017
Epilepsies: Diagnosis and Management, NICE Clinical Guideline 137, Jan 2012
NICE Technology Appraisal No. 79 Newer drugs for epilepsy in children, April 2004
Sabril (Vigabatrin) Summary of Characteristics, Sanofi, accessed via www.medicinescomplete.com 1/3/2017, last updated on eMC 14/7/14
The Ocular Side-Effects Of Vigabatrin (Sabril) Information And Guidelines For Screening, The Royal College of Ophthalmologists, March 2008
CEWT Epileptic Spasms & West Syndrome Guideline
http://www.cewt.org.uk/CEWT/Epilepsy-to-go_files/CEWT%20ratified%20Epileptic%20Spasms%2012_17.pdf

Appendix 1 – Visual Field Defects and Tests

- Pooled data from prevalence surveys suggest that as many as 1/3 of patients receiving vigabatrin therapy have Visual Field Defects (VFDs). Males may be at greater risk than females
- Most patients with perimetry-confirmed defects have not previously spontaneously noticed any symptoms, even in cases where a severe defect was observed in perimetry
- Available evidence suggests that the VFDs are irreversible even after discontinuation of vigabatrin
- If a visual field constriction is observed during follow-up, consideration should be given to gradual discontinuation of vigabatrin. If the decision to continue treatment is made, consideration should be given to more frequent follow-up (perimetry) in order to detect progression or sight threatening defects
- Manufacturer advises that visual field testing and assessment of visual acuity should continue at 6 month intervals for the whole duration of treatment

Children

Screening for visual field deficits requires specialist input for children with a cognitive age of 9 years and above. Children with epilepsy should be under regular review by a paediatrician with expertise in epilepsy (see NICE guidelines) and where necessary a paediatric neurologist. Where required, the hospital team will seek ophthalmology assessment. These specialists should arrange visual screening for children (above the age of 12) taking vigabatrin at the appropriate time.

Appendix 2 – Sample transfer letter

{Insert Hospital Logo here}

Hospital No: «HOSPITAL_NUMBER»

NHS No: «NHS_NUMBER»

{Insert date}

PRIVATE & CONFIDENTIAL

«GP_TITLE» «GP_INITIALS» «GP_SURNAME»

«GP_ADDRESS_1»

«GP_ADDRESS_2»

«GP_ADDRESS_3»

«GP_ADDRESS_4»

«GP_POSTCODE»

DERBYSHIRE JAPC SHARED CARE AGREEMENT LETTER

Dear «GP_TITLE» «GP_SURNAME»

«FORENAME_1» «SURNAME» «DATE_OF_BIRTH»

«CURRENT_ADDRESS_1» «CURRENT_ADDRESS_2» «CURRENT_ADDRESS_3»

«CURRENT_ADDRESS_4» «CURRENT_POSTCODE»

Your patient was seen on *{Insert date}* with a diagnosis of *{Insert diagnosis}*. I have initiated the following medication *{Insert drug name}* and am writing to ask you to participate in the shared care for this patient.

This medication has been accepted as suitable for shared care by the Derbyshire Joint Area Prescribing Committee (JAPC). I agree to the secondary care responsibilities set out in the shared care agreement for this medication (available from www.derbyshiremedicinesmanagement.nhs.uk/clinical_guidelines/shared_care_guidelines). I am therefore requesting your agreement to share the care of this patient. Where preliminary tests are set out in the agreement I have carried these out and results are below.

Dose Regimen	Date <i>{Insert medicine name}</i> started	Date for GP to start prescribing <i>{Insert medicine name}</i> from
The baseline test results are (if applicable):		

I confirm I have explained to the patient: the risks and benefits of treatment, the baseline tests conducted the need for monitoring, how monitoring will be arranged, and the roles of the consultant / nurse specialist, GP and the patient in shared care. I confirm the patient has understood and is satisfied with this shared care arrangement at this time.

If you do **NOT** wish to participate in shared care for this patient, usually under clinical grounds, please complete the attached form.

Yours sincerely

{Consultant name}

GP RESPONSE TO SHARED CARE (only complete & send if **NOT** participating in shared care)

Shared care is produced by GPs and specialists knowledgeable in the field of that drug usage. The shared care has been approved by the JAPC. This allows a more convenient service to the patient and cost effective use of NHS resources.

Patient:	NHS No:
Consultant:	Medicine requested for shared care:

I will **NOT** be undertaking the GP responsibilities as described in the agreed shared care guideline.

My clinical reasons for declining shared care for this patient are listed in the box below:

Yours sincerely

{GP name}

{Surgery}

Please send a copy of this response to:

1. The specialist/consultant requesting shared care
2. **AN ANONYMISED COPY OF THIS FORM ONLY** to the Medicines Management and Clinical Policies and Decisions Team, 1st Floor East Point, Cardinal Square, 10 Nottingham Road, Derby, DE1 3QT or E-MAIL: ddccg.medicinesmanagement@nhs.net

(sending a copy of this form to the Medicines Management and Clinical Policies and Decisions Team will help to identify any inappropriate requests for shared care e.g. indication not covered, hospital monitoring requirements not fulfilled. It will also help to inform the CCG prescribing group of the reasons shared care is not being undertaken allowing for changes to be made in future updates to improve patient care)

Appendix 3 West Syndrome (Epileptic Spasms) management algorithm

CEWT Epileptic Spasms & West Syndrome Guideline

http://www.cewt.org.uk/CEWT/Epilepsy-to-go_files/CEWT%20ratified%20Epileptic%20Spasms%2012_17.pdf

Initial assessment & diagnosis

- History & examination (including OFC, Wood's (UV) light, BP, developmental status)
- Urgent EEG (within 3 days) capturing sleep and awake periods confirming 'hypsarrhythmia' or 'modified hypsarrhythmia'
- Discuss with paediatric neurology

First line treatment

- Treatment to be commenced as soon as possible after confirmatory EEG
- Discuss potential adverse reactions of treatment with family
- Take varicella serology pre-treatment
- Start combined treatment, if no known evidence of TSC, of:
 - Prednisolone 10 mg four times daily plus gastric protection
 - Vigabatrin 25 mg/kg twice daily and increasing to 50mg/kg twice daily on day 2(Refer to guideline for further information)
*if at any point a diagnosis of TSC is made it is recommended that discussions with the family about potentially using monotherapy treatment with vigabatrin should be made
- Start monotherapy, if known to have TSC, of:
 - Vigabatrin 25 mg/kg/twice daily and increasing to 50mg/kg twice daily on day 2
- Monitor BP, urine for glycosuria, U&E

Further investigations

- Repeat EEG at 2 weeks
- Diagnostic investigations if cause of ES unknown performed in the following order until cause identified:
 - MRI brain
 - CGH array, plasma lactate, plasma amino acids and urine organic acids
 - Consider testing for epilepsy gene panel in discussion with paediatric neurology
 - Ophthalmology assessment (may be helpful in identifying a diagnosis)
 - Discuss further investigations with paediatric neurology team