North of Tyne
Area Prescribing Committee

Shared Care Guidance

Vigabatrin

July 2014
(Review date July 2016)

This guidance has been prepared and approved for use in Newcastle, North Tyneside and Northumberland. It gives details of the responsibilities of GPs and specialist services in shared care arrangements and is intended to provide sufficient information to enable GPs to prescribe this treatment within the shared care arrangement.

Further copies and additional information are available from:

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Further copies of this document can also be viewed / downloaded from the North of Tyne Area Prescribing Committee Website: http://www.northoftyneapc.nhs.uk and the NECS Medicines Optimisation website medicines.necsu.nhs.uk (no www. needed in front of the address).

Approved on behalf of the	Name	Signature	Date
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Shared Care Guideline

Vigabatrin

Introduction / Background

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 GABA[1] in the central nervous system. It is very effective for partial onset seizures and infantile 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.

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 spasms (West's Syndrome). Treatment with vigabatrin should be initiated only by a physician with expertise in epilepsy, a neurologist or paediatric neurologist [NICE - 1,2].

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.

Adults

Patients should have their visual fields assessed prior to treatment with vigabatrin and every 6 months while taking vigabatrin (Royal College of Ophthalmologists – [3]). The ophthalmology department at the RVI provides a vigabatrin visual field service with automatic recall every 6 months. Checking attendance for visual field checks and enquiry about visual symptoms should be a part of the annual primary care review of all patients taking vigabatrin.

Patients with learning difficulties may be unable to cooperate with visual field tests. A risk / benefit assessment should be made for each individual.

Children

Screening for visual field deficits is not possible much below the cognitive age of 9 years. Children with epilepsy should be under regular review by a paediatrician with expertise in epilepsy (see NICE guidelines [2]) and where necessary a paediatric neurologist. These specialists should arrange visual screening for children taking vigabatrin at the appropriate time.

[1] GABA = Gamma Amino Butyric Acid

The use of vigabatrin has been considered by NICE and its guidance [1,2] states that:

- 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 monotherapy except in West's 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.

Referral criteria
Patient on maintenance therapy with vigabatrin for the treatment of epilepsy or infantile spasms (West's Syndrome) where therapy has been stabilised.

Responsibilities of Hospital Specialist Team

- Initiation and provision of treatment with vigabatrin until patient is stabilised on the optimal dose.
- Discussion with the patient/carer regarding the benefits, side effects and risks of treatment including the need for regular visual field monitoring.
- To make appropriate arrangements for 6 monthly visual field checks or where these are not practical, alternative arrangements for visual screening/ monitoring.
- Obtaining agreement of GP to participate in shared-care arrangement for vigabatrin therapy.
- Regular follow up of the patient and subsequent adjustment of anti-epileptic therapy, as appropriate - if the patient is seizure-free on vigabatrin and the GP has agreed to supervise regular visual field checks, the patient will not need to be seen regularly by the hospital specialist team.
- Prompt communication with the GP regarding the patient's progress, any reassessment and changes in treatment.
- 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.

Responsibilities of General Practitioner:

- Reply to request for shared care as soon as practical (within 28 days).
- Prescribe vigabatrin in accordance with the specialist's recommendations.
- Adjust the dosage of vigabatrin and if appropriate other therapy on the advice of the specialist.
- Stop treatment on advice of, or in consultation with, a specialist - treatment should be withdrawn gradually.
- As part of the annual primary care review of all patients with epilepsy: to enquire about visual symptoms and ensure that the patient has attended the hospital eye department for planned visual field checks.
- To seek advice from the specialist immediately if a visual field defect is detected.
- 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.
- Referral to a specialist in the event of unsatisfactory control of the patient's epilepsy.
- Report adverse events to specialist and CSM.

Prescribing Information Sheet

Vigabatrin (Sabril)

Shared Care Status: AMBER

Characteristic	Information / Comments
Indication(s)	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. Monotherapy in the treatment of infantile spasms (West's syndrome).
Usual Initiation and Maintenance Dose	***Epilepsy*** With current antiepileptic therapy: ADULT initially 1g daily in single or 2 divided doses then increased according to response in steps of 500 mg at weekly intervals; usual range 2–3g daily (max. 3g daily); CHILD initially 40 mg/kg daily in single or 2 divided doses then adjusted according to body-weight 10–15kg, 0.5–1g daily; body-weight 15–30kg, 1–1.5g daily; body-weight 30–50kg, 1.5–3g daily; body-weight over 50kg, 2–3g daily. ***Infantile spasms (West's syndrome)***, *monotherapy*, 50 mg/kg daily, adjusted according to response over 7 days; up to 150mg/kg daily used with good tolerability.
Likely duration of treatment	Indefinite, as long as treatment is considered appropriate by specialist (epilepsy specialist, adult or paediatric neurologist).
Formulations and Strengths available	500mg scored film-coated tablets. Powder (sugar-free) in 500mg sachets, for dissolving in water or soft drink immediately before administration.
NHS Cost (for 28 days treatment) March 2011	Tablets – 2g / day £34.54 - 3g / day £51.81 Sachets – 2g / day £38.26 - 3g / day £57.39
Potential Problems and Their Management	Visual Field Defects Encephalopathic symptoms (rare) consisting of marked sedation, stupor, and confusion with non-specific slow wave EEG. — Seek advice from specialist regarding reducing dose or withdrawing treatment.
Adverse Effects	Drowsiness, fatigue, visual field defects (see also under Cautions), 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.

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Contraindications	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.
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).
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.
Monitoring By GP By Hospital specialist	Annual primary care review should include enquiry about visual symptoms. Any concerns should be reported to the specialist. Patients should undergo systematic screening examination when starting vigabatrin and at regular intervals for detection of visual field defects. Visual field testing should continue at 6-month intervals for the whole duration of treatment.
Drug Interactions	Anticonvulsant effect of vigabatrin may be reduced by antidepressants (tricyclics, SSRIs and MAOIs) 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.

References

1. NICE Technology Appraisal No. 76 Newer drugs for epilepsy in adults, March 2004
2. NICE Technology Appraisal No. 79 Newer drugs for epilepsy in children, April 2004
3. The Ocular Side-Effects Of Vigabatrin (Sabril) Information And Guidelines For Screening, The Royal College of Ophthalmologists, April 2000