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Coventry & Warwickshire Area Prescribing Committee

Shared Care Agreement

Retigabine (Trobalt®▼)

SCA: For the adjunctive treatment adjunctive treatment of partial onset seizures with or without secondary generalisation in adults aged 18 years and above with epilepsy

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of retigabine for epileptic seizures can be shared between the specialist and general practitioner (GP).* GPs are **invited** to participate. If the GP is not confident to undertake these roles, then he or she is 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 practicable.**

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care is usually explained to the patient by the doctor initiating treatment. It is important that patients are consulted about treatment and are in agreement with it. Patients with epilepsy are under regular follow-up. This provides an opportunity to discuss drug therapy.

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

Specialist responsibilities
1. Initiate Retigabine and stabilise patient on initial target dose.
2. Perform baseline assessment and periodic review of renal and hepatic function (as indicated for each patient)
3. Record ECG in patients taking medication that prolongs QT interval or have conditions as defined under monitoring,
4. Discuss the benefits and side effects of treatment with the patient.
5. Ask the GP if he or she is willing to participate in shared care, and agree with the GP as to who will discuss the shared care agreement with the patient.
6. Regular follow-up of patient (suggest at least annually). If the patient becomes seizure free then providing there is a channel of communication between the specialist and GP, the specialist does not need to see the patient again.
7. Communicate promptly with the GP when the treatment is changed.
8. Have a mechanism in place to receive rapid referral of a patient from the GP in the event of deteriorating clinical condition.
9. Advise GP on dosage adjustment and when and how to stop treatment.
10. Report adverse events to CSM.
11. Ensure that clear backup arrangements exist for GPs to obtain advice and support.

General Practitioner responsibilities
1. Reply to the request for shared care as soon as practicable.
2. Prescribe retigabine at the dose recommended.
3. Adjust the dose as advised by the specialist and review any further monitoring needs (see monitoring).
4. Report to and seek advice from the specialist on any aspect of patient care that is of concern and may affect treatment.
5. Refer patient to the specialist if his or her condition deteriorates.
6. Stop treatment on the advice of the specialist or initiate tapered withdrawal if advised to do so.
7. Monitoring of seizure control and referral to a specialist in the event of unsatisfactory control.
8. Refer adverse events to the specialist and MHRA.

Patient/carer's role
1. Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
2. Share any concerns in relation to treatment with retigabine.
3. Report any adverse events e.g. mood swings to the specialist or GP whilst taking retigabine.

BACK-UP ADVICE AND SUPPORT:

See patient letter and/or other supporting information for contact details of clinician(s) initiating and stabilising patient prior to request for shared care

SUPPORTING INFORMATION:

Licensed indications: Retigabine is indicated as adjunctive treatment of partial onset seizures with or without secondary generalisation in adults aged 18 years and above with epilepsy.
NICE TA 232 states that Retigabine is recommended as an option for the adjunctive treatment of partial onset seizures with or without secondary generalisation in adults aged 18 years and older with epilepsy, only when previous treatment with carbamazepine, clobazam, gabapentin, lamotrigine, levetiracetam, oxcarbazepine, sodium valproate and topiramate has not provided an adequate response, or has not been tolerated.

Dosage and administration: Retigabine must be titrated, according to individual patient response, in order to optimise the balance between efficacy and tolerability.

The maximum total daily starting dose is 300 mg (100 mg three times daily). Thereafter, the total daily dose is increased by a maximum of 150 mg every week, according to the individual patient response and tolerability. An effective maintenance dose is expected to be between 600 mg/day and 1,200 mg/day. The maximum total maintenance dose is 1,200 mg/day.

If patients miss one dose or more, it is recommended that they take a single dose as soon as they remember.

After taking a missed dose, at least 3 hours should be allowed before the next dose and then the normal dosing schedule should be resumed.

When withdrawing Retigabine, the dose must be gradually reduced

Renal impairment: A 50% reduction in the initial and maintenance dose of retigabine is recommended in patients with moderate or severe renal impairment (creatinine clearance <50 ml/min). The total daily starting dose is 150 mg, and it is recommended that during the titration period, the total daily dose is increased by 50 mg every week, to a maximum total dose of 600 mg/day

Hepatic impairment: A 50% reduction in the initial and maintenance dose of retigabine is recommended in patients with moderate or severe hepatic impairment (Child-Pugh score $\geq$7; see section 5.2). The total daily starting dose is 150 mg, and it is recommended that during the titration period, the total daily dose is increased by 50 mg every week, to a maximum total dose of 600 mg/day.

Elderly (65 years of age and above): There are only limited data on the safety and efficacy of retigabine in patients aged 65 years and above. A reduction in the initial and maintenance dose of retigabine is recommended in elderly patients. The total daily starting dose is 150 mg/day and during the titration period the total daily dose should be increased by a maximum of 150 mg every week, according to the individual patient response and tolerability. Doses greater than 900 mg/day are not recommended.

Monitoring:
Baseline measurement of urea, electrolytes, and liver function is recommended because a slower dose titration may be necessary if renal or hepatic function is impaired. Renal and liver function should then be assessed subsequently by the GP if there are factors or conditions that suggest deterioration.

ECG to be recorded when retigabine is prescribed with medicinal products known to increase QT interval and in patients with known prolonged QT interval, congestive cardiac failure, ventricular hypertrophy, hypokalaemia or hypomagnesaemia and in patients initiating treatment who are 65 years of age and above. Iin those with a corrected QT interval>440ms at baseline, an ECG should be recorded on reaching the maintenance dose.

Contra-indications/Cautions: Retigabine must be used with caution in patients at risk of urinary retention, and it is recommended that patients are advised about the risk of these possible effects.

Caution should be taken when retigabine is prescribed **with medicinal products known to increase QT interval and in patients with known prolonged QT interval, congestive cardiac failure, ventricular hypertrophy, hypokalaemia or hypomagnesaemia and in patients initiating treatment who are 65 years of age and above**.

Confusional state, psychotic disorders and hallucinations were reported in controlled clinical studies with retigabine. These effects generally occurred within the first 8 weeks of treatment, and frequently led to treatment withdrawal in affected patients. It is recommended that patients are advised about the risk of these possible effects.

Suicide risk: **Suicidal ideation and behaviour** have been reported in patients treated with antiepileptic agents in several indications. A meta-analysis of randomised placebo-controlled trials of antiepileptic drugs has also shown a small increased risk of suicidal ideation and behaviour. The mechanism of this risk is not known and the available data do not exclude the possibility of an increased risk for retigabine. Therefore patients should be monitored for signs of suicidal ideation and behaviours and appropriate treatment should be considered. Patients (and caregivers of patients) should be advised to seek medical advice if signs of suicidal ideation or behaviour emerge.

Elderly patients may be at increased risk of central nervous system events, urinary retention and atrial fibrillation. Retigabine must be used with caution in this population and a reduced initial and maintenance dose is recommended. As with other antiepileptic drugs, retigabine must be **withdrawn gradually** to minimise the potential for rebound seizures. It is recommended that the retigabine dose is reduced over a period of at least 3 weeks, unless safety concerns require an abrupt withdrawal.

Side effects: In pooled safety data from three multicentres, randomised, double-blind, placebo-controlled studies, adverse reactions were generally mild to moderate in intensity, and were most commonly reported in the first 8 weeks of treatment. There was an apparent dose-relationship for dizziness, somnolence, confusional state, aphasia, coordination abnormal, tremor, balance disorder, memory impairment, gait disturbance, blurred vision and constipation.

Adverse reactions that were most frequently reported to lead to discontinuation were dizziness, somnolence, fatigue and confusional state.

Drug interactions (see also above under cautions): Steady-state data from a limited number of patients in smaller phase II studies indicated that phenytoin can reduce retigabine systemic exposure by 35% and carbamazepine can reduce retigabine systemic exposure by 33%

Administration of retigabine at therapeutic doses may increase digoxin serum concentrations.

Cost (www.mims.co.uk): At current prices, one year's treatment costs £1012.18 to £1659.84 with retigabine 600 mg to 1200 mg/day.

References:

1. SPC. (Trobalt®) GSK 12/5/2012
2. NICE TA 232. Retigabine for the adjunctive treatment of partial onset seizures in epilepsy. July 2011