Health and Social Care Board

Interface Pharmacist Network Specialist Medicines

Stiripentol

GP Information Sheet

Introduction

Stiripentol is indicated for use in conjunction with clobazam and valproate, as adjunctive therapy of refractory generalized tonic-clonic seizures in patients with severe myoclonic epilepsy in infancy (SMEI, Dravet's syndrome) whose seizures are not adequately controlled with clobazam and valproate.

Stiripentol may also potentiate the effect of other antiepileptic drugs (AEDs).

Stiripentol should only be used under the supervision of a paediatrician / paediatric neurologist experienced in the diagnosis and management of epilepsy in infants and children.

Stiripentol appears to increase brain levels of gamma-aminobutyric acid (GABA) - the major inhibitory neurotransmitter in the brain. This could occur by inhibition of uptake of GABA and/or inhibition of GABA transaminase.

Dosage and Administration

The dose of stiripentol is calculated on a mg/kg body weight basis, and the daily dose is administered in 2 or 3 divided doses. AED regimes may vary and the information below reflects usual practice.

The initiation of adjunctive therapy with stiripentol should be undertaken gradually using upwards dose escalation to reach the recommended dose of 50 mg/kg/day administered in conjunction with clobazam and valproate.

- Child 3–5 years: Initially 20 mg/kg daily in 2–3 divided doses for 1 week, then increased to 30 mg/kg daily in 2–3 divided doses for 1 week, then increased to 50 mg/kg daily in 2–3 divided doses.
- Child 6–11 years: Initially 20 mg/kg daily in 2–3 divided doses for 1 week, then increased in steps of 10 mg/kg daily in 2–3 divided doses, dose to be increased at intervals of 1 week to 50 mg/kg daily in 2–3 divided doses.
- Child 12–17 years: Initially 20 mg/kg daily in 2–3 divided doses for 1 week, then increased to 30 mg/kg daily in 2–3 divided doses for 1 week, then increased in steps of 5 mg/kg daily in 2–3 divided doses, dose to be increased at intervals of 1 week, until the optimum dose is reached based on clinical judgement; maximum 50 mg/kg per day.
- Adult: Doses of up to 50 mg/kg daily in 2–3 divided doses should be continued for as long as efficacy is observed.

Dose adjustment

The specialist will provide detailed written instructions on how to adjust dose during the titration phase.

Parents/carers will be provided with written information on dose titration and the use of stiripentol to control seizures, and will be given contact details for the paediatric epilepsy service, should further advice or information be required.

Specialist will advise on dose adjustment throughout therapy, and will provide GP with updates following review appointment

Note: Reduction of clobazam (or other AED's) may be required as concurrent use can affect plasma levels (specialist will monitor for clinical effects and advise if action required).

Counselling for parent/carer

- Stiripentol must always be taken with food as it degrades rapidly in an acidic environment (e.g. exposure to gastric acid in an empty stomach)
- Stiripentol should not be taken with milk or dairy products (yoghurt, soft cream cheese, etc.), carbonated drinks, fruit juice or food and drinks that contain caffeine or theophylline.
- Capsules should be swallowed whole with a glass of water.
- The powder should be mixed in a glass of water and should be taken immediately after mixing.

Patients 18yrs and over: treatment is continued for as long as efficacy is observed, therefore patients may remain on therapy into adulthood under neurologist care.

Available as

Diacomit® Capsules, stiripentol 250mg and 500mg, 60 capsule pack

Diacomit® Powder, stiripentol 250mg and 500mg, 60 sachet pack

Switching between preparations: Bioequivalence between the capsules and oral suspension formulations has not been established. Clinical supervision is recommended if changing stiripentol formulation.

Monitoring Requirements

All monitoring will be performed by the specialist at clinic appointments.

- Baseline full blood count and liver function tests.
- Unless otherwise clinically indicated, full blood count and liver function tests every 6 months.
- Growth rate.

Adverse Effects, Precautions and Contraindications

Stiripentol is contraindicated:

- In maintenance therapy in conjunction with carbamazepine, or phenytoin or phenobarbital.
- Where there is a history of episodes of delirium.
- In patients with impaired hepatic and/or renal function

Concurrent use of Stiripentol with other AED's may potentiate side effects as well as the therapeutic effect of these medicines (e.g. increased drowsiness with clobazam). The daily dosage of clobazam and/or valproate should be reduced according to the onset of side effects whilst on stiripentol therapy.

Common or very common adverse effects include:

- GI adverse effects (anorexia, loss of appetite, nausea, vomiting),weight loss
- Neutropenia
- Drowsiness, ataxia, dystonia, hyperkinesia, hypotonia.
- Aggression, irritability, behaviour disorders, opposing behaviour, hyper-excitability, sleep disorders

Less commonly: fatigue, photosensitivity, rash, and urticaria.

Common Drug Interactions

Stiripentol inhibits several CYP450 enzymes. Caution is therefore advised when combining stiripentol with other drugs that inhibit or induce one or more of these enzymes, particularly those with a narrow therapeutic index. Examples of drugs metabolised by these enzymes include beta blockers, antidepressants, antipsychotics, analgesics.

Ergot alkaloids, immunosuppressants, statins: Avoid co-prescribing unless clinically necessary.

Other antiepileptic drugs: plasma levels may increase due to inhibition of hepatic metabolism, so clinical monitoring advised (dose reduction may be required).

Use with caution: Midazolam, triazolam, alprazolam; chlorpromazine, theophylline, caffeine

Communication

For any queries relating to the patients treatment with stiripentol, contact the specialist.

This information is not inclusive of all prescribing information and potential adverse effects.
Please refer to full prescribing data in the SPC or the BNF

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