Health and Social Care Board

Interface Pharmacist Network Specialist Medicines

Stiripentol

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 regimens 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 3–18 years: Initially 10 mg/kg in 2–3 divided doses; titrate dose over minimum of 3 days to maximum 50 mg/kg/day in 2–3 divided doses.

Further details on dose escalation are available in the Summary of Product Characteristics for Diacomit® (see below), but dose initiation at 10mg/kg/day is the preferred regime in RBHSC.

Stiripentol dosage escalation should be gradual, starting with 20mg/kg/day for 1 week, then 30mg/kg/day for 1 week. Further dosage escalation is age dependent:

- children less than 6 years should receive an additional 20 mg/kg/day in the third week, thus achieving the recommended dose of 50 mg/kg/day in three weeks;

- children from 6 to less than 12 years should receive an additional 10 mg/kg/day each week, thus achieving the recommended dose of 50 mg/kg/day in four weeks;

- children and adolescents 12 years and older should receive an additional 5 mg/kg/day each week until the optimum dose is reached based on clinical judgment.

Children aged less than 3 years: The clinical decision for use of stiripentol in children with SMEI less than 3 years of age needs to be made on an individual patient basis taking into consideration the potential clinical benefits and risks. In this younger group of patients, adjunctive therapy with stiripentol should only be started when the diagnosis of SMEI has been clinically confirmed.

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 during a meal.
- The powder should be mixed in a glass of water and should be taken immediately after mixing during a meal.

Patients ≥ 18 years of age: Treatment is continued for as long as efficacy is observed therefore patients may remain on therapy into adulthood under neurologist care.

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

Available as

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

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

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).

- GI adverse effects can occur frequently (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.

Stiripentol is contraindicated where there is a history of allergy to stiripentol or excipient, or a history of attacks of delirium.

Stiripentol is not recommended for use in patients with impaired hepatic and/or renal function

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, immunosuppressant's, 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.

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