

Clinical Expert Summary
Stiripentol (Diacomit[®]) 250 mg and 500 mg hard capsules; 250 mg and 500 mg powder for oral suspension in sachet

Stiripentol (Diacomit[®]) 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 syndrome) whose seizures are not adequately controlled with clobazam and valproate.

1. Existing guidelines

Some experts referred to the National Institute for Health and Care Excellence (NICE) guideline (CG137), which recommends considering stiripentol or clobazam as adjunctive treatment for Dravet syndrome that has not responded to first-line treatment with sodium valproate or topiramate.

2. Disease prevalence/incidence

One expert confirmed that there are 6 children with Dravet syndrome in an area of Wales with a population of around 1 million; two or three of these children are being treated with stiripentol. Another highlighted recent US research showing the incidence of Dravet syndrome as 1 in 20,000 births when diagnosed by a change in the SCN1A gene compared with a previously published incidence of 1 in 40,000 when diagnosed by clinical presentation. Using the most recent US data and the current birth rate in Wales it was predicted that there would be at least 1–2 children born with Dravet syndrome each year in Wales. It was also highlighted that the number of children in Cardiff is expected to increase by 20% between 2006 and 2026.

3. Current treatment options

Sodium valproate was confirmed as the main first-line treatment option for Dravet syndrome. Medicines to consider adding in to sodium valproate were identified as topiramate, levetiracetam, clobazam and clonazepam, though some experts commented that they preferred to avoid clobazam in the long term and instead reserve this for short-term rescue treatment. It was reported that some patients want to try the ketogenic diet or a vagal nerve stimulator, but that these have not been particularly effective. Some experts are also already using adjunctive stiripentol in Wales, with one suggesting that this is “widely used”. Another commented that, in their experience, the early efficacy of valproate is often not sustained and cycling through multiple anticonvulsant medications is not uncommon.

4. Unmet needs

Experts highlighted that, with the availability of genetic testing, earlier diagnosis is now much easier and relatively straightforward. In light of this, one expert predicted that the demand for stiripentol will increase. Another commented that access to the ketogenic diet is a problem with regard to funding and dietetic support.

One expert referred to the association of Dravet syndrome with intellectual and physical disability and increased mortality, including sudden unexplained death in epilepsy, as well as poor quality of life affecting patients’ appetite, sleep, gait and behaviour.

5. Knowledge of product in given indication

Some experts stated that they already used stiripentol as an adjunct to other anti-epileptic medicines in children with Dravet syndrome, with one commenting that they prescribe this for all their patients at some stage during their care. In terms of place in therapy, experts indicated that they may add stiripentol to valproate plus clobazam, valproate plus topiramate, valproate plus levetiracetam or use alongside

clonazepam if valproate and clonazepam had lost efficacy. One expert stated that they would try using stiripentol before referring a patient for the ketogenic diet.

It was suggested that patients successfully being treated with adjunctive stiripentol at the age of 18 years would likely continue on this. One expert commented that children with Dravet syndrome “are rarely weaned off stiripentol” and that most of them are taking it at the time of transition to adult services. Conversely, another expressed a view that by the age of 18 years other therapies were likely to have replaced stiripentol. One expert commented that familiarisation with stiripentol would help the transition of patients from paediatric to adult services and is important for continuity of care.

Opinion was divided about whether stiripentol should be prescribed under specialist recommendation or with a shared care agreement.

It should be noted that one expert involved in compiling this response declared a non-personal specific interest in relation to stiripentol for the indication under consideration.