stiripentol (Diacomit®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO063

Description

Stiripentol (Diacomit) is an orally administered anticonvulsant with direct effects mediated through the GABAa receptor.

Length of Authorization

- Initial: Three months
- Renewal: 12 months

Quantity limits

Product Name	Indication	Dosage Form	Quantity Limit
stiripentol (Diacomit)	Dravet Syndrome	250 mg capsules	180 capsules/30 days
		500 mg capsules	
		250 mg powder for oral suspension	180 packets/30 days
		500 mg powder for oral suspension	

Initial Evaluation

I. **Stiripentol (Diacomit)** may be considered medically necessary when the following criteria below are met:
   A. Member is 6 months of age or older; **AND**
      1. Member weighs at least 7 kg (15 lbs); **AND**
   B. Medication is prescribed by or in consultation with a neurologist; **AND**
   C. Medication will not be used as monotherapy (i.e., will be used in combination with another antiepileptic agent); **AND**
   D. A diagnosis of **Dravet Syndrome** when the following are met:
      i. Treatment with clobazam (Onfi) and valproate (Depakote) has been ineffective, contraindicated, or not tolerated; **AND**
      ii. Medication will be used in combination with clobazam (Onfi)

II. Stiripentol (Diacomit) is considered investigational when used for all other conditions, including but not limited to:
   A. Epileptic encephalopathies associated with SCN1A mutations
   B. Pharmacoresistant Focal Seizures
   C. Other non-FDA approved seizure disorder
   D. Primary Hyperoxaluria
   E. When used as monotherapy

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Member has exhibited improvement or stability of disease symptoms [e.g., reduction in seizure frequency, seizure duration, incidence of ER visits or hospitalization due to seizure, etc.]; **AND**
IV. Medication will be used in combination with clobazam (Onfi)

Supporting Evidence

I. Dravet syndrome, previously known as severe myoclonic epilepsy in infancy, is a rare pediatric genetic epilepsy syndrome that typically presents within the first year of life (infancy) and is characterized by refractory epilepsy and neurodevelopmental problems. It can be difficult to diagnose, with common misdiagnoses including Lennox-Gastaut syndrome, cerebral palsy and vaccine encephalopathy. Because Dravet syndrome is generally treatment refractory, with high-touch care and monitoring required, stiripentol (Diacomit) must be prescribed by, or in consultation with a neurologist.
II. The use of stiripentol (Diacomit) has not been studied as monotherapy, and FDA labeling notes that there are no clinical data to support the use of stiripentol (Diacomit) as monotherapy. Therefore, if a member has a contraindication to therapy with clobazam, then another antiepileptic agent will be required to be used in combination with stiripentol (Diacomit).
III. Stiripentol (Diacomit) was studied in two Phase III, multicenter, randomized, placebo-controlled trials in 64 patients between the ages of three and 18 years who have been diagnosed with Dravet syndrome with previous inadequately controlled seizures on clobazam and valproate. Patients received stiripentol (Diacomit) as add-on therapy to on-going use of clobazam and

valproate. The primary efficacy endpoint was responder rate, defined as a patient who experienced a >50% decrease in the frequency (per 30 days) of generalized clonic or tonic-clonic seizures, which was statistically significant for stiripentol (Diacomit) compared to placebo in both studies.

IV. The effectiveness of stiripentol (Diacomit) for patients aged six months to less than three years of age was extrapolated from the demonstration of effectiveness in patients aged three years to less than 18 years of age in the trials pivotal trials described above (supporting evidence I).

V. Although stiripentol (Diacomit) was studied in combination with both clobazam and valproate, the FDA indication is for the treatment of seizures associated with Dravet syndrome in patients taking clobazam. Pharmacokinetic data from the clinical trial revealed that the serum levels of both clobazam and its active component, norclobazam, were increased substantially with stiripentol (Diacomit), while the serum levels of valproate were unchanged. Because the relative contribution of efficacy of the increased levels of clobazam and norclobazam with stiripentol (Diacomit) treatment remains incompletely defined, along with concerns for long-term teratogenicity and side effects of valproate, the FDA concluded that stiripentol (Diacomit) will be indicated in patients taking clobazam only.

VI. The NICE guidelines for Dravet syndrome recommend valproate as first-line therapy, then clobazam, and stiripentol (Diacomit) as adjunct first-line therapy. Cannabidiol (Epidiolex), in combination with clobazam, and fenfluramide (Fintepla) can also be considered as second-line add-on therapy. In addition to these guidelines, the international consensus on diagnosis and treatment of Dravet syndrome recommend first-line treatment with valproate, second-line with stiripentol (Diacomit), clobazam, or fenfluramine (Fintepla), and third-line with cannabidiol (Epidiolex).

Investigational or Not Medically Necessary Uses

I. Stiripentol (Diacomit) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   A. Epileptic encephalopathies associated with SCN1A mutations
   B. Pharmacoresistant Focal Seizure
   C. Other non-FDA approved seizure disorder
   D. Primary hyperoxaluria
   E. When used as monotherapy
      i. Stiripentol (Diacomit) has not been studied as monotherapy in Dravet syndrome. Package label also notes lack of clinical data to support the use as monotherapy.

References

1. Diacomit [Prescribing Information]. Redwood City, CA: Biocodex, Beauvais, France. July 2022.
2. Center for Drug Evaluation and Research. Application Number 206709Orig1s000/207223Orig1s000 Summary Review. Summary Review for Regulatory Action: NDA206709/207223. Updated August 20, 2018. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2018/206709Orig1s000,207223Orig1s000SumR.pdf
3. Stiripentol (Diacomit): For Severe Myoclonic Epilepsy in Infancy (Dravet Syndrome) [Internet]. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2015 Apr. 3, RESULTS. Available from: https://www.ncbi.nlm.nih.gov/books/NBK349320/
4. Chiron C, Marchand MC, Tran A, Rey E, d'Athis P, Vincent J, et al. Stiripentol in severe myoclonic epilepsy in infancy: a randomised placebo-controlled syndrome-dedicated trial. STICLO study group. Lancet. 2000 Nov 11;356(9242):1638–1642.
5. National Institute for Health and Care Excellence. Epilepsies in children, young people, and adults. Nice.org.uk. April 27, 2022. Accessed September 7, 2022.
6. National Institute for Health and Care Excellence. Fenfluramine for treating seizures associated with dravet syndrome. Nice.org.uk. July 8, 2022. Accessed September 7, 2022.
7. Wirrell EC, Hood V, Knupp KG, et al. International consensus on diagnosis and management of Dravet syndrome. Epilepsia. Published online May 12, 2022:epi.17274.

Related Policies

Policies listed below may be related to the current policy. Related policies are identified based on similar indications, similar mechanisms of action, and/or if a drug in this policy is also referenced in the related policy

Policy Name	Disease state
cannabidiol (Epidiolex)	Lennox-Gastaut syndrome Dravet syndrome Tuberous Sclerosis Complex
fenfluramine (Fintepla)	Dravet syndrome Lennox-Gastaut syndrome

Policy Implementation/Update:

Action and Summary of Changes	Date
Updated formatting of policy and quantity limit table; updated age requirement to 6 months and older; removed requirement for combination use with valproate from initial criteria; removed concomitant use with cannabidiol (Epidiolex) from E/I section	09/2022
Policy created	05/2019