DIACOMIT® Pivotal Randomized Studies Summary

DIACOMIT® (stiripentol) 250 mg, 500 mg capsules or for oral suspension

STICLO France and STICLO Italy

The efficacy of DIACOMIT (stiripentol) in patients with Dravet syndrome was demonstrated in two randomized, double-blind, placebo-controlled, Phase 3 clinical trials: STICLO France and STICLO Italy. In these trials, DIACOMIT was used as an add-on therapy to optimize treatment with valproic acid and clobazam. The trials had identical protocol designs, enabling for comparisons and the pooling of data.[1,2] STICLO Italy was not published; however, both studies are included in DIACOMIT's full Prescribing Information.

The STICLO France and STICLO Italy studies were divided into a baseline, comparison, and 30-day follow-up period:[1,6]

Baseline Period

A one-month baseline period where eligible patients continued to receive valproic acid and clobazam.

Comparison Period

A two-month, double-blind, comparison period involving patients who had at least four generalized clonic or tonic-clonic seizures during the baseline period. Patients were randomly allocated to receive DIACOMIT or a placebo with their antiepileptic treatment for two months. The DIACOMIT dose was fixed at 50 mg/kg/day and administered in two or three doses.

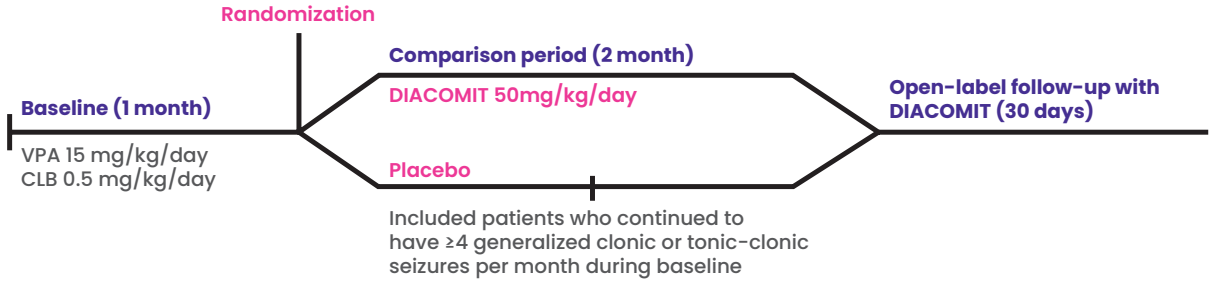
Follow Up Period

Patients received DIACOMIT under the open-label extension trial for 30 days.

Quick Fact

Both STICLO France and STICLO Italy were short-term studies with a duration of two months. After their completion, long-term studies were performed and confirmed that DIACOMIT's efficacy and safety profile is maintained over long-term treatment up to several years.[3-5]

Study Design



CLB, clobazam; VPA, valproic acid

Learn More at **DIACOMIT.com/hcp**

Indication

DIACOMIT (stiripentol) is indicated for the treatment of seizures associated with Dravet syndrome (DS) in patients taking clobazam who are 6 months of age and older and weighing 7 kg or more.

There are no clinical data to support the use of DIACOMIT as monotherapy in Dravet syndrome.

Important Safety Information

Contraindications

None

Warnings & Precautions

Somnolence

DIACOMIT can cause somnolence. Monitor patients for somnolence, particularly when DIACOMIT is used concomitantly with other CNS depressants or clobazam, which is also known to cause somnolence.

Additional Important Safety Information on reverse side.

Summary of STICLO Studies[1,2,5]	
Design	Multicenter, randomized, placebo-controlled, double-blind, Phase 3 clinical trials
Location	Pooled data from multiple centers in France and Italy
Participants	• STICLO France: 41 • STICLO Italy: 23 • Patients ages 3 to 18 years
Objectives	• Evaluate the efficacy of DIACOMIT as an add-on therapy to valproic acid and clobazam • Study the safety profile of different drug combinations • Record steady-state concentrations
Interventions	• Baseline period: valproic acid 15 mg/kg/day and clobazam 0.5 mg/kg/day • Comparison period: DIACOMIT for two months at 50 mg/kg/day divided into two or three daily doses
Primary endpoint	Percentage of responders (defined as > 50% reduction in clonic or tonic-clonic seizure frequency during the second month of the double-blind period compared with baseline)
Secondary endpoints	• Mean percentage change from baseline in frequency of generalized clonic or tonic-clonic seizures • Change in number of seizures

Important Safety Information (cont'd)

Decreased Appetite and Decreased Weight

DIACOMIT can cause decreases in appetite and weight. The growth and weight of pediatric patients treated with DIACOMIT should be carefully monitored.

Neutropenia and Thrombocytopenia

DIACOMIT can cause significant declines in neutrophil and platelet counts. Hematologic testing should be obtained prior to starting treatment with DIACOMIT and then every 6 months.

Withdrawal Symptoms

As with most antiepileptic drugs (AEDs), DIACOMIT should be gradually withdrawn to minimize the risk of increased seizure frequency and status epilepticus.

Risks in Patients with Phenylketonuria (PKU)

DIACOMIT for oral suspension contains phenylalanine, which can be harmful to patients with PKU. Before prescribing DIACOMIT for oral suspension to a patient with PKU, consider the total daily intake of phenylalanine from all sources, including DIACOMIT for oral suspension. DIACOMIT capsules do not contain phenylalanine.

Suicidal Behavior and Ideation

AEDs, including DIACOMIT, increase the risk of suicidal thoughts or behavior. Patients treated with any AED for any indication should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.

Adverse Reactions

The most common adverse reactions that occurred in at least 10% of DIACOMIT-treated patients and more frequently than on placebo were somnolence, decreased appetite, agitation, ataxia, decreased weight, hypotonia, nausea, tremor, dysarthria, and insomnia.

Pregnancy

There are no adequate data on the developmental risks associated with the use of DIACOMIT in pregnant women. Based on animal data, DIACOMIT may cause fetal harm.

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to AEDs, such as DIACOMIT, during pregnancy. Physicians are advised to recommend that pregnant patients taking DIACOMIT enroll in the North American Antiepileptic Drug (NAAED) Pregnancy Registry (information at **www.aedpregnancyregistry.org**.) This can be done by calling the toll free number 1-888-233-2334, and must be done by patients themselves or their caregiver.

To report suspected adverse reactions, contact Biocodex at 1-866-330-3050 or FDA at 1-800-FDA-1088 or **www.fda.gov/medwatch.**

Please see full Prescribing Information at **www.DIACOMIT.com**.

References:

1. DIACOMIT. Prescribing information. Biocodex; July 2022. Accessed August 2, 2022. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/206709s003;207223s003lbl.pdf
2. Kassaï B, Chiron C, Augier S, et al. Severe myoclonic epilepsy in infancy: a systematic review and a meta-analysis of individual patient data. *Epilepsia*. 2008;49(2):343-348. doi:10.1111/j.1528-1167.2007.01423.x
3. De Liso P, Chemaly N, Laschet J, et al. Patients with dravet syndrome in the era of stiripentol: A French cohort cross-sectional study. *Epilepsy Res*. 2016;125:42-46. doi:10.1016/j.eplepsyres.2016.05.012
4. Myers KA, Lightfoot P, Patil SG, Cross JH, Scheffer IE. Stiripentol efficacy and safety in Dravet syndrome: a 12-year observational study. *Dev Med Child Neurol*. 2018;60(6):574-578. doi:10.1111/dmcn.13704
5. Chiron C, Helias M, Kaminska A, et al. Do children with Dravet syndrome continue to benefit from stiripentol for long through adulthood? *Epilepsia*. 2018;59(9):1705-1717. doi:10.1111/epi.14536
6. Chiron C, Marchand MC, Tran A, et al. Stiripentol in severe myoclonic epilepsy in infancy: a randomised placebo-controlled syndrome-dedicated trial. STICLO study group. *Lancet*. 2000;356(9242):1638-1642. doi:10.1016/s0140-6736(00)03157-3

BBD-00231-042023

BIOCODEX