

Cenobamate Prescribing Guidance

Document history:

Version	Date	Main Changes/ Comments
1	16 th May 2022	Developed following request by Kent and Medway Joint Prescribing Committee (JPC)
1.1	24 th May 2022	Amended to include titration and dose stabilisation
1.2	30 th May 2022	Amended to include epilepsy service contact details
1.3	27 th July 2022	Amended to include special warnings, precautions, and potential drug interactions as suggested by JPC (July 2022)

Produced in consultation with:

Chloe Lewis	Principal Pharmacist – Formulary & Clinical Effectiveness, King's College Hospital NHS Foundation Trust
Deborah Clarke	Specialist Neurology Pharmacist, King's College Hospital NHS Foundation Trust
Trudy Thomas	Epilepsy Specialist Pharmacist, Medway NHS Trust, NHS Kent & Medway

Specialist Initiated Drugs

Cenobamate

May 2022

Cenobamate (Ontozry[®]) - Adjunctive therapy in the treatment of focal-onset seizures with or without secondary generalisation in adult patients with epilepsy who have not been adequately controlled despite treatment with at least 2 anti-epileptic medicinal products.

Formulations available on Formulary

Film coated tablets available in 50mg, 100mg, 150mg and 200mg

Prescribing

Initiation:

The specialist will initiate the medication accordingly and adjust the dose until the patient is stable.

Patients are expected to reach their stable dose after approximately 3 months, at which point GPs will be asked to continue prescribing. Some patients may require a slower titration, in which case the GP would not be asked to prescribe until the patient has reached their stable dose.

Continuation:

On-going prescribing can be continued by a GP. The GP is **NOT** expected to titrate the dose. The responsibility for titrating the dose or stopping treatment due to lack of effect or side effects remains with the specialist.

Specialist services should respond to **urgent** queries from primary care prescribers within 48 hours.

Kings College Hospital Specialist Team Contact Details

Email: kch-tr.epilepsycns@nhs.net

Special warnings and precautions

Risk of suicidal thoughts and behaviour:

Antiepileptic treatment is associated with a small risk of suicidal thoughts and behavior. Patients and caregivers of patients should be alert to any mood changes, distressing thoughts, or feelings about suicide or harming themselves at any point during treatment and should be advised to seek medical advice should any signs emerge. Please see MHRA advice available [here](#).

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS):

DRESS has been reported in association with Cenobamate when started at higher doses and titrated rapidly (weekly or faster titration). Patients should be advised of the signs and symptoms of DRESS and monitored closely for skin reactions. Symptoms of DRESS include typically, although not exclusively, fever, rash associated with other organ system involvement, lymphadenopathy, liver function tests abnormalities and eosinophilia.

If signs and symptoms suggestive of these reactions appear, Cenobamate should be withdrawn immediately, and an alternative treatment considered (as appropriate).

QT Shortening:

A dose-dependent shortening of the QTcF interval has been observed with Cenobamate. Clinicians should use caution when prescribing Cenobamate in combination with other medicinal products that are known to shorten the QT. Cenobamate must not be used in patients with Familial Short-QT syndrome.

Pregnancy:

There is no adequate data from the use of Cenobamate in pregnant women. Women of childbearing potential must use effective contraception during use of cenobamate and until 4 weeks after treatment discontinuation.

Any woman of childbearing potential or planning a pregnancy whilst on this drug should be referred for specialist review.

Potential Drug Interactions with other Antiepileptic Drugs (AEDs)

When used concomitantly with Cenobamate, no dosage adjustments are needed for: Carbamazepine, Lacosamide, Levetiracetam, Oxcarbazepine and Valproic acid.

Recommended dose adjustments depending on individual patient response:

Concomitant AED	Cenobamate
Lamotrigine	Depending on individual response, the dose of cenobamate may need to be increased.
Clobazam <ul style="list-style-type: none">May require dose reduction	No dose adjustment required.
Phenobarbital <ul style="list-style-type: none">May require dose reduction based on individual response (Phenobarbital concentration should be monitored during Cenobamate titration)	
Phenytoin <ul style="list-style-type: none">May require dose reduction based on individual response (Phenytoin concentration should be monitored during Cenobamate titration)	

For additional information please see the Summary of Product Characteristics
<https://www.medicines.org.uk/emc/search?q=cenobamate>

References

1. Summary of Product Characteristics Ontozry[®], Arvelle Therapeutics UK. Updated 20/07/2021 <https://www.medicines.org.uk/emc/product/13012/smpc>
2. NICE Technology appraisal guidance [TA753] [Cenobamate for treating focal onset seizures in epilepsy](#)
3. MHRA Drug Safety Update, Antiepileptics: risk of suicidal thoughts and behaviour, published 2014