Therapeutics Advisory Group

Improving lives together
Norfolk and Waveney Integrated Care System

Prescribing Guidance Update
Cenobamate for focal onset seizures in epilepsy - TA753
June 2025 v2.0

Key Message

In Norfolk and Waveney, **Cenobamate** has been awarded a classification of **AMBER INITIATE** for treating focal onset seizures in epilepsy as per NICE TA753. As per NICE guidance, **"treatment should be started by a healthcare professional with expertise in epilepsy, after which treatment can be continued in primary care."** Locally, this would be initiated in secondary care.

Amber Initiate - Specialist initiation. Treatment is initiated by a secondary care healthcare professional with expertise in epilepsy, after which it can be continued in primary care when clinically appropriate.

NICE Guidance

NICE TA753 - Cenobamate for treating focal onset seizures in epilepsy was published in December 2021 and updated in May 2025.

Cenobamate is recommended as an option as an add-on treatment for focal onset seizures with or without secondary generalised seizures in adults with drug-resistant epilepsy that has not been adequately controlled with at least 2 antiseizure medicines. It is recommended only as a second-line add-on treatment if:

- it is used after at least 1 first-line add-on treatment has not controlled seizures, and other first-line add-on treatments are contraindicated or not tolerated, and
- treatment is initiated by a secondary care healthcare professional with expertise in epilepsy, after which treatment can be continued in primary care.

Prescribing and Monitoring

The SPC table shows recommended dosage in adults with focal-onset seizures in epilepsy:

Treatment phase	Dose (per day, oral)	Duration
Treatment initiation	12.5 mg	Weeks 1 and 2
	25 mg	Weeks 3 and 4
Titration	50 mg	Weeks 5 and 6
	100 mg	Weeks 7 and 8
	150 mg	Weeks 9 and 10
Target dose	200 mg	Weeks 11 and 12 and onwards
Dose optimisation	Some patients, who do not reach optimal seizure control, may benefit from doses above 200 mg (increased by increments of 50 mg/day every two weeks) up to a maximum of 400 mg daily.	

The recommended starting dose of Cenobamate is 12.5mg per day, titrated gradually to the recommended target dose of 200mg per day. Based on clinical response, dose may be increased to a maximum of 400mg per day.

If Cenobamate is to be stopped, discontinuation should be gradual to prevent potential for rebound seizures, unless safety concerns require abrupt withdrawal. Specialist will advise the patient's GP on Cenobamate withdrawal.

Monitoring

Cenobamate should be used with caution. Reduction of the target dose may be considered in patients with renal or hepatic impairment.

The specialist will arrange baseline blood tests (FBC, LFTs AND U&Es) and repeat these after three months of treatment with Cenobamate if clinically indicated. If deemed appropriate, an ECG at baseline may be requested by the specialist and repeated if necessary. The GP may be asked to conduct ongoing monitoring of renal and hepatic function as necessary to ensure safe prescribing.

The specialist may undertake additional investigations as required, e.g., therapeutic drug levels of anti-seizure medication(s). The results will be sent to the GP.

Special warnings and precautions

MHRA published a Drug Safety Update - Antiepileptics: risk of suicidal thoughts and behaviour in December 2014.

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.

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 • May require dose reduction	No dose adjustment required
Phenobarbital • May require dose reduction based on individual response (Phenobarbital concentration should be monitored during Cenobamate titration)	
Phenytoin • May require dose reduction based on individual response (Phenobarbital concentration should be monitored during Cenobamate titration)	

Patient Counselling

- Patients (and caregivers of patients) should seek the advice of their specialist or GP if they experience any adverse effects. Treatment must not be stopped without first seeking medical advice.
- Patients should be advised to seek medical advice from their specialist or GP should signs of suicidal ideation or behaviour emerge.
- Patients must report any other adverse effects or warning symptoms to the specialist or GP whilst receiving Cenobamate, especially any signs or symptoms of DRESS.
- Cenobamate is not recommended in women of childbearing potential not using contraception. Women of childbearing potential should use effective contraception during treatment and for 4 weeks after stopping treatment. Those using oral contraceptives should practice additional or alternative non-hormonal measures (e.g., barrier methods) of birth control.
- Cenobamate is NOT recommended in pregnancy or during breast feeding. Should a patient discover they are pregnant then they should contact their GP or specialist to obtain an URGENT referral to neurology for review. Treatment should NOT be stopped without medical advice.
- If a patient misses one dose, it is recommended that they take a single dose as soon as they remember, unless it is less than 12 hours until their next regularly scheduled dose.
- Attendance for relevant tests and appointments is essential. Patients (and caregivers of patients) must book and attend all appointments as advised by the specialist team or GP.
- If their GP surgery is changed then they must notify their new GP as soon as possible of this treatment to ensure they can provide the service, and that the next prescription is not delayed.

References (accessed 10/6/2025)

NICE Guidance - Cenobamate for treating focal onset seizures in epilepsy
SPC - Cenbamate
BNF - Cenobamate
MHRA Drug Safety Update - Antiepileptics: risk of suicidal thoughts and behaviour

Adapted for local use from document developed by Kent and Medway Joint Prescribing Committee (JPC)

Title	Prescribing Guidance Update Cenobamate for focal onset seizures in epilepsy - TA753
Description of policy	*To inform healthcare professionals*
Scope	*Norfolk and Waveney Integrated Care System*
Prepared by	Norfolk and Waveney ICB Medicines Optimisation Team
Impact Assessment (Equalities and Environmental)	*Please indicate impact assessment outcome:* *Positive impact* *Adverse impact - low - action plan completed as per guidance* *Adverse impact - medium - action plan completed as per guidance* *Adverse impact - high - action plan completed as per guidance* *No impact* ***No policy will be approved without a completed equality impact assessment***
Other relevant approved documents	
Evidence base / Legislation	Level of Evidence: *A. based on national research-based evidence and is considered best evidence* ***B. mix of national and local consensus*** *C. based on local good practice and consensus in the absence of national research based information.*
Dissemination	Is there any reason why any part of this document should not be available on the public web site? ☐ Yes / No ☒
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1.0	TAG Lead Technician, NWICB	To support prescribing	April 2023
2.0	Senior Interface and Formulary Technician, NWICB	Traffic light classification amended following update to NICE TA	June 2025