



**ONTOZRY**<sup>®</sup> ▼  
cenobamate

# How to start your patient on ONTOZRY<sup>®</sup>

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Adverse events and product complaints should be reported. Reporting forms and information can be found at [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard) for the UK or [www.hpra.ie](http://www.hpra.ie) for Ireland. Adverse events and product complaints should also be reported to Angelini Pharma on (UK) +44 2034889643, (ROI) +353 1 584 4671 or [UKIReporting@angelinipharma.com](mailto:UKIReporting@angelinipharma.com)

**Indication for United Kingdom:** ONTOZRY<sup>®</sup> is indicated for the adjunctive 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.<sup>1</sup>

**Indication for Republic of Ireland:** ONTOZRY<sup>®</sup> is indicated for the adjunctive treatment of focal-onset seizures with or without secondary generalisation in adult patients with epilepsy who have not been adequately controlled despite a history of treatment with at least 2 anti-epileptic medicinal products.<sup>1</sup>

Prescribing information and adverse event reporting information can be found by scanning the QR code or [click here](#) if you are viewing on a digital device.



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## Administration of ONTOZRY®

ONTOZRY® offers once-daily (OD) oral dosing.<sup>1</sup>



### Starting dose

To be **titrated** to a target maintenance dose of 200 mg or a maximum dose of 400 mg<sup>1</sup>



### Oral route of administration

To be taken with a **glass of water, with or without food**, preferably at the same time each day<sup>1</sup>  
The tablet can also be crushed, then mixed with water and administered orally or via a nasogastric tube<sup>1</sup>



### Missed doses

If a patient misses one dose, they should take a single dose as soon as they remember, unless it is **less than 12 hours until their next regularly scheduled dose**<sup>1</sup>

## ONTOZRY® titration regimen

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	<b>200 mg</b>	<b>Weeks 11 and 12 and onwards</b>
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.	

ONTOZRY® starting dose is **12.5 mg OD**, titrated gradually every 2 weeks to the recommended target dose of 200 mg OD. The dose may be increased to a maximum of **400 mg OD** based on individual needs.<sup>1</sup>

The recommended titration schedule should not be exceeded because of the potential for serious adverse events.

**Discontinuation should be gradual** to minimise risk of rebound seizures, unless safety concerns require otherwise.<sup>1</sup>

## Clinical pharmacology of ONTOZRY®<sup>1</sup>

### Special populations

**Elderly:** Clinical studies of cenobamate did not include sufficient numbers of subjects aged 65 and over to determine whether they responded differently from younger patients. It has been reported that elderly subjects on anti-epileptic medicinal products have a higher incidence of adverse reactions. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic or renal function and of concomitant disease as well as the potential interactions in polymedicated patients.

**Renal:** Cenobamate should be used with caution, and reduction of the target dose may be considered in patients with mild to moderate (creatinine clearance 30 to <90 ml/min) or severe (creatinine clearance < 30 ml/min) renal impairment. The maximum recommended dose for patients with mild, moderate or severe renal impairment is 300 mg/day. Cenobamate should not be used in patients with end-stage renal disease or patients undergoing haemodialysis.

**Hepatic:** Exposure to cenobamate was increased in patients with chronic hepatic disease. A change in the starting dose is not required; however, a decrease in target doses of up to 50% may need to be considered. The maximum recommended dose in patients with mild and moderate hepatic impairment is 200 mg/day. Cenobamate should not be used in patients with severe hepatic impairment.

**Paediatric:** The safety profile and efficacy of ONTOZRY® in children aged 0 months to 18 years have not yet been established. No data is available.

## Potential drug–drug interactions

Below is a quick reference checklist of the potential drug–drug interactions to look out for:

Concomitant medication	Drug–drug interactions <sup>1</sup>
Lamotrigine	Pharmacometric analyses of data from healthy subjects and patients showed that concomitant administration of cenobamate with lamotrigine had no effect on cenobamate exposures, but resulted in dose-dependent decreases in lamotrigine concentrations (by –21%, –35% and –52% for cenobamate 100, 200 and 400 mg/day respectively). Based on subpopulation analyses of patients taking concomitant lamotrigine, <b>higher doses (200–400 mg/day) of cenobamate may be required for efficacy when co-administered with lamotrigine</b>
Carbamazepine	No clinically meaningful interactions. Please see ONTOZRY® Summary of Product Characteristics for further information
Lacosamide	
Levetiracetam	
Oxcarbazepine	
Valproic acid ▼	
Clobazam	Pharmacometric analyses of data from healthy subjects and patients predict that clobazam slightly increases cenobamate exposures (by 24%). No dose adjustment of cenobamate is required. Due to a possible increase in exposure of the active metabolite of clobazam ( <i>N</i> -desmethylclobazam), related to the induction of CYP3A4 (formation) and the inhibition of CYP2C19 (elimination), the dose of clobazam may need to be reduced
Phenobarbital	In a study in healthy subjects, concomitant administration of cenobamate 200 mg/day and phenobarbital 90 mg/day did not cause any clinically meaningful changes in cenobamate exposure but led to increased phenobarbital exposures (maximum plasma concentration [ <i>C</i> <sub>max</sub> ] by 34% and area under the curve [AUC] by 37%). No dose adjustment of cenobamate is required. Concentrations of phenobarbital should be monitored during cenobamate titration, and based on individual response, the dose of phenobarbital may need to be reduced
Phenytoin	In a study in healthy subjects, concomitant administration of cenobamate 200 mg/day and phenytoin 300 mg/day slightly reduced cenobamate exposures ( <i>C</i> <sub>max</sub> by –27%, AUC by –28%) and increased phenytoin exposures ( <i>C</i> <sub>max</sub> by 67%, AUC by 84%). No dose adjustment of cenobamate is required. Phenytoin concentrations should be monitored during titration of cenobamate, and based on individual response, the dose of phenytoin may need to be reduced
Oral contraceptives	Cenobamate showed a dose-dependent induction of CYP3A4, reducing exposures (AUC) of the CYP3A4 substrate, midazolam 2 mg by 72% with cenobamate 200 mg/day in healthy subjects. Since hormonal contraceptives may also be metabolised by CYP3A4, their efficacy may be reduced by concomitant use with cenobamate. Therefore, women of reproductive potential concomitantly using oral contraceptives should practise additional or alternative non-hormonal measures of birth control
CYP3A4 substrates	Cenobamate 100 mg and 200 mg once daily reduced exposure (AUC) of the CYP3A4 substrate, midazolam 2 mg by 27% and 72% respectively. An increase in the dose of medicines metabolised by CYP3A4 may be required when used concomitantly with cenobamate
CYP2B6 substrates	In a study in healthy subjects, concomitant administration of cenobamate 200 mg once daily reduced exposures of the CYP2B6 substrate, bupropion 150 mg ( <i>C</i> <sub>max</sub> decreased by 23%, AUC decreased by 39%). An increase in the dose of medicines metabolised by CYP2B6 may be required when used concomitantly with cenobamate
CYP2C19 substrates	In a study in healthy subjects, concomitant administration of cenobamate 200 mg once daily increased exposures of the CYP2C19 substrate, omeprazole 20 mg ( <i>C</i> <sub>max</sub> increased by 83%, AUC increased by 107%). A dose reduction of medicines metabolised by CYP2C19 may be required when used concomitantly with cenobamate

## Remind patients of what they need to look out for

Although not all patients will experience side effects, they must make note of any instances in their **ONTOZRY® Titration Diary**.

The following side effects are very common and may affect **1 in 10 people**:<sup>2</sup>

- **Feeling sleepy (somnolence, hypersomnia), sedated or very tired (fatigue)**
- **Feeling dizzy**
- **Spinning sensation (vertigo)**
- **Having problems with coordination of movements, having problems walking or keeping your balance (ataxia, gait disturbance, abnormal coordination)**
- **Headache**

Patients should be reminded to contact their healthcare professional if any side effects arise. This includes any possible side effects not listed in this leaflet.<sup>2</sup>

A dose-dependent shortening of the QTcF interval has been observed with ONTOZRY®. Thus, caution should be used when prescribing alongside other medicinal products known to shorten the QT. ONTOZRY® is contraindicated in patients with Familial Short-QT syndrome.<sup>1</sup>

In rare cases, drug reaction with eosinophilia and systemic symptoms (DRESS) was reported in association with ONTOZRY® at higher doses or rapid titration, hence the recommended starting dose of 12.5 mg and gradual titration.<sup>1</sup>

Suicidal ideation and behaviour have been reported in patients treated with anti-epileptic medicinal products including cenobamate.<sup>1</sup>

This drug contains lactose. Patients with rare hereditary problems such as galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.<sup>1</sup>

ONTOZRY® is contraindicated in patients with hypersensitivity to the active substance or to any of the excipients.

## References

1. ONTOZRY® Summary of Product Characteristics. United Kingdom and European Union.
2. ONTOZRY® UK Patient Information Leaflet.



If you would like to know more about ONTOZRY®, please scan the QR code or visit [www.harmoniamentis.co.uk/uk-hcp/](http://www.harmoniamentis.co.uk/uk-hcp/)