19 June 2025
EMADOC-1700519818-2230332

# CHMP List of questions

To be addressed by the applicants and marketing authorisation holder(s) for sodium oxybate-containing syrup and oral solution for alcohol dependence

Referral under Article 31 of Directive 2001/83/EC

Procedure number: EMA/REF/0000278933

INN/active substance: sodium oxybate

**Official address** Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
**Address for visits and deliveries** Refer to www.ema.europa.eu/how-to-find-us
**Send us a question** Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

The marketing authorisation holders (MAHs) and applicants as applicable are requested to address the following questions:

Question 1

Concerning your medicinal product(s) and/or marketing authorisation application(s), please provide:

a) information on the type of marketing authorisation(s)/application(s), marketing status (whether currently marketed or not), legal status, approved/applied indication(s), pharmaceutical form(s) and strength(s) by EEA member state (MS). Please specify if special conditions of prescription or dispensation are applied such as limited prescription, hospital use only, limitation to specialists (see Annex);

b) yearly figures on sales and patient exposure with a cut-off date on 30 June 2025 (in patient-years based on the WHO defined daily doses) by medicinal product, indication, sex of patient, and age (i.e. <18 years old, >18 years old), sorted by EEA MS (see Annex);

c) data on the use in clinical practice including information on dose, duration of treatment and concomitant treatment(s) (characterisation of users, prescriptions) (see Annex);

d) information included in the summary of product characteristics (SmPC), package leaflet (PL) on posology, as well as on contraindications, warnings and precautions and undesirable effects related to the risks of abuse and misuse. Please highlight the main differences between the product information (PI) in the different EEA MS (see Annex);

e) an overview of the approved indication(s) of sodium oxybate 175mg/mL outside the EEA.

Question 2

Please provide and critically discuss all the evidence of the therapeutic efficacy of sodium oxybate 175 mg/mL for each approved/applied indication in the EU. This should include all clinical trial data (including both MAH/applicant-sponsored and non-sponsored studies), pharmaco-epidemiological studies (including observational studies), and published literature. Any relevant non-clinical data should also be provided.

Please provide a summary of EU clinical guidelines and relevant supportive publications on the current approach to management of the alcohol dependence, together with a critical discussion.

Question 3

Please provide all available safety data relevant to evaluate the risks of abuse and misuse associated with sodium oxybate 175 mg/mL, together with an analysis and critical discussion of such data. This should include:

a) clinical trial data (including both MAH/applicant sponsored and non-sponsored studies), pharmaco-epidemiological studies (including observational studies) and published literature.

b) a cumulative review of all post-marketing spontaneous case reports (serious and non-serious) related to the risks of abuse and misuse. For this purpose, all the MedDRA Preferred Terms (PTs) should be provided where sodium oxybate 175 mg/mL is reported as a suspected or interacting medicinal product. Causality assessment should be performed for the serious cases using the WHO-UMC scoring system.
The review should include analyses per age, sex of patient, indication of use, duration and dose,

time to onset, outcome, seriousness, concomitant medications and illnesses, relevant medical history.

The possible risk factors should be discussed based on the above data.

Question 4

Based on the above, please provide a full benefit-risk balance assessment of your sodium oxybate-containing product/application in each of its approved/applied indication(s).

The MAH(s)/applicant(s) should provide justified proposals for any measures (including changes to the product information, additional risk minimisation measures) which could be implemented to improve the benefit-risk balance of sodium oxybate 175 mg/mL. Please also comment on how the effectiveness of such measures should be assessed and monitored.

# Annex

Question 1

a)

| Member state | INN | Product name | Type of marketing authorisation/ application | Marketing status | Legal status | Approved/applied indication(s) | Pharmaceutical forms and strengths | Special conditions of prescription or dispensation |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | | |

b)

| Member state | INN | Product name | Approved/applied indication(s) | Age range[1] | Year | Sales figures | Estimated patient exposure[2] |
|---|---|---|---|---|---|---|---|
| | | | | | | | |

[1] I.e. <18 years old, >18 years old.
[2] Expressed in patient years based on the WHO defined daily doses. Reasonable efforts should be made to obtain this information; potential sources in addition to sales data include registries and healthcare databases. If no precise data is available an estimate can be provided.

c)

| Member state | INN | Product name | Approved/applied indication(s) | Clinical practice - dose | Clinical practice – duration of treatment | Clinical practice – concomitant treatment | Clinical practice – other relevant information |
|---|---|---|---|---|---|---|---|
| | | | | | | | |

d)

| **PI**[1] | **SmPC** | **PL** | **Main differences in SmPCs/PLs between the different EEA member states** |
|---|---|---|---|
| Approved/applied indication: | | | |
| Posology (including max daily dose) | | | |
| Specifically on the risks of abuse and misuse: | | | |
| Contraindications | | | |
| Special warnings and precautions | | | |
| Undesirable effects | | | |

[1] Additional row(s) should be added as needed to reflect information on the risks mentioned above that may be included in other PI sections.