From: [redacted]
To: Streamlined Submission
Subject: RE: Request for pre-submission meeting for Sodium Oxybate [SEC=UNCLASSIFIED]
Date: Thursday, 14 June 2018 2:06:53 PM

Dear [redacted]

Thank you for your feedback, much appreciated.

Kind regards,

[redacted]

From: [redacted]@health.gov.au] **On Behalf Of** Streamlined Submission
Sent: Wednesday, 13 June 2018 3:01 PM
To: [redacted]
Subject: RE: Request for pre-submission meeting for Sodium Oxybate [SEC=UNCLASSIFIED]

Dear [redacted]

Thank you for your email.

The TGA's view that this product (Xyrem) does not meet the criteria for orphan drug designation is still applicable. This information was conveyed to you via email on 6 April 2018 in response to the questions raised to the TGA in the pre-submission briefing package, advice which was given without prejudice and is non-binding on the TGA. Further information pertaining to the orphan drug designation process and TGA's administration of same can be found on the TGA website at https://www.tga.gov.au/publication/orphan-drug-designation

This does not preclude you from applying for orphan drug designation for Xyrem. However, the likelihood of Xyrem being granted this designation, as per the advice provided to you in the above mentioned email is not high. The submission of a Category 1 application with the appropriate data package(s) in the future, will be evaluated according to standard practice and time frames.

I trust the above information is of use to you. If you require any clarification or have any further queries please send a return email.

Kind regards,

[redacted]
Stream 1 Case Manager
Evaluation Management Section
Prescription Medicines Authorisation Branch
Phone: [redacted]
Email: xxxxxxxxxxxxxxxxxxxxx@xxx.xxx.xx

Therapeutic Goods Administration
Department of Health

PO Box 100
Woden ACT 2606 Australia
www.tga.gov.au

This response is general information given to you without prejudice; it is not binding on the TGA and you should get your own independent legal advice to ensure that all of the legislative requirements are met.

[redacted]

From: [redacted]
Sent: Tuesday, 12 June 2018 4:19 PM
To: Streamlined Submission
Subject: RE: Request for pre-submission meeting for Sodium Oxybate [SEC=UNCLASSIFIED]

Dear [redacted]

UCB would like to thank the TGA for their feedback on our pre-submission briefing package for Xyrem. We also apologise for the delay with our response as we had many internal stakeholders to align with.

As some background, UCB is a company specialising in two main therapeutic areas: Neurology (Neupro, Keppra, Vimpat, Briviact) and Immunology (Cimzia). Xyrem is owned by Jazz Pharmaceuticals in the US, and UCB has been assigned the rights to register and market Xyrem in markets outside of the US. In Australia, Xyrem was a prohibited substance (S9) until the Australian Sleep Association (ASA) was successful with its application to down schedule sodium oxybate to S8 in 2014. At the same time, the ASA contacted UCB Australia to arrange for Xyrem to be made available for Australian patients. Through the interest of patients and discussions with the sleep specialists as well as interest from the public, we recognised that Xyrem would have value in Australia, therefore UCB decided to help these patients by arranging for the necessary licences and permits for the import of Xyrem under the Special Access Scheme Category B. At that time, we also investigated submitting an orphan application for Xyrem to further assist the ease of access for patients. However, the orphan guidelines at that time precluded this type of submission. In 2017, as the orphan drug designation prevalence criteria was revised (after the TGA conducted consultation with the public, which led to 7 submissions by members of the public specifically requesting the changes to the orphan drug designation prevalence criteria in order to facilitate easier access to sodium oxybate), UCB decided to apply for an orphan drug designation in Australia as a pathway for registration to ease the administrative burden on doctors wishing to prescribe Xyrem. Currently, no registered drugs are specifically indicated in the treatment of cataplexy, even if they have a broad indication of "narcolepsy". In fact, for methylphenidate the indication specifically mentions that it is not effective for loss of voluntary muscle tone and for modafinil and armodafinil, the indication only encompasses excessive daytime sleepiness in narcolepsy.

UCB appreciates that the main concern raised by the TGA is the requirement for comparator studies that show significant benefit over existing treatments. However, currently none of the existing stimulant treatment options have any proven effects on cataplexy. As such, UCB believes

that it would not be ethical to conduct a head-to-head trial with drugs which do not have a proven effect on a specific symptom and it would be difficult to convince investigators to participate and recruit for such a trial. Prior to the revision of the TGA Orphan guidelines in 2017, narcolepsy would not have met the prevalence criteria of the prevailing guidelines at the time. Taking into account the TGA's feedback on narcolepsy not representing a true orphan indication, UCB would like to explore the possibility of the TGA considering narrowing the orphan indication being sought to narcolepsy type 1 (narcolepsy with cataplexy), which is in line with our the intended indication for registration.

UCB's intent to pursue an orphan drug designation for Xyrem was driven to provide an easier to access alternative to patients that have exhausted all drug treatment options which would also be in the interest of their treating sleep physicians. There has also been substantial interest from the media and public on the availability of Xyrem in Australia; this interest has led to members of the public to escalate their unmet needs to the Minister of Health in New South Wales and to the Federal Minister for Health's Pharmaceuticals Advisor. In particular we were asked to keep them updated with the progress of the orphan drug designation application. Should Xyrem not be deemed eligible to be considered for an orphan drug designation, UCB would greatly appreciate a formal response from the TGA so that we are able to provide a definitive response to the relevant external stakeholders and manage their expectations. UCB will make every effort to continue supply of Xyrem on SAS to ease access for patients with unmet needs.

Kind regards,

[redacted]

From: [redacted]@health.gov.au] **On Behalf Of** Streamlined Submission
Sent: Friday, 6 April 2018 11:59 AM
To: [redacted]
Subject: RE: Request for pre-submission meeting for Sodium Oxybate [SEC=UNCLASSIFIED]

Dear [redacted]

Thank you for your email below. There has been a change in the Case Management team with [redacted] leaving the Stream 1 Case Manager position and I taking over. The Clinical Evaluation team have provided responses to the questions raised in the Pre-Submission package with an end to not conduct such a meeting. Please find the responses to these attached.

I trust the above information is of use to you. If you require any clarification please send a return email.

Kind regards,

[redacted]

[redacted]
Stream 1 Case Manager
Evaluation Management Section
Prescription Medicines Authorisation Branch
Phone: [redacted]

Email: xxxxxxxxxxxxxxxxxxxx@xxx.xxx.xx

Therapeutic Goods Administration
Department of Health
PO Box 100
Woden ACT 2606 Australia
www.tga.gov.au

This response is general information given to you without prejudice; it is not binding on the TGA and you should get your own independent legal advice to ensure that all of the legislative requirements are met.

From: [redacted]
Sent: Tuesday, 27 March 2018 2:31 PM
To: Streamlined Submission
Subject: RE: Request for pre-submission meeting for Sodium Oxybate [SEC=No Protective Marking]

Hi,

I just wanted to follow up with the below request for a pre-submission meeting from last month; has the TGA considered this and have a suitable date in mind or does the TGA require any further information in relation to this request? Much appreciated.

Kind regards,

[redacted]

From: [redacted]
Sent: Wednesday, 28 February 2018 4:36 PM
To: 'xxxxxxxxxxxxxxxxxxxx@xxx.xxx.xx' < xxxxxxxxxxxxxxxxxxxx@xxx.xxx.xx >
Cc: [redacted]
Subject: Request for pre-submission meeting for Sodium Oxybate

Hi,

Please find attached a request for a pre-submission meeting with the clinical delegate of Clinical Section 1 for an orphan drug designation application for sodium oxybate.

With this request, the following documents are provided:

Cover letter
Request for a pre-submission meeting form
A background document prepared in line with ARGPM Guidance 5)overview of the product and its development program), which includes list of final questions
A meeting agenda including UCB participants

Our preferred meeting dates would be on the 12th of 16th of March, subject to the TGA's availability. The meeting presentation will be provided no later than 2 days prior to the scheduled meeting. Please let me know should you have any queries or require any additional information further to this request at all.

Kind regards,

[redacted]
Regulatory Manager

UCB Australia Pty Ltd
Level 1, 1155 Malvern Road
MALVERN VIC 3144
Australia

[redacted]
Website: www.ucbaustralia.com.au

Medical Information Email: @.
Drug Safety/Pharmacovigilance E-Mail: .@.

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