Day 48
Updated Assessment Report

Assessment of applicant’s response to Day 30 comments

Repeat use procedure

Dexmedetomidin Ever Pharma
Concentrate for solution for infusion
100 microgram/ml

Dexmedetomidine Hydrochloride

DK/H/2619/001/E/001

CMS: HU, HR, FR, SI, PT

Applicant: EVER Neuro Pharma GmbH

Date: 8 June, 2018
# ADMINISTRATIVE INFORMATION

| Name of the product in the Reference Member State | Dexmedetomidin Ever Pharma |
| INN (or common name) of the active substance | Dexmedetomidine hydrochloride |
| Pharmaco-therapeutic group (ATC code) | N05CM18 |
| Pharmaceutical form(s) and strength(s) | Concentrate for solution for infusion 100 µg/ml |
| Reference number(s) for the Mutual Recognition Procedure | DK/H/2619/001/DC |
| Reference Member State | DK |
| Member States concerned in earlier procedure(s) | AT, BE, CZ, DE, IE, IT, NL, NO, PL, SK, ES, SE, UK |
| Member States concerned in current procedure | HU, HR, FR, SI, PT |
| Authorisation holder’s name and address in RMS | EVER Neuro Pharma GmbH, Oberburgau 3, Unterach am Attersee, 4866, Austria |
| Names and addresses of manufacturer(s) of dosage form | EVER Pharma Jena GmbH Otto-Schott-Straße 15 Jena, 07745 Germany |
| Name and address of manufacturer(s) responsible for batch release in the EEA | EVER Pharma Jena GmbH Otto-Schott-Straße 15 Jena, 07745 Germany |
| Marketing Authorisation number(s) in RMS | 57662 |
| Date of Day 48 Updated Assessment Report | 8 June, 2018 |
| RMS Contact Person |  |
CMS positions by Day 30:
Comments received: SI, HU,
No comment according to CTS: HR
No comment: FR, PT

Module 1:

Annex 5.19 - Product name

RMS Day 48:
Please note the following raised by RMS in the Day 0 RUP AR:

The reference product Dexdor is authorised by the Community. Therefore, according to Regulation EC/726/2004, Article 3(3)c, it is required that, “the generic medicinal product is authorised under the same name in all the Member States where the application has been made. For the purposes of this provision, all the linguistic versions of the INN (international non-proprietary name) shall be considered to be the same name”. Therefore, the name of a generic of a centrally authorised reference medicinal product should be the same in all Member States where it is authorised, regardless of the procedure followed for authorisation, i.e. centralised, mutual recognition or decentralised procedure and throughout the life cycle of the product.
The documentation for the trademark was considered acceptable during the initial procedure.

is kindly requested to indicate a final position.

Module 1.8.1 - RMP

The list of safety concerns in the RMP submitted for this hybrid application is not aligned with the safety concerns in the latest RMP of the reference product.
Please submit a variation within three month following the end of this RUP to update the RMP.

The applicant commits to submit a respective variation within the desired period.
RMS Day 48:
The applicant has provided a Commitment to fulfill 
’s request of an updated RMP.

Commitment accepted → Point resolved.

Product information:
PIL

<table>
<thead>
<tr>
<th>PIL</th>
<th>Section 2:</th>
<th>Content of sodium should be in line with Annex to the European Commission guideline on ‘Excipients in the labelling and package leaflet of medicinal products for human use’.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EVER Response:</td>
<td>The PIL was updated to reflect the changes introduced in the SmPC.</td>
</tr>
<tr>
<td></td>
<td>Please refer to PIL (Annex), working documents and commitment letter</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PIL</th>
<th>Section 4:</th>
<th>Frequency convention should be in line with last revision of QRD template</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EVER Response:</td>
<td>The PIL was updated to reflect the changes introduced in the SmPC.</td>
</tr>
<tr>
<td></td>
<td>Please refer to PIL (Annex), working documents and commitment letter</td>
<td></td>
</tr>
</tbody>
</table>

RMS Day 48:

Section 2:
This update is in accordance to Annex to the guideline on ”Excipients in the labelling and package leaflet of medicinal products for human use”.
Due to the fact that no changes can be introduced to the product information during a RUP, the applicant has agreed to implement the change via a variation. Please refer to the commitment document inserted above.
Point resolved.

Section 4:
The updated is considered acceptable (in accordance with current QRD version dated February 2016). Due to the fact that no changes can be introduced to the product information during a RUP, the applicant has agreed to implement the change via a variation. Please refer to the commitment document inserted above.
Point resolved.
RMS Day 48:

Section 2
This concern is not raised/proposed by DK (RMS), thus, is a outcome of the question raised by (CMS) for the package leaflet (section 2).
The proposed change is not acceptable. Note that since the threshold is below 1 mmol, there is no requirements to add information in section 2 or section 4.4. The current information of the sodium content must be re-inserted in section 2. Please revise the SmPC.
Point to be resolved.

Section 4.4.
The changes are only of minor administrative (stylistic) matter.
Due to the fact that no changes can be introduced to the product information during a RUP, the applicant has agreed to implement the change via a variation. Please refer to the commitment document inserted above. Due to comments re section 2, this is considered of very minor change and the commitment is only accepted by RMS since there are already other changes to the product information (package leaflet).
Point resolved.

Day 48 - Overall conclusion:
There are minor outstanding concerns to be solved prior final conclusion.