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

Doc. Ref: CMDh/339/2015 Rev.1
July 2017

ADMINISTRATIVE INFORMATION

Name of the product in the Reference Member State	Dexmedetomidin Ever Pharma
INN (or commen 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 Name and address of manufacturer(s) responsible for batch release in the EEA	EVER Pharma Jena GmbH Otto-Schott-Straße 15 Jena, 07745 Germany 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	

Day 48 - Updated assessment report

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

MODULE 1		
1. (CMS)	Annex 5.19: The proposed name Deksmedetomidin EVER Pharma 100 mikrogramov/ml koncentrat za raztopino za infundiranje is not acceptable for SI. The Applicant should submit Proof of establishment of trademark "EVER Pharma" or in case of proposing name composed of INN + MAH, MAH should be amended to be in line with MAH, stated in Annex 5.3/AF 2.4.1.	
	EVER Response: The applicant considers the product name Dexmedetomidine EVER Pharma to be appropriate as the Directive 2001/83/EC states in Art. 1 no. 20 that the name of the medicinal product may (i.a.) be "a common or scientific name accompanied by a trade mark". EVER Pharma is a registered trade mark. Thus, the same convention is applied for all medicinal products of EVER Valinject GmbH.	**Please refer to certificate on registered trade mark (eCTD 1.2)**

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

2. (CMS)	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.	
	EVER Response: The applicant commits to submit a respective variation within the desired period.	**Please refer to commitment letter**

RMS Day 48:

The applicant has provided a Commitment to fulfill ’s request of an updated RMP.

common-responses
-commitment.pdf

Commitment accepted → **Point resolved.**

Product information:

PIL

PIL		
1. (CMS)	Section 2 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’	
	EVER Response: The PIL was updated to reflect the changes introduced in the SmPC.	**Please refer to PIL (Annex), working documents and commitment letter**
2. (CMS)	Section 4 Frequency convention should be in line with last revision of QRD template	
	EVER Response: The PIL was updated to reflect the changes introduced in the SmPC.	**Please refer to PIL (Annex), working documents and commitment letter**

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.

SmPC

SmPC		
Amendments to the proposed SmPC are requested. Requested changes are incorporated into the SmPC with the regulatory assessor's comments in a boxed area within the text.		
1. (CMS)	4.4 Special warnings and precautions for use -Monitoring Based on the indications, [Nationally approved name] is intended for use in an intensive care setting, operating room and during diagnostic procedures (stylistic matter): -Subheading Elderly should be written as a new paragraph	
	EVER Response: - The applicant amended the respective section. - The applicant added the requested sub-heading.	**Please refer to SmPC (Annex), working documents and commitment letter**
2. DK (RMS)	Section 2: Sodium is listed in the Annex to the Guideline on the excipients in the label and package leaflet of medicinal product for human use and should therefore be included in section 2, e.g.: Excipient with known effect: Each ml of concentrate contains less than 1 mmol (approximately 3.5 mg) sodium. **Please refer to updated SmPC**	
	EVER Response: The text of section 2 was amended, and text passage on sodium was added as proposed by the RMS.	**Please refer to SmPC (Annex), working documents and commitment letter**

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 informtation 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 conclusiuon.