

## **Annex I**

**Scientific conclusions and grounds for the variation to the terms of the Marketing  
Authorisation(s)**

## **Scientific conclusions**

Taking into account the PRAC Assessment Report on the PSUR(s) for dexmedetomidine, the scientific conclusions of the CHMP are as follows:

In view of available data on diabetes insipidus from the literature, spontaneous reports including in several cases a close temporal relationship, a positive de-challenge and in view of a plausible mechanism of action, the PRAC considers a causal relationship between dexmedetomidine and diabetes insipidus is established. The PRAC concluded that the product information of products containing dexmedetomidine should be amended.

The CHMP agrees with the scientific conclusions made by the PRAC.

## **Grounds for the variation to the terms of the Marketing Authorisation(s)**

On the basis of the scientific conclusions for dexmedetomidine the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing dexmedetomidine is unchanged subject to the proposed changes to the product information.

The CHMP recommends that the terms of the marketing authorisation(s) should be varied.

## **Annex II**

**Amendments to the product information of the nationally authorised medicinal product(s)**

**Amendments to be included in the relevant sections of the Summary of Product Characteristics**  
(new text **underlined and in bold**, deleted text ~~strike through~~)

- Section 4.4

A warning should be added as follows:

**Diabetes insipidus has been reported in association with dexmedetomidine treatment. If polyuria occurs, it is recommended to stop dexmedetomidine and check serum sodium level and urine osmolality.**

- Section 4.8

The following adverse reaction should be added under the SOC Endocrine disorders with a frequency unknown:

**Diabetes insipidus.**

The following adverse reaction should be removed:

~~Polyuria.~~

**Amendments to be included in the relevant sections of the Package Leaflet** (new text **underlined and in bold**, deleted text ~~strike through~~)

- Section 2

Warnings and precautions

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**This medicine may cause large amount of urine and excessive thirst, contact a doctor if these side effects occur. See section 4 for more information.**

- Section 4

Not known (frequency cannot be estimated from the available data):

~~— increased need to pass urine.~~

- **large amount of urine and excessive thirst – may be symptoms of a hormonal disorder called diabetes insipidus. Contact a doctor if these occur.**