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 nalbuphine, the scientific conclusions are as follows:

In view of available data on risk of medication errors in paediatric population from the literature and spontaneous reports including cases of ten-fold overdose, the PRAC concluded that the comprehensibility of dosing instructions should be increased. The product information of products containing nalbuphine should be amended accordingly.

The CMDh 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 nalbuphine the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing nalbuphine is unchanged subject to the proposed changes to the product information.

The CMDh reaches the position that the marketing authorisation(s) of products in the scope of this single PSUR assessment should be varied. To the extent that additional medicinal products containing nalbuphine are currently authorised in the EU or are subject to future authorisation procedures in the EU, the CMDh recommends that the concerned Member States and applicant/marketing authorisation holders take due consideration of this CMDh position.

Annex II

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

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

Summary of Product Characteristics

- Section 4.2

A posology should be amended as follows:

Posology

Dosing is based on patient weight. Take care to avoid dosing errors due to confusion between milligram (mg) and millilitre (mL), which could result in accidental overdose (please see the dosing Table 1 (adult) or Table 2 (paediatric patients) below).

Adults

The recommended dose for adults is 10 – 20 mg nalbuphine hydrochloride for patients with 70 kg body weight, which is equivalent to 0.1 – 0.3 mg/kg body weight. The maximum single dose in adults must not exceed 20 mg.
The dose may be repeated after 3 to 6 hours, if necessary **with maximum total daily dose of 160 mg**.
The posology must be adapted to the intensity of pain and the physical status of the patient.

Table 1: Dosing table for adult patients:

Dose per administration	Maximum Single Dose	Maximum Volume per administration	Maximum Daily Dose	Maximum Volume of Daily Dose
0.1 – 0.3 mg/kg	20 mg	2 mL	160 mg	16 mL

Paediatric population

The recommended dose for children is 0.1 – 0.2 mg/kg body weight. The single maximum dose is 0.2 mg nalbuphine hydrochloride per kilogram body weight.
The dose may be repeated after 3 to 6 hours, if necessary **with maximum total daily dose of 1.6 mg/kg.**

Table 2: Dosing table for paediatric patients:

Dose per administration	Maximum Single Dose	Maximum Volume per administration	Maximum Daily Dose	Maximum Volume of Daily Dose
0.1 – 0.2 mg/kg	0.2 mg/kg	0.02 mL/kg	1.6 mg/kg*	0.16 mL/kg*

*** This dose was calculated based on approved dosing interval. For products recommending repeating of doses after 4 to 6 hours the maximum daily dose is 1.2 mg/kg and maximum volume 0.12 ml/kg.**

There are no adequate data for the treatment of children younger than 1.5 years.

Package Leaflet

Section 3

3. How to take nalbuphine

Nalbuphine will be given to you by a healthcare professional.

The dose you receive is based on your body weight.

Adults

The recommended dose for adults is 10 – 20 mg nalbuphine hydrochloride for patients with 70 kg body weight, which is equivalent to 0.1 – 0.3 mg/kg body weight. The maximum single dose in adults must not exceed 20 mg.
The dose may be repeated after 3 to 6 hours, if necessary **with maximum total daily dose of 160 mg.**
The posology must be adapted to the intensity of pain and the physical status of the patient.

Paediatric population

The recommended dose for children is 0.1 – 0.2 mg/kg body weight. The single maximum dose is 0.2 mg nalbuphine hydrochloride per kilogram body weight.
The dose may be repeated after 3 to 6 hours, if necessary **with maximum total daily dose of 1.6 mg/kg.**

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	January 2024 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	10/03/2024
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	09/05/2024