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 levosalbutamol, salbutamol, the scientific conclusions are as follows:

In view of available data published in the scientific literature from clinical trials and large population-based observational studies, and in view of a plausible mechanism of action, the PRAC considers that overuse of salbutamol-containing reliever medication is significant, and associated with deteriorating asthma control and the risk of life-threatening asthma exacerbations. Furthermore, providing asthma patients solely with salbutamol-containing reliever medication leaves the underlying inflammatory condition untreated and exposes patients to salbutamol overuse with its untoward consequences. Risks of salbutamol overuse should be re-emphasized for patients and healthcare professionals to suppress salbutamol monotherapy in intermittent/apparently mild asthma.

The PRAC concluded that the product information of products containing salbutamol in inhalational dosage forms indicated for asthma reliever therapy 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 levosalbutamol, salbutamol the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing levosalbutamol, salbutamol 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 levosalbutamol, salbutamol 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~~)>

- Section 4.4

Patients who are prescribed regular anti-inflammatory therapy (*e.g.,* inhaled corticosteroids) should be advised to continue taking their anti-inflammatory medication even when symptoms decrease, and they do not require <invented name>.

Increasing use of short-acting bronchodilators, in particular beta-2 agonists to relieve symptoms indicates deterioration of asthma control**, and patients should be warned to seek medical advice as soon as possible**. Under these conditions, the patient's therapy plan should be reassessed.

Overuse of short-acting beta-agonists may mask the progression of the underlying disease and contribute to deteriorating asthma control, leading to an increased risk of severe asthma exacerbations and mortality.

Patients who take more than twice a week "as needed" salbutamol, not counting prophylactic use prior to exercise, should be re-evaluated (*i.e.,* daytime symptoms, night-time awakening, and activity limitation due to asthma) for proper treatment adjustment as these patients are at risk for overuse of salbutamol.

Package Leaflet

Section 3: How to use <invented name>

<Invented name> should be used as required rather than regularly.

If your asthma is active (for example you have frequent symptoms or flare ups, **such as breathlessness that makes speaking, eating or sleeping difficult, cough, wheezing, tight chest** or limited physical ability), you should tell your doctor **right away** who may start or increase a medicine to control your asthma such as an inhaled corticosteroid.

~~If your inhaler fails to give relief for at least 3 hours, check with your doctor.~~

Tell your doctor **as soon as possible** if your medicine does not seem to be working as well as usual **(for example you need higher doses to relieve your breathing problems or your inhaler fails to give relief for at least 3 hours)** as your asthma may be getting worse and you may need a different medicine.

If you use <invented name> more than twice a week to treat your asthma symptoms, not including preventive use before exercise, this indicates poorly controlled asthma and may increase the risk of severe asthma attacks (worsening of asthma) that can have serious complications and may be life-threatening or even fatal. You should contact your doctor as soon as possible to review your asthma treatment.

If you use a medicine against inflammation of your lungs daily, *e.g.,* "inhaled corticosteroid", it is important to continue using it regularly, even if you feel better.

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	October 2023 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	27 November 2023
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	25 January 2024