

**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 levothyroxine, the scientific conclusions are as follows:

Based on a number of reported cases of circulatory collapse in very low birth weight preterm neonates from spontaneous reports and from the literature during the PSUR reporting period, the PRAC considers that a warning regarding circulatory collapse should be added in order to prevent the occurrence of circulatory collapse in this paediatric population due to immature adrenal function. Indeed, hypothyroidism often masks adrenal insufficiency and levothyroxine is therefore well known to reveal adrenal insufficiency.

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 levothyroxine the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing levothyroxine 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 levothyroxine 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 4.4

A warning should be added as follows:

**Haemodynamic parameters should be monitored when levothyroxine therapy is initiated in very low birth weight preterm neonates as circulatory collapse may occur due to the immature adrenal function.**

## Package Leaflet

Section 2

**Blood pressure will be regularly monitored when levothyroxine treatment is started in very low birth weight preterm neonates because rapid fall in blood pressure (known as circulatory collapse) may occur.**

**Annex III**

**Timetable for the implementation of this position**

### Timetable for the implementation of this position

Adoption of CMDh position:	October 2019 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	01/12/2019
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	30/01/2020