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 oxcarbazepine, the scientific conclusions are as follows:

In view of available data on **breastfeeding** from the literature, the Lead Member State (LMS) considered that a revised wording for oxcarbazepine and breastfeeding would be appropriate. The PRAC concluded that the product information of products containing oxcarbazepine should be amended accordingly.

In view of available data on **neurodevelopmental disorders** from the literature, the Lead Member State (LMS) considered that a causal relationship between oxcarbazepine and neurodevelopmental disorders is possible but is not clearly established. The PRAC concluded that the product information of products containing oxcarbazepine should be amended accordingly.

In view of available data on **congenital malformations** from the literature the Lead Member State considered a causal relationship between oxcarbazepine and congenital malformations is possible but is not clearly established. The PRAC concluded that the information regarding oxcarbazepine and congenital malformations is covered sufficiently in the SmPC; however this information should also be reflected in the Package Leaflet.

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 oxcarbazepine the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing oxcarbazepine 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 oxcarbazepine 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 4.6

The information regarding neurodevelopmental disorders should be added as follows:

Pregnancy
[..]
Risk related to oxcarbazepine
There is moderate amount of data on pregnant women (300-1000 pregnancy outcomes). However, the data on oxcarbazepine associated with congenital malformation is limited. There is no increase in the total rate of malformations with [product name] as compared with the rate observed with general population (2-3%). Nevertheless, with this amount of data, a moderate teratogenic risk cannot be completely excluded. **Study results related to the risk of neurodevelopmental disorders in children exposed to oxcarbazepine during pregnancy are conflicting and a risk cannot be excluded.**
[…]

The information regarding breastfeeding should be amended as follows:

Breastfeeding

Oxcarbazepine and its active metabolite (MHD) are excreted in human breast milk. ~~A milk-to-plasma concentration ratio of 0.5 was found for both. The effects on the infant exposed to [product name] by this route are not known. Therefore, [product name] should not be used during breast-feeding.~~ **Limited data indicate that the breastfed infants´MHD plasma concentrations are 0.2-0.8 µg/ml, corresponding to up to 5% of the maternal MHD plasma concentration. Although exposure appears to be low, a risk to the infant cannot be excluded. Therefore, a decision whether to breastfeed while using [product name] should take into consideration both the benefit of breastfeeding and the potential risk of side effects in the infant. If breastfed, the infant should be monitored for adverse effects such as drowsiness and poor weight gain.**

Package Leaflet

- 2. What you need to know before you take [product name]

Pregnancy, breast-feeding and fertility

Pregnancy

If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

It is important to control epileptic seizures during pregnancy. However, there may be a risk to your baby if you take antiepileptic medicines during pregnancy.

Birth defects

Studies have not shown an increased risk of birth defects associated with oxcarbazepine use during pregnancy, however, a risk of birth defects for your unborn child cannot be completely ruled out.

Neurodevelopmental disorders

Some studies have shown that exposure to oxcarbazepine in the womb negatively affects the development of brain function (neurodevelopment) in children, while other studies have not found such an effect. The possibility of an effect on neurodevelopment cannot be ruled out.

Your doctor will tell you the benefits and potential risks involved and help you to decide whether you should take [product name].

Do not stop your treatment with [product name] during pregnancy without first checking with your doctor.

Breastfeeding

~~You should not breast-feed while taking [product name].~~ **If you are taking this medicine, ask your doctor for advice before starting breastfeeding.** The active substance in [product name] passes into breast milk. **Although available data suggest that the amount of [product name] that passes to a breastfed baby is low, a risk of side effects for the baby cannot be ruled out.** ~~This could cause side effects for breast-fed babies. Ask your doctor or pharmacist for advice before taking this medicine while you are breast-feeding.~~ **Your doctor will discuss with you the benefits and potential risks of breastfeeding while taking [product name]. If you are breastfeeding while taking [product name] and you think your baby is having side effects such as excessive sleepiness or poor weight gain, tell your doctor immediately.**

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	April 2022 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	6 June 2022
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	5 August 2022