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 omega-3-acid ethyl esters, the scientific conclusions are as follows:

In view of available data on risk of Atrial fibrillation from clinical trials, the literature and spontaneous reports, the PRAC considers a causal relationship between omega-3-acid ethyl esters and atrial fibrillation is at least a reasonable possibility. The PRAC concluded that the product information of products containing omega-3-acid ethyl esters should be amended accordingly.

Following the adoption of the PRAC recommendation:

- The MAH BASF did not fully agree with the adopted PRAC recommendation and submitted further information in writing and at an Oral explanation to CMDh to support their objection to the calculation of the frequency of atrial fibrillation as "common" based on the meta-analysis of randomised clinical trials, the need to communicate by means of a DHPC and the PSUR frequency change from 3 years to 1 year.
- The MAH SPA provided written observations objecting to the calculation of the frequency of atrial fibrillation as 'common' based on meta-analysis of randomised clinical trials.

Having reviewed the PRAC recommendation, the information provided by the MAH BASF in writing and at an oral explanation and the written observations provided by the MAH SPA following the adoption of the PRAC recommendation, the CMDh agrees with the PRAC overall conclusions and grounds for recommendation.

Grounds for the variation to the terms of the marketing authorisation(s)

On the basis of the scientific conclusions for omega-3-acid ethyl esters, the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing omega-3-acid ethyl esters is unchanged subject to the proposed changes to the product information.

The CMDh 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 Product Information (new text **underlined and in bold**, deleted text ~~strike through~~)

Summary of Product Characteristics

- Section 4.4

Systematic reviews and meta-analyses of randomized controlled clinical trials highlighted a dose-dependent increased risk of atrial fibrillation in patients with established cardiovascular diseases or cardiovascular risk factors treated with omega-3-acid ethyl esters compared to placebo. The observed risk is highest with a dose of 4 g/daily (see section 4.8). If atrial fibrillation develops, treatment should be permanently discontinued.

- Section 4.8

The following adverse reaction should be added under the SOC Cardiac disorders with a frequency
common
Atrial fibrillation

Package Leaflet

2. Warnings and precautions
Talk to your doctor or pharmacist if:
- you have, or have had, heart problems
- you develop light-headedness, asthenia (feeling of weakness), palpitations or shortness of breath as these may be symptoms of an irregular and often very rapid heart rhythm (atrial fibrillation).

4. Possible side effects
Common (may affect up to 1 in 10 people)
- Irregular, rapid rhythm of the heart

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:	25 November 2023
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	24 January 2024