**<Type II> <group of> variation<s>**

**Preliminary Variation Assessment Report**

**<Invented Name>**

**<(Active Substance)>**

**<AB/H/****{nnnn}/II/****{nnn}>**

**<AB/H/{nnnn}/II/{nnn}/G>**

**<AB/H/xxxx/WS/{nnn}>**

**Marketing Authorisation Holder:**

**Date:**

|  |  |
| --- | --- |
| Deadline for Comments by CMS |  |

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**ADMINISTRATIVE INFORMATION**

|  |  |
| --- | --- |
| Name of the medicinal product(s) in the RMS |  |
| Name of the active substance (INN, common name): |  |
| Pharmaco-therapeutic group (ATC code) |  |
| Pharmaceutical form(s) and strength(s) |  |

|  |  |  |
| --- | --- | --- |
| Procedure number |  | |
| Member States concerned |  |

|  |  |
| --- | --- |
| RMS contact person | **Name:**  Tel:  Email: |
| Names of the assessors | **Quality:**  **Name(s):**  Tel:  Email:  **Nonclinical:**  **Name(s):**  Tel:  Email:  **Clinical:**  **Name(s):**  Tel:  Email:  **Pharmacovigilance:**  **Name**  Tel:  Email |

|  |  |
| --- | --- |
| Nature of change/s requested |  |

|  |  |
| --- | --- |
| Active Substance Master File (ASMF) Assessment Report/s  <Active substance> - <ASM> - <ASMF reference number> <ASMF holder’s version> | <Attached as separate document/s <including confidential Annex 1>> <N/A> |

# Recommendation

Based on the review of the data on ,  , the RMS considers that the <group of> variation<s>< following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008> for <medicinal product invented name> (<INN>), in the treatment of <indication>, for the following proposed changes <scope of variation>

<is approvable. >

<is not approvable unless the MAH can provide satisfactory responses to the <X> request for supplementary information. The details of these/this objections/request for supplementary information are provided in section V.>

<is not approvable since major objections (see section V.1) have been identified which preclude a recommendation for such variation and recommend that the variation to the terms of the Marketing Authorisation should be refused.>

*<The section below should only be filled out in case of variation(s) with impact on the conditions to the Marketing Authorisation>*

Conditions to Marketing Authorisation pursuant to Article 21a, 22 or 22a of Directive 2001/83/EC

*Please choose one of the following options and delete the ones not applicable*

For the condition(s)/ to the Marketing Authorisation that have been lifted as a result of the variation assessment, see section IV.

For the previously agreed condition(s) to the Marketing Authorisation that remain(s) valid and is/are still outstanding, see section IV.

For the **new condition(s)** to the Marketing Authorisation that has/have been agreed as a result of the variation assessment, see section IV.

# Executive Summary

## Scope of the variation

<Text>

# Scientific discussion

|  |
| --- |
| This discussion should clearly provide the scientific rationale for the recommendation and for the objections and concerns/request for supplementary information listed in section V.  In case the ASMF procedure is used to introduce a new source for the AS (initial submission of an ASMF in a MAV application), Letter/s of Access in relation to drug product/s should be described. |

## <Quality aspects>

<Text> <N/A>

**III.1.1 <Active substance (related to additional data provided by applicant only)>**

<Text> <N/A>

|  |
| --- |
| It should be mentioned whether a CEP or ASMF procedure or full information in the dossier of the AS is used.  In case the ASMF procedure is used it should be mentioned that the assessment of the Active Substance Master File (ASMF) is provided in a separate ASMF Assessment Report with a confidential annex on the Restricted Part.  When variation concerns more than one ASMF, a separate report is provided for each ASMF.  Where ASMF or CEP is applicable, clarify the source (applicant or ASMF holder or CEP holder) and level of details to be drafted in the assessment report.  The assessment of the drug substance in this VAR should only address additional information provided by the applicant, which is not included in the ASMF. In case a full Module 3.2.S for the Active Substance is provided by the applicant, assessment of the active substance should be included in the PVAR. |

**III.1.2 <Medicinal product>**

<Text> <N/A

## <Non clinical aspects>

<Text> <N/A>

Methods

Results

## < Clinical aspects>

<Text> <N/A>

### <III.3.1 Clinical pharmacology>

<Text> <N/A>

### <III.3.2 Clinical efficacy>

<Text below relevant subheadings as detailed below> <N/A>

Main study(ies)

Methods

Results

Clinical studies in special populations

Analysis performed across trials (pooled analyses and meta-analysis)

Supportive study(ies)

### <III.3.3 Clinical safety>

<Text below relevant subheadings as detailed below> <N/A>

Patient exposure

Adverse events

Serious adverse events and deaths

Laboratory findings

Safety in special populations

### <III.3.4 RMP>

<Text> <N/A>

The following introductory statement can be included

<The MAH has submitted a risk management plan/ an updated risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to (*insert name of medicinal product*).”>

Any update to RMP should be described.

Safety specification

[Insert summary table of proposed safety concerns (RMP Part II: Module SVIII)].

Pharmacovigilance Plan

<[Insert summary of the pharmacovigilance plan (RMP Part III.5)]

*OR*

<Routine pharmacovigilance is suggested and no additional pharmacovigilance activities are proposed by the applicant, which is endorsed.>

Risk minimisation measures

<[Insert summary table of proposed risk minimisation measures (RMP Part V.3].>

*OR*

<Routine risk minimisation is suggested and no additional risk minimisation activities are proposed by the applicant, which is endorsed.>

Summary of the RMP

*In this paragraph the RMS should summarise the conclusion on the assessment of the RMP.*

*The following statements can be used:*

<The submitted Risk Management Plan, version <XX> signed <date> is considered acceptable.> <The submitted Risk Management Plan, version <XX> signed <date> is not considered acceptable. See List of Questions for further details.>

## <Product information>

<Text> <N/A>

<Harmonisation of PL and labelling is included as part of this procedure.>

<PL and labelling are harmonised for this product.>

### <III.4.1 Summary of Product Characteristics>

### <III.4.2 Package leaflet and user test>

### <III.4.3 Labelling>

# OVERALL CONCLUSION <AND Benefit-risk assessment>

Please also indicate

- if existing conditions to the Marketing authorisation pursuant to Article 21a, 22 or 22a of Directive 2001/83/EC remain valid or can be lifted,

-if new conditions to the Marketing authorisation pursuant to Article 21a, 22 or 22a of Directive 2001/83/EC should be imposed,

or that no conditions to the Marketing authorisation are applicable.

Please also provide a justification, by e.g. referring to other parts of the PVAR.

# Request for supplementary information as proposed by the RMS

|  |
| --- |
| Questions must be divided into ‘major objections’ and/or ‘other concerns’, which are defined as follow:  ‘Major objections’ preclude a recommendation to the variation to the term of the marketing authorisation. In principle, one ‘major objection’ may entail more than one question and the use of bullet points or subheadings is encouraged. It is vital that the structure and content of the objection are clear and understandable to the reader. Detailed comments may be necessary along with a reference to guidance documents  Ideally, the objection should include a clarification as to what kind of response/action by the MAH could be considered to solve the problem.  ‘Other concerns’, may affect the proposed conditions to the variation to the terms of the marketing authorisation and product information. |

## V.1 < Major objections>

<Text below relevant subheadings as detailed below> <N/A>

### <V.1.1 Quality aspects>

**<V.1.1.1. Active Substance (related to additional data provided by applicant only)>**

|  |
| --- |
| In case the ASMF procedure is used the following should be stated in case major objections are being raised on the restricted or applicant’s part of the ASMF:  *‘For major objections on the restricted or applicant’s part of the ASMF see separate AR on the ASMF’* |

<**V.1.1.2. Medicinal Product**>

**<V.1.2 Non clinical aspects>**

### <V.1.3 Clinical efficacy>

### <V.1.4 Clinical safety>

### <V.1.5 RMP>

### <V.1.6 Product information>

## V.2 < Other concerns>

<Text below relevant subheadings as detailed below> <N/A>

### <V.2.1 Quality aspects>

< **V.2.1.1 Active Substance (related to additional data provided by the applicant only)**>

|  |
| --- |
| In case the ASMF procedure is used the following should be stated in case other concerns are being raised on the restricted or applicant’s part of the ASMF:  *“For other concerns on the restricted or applicant’s part of the ASMF see separate AR on the ASMF”.* |

< **V.2.1.2 Medicinal Product**>

### <V.2.2 Non clinical aspects>

### <V.2.3 Clinical efficacy>

### <V.2.4 Clinical safety>

### <V.2.5 RMP>

### <V.2.6 Product information>

# <Annex: Proposed changes to the <SmPC>, <PL>, <Labelling> ANNOTATED with THE RMS’s comments AFTER EACH SECTION>