RISK MANAGEMENT PLAN
For
Amlodipine/Valsartan
Version 4.1

RMP Version to be Assessed as Part of this Application:

RMP Version Number	4.1
Data Lock Point for this RMP	31-Aug-2023
Date of Final Sign Off	20-Jun-2024
Rationale for Submitting an Updated RMP	• RMP updated in line with comments received in PRAC Rapporteur's preliminary assessment report for EMEA/H/C/004037/II/0021 dated 29-Apr-2024.
Summary of Significant Changes in this RMP	Version 4.0 of the RMP has been amended to Version 4.1 to delete the extra information about RMP version 3.0 from Part II.I SVII.1 and from Table 2 heading.

Other RMP Versions Under Evaluation:

RMP Version Number	4.0
Submitted On	28-Nov-2023
Procedure Number	EMEA/H/C/004037/II/0021

Details of the Current RMP:

Version Number	3.0
Approved with Procedure	EMEA/H/C004037
Date of Approval (Opinion Date)	22-Mar-2016

Approver	Dr Eiko Soehlke, MD MPH, EEA QPPV *The signatory is authorised by the Global Head PSRM and EEA-QPPV to sign this RMP*
Signature	RMP has been reviewed and approved by the marketing authorisation applicant's QPPV and that the electronic signature is on file.
E-mail address of contact person	PV.RMP@Viatris.com

[redacted]

Table of Contents

LIST OF TABLES

[redacted]

LIST OF ABBREVIATIONS

Abbreviation	Definition
ATC	Anatomical Therapeutic Chemical Classification System
CHMP	Committee for Medicinal Products for Human Use
EEA	European Economic Area
EMA	European Medical Agency
EPAR	European Public Assessment Report
EU	European Union
MAH	Marketing Authorization Holder
PL	Package Leaflet
QPPV	Qualified Person for Pharmacovigilance
MedDRA	Medical Dictionary for Regulatory Activities
RMP	Risk Management Plan
SmPC	Summary of Product Characteristics

PART I: PRODUCT(S) OVERVIEW

Table 1: Part 1.1-Product Overview

Active Substance(s) (INN or Common Name)	Amlodipine/Valsartan
Pharmacotherapeutic Group(s) (ATC Code)	Agents acting on the renin-angiotensin system; angiotensin II antagonists, combinations; angiotensin II antagonists and calcium channel blockers ATC code: C09DB01
Marketing Authorisation Holder	Mylan Pharmaceuticals Ltd
Medicinal Products to Which this RMP Refers	1
Invented Name(s) in the European Economic Area (EEA)	Amlodipine/Valsartan Mylan 5 mg/80 mg film-coated tablets Amlodipine/Valsartan Mylan 5 mg/160 mg film-coated tablets Amlodipine/Valsartan Mylan 10 mg/160 mg film-coated tablets
Marketing Authorisation Procedure	Centralised procedure
Brief Description of the Product	Agents acting on the renin-angiotensin system; angiotensin II antagonists, combinations; angiotensin II antagonists and calcium channel blockers. Amlodipine/Valsartan Mylan combines two antihypertensive compounds with complementary mechanisms to control blood pressure in patients with essential hypertension: amlodipine belongs to the calcium antagonist class and valsartan to the angiotensin II antagonist class of medicines. The combination of these substances has an additive antihypertensive effect, reducing blood pressure to a greater degree than either component alone. Amlodipine/Valsartan The combination of amlodipine and valsartan produces dose-related additive reduction in blood pressure across its therapeutic dose range. The antihypertensive effect of a single dose of the combination persisted for 24 hours.
Hyperlink to the Product Information:	PI available in section 1.3.1 of the dossier
Indication(s) in the EEA	Treatment of essential hypertension. Amlodipine/Valsartan Mylan is indicated in adults whose blood pressure is not adequately controlled on amlodipine or valsartan monotherapy.

Dosage in the EEA	The recommended dose of Amlodipine/Valsartan Mylan is one tablet per day. Amlodipine/Valsartan 5 mg/80 mg film-coated tablets Amlodipine/Valsartan 5 mg/80 mg may be administered in patients whose blood pressure is not adequately controlled with amlodipine 5 mg or valsartan 80 mg alone. Amlodipine/Valsartan 5 mg/160 mg film-coated tablets Amlodipine/Valsartan 5 mg/160 mg may be administered in patients whose blood pressure is not adequately controlled with amlodipine 5 mg or valsartan 160 mg alone. Amlodipine/Valsartan 10 mg/160 mg film-coated tablets Amlodipine/Valsartan 10 mg/160 mg may be administered in patients whose blood pressure is not adequately controlled with amlodipine 10 mg or valsartan 160 mg alone or with Amlodipine/Valsartan 5 mg/160 mg. Individual dose titration with the components (i.e. amlodipine and valsartan) is recommended before changing to the fixed dose combination. When clinically appropriate, direct change from monotherapy to the fixed dose combination may be considered. For convenience, patients receiving valsartan and amlodipine from separate tablets/capsules may be switched to Amlodipine/Valsartan Mylan containing the same component doses. <u>Method of administration</u> Oral use. It is recommended to take Amlodipine/Valsartan Mylan with some water. <u>Amlodipine/Valsartan Mylan can be used with or without food.</u>
Pharmaceutical Form(s) and Strengths	5 mg of amlodipine (as amlodipine besilate) and 80 mg of valsartan. 5 mg of amlodipine (as amlodipine besilate) and 160 mg of valsartan. 10 mg of amlodipine (as amlodipine besilate) and 160 mg of valsartan.
Is the Product Subject to Additional Monitoring in the EU?	No

PART II: SAFETY SPECIFICATION

Part II: Module SI - Epidemiology of the Indication(s) and Target Population(s)

Not applicable.

Part II: Module SII - Non-clinical Part of the Safety Specification

Not applicable.

Part II: Module SIII - Clinical Trial Exposure

Not applicable.

Part II: Module SIV - Populations Not Studied in Clinical Trials

Not applicable.

Part II: Module SV - Post-authorisation Experience

Not applicable.

Part II: Module SVI - Additional EU Requirements for the Safety Specification

Not applicable.

Part II: Module SVII - Identified and Potential Risks

SVII.1 Identification of Safety Concerns in the Initial RMP Submission

Not applicable.

SVII.1.1. Risks Not Considered Important for Inclusion in the List of Safety Concerns in the RMP

Not applicable.

SVII.1.2. Risks Considered Important for Inclusion in the List of Safety Concerns in the RMP

Not applicable.

SVII.2 New Safety Concerns and Reclassification with a Submission of an Updated RMP

The list of safety concerns has been revised as recommended in GVP V R2 and the MAH is proposing to align it with the safety concerns in for Amlodipine/Valsartan published on CMDh website (Amlodipine/Valsartan KRKA Pharma HU/H/0405/001-005/R/001C, Version 2.2 dated 20-Nov-2020).

SVII.3 Details of Important Identified Risks, Important Potential Risks, and Missing Information

[redacted]

SVII.3.1. Presentation of Important Identified Risks and Important Potential Risks

Not applicable as this RMP for amlodipine/valsartan follows the same safety concerns as the safety concerns of the RMP published on CMDh website.

SVII.3.2. Presentation of the Missing Information

Not applicable as this RMP for amlodipine/valsartan follows the same safety concerns as the safety concerns of the RMP published on CMDh website.

Part II: Module SVIII - Summary of the Safety Concerns

As there is no RMP available for the originator product, the MAH assessed the list of safety concerns for amlodipine/valsartan published on the CMDh website. The RMP with the most recent version number and date (Amlodipin/Valsartan KRKA Pharma, procedure HU/H/0405/001-005/R/001C, legal basis 10(1), Version 2.2 dated 20-Nov-2020) was considered to have the most up to date understanding of the current safety profile of the product and was therefore selected as source for the safety concerns in the updated MAH's RMP. The summary of safety concerns is described in Table 2 below:

Table 2: SVIII- Summary of safety concerns

Important Identified Risks	• None.
Important Potential Risks	• None.
Missing Information	• None.

PART III: PHARMACOVILIGANCE PLAN

The Pharmacovigilance System Master File contains details of the system and processes that the MAH has in place to identify and characterize the risks recognised in the safety specification.

III.1 Routine Pharmacovigilance Activities

Routine pharmacovigilance activities only.

III.2 Additional Pharmacovigilance Activities

As current routine pharmacovigilance activities are sufficient, no additional pharmacovigilance activities are recommended.

III.3 Summary Table of Additional Pharmacovigilance Activities

None.

PART IV: PLANS FOR POST-AUTHORISATION EFFICACY STUDIES

Not applicable.

PART V: RISK MINIMISATION MEASURES

Risk Minimisation Plan

The safety information in the proposed product information is aligned to the reference medicinal product (Exforge, by Novartis Europharm Limited).

V.1 Routine Risk Minimisation Measures

Not applicable

V.2 Additional Risk Minimisation Measures

Not applicable.

V.3 Summary Table of Pharmacovigilance and Risk Minimisation Activities by Safety Concern

Not applicable.

PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN

Summary of Risk Management Plan for Amlodipine/Valsartan Mylan 5 mg/80 mg, 5 mg/160 mg and 10 mg/160 mg film-coated tablets (amlodipine/valsartan)

This is a summary of the risk management plan (RMP) for Amlodipine/Valsartan Mylan 5 mg/80 mg, 5 mg/160 mg and 10 mg/160 mg film-coated tablets. The RMP details important risks of amlodipine/valsartan, how these risks can be minimised, and how more information will be obtained about amlodipine/valsartan 's risks and uncertainties (missing information).

Amlodipine/Valsartan Mylan 5 mg/80 mg, 5 mg/160 mg and 10 mg/160 mg film-coated tablets 's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how it should be used.

This summary of the RMP for Amlodipine/Valsartan Mylan 5 mg/80 mg, 5 mg/160 mg and 10 mg/160 mg film-coated tablets should be read in the context of all the information including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current ones will be included in updates of Amlodipine/Valsartan Mylan 5 mg/80 mg, 5 mg/160 mg and 10 mg/160 mg film-coated tablets's RMP.

I. The Medicine and What it is Used For

Amlodipine/Valsartan Mylan 5 mg/80 mg, 5 mg/160 mg and 10 mg/160 mg film-coated tablets is authorised for treatment of essential hypertension. Amlodipine/Valsartan Mylan is indicated in adults whose blood pressure is not adequately controlled on amlodipine or valsartan monotherapy. It contains amlodipine/valsartan as the active substance, and it is given by oral route.

Further information about the evaluation of Amlodipine/Valsartan Mylan 5 mg/80 mg, 5 mg/160 mg and 10 mg/160 mg film-coated tablets's benefits can be found in Amlodipine/Valsartan Mylan 5 mg/80 mg, 5 mg/160 mg and 10 mg/160 mg film-coated tablets's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage.

II. Risks Associated with the Medicine and Activities to Minimise or Further Characterise the Risks

Important risks of 5 mg of Amlodipine/Valsartan Mylan 5 mg/80 mg, 5 mg/160 mg and 10 mg/160 mg film-coated tablets, together with measures to minimise such risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific Information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the public (e.g. with or without prescription) can help to minimises its risks.

[redacted]

Together, these measures constitute routine risk minimisation measures.

In addition to these measures, information about adverse events is collected continuously and regularly analysed, so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

If important information that may affect the safe use of Amlodipine/Valsartan Mylan 5 mg/80 mg, 5 mg/160 mg and 10 mg/160 mg film-coated tablets is not yet available, it is listed under 'missing information' below.

II.A List of Important Risks and Missing Information

Important risks of Amlodipine/Valsartan Mylan 5 mg/80 mg, 5 mg/160 mg and 10 mg/160 mg film-coated tablets are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken by patients. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Amlodipine/Valsartan Mylan 5 mg/80 mg, 5 mg/160 mg and 10 mg/160 mg film-coated tablets. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g., on the long-term use of the medicine/use in special patient populations etc.).

Table 3: Part VI.1- Summary of safety concerns

List of Important Risks and Missing Information	
Important Identified Risks	None.
Important Potential Risks	None.
Missing Information	None.

II.B Summary of Important Risks

The safety information in the proposed Product Information is aligned to the reference medicinal product.

II.C Post-Authorisation Development Plan

II.C.1 Studies Which are Conditions of the Marketing Authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of Amlodipine/Valsartan Mylan 5 mg/80 mg, 5 mg/160 mg and 10 mg/160 mg film-coated tablets.

II.C.2 Other Studies in Post-Authorisation Development Plan

There are no studies required for Amlodipine/Valsartan Mylan 5 mg/80 mg, 5 mg/160 mg and 10 mg/160 mg film-coated tablets.

Annex 4 - Specific Adverse Drug Reaction Follow-up Forms

Not applicable.

Annex 6 - Details of Proposed Additional Risk Minimisation Activities (If Applicable)

Not applicable.