Medicines & Healthcare products Regulatory Agency

MHRA

Public Assessment Report

National Procedure

Amlodipine 5 mg Tablets
Amlodipine 10 mg Tablets

(amlodipine besilate)

PL 36687/0234-0235

Torrent Pharma UK Limited

LAY SUMMARY

Amlodipine 5 mg Tablets
Amlodipine 10 mg Tablets
(amlodipine besilate)

This is a summary of the Public Assessment Report (PAR) for Amlodipine 5 mg and 10 mg Tablets. It explains how these products were assessed and their authorisation recommended, as well as their conditions of use. It is not intended to provide practical advice on how to use these products.

These products will be referred to as Amlodipine tablets in this lay summary for ease of reading.

For practical information about using Amlodipine tablets, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

What are Amlodipine tablets and what are they used for?
These applications are the same as Amlodipine 5 mg and 10 mg Tablets (PL 33410/0044-0045), which are already authorised.

The Company responsible for Amlodipine 5 mg and 10 mg Tablets has agreed that its scientific data can be used as the basis for the grant of identical licences for Amlodipine tablets.

Amlodipine tablets are used in the treatment of:
- high blood pressure (hypertension)
- angina (severe pain in the chest) including Printzmetal's (or variant) angina.

Amlodipine tablets do not provide immediate relief of chest pain from angina.

How do Amlodipine tablets work?
Amlodipine tablets contain the active ingredient amlodipine (as amlodipine besilate). Amlodipine belongs to a group of medicines called calcium antagonists.

In patients with high blood pressure amlodipine works by relaxing blood vessels, so that blood passes through them more easily. In patients with angina, amlodipine works by improving blood supply to the heart muscle, which then receives more oxygen and, as a result, chest pain is prevented.

How are Amlodipine tablets used?
The pharmaceutical form of these medicines is tablets and the route of administration is oral (taken by mouth).
The recommended initial dose is 5 mg once daily. The dose can be increased to 10 mg once daily.

Amlodipine tablets can be used before or after food or drinks. The patient should take these medicines at the same time each day with a drink of water. The patient should not take Amlodipine tablets with grapefruit juice.

Use in children and adolescents
For children and adolescents (6 – 17 years old), the recommended usual starting dose is 2.5 mg a day. The maximum recommended dose is 5 mg a day.

It is important that the patient keeps taking the tablets. The patient should not wait until their tablets are finished before seeing their doctor.

For further information on how Amlodipine tablets are used, refer to the PIL and Summaries of Product Characteristics (SmPCs) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

These medicines can only be obtained with a prescription.

The patient should always take the medicines exactly as their doctor/pharmacist has told them. The patient should check with their doctor or pharmacist if they are not sure.

What benefits of Amlodipine Tablets have been shown in studies?
Amlodipine tablets are considered identical to the previously authorised products with the same benefits and risks. No new studies have been provided for Amlodipine tablets, however, reference is made to the studies for Amlodipine 5 mg and 10 mg Tablets.

What are the possible side effects of Amlodipine Tablets?
For the full list of all side effects reported with these medicines, see Section 4 of the PIL or the SmPCs available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on behalf of someone else they care for, directly via the Yellow Card scheme at www.mhra.gov.uk/yellowcard or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

Amlodipine tablets are considered to be identical to the previously authorised products with the same benefits and risks.

Why were Amlodipine Tablets approved?
The MHRA decided that the benefits of Amlodipine tablets are greater than the risks and recommended that medicines are approved for use.

What measures are being taken to ensure the safe and effective use of Amlodipine tablets?
A Risk Management Plan (RMP) has been developed to ensure that Amlodipine tablets are used as safely as possible. Based on this plan, safety information has been included in the SmPCs and the PIL, including the appropriate precautions to be followed by healthcare professionals and patients.

Known side effects are continuously monitored. Furthermore, new safety signals reported by patients/healthcare professionals will be monitored and reviewed continuously.
Other information about Amlodipine tablets
Marketing Authorisations were granted in the United Kingdom (UK) to Aptil Pharma Limited on 15 November 2012. Subsequent to Change of Ownership procedures, the Marketing Authorisations were transferred to the current Marketing Authorisation Holder (MAH) Torrent Pharma UK Limited (PL 36687/0234-0235) on 01 February 2019.

The full PAR for Amlodipine tablets follows this summary.

This summary was last updated in November 2021.

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I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the applications for Amlodipine 5 mg and 10 mg Tablets (PL 36687/0234-0235; formerly PL 40378/0121-0122) could be approved.

The products are approved for the following indications:

- Hypertension
- Chronic stable angina pectoris
- Vasospastic (Prinzmetal's) angina

The active substance, amlodipine (as amlodipine besilate) is a calcium ion influx inhibitor of the dihydropyridine group (slow channel blocker or calcium ion antagonist) and inhibits the transmembrane influx of calcium ions into cardiac and vascular smooth muscle.

The mechanism of the antihypertensive action of amlodipine is due to a direct relaxant effect on vascular smooth muscle. The precise mechanism by which amlodipine relieves angina has not been fully determined but amlodipine reduces total ischaemic burden by the following two actions:

- amlodipine dilates peripheral arterioles and thus, reduces the total peripheral resistance (afterload) against which the heart works. Since the heart rate remains stable, this unloading of the heart reduces myocardial energy consumption and oxygen requirements.
- the mechanism of action of amlodipine also probably involves dilatation of the main coronary arteries and coronary arterioles, both in normal and ischaemic regions. This dilatation increases myocardial oxygen delivery in patients with coronary artery spasm (Prinzmetal's or variant angina).

These are national abridged applications approved under Article 10c of Directive 2001/83/EC, as amended (equivalent to Regulation 56 of The Human Medicines Regulation 2012, as amended) as informed consent applications. The applications cross-refer to the reference products Amlodipine 5 mg and 10 mg Tablets (PL 33410/0044-0045), which were originally granted in the UK to the Marketing Authorisation Holder Apsla Limited on 05 January 2011.

No new non-clinical or clinical data have been supplied and none are required for these informed consent applications.

Suitable justification has been provided for non-submission of an Environmental Risk Assessment (ERA). As the applications are for identical versions of already authorised products, no increase in environmental exposure is anticipated and no ERA is required.

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for these products at all sites responsible for the manufacture, assembly and batch release of these products.

The Marketing Authorisation Holder has provided details of a suitable pharmacovigilance system that fulfils the requirements and provides adequate evidence that the Marketing Authorisation Holder has the services of a qualified person responsible for pharmacovigilance and has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

Suitable justification has been provided for not submitting a Risk Management Plan for these products.

Marketing Authorisations were granted in the United Kingdom (UK) to Aptil Pharma Limited on 15 November 2012. Subsequent to Change of Ownership procedures, the Marketing Authorisations were transferred to the current Marketing Authorisation Holder (MAH) Torrent Pharma UK Limited (PL 36687/0234-0235) on 01 February 2019.

II. EXPERT REPORT

The applicant cross-refers to the data for Amlodipine 5 mg and 10 mg Tablets (PL 3410/0044-0045; Apsla Limited), to which these applications are claimed to be identical. This is acceptable.

III. ASSESSOR'S COMMENTS ON THE PRODUCT INFORMATION SUMMARY OF PRODUCT CHARACTERITICS (SmPC)

The SmPCs are in line with those for Amlodipine 5 mg and 10 mg Tablets (PL 33410/0044-0045).

PATIENT INFORMATION LEAFLET

A leaflet text has been provided which has been aligned with that for PL 33410/0044-0045). The user test report submitted for PL 33410/0044-0045 has been provided.

LABEL

Label text have been provided.

IV. QUALITY ASPECTS

IV.1 Drug Substance

Drug substance specifications

The sources of the active substance are in line with the cross-reference products. The proposed drug substance specification is consistent with the details registered for the cross-reference products.

IV.2. Drug Product

Name

The product has been named in line with current requirements.

Strength, pharmaceutical form, route of administration, container and pack sizes

Amlodipine 5 mg and 10 mg Tablets are available in clear polyvinylchloride (PVC)/aluminium blisters in pack sizes of 28 tablets.

The appearance of the products is identical to that of the cross-reference products).

The proposed shelf life of the product is 3 years with the recommended storage conditions 'Store below 30°C. Keep the blister in the outer carton in order to protect from light).'

The proposed packaging, shelf life and storage conditions are consistent with the details registered for the reference product.

Legal status

Prescription only medicine (POM)

Manufacturers

The proposed manufacturing sites are consistent with the details registered for the cross-reference products and evidence of Good Manufacturing Practice (GMP) compliance has been provided.

Qualitative and quantitative compositions
The composition of the proposed products is consistent with the details registered for the cross-reference products.

Manufacturing process & control of critical steps
The proposed manufacturing processes and process controls are consistent with the details registered for the reference products and the maximum batch size is stated.

Finished product release/shelf life specifications
The finished product specifications at release and shelf-life are in line with the details registered for the cross-reference products.

TSE Compliance
With the exception of magnesium stearate, no excipients of animal or human origin are used in the final products. The supplier of magnesium stearate has provided a Certificates of Suitability from the European Directorate for the Quality of Medicines (EDQM) to show that it is manufactured in line with current European guidelines concerning the minimising of risk of transmission of Bovine Spongiform Encephalopathy/Transmissible Spongiform Encephalopathies (BSE/TSE).

These products do not contain or consist of genetically modified organisms (GMO).

NON-CLINICAL ASPECTS
As these applications are submitted under Article 10(c) of Directive 2001/83/EC, as amended (equivalent to Regulation 56 of The Human Medicines Regulations 2012, as amended), (as informed consent applications) no new non-clinical data have been supplied and none are required.

V. CLINICAL ASPECTS
As these applications are submitted under Article 10(c) of Directive 2001/83/EC, as amended (equivalent to Regulation 56 of The Human Medicines Regulations 2012, as amended), (as informed consent applications) no new clinical data have been supplied and none are required.

VI. RISK MANAGEMENT PLAN (RMP)
The Marketing Authorisation Holder has provided details of a suitable pharmacovigilance system that fulfils the requirements and provides adequate evidence that the Marketing Authorisation Holder has the services of a qualified person responsible for pharmacovigilance and has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

Suitable justification has been provided for not submitting a Risk Management Plan for these products.

VII. USER CONSULTATION
A full colour mock-up of the Patient Information Leaflet (PIL) has been provided with the application, in accordance with legal requirements.

The PIL has been evaluated via a user consultation study in accordance with legal requirements. The results show that the PIL meets the criteria for readability as set out in the guideline on the readability of the label and package leaflet of medicinal products for human use.

VIII. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION

The quality of the products is acceptable, and no new non-clinical or clinical safety concerns have been identified. The applicant's products are identical to the cross-reference products. The benefit/risk balance is, therefore, considered to be the same as for the cross-reference products and positive.

The SmPCs, PIL and labelling are satisfactory, in line with current guidelines and consistent with the cross reference products.

In accordance with legal requirements, the current approved UK versions of the SmPCs and PIL for these products are available on the MHRA website.

The following text is that approved at the time of licensing of Amlodipine 5 mg and 10 mg Tablets (PL 36687/0234-0235); no label mock-ups were provided for these products at the time. In accordance with legal requirements, these products shall not be marketed until approval of the full-colour label mock-ups has been obtained.

Amlodipine 5 mg Tablets

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Amlodipine 5 mg Tablets
Amlodipine besilate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 6.94 mg amlodipine besilate equivalent to 5 mg amlodipine.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Tablets
28 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For oral use.

Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP: MM/YYYY

9. SPECIAL STORAGE CONDITIONS

Store below 30°C. Keep the blister in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Marketing Authorisation Holder:
Torrent Pharma (UK) Ltd.
3rd Floor, Nexus Building,
4 Gatwick Road,
Crawley,
West Sussex,
RH10 9BG,
United Kingdom

12. MARKETING AUTHORISATION NUMBER(S)

PL 36687/0234

13. BATCH NUMBER

Lot: xxxxxx

14. GENERAL CLASSIFICATION FOR SUPPLY

POM

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Amlodipine 5 mg Tablets

Amlodipine 10 mg Tablets

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
CARTON

1. NAME OF THE MEDICINAL PRODUCT

Amlodipine 10 mg Tablets
Amlodipine besilate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 13.87 mg amlodipine besilate equivalent to 10 mg amlodipine.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Tablets
28 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For oral use.

Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP: MM/YYYY

9. SPECIAL STORAGE CONDITIONS

Store below 30°C. Keep the blister in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Marketing Authorisation Holder:
Torrent Pharma (UK) Ltd.
3rd Floor, Nexus Building,
4 Gatwick Road,
Crawley,
West Sussex,
RH10 9BG,
United Kingdom

12. MARKETING AUTHORISATION NUMBER(S)

PL 36687/0235

13. BATCH NUMBER

Lot: xxxxxx

14. GENERAL CLASSIFICATION FOR SUPPLY

POM

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Amlodipine 10 mg Tablets

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Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations where significant changes are made are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPC and/or PIL available on the MHRA website.

Application type	**Scope**	**Product information affected**	**Date of grant**	**Outcome**	**Assessment report attached Y/N**
Type IB	To update sections 4.2, 4.3, 4.4, 4.8, 5.1 and 5.2 of the SmPCs, and consequentially the PIL, in line with ISTIN 5 mg and 10 mg Tablets.	SmPCs PIL	15/09/2021	Approved	Yes

Annex 1

Reference: PL 36687/0234-0009
PL 36687/0235-0009

Product: Amlodipine 5 mg Tablets
Amlodipine 10 mg Tablets

Type of Procedure: National

Submission category: Type IB Variation

Reason
To update sections 4.2, 4.3, 4.4, 4.8, 5.1 and 5.2 of the SmPCs, and consequentially the PIL, in line with ISTIN 5 mg and 10 mg Tablets.

Supporting evidence
The Company has submitted updated SmPCs and PIL.

Evaluation
The updated documents are satisfactory.

Conclusion
The proposed changes are acceptable.

In accordance with legal requirements, the Summaries of Product Characteristics (SmPCs) and Patient Information Leaflets (PILs) for products granted Marketing Authorisations at a national level are available on the MHRA website.

Decision: Grant

Date: 15 September 2021