**Public Assessment Report**

**National Procedure**

**<NAME(S) OF PRODUCT(S) FROM SmPC(S)>**

**<active substance(s)/common name(s)>**

**<PRODUCT LICENCE NUMBER(S);**

**<MAH Name>LAY SUMMARY**

**<PLEASE NOTE THAT THIS LAY SUMMARY IS INTENDED TO BE INFORMATIVE TO THE PATIENT AND SHOULD CONTAIN NON-PROMOTIONAL INFORMATION TO HELP PATIENTS UNDERSTAND MORE ABOUT THEIR MEDICINES.>**

**< name of product(s) from SmPC(s), including pharmaceutical form and strength(s)> i.e. <X>**

**<active substance(s)/common name(s)>**

This is a summary of the Public Assessment Report (PAR) for [Prodnames]. It explains how this product/these products was/were assessed and its/their authorisation recommended, as well as its/their conditions of use. It is not intended to provide practical advice on how to use this product/these products.

<*If necessary, include shortened name and the following text*:

This product/These products will be referred to as <XX> in this lay summary for ease of reading.> (***Note****: if shortened name is to be used, XX should replace all mentions of X in text below.)*

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

**What is/are <X> and what is it/are they used for?**

<This/These> products is/are <a> generic medicine(s). This means that this/these medicine(s) is/are the same as, and considered interchangeable with, a reference medicine(s) already authorised, called [type or paste reference product name here].

<X is used in the treatment of/X can be used by patients who…>

*<Include the relevant information on indications, e.g. copy the relevant information from PIL section “What X is and what is it used for”. Note that the PL is directed to the patient, rewrite accordingly if necessary.>*

**How does/do <X> work?**

<*Copy the relevant information from Section 1 of the PIL “What X is and what is it used for”.>*

**How is/are <X> used? <AVOID USING GRAPHICS, TEXT ONLY>**

The pharmaceutical form of this/these medicine(s) is <pharmaceutical form> and the route of administration is <route of administration>.

*<This section should include: pharmaceutical form(s); main dosing recommendations; route/method of administration; duration of treatment if specified; need for any specific monitoring of certain parameters or for diagnostic tests; prescription status.>*

*If there are many routes of admin. and multiple strengths, the following form of statement can be used:*

*<Due to the different routes of administration and high-level of detail in the usage instructions it is best to refer directly to the PIL and Summaries of Product Characteristics (SmPCs) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website, for information on the how x product is used.>*

For further information on how <X> is/are used, refer to the PIL and Summary/Summaries of Product Characteristics (SmPC(s)) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

**Either:**

<This/These medicine(s) can only be obtained with a prescription.>

**Or:**

<This/These medicine(s) can be obtained without a prescription.>

**Either (if being administered by the patient themselves):**

<The patient should always take this medicine exactly as their doctor/pharmacist has told them. The patient should check with their doctor or pharmacist if they are not sure.>

**Or (if being administered by a healthcare practitioner):**

<The patient should ask the administering healthcare practitioner if they have any questions concerning their medicine.>

**What benefits of <X> have been shown in studies?**

**Either**

<Because <X> is/are a generic medicine(s), studies in <healthy volunteers> OR <patients> have been limited to tests to determine that it is bioequivalent to the reference medicine. Two medicines are bioequivalent when they produce the same levels of the active substance in the body.>

**Or**

< <X> is/are a generic medicine(s) that fulfils criteria meaning that no additional studies are required. <X> has/have been considered a generic medicine(s) of the reference medicine(s) based on a comparison of their physical and chemical characteristics. >.

**What are the possible side effects of <X>?**

For the full list of all side effects reported with this medicine/these medicines, see Section 4 of the PIL or the SmPC(s) 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 their behalf by someone else who cares for them, directly via the Yellow Card scheme at <https://yellowcard.mhra.gov.uk> or search for ‘MHRA Yellow Card’ online. By reporting side effects, patients can help provide more information on the safety of this medicine.

**Either**

Because <X> is/are a generic medicine(s) and is/are bioequivalent to the reference medicine(s), its benefits and possible side effects are considered to be the same as the reference medicine(s).

**Or**

# Because <X> is/are a generic medicine(s), its benefits and possible side effects are considered to be the same as for the reference medicine(s).

**Why was/were <X> approved?**

It was concluded that, <X> has been shown to be either comparable or bioequivalent to the reference medicine. Therefore, the MHRA decided that, as for the reference medicine, the benefits are greater than the risks and recommended that it can be approved for use.

*If applicable include the following statements:*

<The reference medicinal product(s) of <X> has been authorised under “exceptional circumstances”. This means that because of the rarity of this disease it has been impossible to get complete information on this medicine. Any new information on the reference medicinal product(s) will be reviewed every year and this report will be updated, as necessary.>

<X> has been authorised with the condition to perform further studies and/or to provide additional measures to minimise the risk. See section below “What measures are being taken to ensure the safe and effective use of <X>?”

**What measures are being taken to ensure the safe and effective use of <X>?**

**<PLEASE COMPILE FROM RELEVANT SECTIONS OF THE RISK MANAGEMENT PLAN>**

As for all newly-authorised medicines, a Risk Management Plan (RMP) has been developed for <X>. The RMP details the important risks of <X>, how these risks can be minimised, any uncertainties about <X> (missing information), and how more information will be obtained about the important risks and uncertainties.

The following safety concerns have been recognised for <X>:

Important identified risks: <complete as applicable or state “None”>

Important potential risks: <complete as applicable or state “None”>

Missing information: <complete as applicable or state “None”>

<or>

<if applicable: There are no safety concerns associated with use of <X>.>

<if applicable: describe additional risk management measures (also mentioned in the AR), such as obligations to provide educational materials, establish patient registries, or carry out further studies e.g. in specific populations or for long-term safety/efficacy data.>

The information included in the SmPC and the PIL is compiled based on the available quality, non-clinical and clinical data, and includes appropriate precautions to be followed by healthcare professionals and patients. Side effects of <X> are continuously monitored and reviewed including all reports of suspected side-effects from patients, their carers, and healthcare professionals.

An RMP and a summary of the pharmacovigilance system have been provided with this/these application(s) and are satisfactory.

**Other information about <X>**

A marketing authorisation/Marketing authorisations for <X> was/were granted in the United Kingdom (UK) on [Click and type or paste in date of MA grant dd mmmm yyyy].

The full PAR for <X> follows this summary.

This summary was last updated in February 2024.

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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 application(s) for [Prodnames](Product Licence Number(s)) could be approved.

The product(s) is/are approved for the following indication(s):

*<Include the relevant information on indications, copied from the SmPC(s)>*

<Name(s) of the active substance(s)> is [active substance(s) common name(s)]….

*<Include a summary of the mechanism of action of each active substance, taken from the Overview of the assessment report (MRP/DCP) or from the national assessment report/Module 2 summaries or Section 5.1 of the SmPC*

**Either**

This/These application(s) was/were approved under Regulation Choose an item A= GB B=UK. of The Human Medicines Regulation 2012, as amended (previously Article 10(1) of Directive 2001/83/EC, as amended), as a generic medicine(s) of a suitable originator medicinal product(s), [type or paste reference product name here] that has been licensed for a suitable time, in line with the legal requirements.

**<For Access applications, the following text should be added:**

This/these application(s) was/were evaluated as part of the Access Consortium, which consists of the health regulatory authorities of Australia (TGA) Canada (Health Canada), Singapore (HSA), Switzerland (Swissmedic) and the MHRA. Work-sharing for this application was conducted between <list the regulators involved>. Each regulator made independent decisions regarding approval of the application(s).

No new non-clinical studies were conducted, which is acceptable given that the application(s) is/are for a generic medicinal product(s) of a suitable reference product(s).

**Either**

With the exception of the bioequivalence study(ies), no new clinical studies were conducted, which is acceptable given that the application(s) is/are for (a) generic medicinal product(s) of a suitable reference product(s). The bioequivalence study(ies) was/were conducted in-line with current Good Clinical Practice (GCP).

**Or**

A biowaiver was submitted with this/these application(s), which was accepted. No bioequivalence study was required and no new clinical studies were provided with this/these application(s).

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

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with this/these application(s) and are satisfactory.

**<For applications referred to CHM>**Advice was sought from the Commission of Human Medicines (CHM) on <state dates(s) of CHM discussions> because….

*<A brief description of the main non-clinical/clinical reason(s) (but not quality as commercially confidential) that the application(s) was/were referred to CHM should be given and how the issue(s) was resolved. For example “Advice was sought from the Commission of Human Medicines (CHM) on d mmm yyyyy, following provision of additional data the CHM were reassured on the quality of the product >.*

A marketing authorisation/Marketing authorisations for <X> was/were granted in the United Kingdom (UK) on [Click and type or paste in date of MA grant dd mmmm yyyy].

II QUALITY ASPECTS

**II.1 Introduction**

This/These products consist(s) of…

*<Include the relevant information from Section 2 of the SmPC(s) that describes each product>*

In addition to [active substance(s)common name(s)], this/these product(s) also contain the excipients <list excipients, as per Section 6.1 of the SmPC(s )>.

The finished product(s) is/are packaged in <list packaging, as per Section 6.5 of the SmPC(s*)>. In the case of* ***more than one*** *pack size add the following* ,<Not all pack sizes may be marketed>.

Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary packaging complies with the current regulations concerning materials in contact with food.

**II.2 ACTIVE SUBSTANCE(S)**

**rINN:** [active substance(s)common name(s)]

Chemical Name: <state chemical name, as per the Quality assessment report or Module 3.2.S>

Molecular Formula: <state molecular formula, as per the Quality assessment report or Module 3.2.S>

Chemical Structure: <provide chemical structure, as per the Quality assessment report or Module 3.2.S>

Molecular Weight: <state molecular weight, as per the Quality assessment report or Module 3.2.S>

Appearance: <state appearance, as per the Quality assessment report or Module 3.2.S>

Solubility: <state solubility, as per the Quality assessment report or Module 3.2.S>

**Either**

[active substance(s) common name(s)] is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance are covered by a European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificate of Suitability.

*<Please note that if the packaging and retest period have not been covered by the EDQM certificate, these will have been assessed by the Quality assessor and so the following should be added>*

Suitable specifications have been provided for all packaging used. The primary packaging complies with the current regulations concerning materials in contact with food.

Appropriate stability data have been generated supporting a suitable retest period when stored in the proposed packaging.

**Or**

<The information related to the active substance was provided in an ASMF.  The Active substance is the subject of a Ph.Eur. monograph.>

Synthesis of the active substance from the designated starting materials has been adequately described and appropriate in-process controls and intermediate specifications are applied. Satisfactory specifications are in place for all starting materials and reagents, and these are supported by relevant Certificates of Analysis.

Appropriate proof-of-structure data have been supplied for the active substance. All potential known impurities have been identified and characterised.

An appropriate specification is provided for the active substance. Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specification. Batch analysis data are provided and comply with the proposed specification. Satisfactory Certificates of Analysis have been provided for all working standards.

Suitable specifications have been provided for all packaging used. The primary packaging complies with the current regulations concerning materials in contact with food.

Appropriate stability data have been generated supporting a suitable retest period when stored in the proposed packaging.

*<Repeat the above for each active substance in the medicinal product(s)>*

**II.3 DRUG PRODUCT(S)**

**Pharmaceutical development**

A satisfactory account of the pharmaceutical development was provided. *<If relevant, for complex dosage forms, include other information that is critical for the particular dosage form, if highlighted by assessor in their assessment report>.*

*If relevant, <Include the following for any solid oral formulations>*

Comparative *in vitro* dissolution and impurity profiles were provided for the proposed and reference products.

*If relevant, <Include the following for any liquid or injection/infusion formulations>*

Comparative *in vitro* impurity profiles were provided for the proposed and reference products.

All excipients comply with either their respective European/national monographs, or a suitable in-house specification. Satisfactory Certificates of Analysis were provided for all excipients.

**Either**

No excipients of animal or human origin are used in the final products.

**Or**

With the exception of <state excipient>, no excipients of animal or human origin are used in the final products. *<State whether any EDQM certificates have been provided for the excipients of animal origin>*

<If appropriate: The supplier of lactose monohydrate has confirmed that it is sourced from healthy animals under the same conditions as milk for human consumption.>

<If appropriate: Confirmation has been given that the magnesium stearate used in the tablets is of vegetable origin.>

This product(s) does/do not contain or consist of genetically modified organisms (GMO).

**Manufacture of the product(s)**

A description and flow-chart of the manufacturing method has been provided.

Satisfactory batch formulation data have been provided for the manufacture of the product(s), along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results.

**Finished Product Specifications**

The finished product specifications at release and shelf-life are satisfactory. The test methods have been described and adequately validated. Batch data have been provided that comply with the release specifications. Certificates of Analysis have been provided for any working standards used.

**Stability**

Finished product stability studies have been conducted in accordance with current guidelines, using batches of the finished product stored in the packaging proposed for marketing. Based on the results, a shelf-life of <INSERT SHELF LIFE FROM SMPC>, with the storage conditions <INSERT STORAGE CONDITIONS FROM THE SMPC>, is acceptable.

**<ADDITIONAL SHELF-LIFE/STORAGE CONDITIONS, SUCH AS FROM IN-USE STABILITY STUDIES OR AFTER RECONSTITUTION CAN BE ADDED HERE.>**

**<If applicable>** Suitable post approval stability commitments have been provided to continue stability testing on batches of finished product.

**II.4 Discussion on chemical, pharmaceutical and biological aspects**

The grant of marketing authorisations / a marketing authorisation was recommended.

III NON-CLINICAL ASPECTS

**III.1 Introduction**

As the pharmacodynamic, pharmacokinetic and toxicological properties of [active substance(s) common name(s)] are well‑known, no new non-clinical studies are required, and none have been provided. An overview based on the literature review is, thus, appropriate.

*<If any additional studies have been provided, this section should be restructured in the same or a similar format to a PAR for an 8.3 and the reason given for the assessment of these studies>*

**III.2 Pharmacology**

No new pharmacology data were provided, and none were required for this/these application(s).

**III.3 Pharmacokinetics**

No new pharmacokinetic data were provided, and none were required for this/these application(s).

**III.4 Toxicology**

No new toxicology data were provided, and none were required for this/these application(s).

**III.5 Ecotoxicity/Environmental Risk Assessment**

**Either**

A suitable justification was provided for non-submission of an Environmental Risk Assessment. As the application(s) is/are for generic version(s) of an already authorised product(s), an increase in environmental exposure is not anticipated following approval of the marketing authorisation(s) for the proposed product(s).

**Or**

An Environmental Risk Assessment (ERA) was provided. The results of the ERA show that there is no risk of increased environmental exposure with the use of this/these product(s).

*<You may need to present some results from the conclusion of the ERA assessment here>*

**III.6 Discussion on the non-clinical aspects**

The grant of (a) marketing authorisation(s) was/were recommended.

IV CLINICAL ASPECTS

**IV.1 Introduction**

**Either**

The clinical pharmacology, efficacy and safety of [active substance(s)common names(s)] is/are well‑known. With the exception of data from <INSERT NUMBER OF BIOEQUIVALENCE STUDY(IES)   undertaken> bioequivalence study(ies), no new clinical data are provided or are required for this type of application. An overview based on a literature review and a review of this/these study(ies) is, thus, satisfactory.

**Or**

The clinical pharmacology, efficacy and safety of <INSERT NAMES OF ACTIVE SUBSTANCE(S)> is/are well‑known. According to the regulatory requirements, the applicant has provided a suitable biowaiver and a bioequivalence study is not required for this product. An overview based on a literature review is, thus, satisfactory.

**IV. 2 Pharmacokinetics**

**Either**

No new pharmacokinetic data were submitted for this/these application(s) and none were required.

**Or**

In support of the application, the applicant submitted the following <BIOEQUIVALENCE STUDY 1>

This study was a… *<A one-sentence description of the study should be included here, including whether it is open- or closed-label, randomised or non-randomised, how many treatments, how many periods, how many sequences, single- or multiple-dose, crossover or parallel study>* comparing the test product <STATE TEST PRODUCT> versus the reference product(s) <STATE REFERENCE PRODUCT(S)> in subjects/patients under fasted/fed conditions.

Subjects were administered…*<A one- or two-sentence description of the drug administration should be provided, including whether it is single or multiple dosing of test/reference products, and when these are taken in relation to meals>*. Blood samples were taken pre-dose and up to <Y> hours post dose, with a washout period of <Z> days between the treatment periods.

A summary of the pharmacokinetic results is presented below:

*<A summary table should be provided for each active variable measured, including Test and Reference Cmax, and AUC calculations by either arithmetic or geometric calculations (depending on what the conclusions are based on). The Test/Reference ratio and 90% Confidence Intervals should also be provided. More than one summary table may be required if there is more than one active variable being measured or more than one reference product used in comparison with the test product.>*.

**Either**

In accordance with the regulatory requirements, the Test/Reference ratios and their 90% confidence intervals were within the specified limits to show bioequivalence between the test product and the reference product.

**Or**

The Test/Reference ratios and their 90% confidence intervals were not within the specified limits to show bioequivalence between the test product and the reference product.

*<Please note that in instances where the bioequivalence study was not accepted or bioequivalence was not shown, this needs to be stated along with the reasons why the bioequivalence study was not accepted and the reason why this was considered acceptable>*.

*<In instances where there is more than one strength relying on same bioequivalence data>*

As the additional <(insert strengths of products that were not subject of the BE study in brackets)> strengths of the product meet the biowaiver criteria specified in the current bioequivalence guideline, the results and conclusions from the bioequivalence study on the product strength can be extrapolated to the other strengths.

<BIOEQUIVALENCE STUDY 2>

*<In instances where more than one bioequivalence study was performed, each should be described as per above>*.

**IV.3 Pharmacodynamics**

No new pharmacodynamic data were submitted for this/these application(s) and none were required.

**IV.4 Clinical efficacy**

No new efficacy data were submitted with this/these application(s) and none were required.

**IV.5 Clinical safety**

**Either**

With the exception of the safety data submitted with the bioequivalence study(ies), no new safety data were submitted with this/these application(s).

The safety data from the bioequivalence study(ies) showed that the test and reference products were equally well tolerated. No new or unexpected safety issues were raised from the bioequivalence study.

**Or**

No new safety data were submitted with this/these application(s) and none were required. The safety profile for this/these product(s) is considered to be the same as [type or paste reference product name here].

**IV.6 Risk Management Plan (RMP)**

**Either**

The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, as amended. The applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns. This is acceptable.

**Or**

The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, as amended. In addition to routine pharmacovigilance and risk minimisation measures, the following additional < if applicable: pharmacovigilance> <and> < if applicable: risk minimisation> measures have been proposed:

<Insert table of risk minimisation and additional pharmacovigilance measures from part VI ‘II.B Summary of important risks‘ of the final RMP in the case folder>. If MAH has used EU RMP template, use table in Part V.3. Summary of risk minimization measures.

This is acceptable.

**IV.7 Discussion on the clinical aspects**

The grant of (a) marketing authorisation(s) was/were recommended for this/these application(s).

V USER CONSULTATION

A full colour mock-up of the Patient Information Leaflet (PIL) was provided with the application in accordance with legal requirements, including user consultation.

<Or>

A text draft of the Patient Information Leaflet (PIL) was presented. A commitment to provide a mock-up and evidence of user consultation of the PIL to the MHRA prior to marketing was accepted.

VI OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the product(s) is acceptable, and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with [active substance(s) common name(s)] is considered to have demonstrated the therapeutic value of the compound. The benefit/risk is, therefore, considered to be positive.

The Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling are satisfactory, in line with current guidelines and consistent with the reference product(s).

In accordance with legal requirements, the current approved UK version(s) of the SmPC</s> and PIL</s> for this/these product(s) are available on the MHRA website.

TABLE OF CONTENT OF THE PAR UPDATE

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** |
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