15 November 2018
EMA/CHMP/845183/2018
Committee for Medicinal Products for Human Use (CHMP)

Assessment report

Silodosin Recordati

International non-proprietary name: silodosin

Procedure No. EMEA/H/C/004964/0000

Note

Assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.

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List of abbreviations

ADR – Adverse Drug Reaction

Al / Alu – Aluminium

AP – Applicant's Part

API – Active Pharmaceutical Ingredient

AR – Assessment Report

ASM – Active Substance Manufacturer

DMF – Drug Master File = Active Substance Master File, ASMF

BCS – Biopharmaceutics Classification System

BE – Bioequivalence

BMI – Body Mass Index

BPH – Benign Prostatic Hyperplasia

BSE/TSE – Bovine Spongiform Encephalopathy / Transmissible Spongiform Encephalopathy

CEP – Certificate of Suitability

CHMP – Committee for Medicinal Products for Human Use

CoA – Certificate of Analysis

CQA – Critical quality attribute

CV – Coefficient of variation

CYP – Cytochrome P450

DILI – Drug Induced Liver Injury

DLP – Data Lock Point

DPM – Drug Product Manufacturer

EDQM – The European Directorate for the Quality of Medicines & HealthCare

EEA – European Economic Area

EGFR-TK - epidermal growth factor receptor tyrosine kinase

EMA – European Medicine Agency

EPAR – European Public Assessment Report

ERA - Environmental Risk Assessment

FDA – Food and Drug Administration

FU – Follow-up

GC – Gas Chromatography

GCP – Good Clinical Practice

GLP – Good Laboratory Practice

GMP – Good Manufacturing Practice

GVP – Good Pharmacovigilance Practices

HCP – Healthcare Professional

HPLC – High Pressure Liquid Chromatography

IBD – International Birth Date

ICH – International Conference on Harmonisation

INN – International Non-proprietary Name

IPC – In-Process Control

IR – Infrared spectroscopy

JP – Japanese Pharmacopoeia

LC-MS – liquid chromatography-mass spectrometry

LFTs – Liver Function Tests

LOD – Loss of drying (1), Limit of Detection (2)

LOQ – Limit of Quantification

LoQ – List of questions

MAA – Marketing Authorisation Application

MAH- Marketing Authorisation Holder

MO – Major objection

MS – Mass spectroscopy (1), Member State (2)

N/A – not applicable

NLT – not less than

NMR – Nuclear magnetic resonance spectroscopy

NMT – not more than

NSCLC - non-small cell lung cancer

OC – other concern

PE – polyethylene

PEC – Predicted Environmental Concentration

Ph. Eur. – European Pharmacopoeia

PI – Product of Information

PIL – Patient Information Leaflet

PK – pharmacokinetic(s)

PKWP – Pharmacokinetics Working Party

PSUR – Periodic Safety Update Report

PT – Preferred Terms

PVC – polyvinyl chloride

PVDC – polyvinylidene chloride

QbD – Quality by Design

QC – Quality Control

QOS – Quality Overall Summary

QP – Qualified Person

QRD – Quality Review of Documents

q.s. – quantity sufficient

QTPP – Quality Target Product Profile

RH – Relative Humidity

RMP – Reference Medicinal Product (1), Risk Management Plan (2)

RP – Restricted Part

RSD – Relative Standard Deviation

RUT – Readability User Test

SmPC – Summary of Product Characteristics

SOC – System Organ Class

TEAEs – treatment emergent adverse events

1. Background information on the procedure

1.1. Submission of the dossier

The applicant Recordati Ireland Ltd submitted on 10 April 2018 an application for marketing authorisation to the European Medicines Agency (EMA) for Silodosin Recordati, through the centralised procedure under Article 3 (3) of Regulation (EC) No. 726/2004– 'Generic of a Centrally authorised product'. The eligibility to the centralised procedure was agreed upon by the EMA/CHMP on 14 December 2017.

The application concerns a generic medicinal product as defined in Article 10(2)(b) of Directive 2001/83/EC and refers to a reference product, as defined in Article 10 (2)(a) of Directive 2001/83/EC, for which a marketing authorisation is or has been granted in the Union the basis of a complete dossier in accordance with Article 8(3) of Directive 2001/83/EC.

The applicant applied for the following indication :

"Treatment of the signs and symptoms of benign prostatic hyperplasia (BPH) in adult men."

The legal basis for this application refers to:

Generic application (Article 10(1) of Directive No 2001/83/EC).

The application submitted is composed of administrative information, complete quality data and a bioequivalence study with the reference medicinal product Urorec instead of non-clinical and clinical, unless justified otherwise.

This application is submitted as a multiple of Urorec authorised on 29 January 2010 in accordance with Article 82.1 of Regulation (EC) No 726/2004.

The chosen reference product is : Urorec

Medicinal product which is or has been authorised in accordance with Union provisions in force for not less than 8 years in the EEA:

- Product name, strength, pharmaceutical form: Urorec, 4 and 8 mg, capsule hard.
- Marketing authorisation holder: Recordati Ireland Ltd.
- Date of authorisation: 29-01-2010
- Marketing authorisation granted by: Union
- Marketing authorisation number: EU/1/09/608/001-014

Medicinal product authorised in the Union/Members State where the application is made or European reference medicinal product:

- Product name, strength, pharmaceutical form: Urorec, 4 and 8 mg, capsule hard.
- Marketing authorisation holder: Recordati Ireland Ltd.
- Date of authorisation: 29-01-2010
- Marketing authorisation granted by: Union
- Marketing authorisation number: EU/1/09/608/001-014

Medicinal product which is or has been authorised in accordance with Union provisions in force and to which bioequivalence has been demonstrated by appropriate bioavailability studies:

N/A as this application is submitted as a multiple of Urorec.

Information on paediatric requirements

Not applicable

Information relating to orphan market exclusivity

Similarity

Pursuant to Article 8 of Regulation (EC) No. 141/2000 and Article 3 of Commission Regulation (EC) No 847/2000, the applicant did not submit a critical report addressing the possible similarity with authorised orphan medicinal products because there is no authorised orphan medicinal product for a condition related to the proposed indication.

1.2. Steps taken for the assessment of the product

The Rapporteur appointed by the CHMP was:

Rapporteur: Katarina Vučić

The application was received by the EMA on	10 April 2018
The procedure started on	30 April 2018
The Rapporteur's first Assessment Report was circulated to all CHMP members on	4 June 2018
The PRAC Rapporteur's first Assessment Report was circulated to all PRAC members on	4 June 2018
The PRAC agreed on the PRAC Assessment Overview and Advice to CHMP during the meeting on	14 June 2018
The CHMP agreed on the consolidated List of Questions to be sent to the applicant during the meeting on	28 June 2018
The applicant submitted the responses to the CHMP consolidated List of Questions on	13 September 2018
The Rapporteurs circulated the Joint Assessment Report on the applicant's responses to the List of Questions to all CHMP members on	22 October 2018
The PRAC agreed on the PRAC Assessment Overview and Advice to CHMP during the meeting on	31 October 2018
The CHMP, in the light of the overall data submitted and the scientific discussion within the Committee, issued a positive opinion for granting a marketing authorisation to Silodosin Recordati on	15 November 2018

2. Scientific discussion

2.1. Introduction

This application for a marketing authorisation of Silodosin Recordati 4 mg hard capsules and Silodosin Recordati 8 mg hard capsules, concerns a generic application of a centrally authorised medicinal product according to Article 10(1) of Directive 2001/83/EC.

The reference medicinal product (RMP) is Urorec 4 mg hard capsules and Urorec 8 mg hard capsules EU/1/09/608-001-014, for which marketing authorisation was granted in the European Union on 29 January 2010 on the basis of a complete dossier in accordance with Article 8(3) of Directive 2001/83/EC.

Recordati Ireland Ltd. is the applicant of the generic MAA and the MAH of the RMP, and they will be produced to identical quality standards using identical manufacturing processes and batch testing processes at the same manufacturing sites. Qualitative and quantitative composition of Silodosin Recordati capsules is the same as in the RMP, thus the proposed generic product is identical in every respect to the reference product aside from the invented product name.

Silodosin Recordati is indicated for treatment of the signs and symptoms of benign prostatic hyperplasia (BPH) in adult men.

The recommended dose is one capsule of Silodosin Recordati 8 mg daily. For special patient populations, one capsule of Silodosin Recordati 4 mg daily is recommended.

Silodosin is an α-adrenoceptor antagonist with high selectivity for the α_{1A}-adrenoreceptors (primarily located in the lower urinary tract) relative to α_{1B}-adrenoreceptors (primarily located in the cardiovascular system). *In vitro* studies have shown that silodosin has a remarkably high α_{1A}:α_{1B} binding ratio (162:1). Blockade of α_{1A}-adrenoreceptors causes smooth muscle in these tissues to relax, thus decreasing bladder outlet resistance, without affecting detrusor smooth muscle contractility. This causes an improvement of both storage (irritative) and voiding (obstructive) symptoms (lower urinary tract symptoms, LUTS) associated with benign prostatic hyperplasia.

2.2. Quality aspects

2.2.1. Introduction

The finished product is presented as hard capsules containing 4 and 8 mg of silodosin as active substance.

Other ingredients are:

Capsule content - starch, pregelatinised (maize), mannitol (E421), magnesium stearate, sodium laurilsulfate.

Capsule shell – gelatin, titanium dioxide (E171), yellow iron oxide (E172) (4 mg capsules only).

The product is available in PVC/PVDC/aluminium blisters in carton pack.

2.2.2. Active Substance

General information

The chemical name of silodosin is
(-)-1-(3-hydroxypropyl)-5-[(2R)-2-({2-[2-(2,2,2-trifluoroethoxy)phenoxy]ethyl}amino)propyl]-2,3-dihydro-1

H-indole-7-carboxamid corresponding to the molecular formula $C_{25}H_{32}F_3N_3O_4$. It has a relative molecular mass of 495.53 g/mol and the following structure:

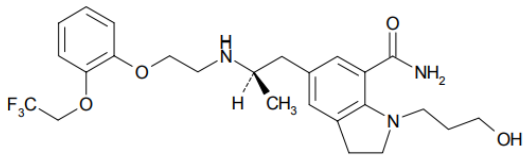

Figure 1: active substance structure

The chemical structure of silodosin was elucidated by a combination of MS (ESI-MS and ESI-MS/MS), UV, IR, 1H-NMR, 13C-NMR, 19F-NMR spectroscopy, two dimensional NMR spectroscopy (COSY, NOESY, HMCQ and HMBC) and elemental analysis. The absolute stereochemistry was confirmed by single-crystal X-ray crystallography and optical rotation. The solid state properties of the active substance were measured by powder X-ray diffraction, IR, solid-state 13C-NMR and thermal analysis (TG/DSC and TG/DTA).

Silodosin is a white to pale yellowish white powder and it is odourless. It is not considered to be hygroscopic and it is very soluble in acetic acid, freely soluble in methanol, *N,N*-dimethylformamide, and ethanol, sparingly soluble in 1-octanol, and very slightly soluble in water. Silodosin can exist in three polymorphic forms. The consistency and stability of produced crystalline form has been sufficiently demonstrated as well.

Silodosin exhibits stereoisomerism due to the presence of one chiral centre. Enantiomeric purity is controlled routinely by chiral HPLC.

Silodosin is not included in current European Pharmacopoeia

Manufacture, characterisation and process controls

Two ASMFs of the same holder with different manufacturing sites are submitted, with the same synthesis route applied for production of the same polymorphic form and the same quality requirements established for silodosin active substance manufactured by the processes described in each ASMF.

Detailed information on the manufacturing of the active substance has been provided in the restricted part of each ASMF and it was considered satisfactory.

Silodosin is synthesized from commercially available well defined starting materials with acceptable specifications.

Adequate in-process controls are applied during the synthesis. The specifications and control methods for raw materials (starting materials, reagents, solvents and auxiliary materials) have been presented. One critical step as well as one critical intermediate in the production of Silodosin has been identified with adequate in-process controls in place.

The characterisation of the active substance and its impurities are in accordance with the EU guideline on chemistry of new active substances.

Silodosin related substances including degradation products and potential impurities such as by-products produced during the manufacturing process were well discussed with regards to their origin and characterised. In addition, residual solvents, elemental impurities and genotoxic impurities were adequately identified and controlled.

Compliance of the primary packaging with the Ph. Eur. and Regulation (EU) No 10/2011 (as amended) has been confirmed by each ASM.

Specification

Release and shelf life specifications for active substance are presented in the relevant ASMF. The release specification includes tests for description, identification, melting point, heavy metals, residue on ignition, related substances, optical isomer, assay and residual solvents. In shelf life specification only stability indicating parameters are proposed with addition of water content testing. When available and applicable, compendial JP methods are used.

The appropriate specifications for impurities including residual solvents, in line with ICH Q3C have been set. The batch analysis results of recent active substance batches (3 pilot and at least 3 at commercial scale) manufactured with the current process of drug substance are provided. The currently approved analytical methods were applied. All results are within the acceptance criteria. The current information on reference standards is presented as well.

The results for representative batches of silodosin (3 batches manufactured at each active substance manufacturing site) are provided by the applicant. The results are within the specifications and consistent from batch to batch.

Stability

Stability data for 6 batches (3 pilot and 3 productions scale) of active substance stored in the intended commercial package for up to 60 months under long term conditions (25 ºC / 60% RH) and for up to 6 months under accelerated conditions (40 ºC / 75% RH) according to the ICH guidelines were provided. Photostability testing following the ICH guideline Q1B was performed on one batch.

The analytical methods used were the same as for release.

All tested parameters were within the specifications. Degradation products increased under accelerated conditions but remained within the specification. One batch was also exposed to light as defined in the ICH Guideline on Photostability Testing of New Drug Substances and Products. According to the results of photostability testing the active substance exposed directly to light showed increased levels of three known impurities as well as unspecified impurities. When protected from the light, the active substance has shown good stability.

The stability results indicate that the active substance is sufficiently stable. The stability results justify the proposed retest period of 60 months for the active substance, when stored in the original container at room temperature and protected from light.

2.2.3. Finished Medicinal Product

Description of the product and Pharmaceutical development

The finished product consists of hard gelatin capsules, containing 4 mg or 8 mg of silodosin, in a homothetic formulation that uses well known pharmaceutical excipients. Qualitative and quantitative composition of the generic finished product, dosage form and strengths are the same as of the reference medicinal product, thus the proposed generic product is identical in every respect to the reference product. Information on the development of the generic finished product is the same as for the reference medicinal product as well (the applicant of the generic finished product and the MAH of the reference medicinal product is the same).

All information regarding the choice of the active substance and the excipients are sufficiently justified. The main aim of the formulation development was to obtain a composition with good homogeneity and performance (disintegration and dissolution) characteristics. The manufacturer developed silodosin 8 mg capsules with a content which is proportionally similar in its active and inactive ingredients to the 4 mg capsules already marketed. It is noted that there are no changes in the manufacture of the blend of the two strengths. Comparative dissolution profiles were obtained for the 4 mg and 8 mg capsules using three different dissolution media pH 1.2, 4.5, 6.8. Based on the disintegration data and dissolution results provided and according to the "Note of Guidance on the Investigation of Bioavailability and Bioequivalence" CPMP/EWP/QWP/1401/98 the applicant justified the absence of an in-vivo test to demonstrate the equivalence of the different capsules formulations.

All excipients are well known pharmaceutical ingredients and their quality is compliant with Ph. Eur standards. There are no novel excipients used in the finished product formulation. The list of excipients is included in section 6.1 of the SmPC and in paragraph 2.1.1 of this report.

The primary packaging is opaque PVC/PVCD/aluminium blisters. The materials comply with Ph. Eur. and EC requirements. The choice of the container closure system has been validated by stability data and is adequate for the intended use of the product.

Manufacture of the product and process controls

The manufacturing process consists of 7 main steps: mixing, kneading, granulation, drying, sieving and mixing, capsule filling and packaging. The process is considered to be a standard manufacturing process and is adequately described.

Process validation data for all proposed batch sizes at both proposed manufacturing sites are provided demonstrating that the manufacturing process is validated. Recordati Ireland Ltd. is the applicant of the generic MAA and the MAH of the RMP, and they will be produced to identical quality standards using identical manufacturing processes and batch testing processes at the same manufacturing sites.

It has been demonstrated that the manufacturing process is capable of producing the finished product of intended quality in a reproducible manner. The in-process controls are adequate for this type of manufacturing process and pharmaceutical form.

Product specification

The finished product release specifications include appropriate tests for this kind of dosage form: appearance, dosage uniformity, identity, assay, impurities, dissolution, and microbial count. All parameters tested at release are included in the shelf life specifications as well.

Impurities present at higher than the qualification threshold according to ICH Q3A were qualified by toxicological and clinical studies and appropriate specifications have been set. A risk assessment on elemental impurities according to ICH Q3D has been carried out.

The analytical methods used have been adequately described and appropriately validated in accordance with the ICH guidelines. Satisfactory information regarding the reference standards used has been presented.

Batch analysis results are provided for three manufacturing scale batches for each site and strength confirming the consistency of the manufacturing process and its ability to manufacture in compliance with the intended finished product specification.

Stability of the product

Stability data on 4 pilot and 3 industrial scale batches of 4 mg strength as well as 2 pilot and 3 industrial scale batches of 8 mg strength and 2 commercial scale batches of both strengths of the finished product stored for up to 36 months under long term conditions (25°C/60% RH), for up to 12 months at 30ºC/65%RH and for up to 6 months under accelerated conditions (40 ºC / 75% RH) according to the ICH guidelines were provided. The batches of the finished product are identical to those proposed for marketing and were packed in the primary packaging proposed for marketing.

For batches of both finished product strengths, the results for appearance and dissolution at each testing conditions comply with specifications as well as the results for assay, related substances and microbial count at long term and intermediate storage conditions.

At accelerated storage conditions (40°C/75% RH) an increase in degradation product is observed at the 3 month time-point with out of specification results obtained for some of the 4 mg capsules batches. At the 6 month time-point the degradation product is out of specification in almost all batches, for both strengths. The assay values are out of specification in some batches, mainly for the 4 mg strength. Results for appearance, dissolution and microbial count are within acceptance criteria.

In addition, one batch was exposed to light as defined in the ICH Guideline on Photostability Testing of New Drug Substances and Products. According to the results of photostability studies capsules exposed directly to light showed increased levels of both specified impurities as well as unspecified impurities, while the samples in the proposed market packaging showed no significant change in the appearance of the capsules, assay or content of related substances.

Based on the available stability data, the proposed shelf life and storage conditions as stated in the SmPC are acceptable.

Based on available stability data, the proposed shelf-life of 36 months and storage conditions: “Store the product in the original package in order to protect the product from light and moisture. Do not store above 30°C.”, as stated in the SmPC (section 6.3) are acceptable.

Adventitious agents

Gelatine obtained from bovine sources is used in the product. Valid TSE CEPs from the suppliers of gelatine used in the manufacture of finished product are provided.

2.2.4. Discussion and conclusions on chemical, pharmaceutical and biological aspects

Information on development, manufacture and control of the active substance and finished product has been presented in a satisfactory manner. The results of tests carried out indicate consistency and uniformity of important product quality characteristics, and these in turn lead to the conclusion that the product should have a satisfactory and uniform performance in clinical use. Data has been presented to give reassurance on viral/TSE safety.

2.2.5. Conclusions on the chemical, pharmaceutical and biological aspects

The quality of this product is considered to be acceptable when used in accordance with the conditions defined in the SmPC. Physicochemical and biological aspects relevant to the uniform clinical performance of the product have been investigated and are controlled in a satisfactory way.

2.3. Non-clinical aspects

2.3.1. Introduction

A non-clinical overview on the pharmacology, pharmacokinetics and toxicology has been provided, which is based on up-to-date and adequate scientific literature. The overview justifies why there is no need to generate additional non-clinical pharmacology, pharmacokinetics and toxicology data. The non-clinical aspects of the SmPC are in line with the SmPC of the reference product. The impurity profile has been discussed and was considered acceptable.

Therefore, the CHMP agreed that no further non-clinical studies are required.

2.3.2. Ecotoxicity/environmental risk assessment

No Environmental Risk Assessment studies were submitted. This was justified by the applicant as the introduction of Silodosin Recordati is considered unlikely to result in any significant increase in the combined sales volumes for all Silodosin containing products and the exposure of the environment to the active substance. Thus, the ERA is expected to be similar.

2.3.3. Discussion on non-clinical aspects

The non-clinical overview provided is based on literature review and studies submitted in Module 2.6 in the Marketing Authorisation Application of the reference medicinal product. Recordati Ireland Ltd. is the applicant of the generic MAA and the MAH of the RMP and this summary is considered acceptable.

Justification for not providing ERA studies for this generic product is accepted.

2.3.4. Conclusion on the non-clinical aspects

There are no objections to approval of Silodosin Recordati 4 mg hard capsules and Silodosin Recordati 8 mg hard capsules from the nonclinical point of view.

2.4. Clinical aspects

2.4.1. Introduction

This is an application for Silodosin Recordati 4 mg and 8 mg hard capsules containing Silodosin. The applicant provided a Clinical Overview outlining the pharmacokinetics and pharmacodynamics as well as efficacy and safety of silodosin based on published literature. The SmPC is in line with the SmPC of the reference medicinal product.

Since Silodosin Recordati is an auto-generic of Urorec, the clinical data in support of the Silodosin Recordati application are identical to the up-to-date clinical data of the Urorec dossier, which have been assessed and authorised (including all post-marketing procedures).

Exemption

Exemption for bioequivalence studies for Silodosin Recordati 4 mg and 8 mg hard capsules can be justified considering that the proposed generic medicinal product is a duplicate of the RMP. Silodosin Recordati and the

related RMP are both manufactured by the same manufacturing sites and apart from the invented name they are identical in every respect (composition, pharmaceutical formulation, strength, manufacturing process, testing).

2.4.2. Pharmacodynamics

No new pharmacodynamic studies were presented and no such studies are required for this application.

2.4.3. Post marketing experience

No post-marketing data are available. The medicinal product has not been marketed in any country.

2.4.4. Discussion on clinical aspects

An adequate Clinical Overview containing a sufficient outline of the published literature regarding the clinical pharmacology, efficacy and safety of silodosin has been submitted.

2.4.5. Conclusions on clinical aspects

There are no objections to approval of Silodosin Recordati 4 mg hard capsules and Silodosin Recordati 8 mg hard capsules from the clinical point of view.

2.5. Risk management plan

Safety concerns

Important identified risks	None
Important potential risks	Misdiagnosis of prostate cancer
Important missing information	None

Pharmacovigilance plan

Routine pharmacovigilance activities are considered appropriate to characterise the important potential risk of misdiagnosis of prostate cancer. Routine pharmacovigilance activities beyond adverse reporting and signal detection include a specific adverse reaction follow-up questionnaires for misdiagnosis of prostate cancer.

No additional pharmacovigilance activities are considered needed.

Risk minimisation measures

Important potential risks

Safety Concern	Risk minimisation measures	Pharmacovigilance activities
Misdiagnosis of prostate cancer	Routine risk minimisation activities recommending specific clinical measures to address the risk: • SmPC section 4.4 • PL section 2	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: *AE follow-up form for adverse reaction*

Routine risk minimisation measures are considered appropriate. No additional risk minimisation measures are considered needed.

Conclusion

The CHMP and PRAC considered that the risk management plan version 11.5 is acceptable.

2.6. Pharmacovigilance

Pharmacovigilance system

The CHMP considered that the pharmacovigilance system summary submitted by the applicant fulfils the requirements of Article 8(3) of Directive 2001/83/EC.

Periodic Safety Update Reports submission requirements

The requirements for submission of periodic safety update reports for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

2.7. Product information

2.7.1. User consultation

No full user consultation with target patient groups on the package leaflet has been performed on the basis of a bridging report making reference to Urorec 4 mg/8 mg hard capsules. The bridging report submitted by the applicant has been found acceptable.

3. Benefit-risk balance

This application concerns a generic version of Silodosin 4 mg hard capsules and Silodosin 8 mg hard capsules. The reference product Urorec is indicated for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH) in adult men. No non-clinical studies have been provided for this application but an adequate summary of the available nonclinical information for the active substance was presented and considered sufficient. From a clinical perspective, this application does not contain new data on the pharmacokinetics and pharmacodynamics as well as the efficacy and safety of the active substance; the applicant's clinical overview on these clinical aspects based on information from published literature was considered sufficient.

The proposed generic medicinal product is a duplicate of the reference medicinal product and both products are

manufactured by the same manufacturing sites and apart from the invented name they are identical in every respect (composition, pharmaceutical formulation, strength, manufacturing process, testing). Therefore demonstration of bioequivalence by means of further studies can be waived and a benefit/risk ratio comparable to the reference product can be concluded.

The CHMP, having considered the data submitted in the application and available on the chosen reference medicinal product, is of the opinion that no additional risk minimisation activities are required beyond those included in the product information.

4. Recommendation

Based on the CHMP review of data on quality, safety and efficacy, the CHMP considers by consensus that the benefit-risk balance of Silodosin Recordati is favourable in the following indication:

Treatment of the signs and symptoms of benign prostatic hyperplasia (BPH) in adult men.

The CHMP therefore recommends the granting of the marketing authorisation subject to the following conditions:

Conditions or restrictions regarding supply and use

Medicinal product subject to medical prescription.

Other conditions and requirements of the marketing authorisation

Periodic Safety Update Reports

The requirements for submission of periodic safety update reports for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

Conditions or restrictions with regard to the safe and effective use of the medicinal product

Risk Management Plan (RMP)

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.