COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

Public Assessment Report

Scientific discussion

Irbesartan + Hidroclorotiazida Aurobindo 150 mg + 12.5 mg, 300 mg + 12.5 mg, 300 mg + 25 mg, film coated tablets (irbesartan + hydrochlorothiazide)

NL/H/5155/001-003/DC

Date: 6 December 2022

This module reflects the scientific discussion for the approval of Irbesartan + Hidroclorotiazida Aurobindo 150 mg + 12.5 mg, 300 mg + 12.5 mg, 300 mg + 25 mg, film coated tablets. The procedure was finalised on 2 November 2012 in Portugal (PT/H/0682/001-003/DC). After a transfer on 9 June 2020, the current RMS is the Netherlands. For information on changes after this date please refer to the 'steps taken after finalisation' at the end of this PAR.

List of abbreviations

ASMF	Active Substance Master File
CEP	Certificate of Suitability to the monographs of the European Pharmacopoeia
CHMP	Committee for Medicinal Products for Human Use
CMD(h)	Coordination group for Mutual recognition and Decentralised procedure for human medicinal products
CMS	Concerned Member State
EDMF	European Drug Master File
EDQM	European Directorate for the Quality of Medicines
EEA	European Economic Area
ERA	Environmental Risk Assessment
ICH	International Conference of Harmonisation
MAH	Marketing Authorisation Holder
Ph.Eur.	European Pharmacopoeia
PL	Package Leaflet
RH	Relative Humidity
RMP	Risk Management Plan
SmPC	Summary of Product Characteristics
TSE	Transmissible Spongiform Encephalopathy

I. INTRODUCTION

Aurobindo Pharma (Malta) Limited has applied for a marketing authorisation for Irbesartan + Hidroclorotiazida Aurobindo 150 mg + 12.5 mg, 300 mg + 12.5 mg, 300 mg + 25 mg, film-coated tablets, containing Irbesartan + Hydrochlorothiazide as the active substance, indicated in treatment of essential hypertension in adult patients whose blood pressure is not adequately controlled on irbesartan or hydrochlorothiazide alone.

This application concerns a generic application claiming essential similarity with the reference product CoAprovel film-coated tablets by Sanofi Pharma Bristol-Myers Squibb SNC.

The marketing authorization was granted on 02/11/2012 based on Directive 2001/83/EC article 10.1 (a) (iii) first paragraph in Portugal. After a transfer on 9 June 2020, the current RMS is the Netherlands.

This type of application refers to information that is contained in the pharmacological-toxicological and clinical part of the dossier of the authorisation of the reference product. A reference product is a medicinal product authorised and marketed on the basis of a full dossier, i.e. including chemical, biological, pharmaceutical, pharmacological-toxicological and clinical data. This information is not fully available in the public domain. Authorisations for generic products are therefore only allowed once the data protection time of the dossier of the reference product has expired. For this kind of application, it has to be demonstrated that the pharmacokinetic profile of the product is similar to the pharmacokinetic profile of the reference product. This generic product can be used instead of its reference product.

II. QUALITY ASPECTS

II.1 Introduction

Irbesartan + Hidroclorotiazida Aurobindo 150 mg + 12.5 mg, 300 mg + 12.5 mg, 300 mg + 25 mg, film-coated tablets, containing irbesartan and hydrochlorothiazide as the active substance.

The excipients are:
Tablet core

- Lactose monohydrate
- Sodium Starch Glycolate (Type A)
- Povidone K30
- Silica Colloidal Anhydrous
- Talc
- Sodium stearyl fumarate

Film coating
150mg/12.5mg & 300mg/12.5mg film-coated tablets
- Lactose monohydrate
- Hypromellose (E464)
- Titanium dioxide (E171)
- Macrogol 4000
- Iron oxide yellow (E172)
- Iron oxide red (E172)

300/25 film-coated tablets
- Hypromellose (E464)
- Titanium dioxide (E171)
- Macrogol 4000
- Iron oxide red (E172)
- Iron oxide black (E172)

The film-coated tablets are available in Polyamide/Aluminium/PVC/Aluminium blister pack and white opaque HDPE bottle with white opaque polypropylene closure pack.

II.2 Drug Substance

The chemical-pharmaceutical documentation and Expert Report in relation to the drug substances Irbesartan + Hydrochlorothiazide are of sufficient quality in view of the present European regulatory requirements.

Stability studies have been performed with the drug substances. No significant changes in any parameters were observed.

II.3 Medicinal Product

The drug product is film-coated tablets, manufactured using the conventional pharmaceutical excipients and with the standard manufacturing process. The development of the product has been described, the choice of excipients is justified and their functions explained.

III. NON-CLINICAL ASPECTS

Pharmacodynamic, pharmacokinetic and toxicological properties of irbesartan + hydrochlorothiazide are well known. As irbesartan + hydrochlorothiazide are widely used, well-known active substances, the applicant has not submitted additional studies and further studies are not required. An overview based on literature review is, thus, appropriate.

IV. CLINICAL ASPECTS

IV.1 Pharmacokinetics

The application concerns 150 mg + 12.5 mg, 300 mg + 12.5 mg, 300 mg + 25 mg, film-coated tablets Irbesartan + Hydrochlorothiazide. A bioequivalence study was carried out with the 300 mg + 25 mg strength. The conditions for bio-waivers in section 5.4 of the Bioequivalence guideline have been fulfilled: same manufacturer and process, drug input has been shown to be linear over the therapeutic dose range, same qualitative composition, same ratio between active and excipients and similar dissolution profile under identical conditions between the 150 mg + 12.5 mg, 300 mg + 12.5 mg and 300 mg + 25 mg strengths.

IV.2 Clinical efficacy & Clinical safety

Irbesartan + Hydrochlorothiazide has a well-recognised efficacy and acceptable level of safety in the indications approved for 150 mg + 12.5 mg, 300 mg + 12.5 mg, 300 mg + 25 mg, film-coated tablets and has been widely used in many countries.

IV.3 Pharmacovigilance System

The RMS considers that the Pharmacovigilance system as described by the applicant fulfils the requirements and provides adequate evidence that the applicant 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.

V. USER CONSULTATION

The readability of the package leaflet was successfully demonstrated.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The application contains adequate quality, non-clinical and clinical data and the bioequivalence has been shown. A benefit/risk ratio comparable to the reference product can therefore be concluded.

STEPS TAKEN AFTER THE FINALISATION OF THE INITIAL PROCEDURE - SUMMARY

Procedure number*	Scope	Product Information affected	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse
NL/H/5155/1-3/IB/031	Changes (Safety/Efficacy) to Human and Veterinary Medicinal Products - To update SmPC and Leaflet	Yes	17-10-2020	Approved	N/A
NL/H/5155/1-3/IA/032	Submission of Updated CEP for Irbesartan from currently approved manufacturer	No	17-6-2021	Approved	N/A
NL/H/5155/1-3/IB/033	Implementation of product information change(s) for which no new additional data are submitted by the MAH – to be in-line with the innovator	Yes	3-7-2021	Approved	N/A
NL/H/5155/1-3/IB/034	To submit the supporting data in order to justify waiver from including nitrosamine testing in the drug product specification.	No	8-2-2022	Approved	N/A
NL/H/5155/1-3/IA/035	Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the risk management plan - Implementation of wording agreed by the competent authority	No	11-12-2021	Approved	N/A
NL/H/5155/1-3/IA/036	To notify present the blend batch size as a range – and to increase the maximum batch size of blend and compressed tablets for one strength (within 10 times the initial approved size)	No	15-12-2021	Approved	N/A
NL/H/5155/1-3/IB/037	Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet of human medicinal products intended to implement the outcome of a procedure concerning PSUR	Yes	22-3-2022	Approved	N/A
NL/H/5155/1-3/IA/038	Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet of human medicinal products intended to implement the outcome of a procedure concerning PSUR or PASS, or the outcome of the assessment done by the competent authority - Implementation of wording agreed by the competent authority	Yes	4-2-2022	Approved	N/A

NL/H/5155/1-3/IA/039/G	Submission of Updated CEP for Irbesartan from currently approved manufacturer(s) Deletion of existing Ph.Eur. CEP for Irbesartan from currently approved manufacturer(s)	No	1-7-2022	Approved	N/A