Public Assessment Report
Scientific discussion

Voriconazole Gobens 200 mg powder for solution for infusion
Voriconazole Amneal 200 mg powder for solution for infusion

(voriconazole)
Registration number in Spain:

EU-procedure number:
ES/H/0315/001/DC
ES/H/0319/001/DC

Applicant: Laboratorios Normon, S.A.

This module reflects the scientific discussion for the approval of **Voriconazole Gobens 200 mg powder for solution for infusion and Voriconazole Amneal 200 mg powder for solution for infusion**. The procedure was finalised on February 2016. For information on changes after this date please refer to the module 'Update'.

I. INTRODUCTION

This decentralised procedure concerns a generic application claiming essential similarity with the innovator product Vfend® 200 mg powder for solution for infusion (Pfizer Limited). Vfend® 200 mg powder for solution for infusion has been registered in Europe since March 2002.

The legal basis of the application is Article 10(1) of Directive 2001/83/EC.

The Concerned Member States involved in these procedures are DE and PT in ES/H/0315/001/DC procedure and DE, DK, FI, SE, NO, UK in ES/H/0319/001/DC procedure.

The product is indicated in the treatment of:

- Treatment of invasive aspergillosis.
- Treatment of candidemia in non-neutropenic patients.
- Treatment of fluconazole-resistant serious invasive Candida infections (including *C. krusei*).
- Treatment of serious fungal infections caused by Scedosporium spp. and Fusarium spp.

A comprehensive description of the product information is given in the SmPC.

The RMS has been assured that acceptable standards of GMP are in place for these product types at all sites responsible for the manufacture and assembly of this product.

For manufacturing sites within the Community, the RMS has accepted copies of current manufacturer authorisation issued by inspection services of the competent authorities as certification that acceptable standards of GMP are in place at those sites.

RECOMMENDATION

Based on the review of the data on quality, safety and efficacy, the Member States have granted a marketing authorisation for **Voriconazole Gobens 200 mg powder for solution for infusion** and **Voriconazole Amneal 200 mg powder for solution for infusion** for Laboratorios Normon S.A.

II. SCIENTIFIC OVERVIEW AND DISCUSSION

II-1 Quality aspects

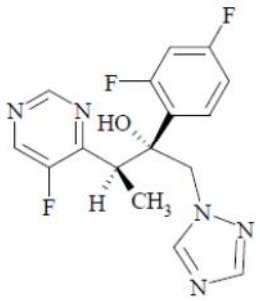
INTRODUCTION

The drug product is a powder for solution for infusion and contains 200 mg voriconazole, as active ingredient.
The excipients present in the product are hydroxylpropylbetadex, sodium chloride and water for injection. The excipients used are common for the manufacture of pharmaceutical preparations. The specifications for excipients are based on the specification given in the corresponding Eur. Ph. monographs.

The drug product is packed in glass vial type I, closed with a stopper and sealed with an aluminium cap placed in a suitable cardboard box.

Primary packaging complies with the current European regulations concerning materials in contact with food.

DRUG SUBSTANCE

INN Name	:	Voriconazole
Chemical name	:	(2R,3S)-2-(2,4-Difluorophenyl)-3-(5-fluoropyrimidin-4- yl)-1-(1H-1,2,4-triazol-1-yl)butan-2-ol.
Structure	:	
Molecular Formula	:	$C_{16}H_{14}F_3N_5O$
Molecular Weight	:	349.31 g/mol
Description	:	White powder

Voriconazole is the subject of a European Pharmacopoeia moograph.

The manufacture and control of Voriconazole are covered by a Certificate of Suitability.

MEDICINAL PRODUCT

Vials containing 200 mg of voriconazole similar to VFEND® 200 mg powder for solution for infusion (reference) is proposed.

The Pharmaceutical development has been supported on the basis of the similarity between the reference product and the proposed formulation.

The Applicant cross-refers to the reference product VFEND® 200mg powder for solution for infusion. Comparative studies between the proposed product and the reference product were performed and show essential similarity with respect to major physicochemical parameters.

The manufacturing process of the product is well described. Process validation data on three industrial batches have been provided. The results are satisfactory.

The finished product specifications are considered acceptable. The analytical procedures have been described and are considered suitably validated. The analytical batch data results confirm the satisfactory uniformity of the product and indicate the manufacturing process is under control.

Finished product stability studies have been conducted in accordance with current guidelines and in the packaging proposed for marketing.

Based on the results, a shelf-life of 18 months (unopened) with the storage condition "Store below 25ºC" is authorized.

For the reconstituted vials the following condition is accepted: "From the microbiological point of view, the product should be used immediately. If not used immediately, the storage times and conditions of the reconstituted solution with 19 ml of water for injection or with 19 ml of sodium chloride before use should not be more than 24 hours at 2-8 ºC".

II-2 Non-clinical aspects

A non-clinical overview on the pharmacology, pharmacokinetics and toxicology of the active substance has been provided, which is based on up-to-date and adequate scientific literature. The non-clinical overview on the pre-clinical pharmacology, pharmacokinetics and toxicology is adequate and the Member States agreed that no further non-clinical studies are required.

Environmental Risk Assessment (ERA)

An ERA was submitted with a justification for not conducting ERA studies. The medicinal product has the same quantitative and qualitative composition in active substances and a similar pharmaceutical form to the reference product. The introduction on the market of this medicinal product will not mean an increased exposure to the environment, since the generic medicinal product is intended to substitute the reference medicinal product as well as other generic products in the market.
In accordance with the Guideline on the Environmental Risk Assessment for medicinal products for human use (CPMP/SWP/4447/00), the absence of this Environmental Risk Assessment is therefore justified.

II.3 Clinical aspects

Introduction

Voriconazole is a well-known drug with established efficacy and safety.

No new clinical efficacy or safety studies were conducted, which is acceptable for this abridged application. A clinical overview has been provided, which is based on scientific literature. The Member States agreed that no further clinical studies are required.

Biowaiver

The generic product Voriconazole Gobens 200 mg powder for injection could be considered to be exempted from bioequivalence studies with the reference product Vfend® 200 mg powder for solution for infusion as these products are solutions for injection. The difference in solubilising agent was adequately justified and it does not influence the *in vivo* disposition of Voriconazole.

Bioequivalence

Not applicable as no bioequivalence study has been submitted since it is not considered necessary according to the Guideline on the Investigation of Bioequivalence (CPMP/QWP/EWP/1401/98 Rev. 1).

Risk Management Plan

A risk management plan in accordance with the requirements of Directive 2001/83/EC as amended has been submitted.

No additional risk minimization activities were required beyond those included in the product information.

Discussion on the clinical aspects

No bioequivalence study has been submitted since it is not considered necessary according to the Guideline on the Investigation of Bioequivalence (CPMP/QWP/EWP/1401/98 Rev. 1).

Efficacy and safety of the active substance voriconazole are well documented for the reference medicinal product.

III OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

No bioequivalence study has been submitted since it is not considered necessary according to the Guideline on the Investigation of Bioequivalence (CPMP/QWP/EWP/1401/98 Rev. 1).

The SmPC, PIL and labelling are considered satisfactory and consistent with the information for the reference medicinal product. The user testing of the Package Information Leaflet has been tested in accordance with Article 59(3) of Directive 2001/83/EC, as amended by Directive 2004/27/EC.

The benefit/risk balance was considered to be positive.

Agreement between Member States was reached during the procedure. The decentralised procedure was finalised with a positive outcome in February 2016.