Medicines & Healthcare products
Regulatory Agency

Public Assessment Report

National Procedure

Rezzayo 200 mg powder for concentrate for solution for infusion

rezafungin acetate

PLGB 16950/0390

Napp Pharmaceuticals Limited

LAY SUMMARY

Rezzayo 200 mg powder for concentrate for solution for infusion. rezafungin acetate

This is a summary of the Public Assessment Report (PAR) for Rezzayo 200 mg powder for concentrate for solution for infusion. It explains how this product was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use this product.

This product will be referred to as Rezzayo in this lay summary for ease of reading.

This product has been authorised by the Medicines and Healthcare products Regulatory Agency (MHRA) for Great Britain (consisting of England, Scotland and Wales). In coming to its decision, MHRA has relied on a European Commission (EC) decision on 22nd December 2023 (EMEA/H/C/005900/0000), in accordance with the advice from the Committee for Medicinal Products for Human Use (CHMP). This is known as the EC Decision Reliance Procedure.

This application was approved under Regulation 50 of the Human Medicines Regulation 2012, as amended (previously Article 8(3) of Directive 2001/83/EC, as amended).

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

What is Rezzayo and what is it used for?
Rezzayo contains the active substance rezafungin, which is an antifungal. Rezafungin belongs to a group of medicines called echinocandins. This medicine is given to adults to treat invasive candidiasis, a serious fungal infection in tissues or organs that is caused by a type of yeast called *Candida*.

This application is a full-dossier application. This means that the results of pharmaceutical, non-clinical and clinical tests have been submitted to show that this medicine is suitable for treating the specified indications.

How does Rezzayo work?
This medicine blocks the action of an enzyme (a type of protein) that is needed by fungal cells to make a molecule that strengthens their cell walls. This makes the fungal cells fragile and stops the fungus from growing. This stops the infection from spreading and gives the body's natural defences a chance to remove the infection.

How is Rezzayo used?
The pharmaceutical form of this medicine is powder for concentrate for solution for infusion (sterile concentrate) and the route of administration is intravenous infusion (drip into a vein).

Treatment with Rezzayo should be initiated by a physician experienced in the management of invasive fungal infections.

The medicine is given once a week as an infusion (drip) into a vein lasting at least 1 hour. The duration of treatment depends on how the patient responds but should continue for at least 2 weeks after the last day that *Candida* is found in the patient's blood.

For further information on how Rezzayo is used, refer to the PIL and Summary of Product Characteristics (SmPC) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

This medicine can only be obtained with a prescription.

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

What benefits of Rezzayo have been shown in studies?
A main study involving 187 people with invasive candidiasis showed that Rezzayo was as effective as caspofungin (another antifungal medicine) in the treatment of invasive candidiasis. After 14 days of treatment, 59% (55 out of 93) of people who received Rezzayo had no signs or symptoms of *Candida* infection compared with 61% (57 out of 94) of those who received caspofungin.

What are the possible side effects of Rezzayo?
For the full list of all side effects reported with this medicine, see Section 4 of the PIL or the SmPC 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.

Why was Rezzayo approved?
MHRA decided that the benefits are greater than the risks and recommended that this medicine can be approved for use.

Rezzayo has been authorised as a GB Orphan medicine. Orphan medicines are intended for use against rare conditions that are life-threatening or chronically debilitating. To qualify as an orphan medicine, certain criteria, for example concerning the rarity of the disease and the lack of currently available treatments, must be fulfilled.

What measures are being taken to ensure the safe and effective use of Rezzayo?
As for all newly-authorised medicines, a Risk Management Plan (RMP) has been developed for Rezzayo. The RMP details the important risks of Rezzayo, how these risks can be minimised, any uncertainties about Rezzayo (missing information), and how more information will be obtained about the important risks and uncertainties.

There are no safety concerns associated with use of Rezzayo.

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 Rezzayo 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 application and are satisfactory.

Other information about Rezzayo.
A marketing authorisation was granted in Great Britain on 29 January 2024.

The full PAR for Rezzayo 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 for Rezzayo 200 mg powder for concentrate for solution for infusion (PLGB 16950/0390) could be approved.

The product is approved for the treatment of invasive candidiasis in adults.

Rezafungin acetate is an antifungal. Rezafungin belongs to a group of medicines called echinocandins. Rezafungin selectively inhibits fungal 1,3-β-D-glucan synthase. This results in inhibition of the formation of 1,3-β-D-glucan, an essential component of the fungal cell wall which is not present in mammalian cells. Inhibition of 1,3-β-D-glucan synthesis results in rapid and concentration-dependent fungicidal activity in Candida species (spp.).

This product has been authorised by MHRA for Great Britain (consisting of England, Scotland and Wales). In coming to its decision, MHRA has relied on a European Commission (EC) decision on 22nd December 2023 (EMEA/H/C/005900/0000), in accordance with the advice from the Committee for Medicinal Products for Human Use (CHMP).

For the scientific discussion of the quality, non-clinical and clinical assessment conducted by the European Medicines Agency (EMA), please refer to the European Public Assessment Report, available on the EMA website.

This application was approved under Regulation 50 of the Human Medicines Regulation 2012, as amended (previously Article 8.3 of Directive 2001/83/EC, as amended).

This application was evaluated for fulfilment of orphan designation criteria. It was concluded that fulfilment of the criteria for approval as an orphan medicinal product was satisfactorily demonstrated. Please see Annex 1 for a summary of the orphan approval.

In line with the legal requirements for children's medicines, the application included a licensing authority decision on the agreement of a paediatric investigation plan (PIP) MHRA-100349-PIP01-21- M02. At the time of the submission of the application, the PIP was not yet completed as some measures were deferred.

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

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

A marketing authorisation was granted on 29 January 2024.

II. PRODUCT INFORMATION

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

The SmPC is in line with current guidelines and is satisfactory.

PATIENT INFORMATION LEAFLET (PIL)

The PIL is in line with current guidelines and is satisfactory.

LABEL
The labelling is in line with current guidelines and is satisfactory.

III. QUALITY ASPECTS
MHRA considered that the quality data submitted for this application is satisfactory. The grant of a marketing authorisation was recommended.

IV. NON-CLINICAL ASPECTS
MHRA considered that the non-clinical data submitted for this application is satisfactory. The grant of a marketing authorisation was recommended.

V. CLINICAL ASPECTS
MHRA considered that the clinical data submitted for this application is satisfactory. The grant of a marketing authorisation was recommended.

VI. RISK MANAGEMENT PLAN (RMP)
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.

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 product is acceptable. The non-clinical and clinical data submitted have shown the positive benefit/risk of this product in the treatment of invasive candidiasis in adults.

The Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling are satisfactory.

In accordance with legal requirements, the current approved GB versions of the SmPC and PIL for this product is available on the MHRA website.

IX. 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 SmPCs and/or PIL available on the MHRA website.

Application type	**Scope**	**Product information affected**	**Date of grant**	**Outcome**	**Assessment report attached Y/N**

Medicines & Healthcare products Regulatory Agency

Annex 1
Summary of fulfilment of the criteria for orphan drug designation

Product:	*Rezzayo 200 mg powder for concentrate for solution for infusion*
Active substance:	*rezafungin acetate*
Orphan Designation Number:	*PLGB 16950/0390/OD1*

Background:
This application was evaluated for fulfilment of orphan designation criteria and the designation criteria were considered fulfilled.

Evaluation:

Orphan condition
The orphan condition is invasive candidiasis. This is a recognised distinct medical condition with defined pathophysiological and clinical characteristics. These characteristics determine the group of patients in whom development of a medicinal product is plausible, based on the pathogenesis of the condition and pharmacodynamic evidence and assumptions. Different degrees of severity or stages/types of a disease would generally not be considered as distinct conditions.

Orphan indication
The orphan indication is treatment of invasive candidiasis.

Life threatening/ debilitating condition
The condition can be a severe and seriously debilitating disease in some patients and if left untreated, could lead to life-threatening complications and even death.

Prevalence of the Condition in Great Britain (GB)
Suitable evidence has been provided that demonstrates that, at the time of orphan designation, the condition affects an estimate of 0.5 to 0.69 in 10,000 people in GB. This does not exceed the upper limit of prevalence for orphan designation, which is 5 in 10,000 people in GB.

Existing methods of treatment
The condition can be a severe and seriously debilitating disease. A number of treatment options are available for treating this condition but each therapy has some limitations.

There are three main classes of monotherapy drugs authorised for the treatment of invasive *Candida* infections in Great Britain: azoles, echinocandins (the class to which rezafungin belongs), and polyenes. For invasive or disseminated candidiasis, the British National Formulary advises an echinocandin to be used as first-line treatment.

Fluconazole is an alternative for *Candida albicans* infection in clinically stable patients who have not received an azole antifungal recently. Amphotericin B is an alternative when an echinocandin or fluconazole cannot be used, however, amphotericin B should be considered for the initial treatment of central nervous system candidiasis. Voriconazole can be used for infections caused by fluconazole- resistant *Candida* species when oral therapy is required, or in patients intolerant of amphotericin B or an

echinocandin. In refractory cases, the British National Formulary advises that flucytosine can be used with intravenous amphotericin B.

Although various antifungal classes are currently in use, several aspects such as toxicity, formulation, and drug-drug interactions in some cases limit their use in daily clinical practice. The high morbidity and mortality rates in patients with invasive *Candida* infections indicate there remains room for improvement. Furthermore drug-resistant fungi are now emerging which makes the development of new antifungals for the treatment of severe *Candida* infection, including invasive candiasis, of great importance.

Justification of significant benefit
Methods for the treatment of the orphan condition already exist in GB. Suitable justification has been provided that Rezzayo 200 mg powder for concentrate for solution for infusion provides a significant benefit to those affected by the condition as specified in the orphan indication.

Rezafungin has shown promising efficacy and safety in adults for treatment of invasive candidiasis, based on the results of the clinical studies provided. The applicant has not been able to establish that rezafungin has any important advantages in terms of spectrum, efficacy or safety over the approved agents in the same class for treatment of candidiasis. At the same time, there are relatively few antifungal agents available and the overall assessment of the efficacy findings, supports a conclusion that rezafungin has efficacy in the population studied. There is also a potential for hepatic effects, including elevations in liver enzymes. In some patients with serious underlying medical conditions and multiple concomitant medications, hepatic dysfunction has occurred; a warning to this effect is present in the Summary of Product Characteristics.

Despite this, the product is considered to have some advantages. Clinical data has been provided showing improved efficacy compared to the azoles and polyenes which corresponds to a clinically relevant advantage. In addition, the reduced hospital stay in intensive care unit constitutes a major contribution to patient care over the other echinocandins. The major contribution to patient care is also supported by the once weekly administration of rezafungin over the daily intravenous administration. Therefore, the significant benefit claim is acceptable.

Conclusion:

Conclusion on acceptability of orphan designation
The applicant has demonstrated fulfilment of the criteria for approval as an orphan medicinal product.

All medicines that gain an orphan marketing authorisation from the UK Licensing Authority are listed on its publicly available Orphan Register until the end of the market exclusivity period. The authorised orphan indication defines the scope of orphan market exclusivity.

Decision: Grant

Date: 29 January 2024