swissmedic

Date: 28 October 2026
Swissmedic, Swiss Agency for Therapeutic Products

Swiss Public Assessment Report

Rezzayo

International non-proprietary name:	rezafungin
Pharmaceutical form:	Powder for concentrate for solution for infusion
Dosage strength(s):	200 mg
Route(s) of administration:	i.v.
Marketing authorisation holder:	Mundipharma Medical Company, Hamilton, Bermuda, Basel Branch
Marketing authorisation no.:	68394
Decision and decision date:	approved on 27 August 2026

Note:

This assessment report is as adopted by Swissmedic with all information of a commercially confidential nature deleted.

SwissPARs are final documents that provide information on submissions at a particular point in time. They are not updated after publication.

Table of contents

1 Terms, Definitions, Abbreviations 3
2 Background information on the procedure 4
2.1 Applicant's request(s) and information regarding procedure 4
2.2 Indication and dosage 4
2.2.1 Requested indication 4
2.2.2 Approved indication 4
2.2.3 Requested dosage 4
2.2.4 Approved dosage 4
2.3 Regulatory history (milestones) 5
3 Medical context 6
4 Quality aspects 6
5 Nonclinical aspects 6
6 Clinical aspects 6
6.1 Efficacy 6
6.2 Final clinical benefit risk assessment 7
7 Risk management plan summary 7
8 Appendix 8

1 Terms, Definitions, Abbreviations

ADA	Anti-drug antibody
ADME	Absorption, distribution, metabolism, elimination
AE	Adverse event
ALT	Alanine aminotransferase
API	Active pharmaceutical ingredient
AST	Aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical Classification System
AUC	Area under the plasma concentration-time curve
$AUC_{0\text{-}24h}$	Area under the plasma concentration-time curve for the 24-hour dosing interval
CI	Confidence interval
C_{max}	Maximum observed plasma/serum concentration of drug
CYP	Cytochrome P450
DDI	Drug-drug interaction
EMA	European Medicines Agency
ERA	Environmental risk assessment
FDA	Food and Drug Administration (USA)
GI	Gastrointestinal
GLP	Good Laboratory Practice
HPLC	High-performance liquid chromatography
IC/EC_{50}	Half-maximal inhibitory/effective concentration
ICH	International Council for Harmonisation
Ig	Immunoglobulin
INN	International non-proprietary name
ITT	Intention-to-treat
i.v.	intravenous
LoQ	List of Questions
MAH	Marketing authorisation holder
Max	Maximum
Min	Minimum
mITT	modified intention-to-treat
MRHD	Maximum recommended human dose
N/A	Not applicable
NI	non-inferiority
NO(A)EL	No observed (adverse) effect level
PBPK	Physiology-based pharmacokinetics
PD	Pharmacodynamics
PIP	Paediatric investigation plan (EMA)
PK	Pharmacokinetics
PopPK	Population pharmacokinetics
PSP	Pediatric study plan (US FDA)
RMP	Risk management plan
SAE	Serious adverse event
SwissPAR	Swiss Public Assessment Report
TEAE	Treatment-emergent adverse event
TPA	Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (SR 812.21)
TPO	Ordinance of 21 September 2018 on Therapeutic Products (SR 812.212.21)

2 Background information on the procedure

2.1 Applicant's request(s) and information regarding procedure

New active substance status
The applicant requested new active substance status for rezafungin in the above-mentioned medicinal product.

Orphan drug status
The applicant requested orphan drug status in accordance with Article 4 paragraph 1 letter a^{decies} no. 2 TPA.
Orphan drug status was granted on 19 August 2021

Authorisation as human medicinal product in accordance with Article 13 TPA
The applicant requested a reduced assessment procedure in accordance with Article 13 TPA.

2.2 Indication and dosage

2.2.1 Requested indication

REZZAYO is indicated for the treatment of invasive candidiasis in adults. Consideration should be given to official guidance on the appropriate use of antifungal agents.

2.2.2 Approved indication

REZZAYO is indicated for the treatment of invasive *Candida* infection in adults who have limited or no alternative treatment options for candidaemia and invasive candidiasis.

Consideration should be given to official guidance on the appropriate use of antifungal agents.

2.2.3 Requested dosage

Summary of the requested standard dosage:
A single 400 mg loading dose on Day 1, followed by 200 mg on Day 8 and once weekly thereafter. The duration of treatment should be based upon the patient's clinical and microbiological response. In general, antifungal therapy should continue for at least 14 days after the last positive culture. During clinical trials patients were treated with rezafungin for up to 28 days. The safety information on rezafungin treatment durations longer than 4 weeks is limited.
[…]

2.2.4 Approved dosage

(see appendix)

2.3 Regulatory history (milestones)

Application	28 July 2025
Formal objection	13 August 2025
Response to formal objection	29 August 2025
Formal control completed	30 September 2025
Preliminary decision	28 January 2026
Response to preliminary decision	22 April 2026
Labelling corrections (informal exchange)	31 July 2026
Response to labelling corrections (informal exchange)	10 August 2026
Final decision	27 August 2026
Decision	approval

Based on Art. 13 TPA Swissmedic has only assessed parts of the primary data submitted with this application. As regards the remaining data, Swissmedic relies for its decision on the assessment of the foreign reference authority, the EMA. This SwissPAR relates to the assessment report Rezzayo, Procedure No. EMEA/H/C/005900/0000 (12 October 2023, EMA/487522/2023) issued by the EMA.

3 Medical context

Candidaemia and invasive candidiasis are serious infections associated with substantial morbidity and mortality. Echinocandins are established intravenous (i.v.) treatment options and, in clinically stable patients with isolates susceptible to azoles, after 5 to 7 days of i.v. administration, treatment is commonly de-escalated to an oral azole to complete therapy. Rezafungin is an echinocandin with an antifungal spectrum broadly similar to that of other approved members of the class. Its prolonged half-life permits once-weekly intravenous administration, rather than daily administration.

4 Quality aspects

Swissmedic has not assessed the primary data relating to quality aspects submitted with this application and relies on the assessment of the foreign reference authority, the EMA (see section 2.3 Regulatory history (milestones).

5 Nonclinical aspects

Swissmedic has not assessed the primary data relating to nonclinical aspects submitted with this application and relies on the assessment of the foreign reference authority, the EMA (see section 2.3 Regulatory history (milestones))

6 Clinical aspects

Based on Art. 13 TPA Swissmedic has only assessed parts of the primary data submitted with this application. As regards the remaining data, Swissmedic relies for its decision on the assessment of the foreign reference authority, the EMA (Procedure No. EMEA/H/C/005900/0000). The evaluation focused on data submitted to support the efficacy claim for the wording of the indication, as well as the difference in indication wording as approved by the EMA and FDA (NDA 217417).

6.1 Efficacy

The pivotal evidence was provided by the single Phase 3 study ReSTORE, a randomised, double-blind, active-controlled Phase 3 non-inferiority study in patients with candidaemia or invasive candidiasis, where rezafungin was compared to caspofungin. STRIVE, a Phase 2 dose-ranging study in a similar population, provided supportive efficacy evidence.

The original ReSTORE database lock included 187 patients in the modified intention-to-treat population. An expanded database lock, which incorporated a China extended-enrolment phase, increased the modified intention-to-treat population to 232 patients. The China extension followed the clinical study protocol, with the exception of one additional endpoint to demonstrate that the results for Global Response (determined from clinical cure as assessed by the investigator, mycological eradication, and radiological cure – if applicable) at Day 14 in the mITT population of the ReSTORE China cohort were consistent with those obtained from the analysis of the data from all subjects in the mITT population.

ReSTORE met the prespecified non-inferiority criterion using a 20% non-inferiority margin. In the expanded dataset, the adjusted treatment difference for global response at Day 14 was -1.0% (95% CI [-13.5; 11.6]). The study also met the prespecified criterion for all-cause mortality at Day 30 with a treatment difference for global response of 0.4% (95% CI [-10.8; 11.6]). Superiority over caspofungin was not demonstrated for either endpoint.

6.2 Final clinical benefit risk assessment

The choice of a 20% non-inferiority margin is the principal limitation of the efficacy evidence, as this allows a potentially clinically important loss of efficacy relative to an established active comparator. A smaller NI margin would require a larger sample size, and challenges to include sufficient participants in this situation are acknowledged. However, given the high mortality associated with the disease, a non-inferiority margin of 10% would have been preferable.

Generalisability of results is limited as patients with *Candida* endocarditis, osteomyelitis, and other complex or chronic infections were excluded, and few neutropenic patients were enrolled. No firm conclusion can be drawn regarding efficacy in these populations.

The current efficacy evidence is not sufficiently precise for unrestricted first-line treatment of invasive candidiasis. The convenience of weekly administration does not, by itself, outweigh the possibility of a clinically relevant loss of efficacy compared with established therapy, particularly as no compensating safety advantage has been demonstrated. However, once-weekly administration may offer clinically meaningful value in a properly defined population. In consequence, the benefit-risk profile is considered favourable for adults with candidaemia or invasive candidiasis who have limited or no alternative treatment options. The approved indication appropriately reflects the residual uncertainty and is also consistent with antimicrobial stewardship principles (e.g. unless needed, echinocandin treatment should not be unnecessarily prolonged and de-escalation approaches (e.g. to fluconazole) should be used.

For further information regarding clinical and clinical pharmacology aspects, please refer to the attached Information for healthcare professionals.

7 Risk management plan summary

The RMP summaries contain information on the medicinal products' safety profiles and explain the measures that are taken to further investigate and monitor the risks, as well as to prevent or minimise them.
The RMP summaries are published separately on the Swissmedic website. It is the responsibility of the marketing authorisation holder to ensure that the content of the published RMP summaries is accurate and correct. As the RMPs are international documents, their summaries might differ from the content in the Information for healthcare professionals / product information approved and published in Switzerland, e.g. by mentioning risks that occur in populations or indications not included in the Swiss authorisations.

8 Appendix

Approved Information for healthcare professionals

Please be aware that the following version of the Information for healthcare professionals for Rezzayo was approved with the submission described in the SwissPAR. This Information for healthcare professionals may have been updated since the SwissPAR was published.

Please note that the valid and relevant reference document for the effective and safe use of medicinal products in Switzerland is the Information for healthcare professionals currently authorised by Swissmedic (see www.swissmedicinfo-pro.ch).

Note:
The following Information for healthcare professionals has been translated by the MAH. It is the responsibility of the authorisation holder to ensure the translation is correct. The only binding and legally valid text is the Information for healthcare professionals approved in one of the official Swiss languages.

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected new or serious adverse reactions. See the “Undesirable effects” section for advice on the reporting of adverse reactions.

REZZAYO® 200 mg powder for concentrate for solution for infusion

Composition

Active substances

Rezafungin as rezafungin acetate

Excipients

Mannitol, histidine, polysorbate 80, hydrochloric acid (for pH- -adjustment), sodium hydroxide (for pH- -adjustment)

Pharmaceutical form and active substance quantity per unit

Powder for concentrate for solution for infusion.
White to pale yellow cake or powder.
Each vial contains 200 mg rezafungin (as acetate).

Indications/Uses

REZZAYO is indicated for the treatment of invasive Candida infection in adults who have limited or no alternative treatment options for candidaemia and invasive candidiasis.

Consideration should be given to official guidance on the appropriate use of antifungal agents.

Dosage/Administration

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

Dosage
A single 400 mg loading dose on Day 1, followed by 200 mg on Day 8 and once weekly thereafter.

The duration of treatment should be based upon the patient's clinical and microbiological response. In general, antifungal therapy should continue for at least 14 days after the last positive culture. During clinical trials patients were treated with rezafungin for up to 28 days. Safety information on treatment with rezafungin for more than 4 weeks is limited.

If a scheduled dose is missed (not given on the assigned day) the missed dose should be administered as soon as possible.

- If the missed dose is administered within 3 days of the assigned day, the next weekly dose may be given on schedule.
- If the missed dose is administered more than 3 days after the assigned day, the dosing schedule should be revised to ensure there are at least 4 days before the next dose.

If administration is restarted more than 2 weeks after the missed dose, the dosing should be started again at the 400 mg loading dose.

Special populations

Elderly patients

No dose adjustment is required in elderly patients aged 65 years or more (see under "*Pharmacokinetics*").

Hepatic impairment

No dose adjustment is required for patients with hepatic impairment (see under "*Pharmacokinetics*").

Renal impairment

No dose adjustment is required for patients with renal impairment. This medicinal product can be given without regard to the timing of haemodialysis (see under "*Pharmacokinetics*").

Other populations

No dose adjustment is required based on patients' weight (see under "*Pharmacokinetics*").

Paediatric population

The safety and efficacy of REZZAYO in children below 18 years have not yet been established. No data are available.

Method of administration

For intravenous use only.

After reconstitution and dilution (see under "*Instructions for handling*"), the solution should be administered by slow intravenous infusion over approximately 1 hour. The infusion time may be

increased up to 180 minutes to manage any evolving symptoms of infusion-related reaction (see under «*Warnings and precautions*»)..

For instructions on reconstitution and dilution of the medicinal product before administration, see under *"Instructions for handling".*

Contraindications

Hypersensitivity to the active substance or to any of the excipients listed under «*Composition*».

Hypersensitivity to other medicinal products of the echinocandin class.

Warnings and precautions

The authorisation of this indication is based on limited clinical data on the safety and efficacy of REZZAYO (see "Properties/Effects").

The efficacy of rezafungin has only been evaluated in a limited number of neutropenic patients.

Hepatic effects

In clinical trials, elevations in liver enzymes have been seen in some patients treated with rezafungin. In some patients with serious underlying medical conditions who were receiving multiple concomitant medications along with rezafungin, clinically significant hepatic dysfunction has occurred. A causal relationship to rezafungin has not been established. Patients who develop elevations in liver enzymes during rezafungin therapy should be monitored and the benefit/risk of continuing rezafungin therapy should be re-evaluated.

Infusion-related reactions

Transient infusion-related reactions have occurred with rezafungin, characterised by flushing, sensation of warmth, nausea, and chest tightness.

In clinical trials, infusion reactions resolved within minutes, some without interruption or discontinuation of the infusion. Patients should be monitored during the infusion. If the infusion is stopped due to a reaction, consideration may be given to restarting the infusion at a slower rate after the symptoms have resolved.

Phototoxicity

Rezafungin may cause increased risk of phototoxicity. Patients should be advised to avoid sun exposure and other sources of UV radiation without adequate protection during treatment and for 7 days after the last administration of rezafungin.

Sodium content

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

Interactions

The drug-drug interaction potential of rezafungin with a number of probe substrates of cytochrome-P450- enzymes and/or transporter proteins has been assessed clinically. The need for dose adjustments is considered unlikely for medicinal products that are substrates for the CYP2C8, CYP3A4, CYP1A2, and CYP2B6 enzymes and P-gp, BCRP, OATP, OCT1, OCT2, MATE1, and MATE2 transporter proteins, when administered with rezafungin.

The drug-drug interaction potential of rezafungin with a number of co-administered medicinal products has also been assessed clinically. The need for dose adjustments is considered unlikely for tacrolimus, cyclosporine, ibrutinib, mycophenolate mofetil, and venetoclax when administered with rezafungin.

In vitro rezafungin is metabolically stable and was found not to be a substrate for BCRP, P-gp, MRP2, OATP1B1, OATP1B3, OCT1, OCTN1, and OCTN2 transporter proteins. Therefore, the need for dose adjustments of rezafungin is considered unlikely when rezafungin is co-administered with other medicinal products.

Pregnancy, lactation

Pregnancy

There are no data from the use of rezafungin in pregnant women.
Studies in animals did not show reproductive or developmental toxicity (see under "*Preclinical data*").
Rezafungin has been shown to cross the placental barrier in animal studies. The potential risk for humans is unknown.

Rezafungin is not recommended to be used during pregnancy and in women of childbearing potential not using contraception unless the benefit outweighs the potential risk to the foetus.

Lactation

There are no data from the use of rezafungin in lactating women. It is unknown whether rezafungin or its metabolites are excreted in human milk. Rezafungin excretion into milk was observed in rats (see under "*Preclinical data*").

A risk to the breastfed child cannot be excluded.

A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from rezafungin therapy. Both the benefit of breast-feeding for the child and the benefit of therapy for the woman should be taken into account.

Fertility

No data on the effect of rezafungin on human fertility are available. Rezafungin did not affect fertility in female rats or reproductive performance in male rats, despite reversible testicular effects in male rats (see under "*Preclinical data*").

Effects on ability to drive and use machines

REZZAYO has no or negligible influence on the ability to drive and use machines.

Undesirable effects

Summary of the safety profile

Based on clinical trial experience, the most frequently reported adverse reactions for rezafungin were hypokalaemia, pyrexia, anaemia, and diarrhoea (very common adverse reactions).

Transient infusion-related reactions have occurred with rezafungin, characterised by flushing, sensation of warmth, nausea, and chest tightness (see section 4.4).

Tabulated list of adverse reactions

The following table lists the adverse reactions reported in 173 patients treated with rezafungin 400/200 mg by System Organ Class (SOC) and MedDRA preferred term. They are listed according to the frequency categories very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000) and very rare (< 1/10,000), as well as adverse reactions from spontaneous reports with a frequency of "not known (cannot be estimated from the available data)". Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 1. Table of adverse reactions

System organ class	Very common ≥ 1/10	Common ≥ 1/100 to < 1/10	Uncommon ≥ 1/1 000 to < 1/100	Not known
Blood and lymphatic system disorders	Anaemia			
Metabolism and nutrition disorders	Hypokalaemia	Hypomagnesaemia, Hypophosphataemia	Hyperphosphataemia, Hyponatraemia	
Vascular disorders		Hypotension		
Respiratory, thoracic and mediastinal disorders		Wheezing		
Gastrointestinal disorders	Diarrhoea	Vomiting, Nausea, Abdominal pain, Constipation		
Skin and subcutaneous tissue disorders		Erythema, Rash	Phototoxicity	Urticaria
Musculoskeletal and connective tissue disorders			Tremor	
General disorders and administration site conditions	Pyrexia			
Investigations		Blood alkaline phosphatase increased, Hepatic enzymes increased, Alanine aminotransferase increased, Aspartate aminotransferase increased, Blood bilirubin increased	Eosinophil count increased	
Injury, poisoning and procedural complications		Infusion-related reactions		

Reporting suspected adverse reactions after authorisation of the medicinal product is very important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions online via the ElViS portal (Electronic Vigilance System). You can obtain information about this at www.swissmedic.ch.

Overdose

In the event of overdose, supportive care and symptomatic treatment are advised, with maintenance of homeostasis and vital functions.

In a Phase 1 clinical trial, single doses of 600 mg and 1400 mg were administered with no reported dose-limiting toxicity. Rezafungin doses of 400 mg once weekly for up to 4 weeks were administered in a Phase 2 clinical trial with no reported dose-limiting toxicity.

Rezafungin is highly protein-bound and not expected to be dialysable (see under “Pharmacokinetics”).

Properties/Effects

ATC Code

J02AX08

Mechanism of action

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 that is not present in mammalian cells. Inhibition of 1,3-β-D-glucan synthesis results in rapid and concentration-dependent fungicidal activity against *Candida*- species (spp.).

Activity in vitro

The MIC90 values for rezafungin (determined using a modified EUCAST method) are generally ≤ 0.016 mg/L for all species other than Candida parapsilosis (Candida parapsilosis MIC90 = 2 mg/L).

In a study using a collection of clinical isolates of Candida spp. enriched with echinocandin-resistant and/or azole-resistant strains, the activity of rezafungin was comparable to that of anidulafungin.

Resistance

Reduced susceptibility to echinocandins, including rezafungin, arises from mutations in glucan synthase catalytic subunit-encoding FKS genes (*FKS1* for most *Candida spp.*; *FKS1 and FKS2* for *C. glabrata*).

Susceptibility testing interpretative criteria

MIC [minimum inhibitory concentration] interpretative criteria for susceptibility testing have been established by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) for rezafungin. These are listed here:

https://www.ema.europa.eu/documents/other/minimum-inhibitory-concentration-mic-breakpoints_en.xlsx

A modified EUCAST broth microdilution MIC methodology has been used for testing the susceptibility of Candida spp. to rezafungin as well as to obtain the respective interpretative breakpoints.

Clinical efficacy

Candidaemia and invasive candidiasis in adult patients
The efficacy of rezafungin in the treatment of patients with candidaemia and/or invasive candidiasis (C/IC) was evaluated in a single Phase-3-study.

The Phase-3- study was multicentre, prospective, randomised and double-blind. Patients with septic arthritis in a prosthetic joint, osteomyelitis, endocarditis or myocarditis, meningitis, endophthalmitis, chorioretinitis or any central nervous system infection, chronic disseminated candidiasis and urinary tract- candidiasis secondary to obstruction or surgical instrumentation were excluded from the study. Subjects were randomised in a 1:1 ratio to receive rezafungin as a 400 mg loading dose on Day 1, followed by 200 mg on Day 8 and once weekly thereafter, for a total of 2 to 4 weeks or caspofungin as a single 70-mg- intravenous loading dose on Day 1 followed by caspofungin 50 mg intravenous once daily for a total - treatment duration of 14 days to 28 days.

For rezafungin and caspofungin treatment groups, 77.0% and 74.2% of patients, respectively, had a final diagnosis of candidaemia only. Most of them had a modified APACHE II score < 20, representing 84.4% and 81.5% of rezafungin and caspofungin subjects, respectively. In the rezafungin and caspofungin treatment groups, 88.5% and 91.1% of patients, respectively, had an absolute neutrophil count (ANC) ≥ 500/mm³ at baseline.

The primary efficacy endpoint was global response (confirmed by the Data Review Committee [*DRC]) at Day 14. Global response was determined based on clinical response, mycological response and radiological response (for patients with IC who qualified for the study). Non-inferiority was concluded if the lower bound of the 95-%- confidence interval (CI) for the difference in global response at Day 14 (rezafungin-caspofungin) was > −-20%. Secondary efficacy endpoints included all-cause mortality at Day 30 [Day 30 ACM (All Cause Mortality)] and global response at Day 5. The results for these endpoints are shown in Table 2 for the mITT- analysis set. This was defined as all subjects with a documented Candida infection based on Central Laboratory evaluation of a blood culture or a culture from a normally sterile site obtained ≤ 4 days (96 hours) before randomisation. The patients in this set had to have received ≥ 1 dose of investigational medicinal product.*

Table 2. Summary of results from the Phase-3- ReSTORE study (mITT- analysis set)

	Rezafungin (R) (N = 115) n (%)	Caspofungin (C) (N = 117) n (%)	Difference (R-C) (95% CI)
Global Response [1]			
Day 5	60 (52.2)	57 (48.7)	3.5 (-9.4; 16.2)
Day 14	65 (56.5)	67 (57.3)	-1.0 (-13.5; 11.6)
Day 30 ACM (deceased) [2, 3]	29 (25.2)	29 (24.8)	0.4 (-10.8; 11.6)

[1] Two-sided 95% confidence intervals (CIs) for the observed differences in global response (rezafungin minus caspofungin) were calculated using the Miettinen and Nurminen method, unadjusted for global response at Day 5 and adjusted for the two randomisation strata for global response at Day 14 (diagnosis [candidaemia only; invasive candidiasis] and APACHE II score/ANC [APACHE II score ≥ 20 or ANC < 500 cells/mm³; APACHE II score < 20 and ANC ≥ 500 cells/mm³] at screening). Cochran-Mantel-Haenszel weights are used for the stratum weights.
[2] The two-sided 95% confidence interval (CI) for the observed difference in Day 30 mortality rates (rezafungin minus caspofungin treatment group) was calculated using the unadjusted Miettinen and Nurminen method.
[3] Subjects who died on or before Day 30, or with unknown survival status.

Paediatric population

The European Medicines- Agency has deferred the obligation to submit the results of studies with REZZAYO in one or more subsets of the paediatric population in treatment of invasive candidiasis (see under "*Dosage/Administration*" for information on paediatric use).

Pharmacokinetics

General pharmacokinetic characteristics

The pharmacokinetics of rezafungin have been characterised in healthy subjects, special populations and patients. Rezafungin has a long half-life, allowing for once-weekly dosing. *Steady state* is achieved with the first loading dose (twice the weekly maintenance dose).

Distribution

Rezafungin is rapidly distributed with a volume of distribution approximately equal to total body water (~ 40 L). Protein binding of rezafungin is high in humans (> 97%).

Metabolism

In vitro, rezafungin was stable across species after incubation with liver- and intestinal microsomes and with hepatocytes.

In a clinical single-dose- study, radiolabelled (^{14}C)-rezafungin (approximately 400 mg/200 µCi radioactivity) was administered to healthy volunteers. The main circulating moiety was parent rezafungin-. Rezafungin plasma- AUC accounted for approximately 77% of the total- radiocarbon AUC, with individual metabolites each accounting for less than 10%.

Elimination

Following administration of single doses of rezafungin- (1-hour intravenous infusion; 50, 100, 200 and 400 mg), the mean total- body clearance of rezafungin was low at approximately 0.2 L/hour across all dose levels, with a mean terminal half-life of 127 to 146 hours. The fraction of the dose excreted in urine as unchanged rezafungin was <1% at all dose levels, indicating that renal clearance makes only a minor contribution to the elimination of rezafungin.

In a clinical single-dose- study, radiolabelled (^{14}C)-rezafungin (approximately 400 mg/200 µCi radioactivity) was administered to healthy volunteers. The estimated mean total- recovery of radioactivity was 88.3% at Day 60; this was based on interpolated data (obtained at return visits to the clinical facility on Day 29 and Day 60). Approximately 74% of the recovered radioactive dose was in faeces (primarily as unchanged rezafungin) and 26% in urine (mainly as metabolites). This indicates that rezafungin is eliminated primarily in the faeces as unchanged rezafungin.

Linearity

Following intravenous infusion of a single dose, the pharmacokinetics of rezafungin are linear over a dose range of 50 to 1400 mg. The observed time to maximum plasma concentration (T_{max}) was at the end of the infusion (as expected) for all doses, and AUC increased in a dose-proportional manner.

Kinetics in specific patient groups

Hepatic impairment

The pharmacokinetics of rezafungin were evaluated in patients with moderate (Child-Pugh- Class B, n = 8) and severe (Child-Pugh- Class C, n = 8) hepatic impairment. Mean rezafungin exposure was reduced by approximately 30% in patients with moderate and severe hepatic impairment compared with matched patients with normal hepatic function. The pharmacokinetics of rezafungin were similar in patients with moderate and severe hepatic impairment, and rezafungin exposure did not change

with increasing severity of hepatic impairment. Hepatic impairment had no clinically meaningful effect on the pharmacokinetics of rezafungin.

Renal impairment
A population pharmacokinetic analysis including data from Phase-1-, Phase-2- and Phase-3- studies showed that creatinine- clearance was not a significant covariate of rezafungin pharmacokinetics.

Elderly patients
A population pharmacokinetic analysis including data from Phase-1-, Phase-2- and Phase-3- studies showed that age was not a significant covariate of rezafungin pharmacokinetics.

Weight
A population pharmacokinetic analysis including data from Phase-1-, Phase-2- and Phase-3- studies showed that body surface area was a significant covariate of rezafungin pharmacokinetics. A simulation of exposure in clinically obese patients (Body- Mass- Index (BMI) ≥ 30) showed that exposure was reduced in these patients; however, this reduction is not considered clinically meaningful.

Sex/ethnicity
A population pharmacokinetic analysis including data from Phase-1-, Phase-2- and Phase-3- studies showed that sex and ethnicity were not significant covariates of rezafungin pharmacokinetics.

Preclinical data

Rezafungin induced an acute histamine- release response in rats; this response was not induced in monkeys.

Reversible intention tremors (defined as a tremor that becomes more pronounced when performing goal-directed movements) were observed in a 3--month study in monkeys with administration once every 3 days and occurred more frequently at ≥ 30 mg/kg. The no observed effect level (*No Observed Effect Level*, NOEL) for intention tremors in this study was established as 10 mg/kg (approximately 2.5--fold the clinical exposure based on AUC comparison). Intention tremors were not observed in the 6--month study in monkeys in which animals received an intravenous dose of up to 30 mg/kg once weekly (approximately 5.8-fold the clinical exposure based on AUC comparison), or in studies in rats.

Rezafungin tested negative for genotoxicity in *in- vitro*- studies conducted in bacterial- and mammalian cells and in a micronucleus- test in rats.

No carcinogenicity studies were conducted.

In reproductive toxicity studies, rezafungin had no effect on mating or fertility in male and female rats following intravenous administration (rapid bolus injection) once every 3 days at doses up to 45 mg/kg (6--fold the clinical exposure based on the AUC determined in a separate study in rats). In the male fertility study, decreased sperm motility was observed at ≥ 30 mg/kg, and at 45 mg/kg most males showed mild/moderate hypospermia and had no detectable motile sperm. There was an increased incidence of abnormal sperm morphology and mild to moderate degeneration of the seminiferous tubules at rezafungin- doses of ≥ 30 mg/kg.

In a 3--month toxicology study in rats, rezafungin was administered intravenously (by rapid bolus injection) once every 3 days. Male animals receiving a dose of 45 mg/kg showed minimal tubular degeneration/atrophy in the testes and cellular debris in the epididymides after 3 months. The incidence of this finding decreased by the end of a 4--week reversibility period.

In contrast, there were no effects on the testes, epididymides or spermatogenesis in rats receiving an intravenous dose (by rapid bolus injection) once weekly for 6 months or following a 6--month recovery period at a dose of 45 mg/kg (i.e. approximately 4.7--fold the clinical exposure based on AUC comparison).

Sperm concentration, production rate, morphology and motility were unaffected in adult monkeys receiving rezafungin once weekly for 11 or 22 weeks at doses up to 30 mg/kg (approximately 6--fold the clinical exposure based on AUC comparison), or following a 52--week recovery period.

No reproductive- or developmental toxicity was observed following intravenous administration of rezafungin to pregnant rats and rabbits at ≥ 3.0--fold the predicted human steady--state plasma AUC- exposure.

In a study of pre-- and postnatal development in rats administered up to 45 mg/kg rezafungin intravenously, no adverse effects on growth, maturation or indicators of neurobehavioural or reproductive function were observed. Rezafungin was measurable at low concentrations in the plasma of foetuses of treated animals (concentrations in foetal plasma were 2.0–3.6% of those observed in maternal plasma) and was excreted in milk (concentrations in milk were 22–26% of those observed in maternal plasma).

Other information

Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products except those listed under "*Instructions for handling*".

Shelf life

Unopened vial

The medicinal product may only be used up to the date marked "EXP" on the container.

Stability of the reconstituted solution in the vial and the diluted solution for infusion

Chemical and physical stability after reconstitution with water for injections has been demonstrated for up to 24 hours at 25 °C and at 2 °C to 8 °C.

Chemical and physical stability of the diluted solution for infusion (immediately after reconstitution) has been demonstrated for 48 hours at 25 °C and at 2 °C to 8 °C.

From a microbiological point of view, the reconstituted solution and the diluted solution for infusion should be used immediately. If not used immediately, in-use storage conditions prior to use are the responsibility of the user. Storage after first opening should normally not exceed 24 hours at 2 °C to 8 °C, unless reconstitution and dilution have taken place under controlled and validated aseptic conditions.

Special precautions for storage

Do not store above 25 °C.
Keep the vial in the outer carton in order to protect from light.
For storage conditions after reconstitution and dilution of the medicinal product, see under "*Shelf life*".

Instructions for handling

REZZAYO should be administered as a single agent by intravenous infusion in sodium chloride- 9 mg/mL (0.9%) solution for injection, sodium chloride- 4.5 mg/mL (0.45%) solution for injection or 5% glucose solution.

INSTRUCTIONS FOR USE IN ADULT PATIENTS

REZZAYO must be reconstituted and diluted before administration.

From a microbiological point of view, the reconstituted solution and the diluted solution for infusion should be used immediately. If not used immediately, in-use storage conditions prior to use are the responsibility of the user. Storage after first opening should normally not exceed 24 hours at 2 °C to 8

°C, unless reconstitution and dilution have taken place under controlled and validated aseptic conditions.

Each vial should be reconstituted under aseptic conditions with 9.5 mL of water for injections. The concentration of the reconstituted vial will then be 20 mg/mL. Do not use sterile sodium chloride- 9 mg/mL (0.9%) solution for injection to reconstitute the contents of the vial; use only water for injections.

To minimise foaming, the medicinal product must not be shaken or mixed vigorously. The white to pale yellow powder will dissolve completely. Mix with a gentle swirling motion for 5 minutes until the reconstituted solution is clear and colourless to pale yellow. The reconstituted solution must be inspected visually for particulate matter or discolouration. If any irregularities are identified, do not use the vial.

The vial is for single use only. Therefore, any unused reconstituted concentrate must be discarded immediately.

For the 400- mg- loading dose, the reconstitution step should be repeated for a second REZZAYO- vial (see dosing table).

The total volume to be infused should be 250 mL; therefore, the volume of the intravenous infusion bag (or bottle) should be adjusted accordingly, as shown in the dosing table. Using aseptic technique, transfer 10 mL from each reconstituted vial into an intravenous infusion bag (or bottle) containing sodium chloride- 9 mg/mL (0.9%) solution for injection, sodium chloride- 4.5 mg/mL (0.45%) solution for injection or 5% glucose solution. The total reconstituted volume to be added to the intravenous infusion bag or bottle is shown in the dosing table. Mix the solution by gently inverting the intravenous infusion bag (or bottle). Do not shake excessively.

After dilution, discard the solution if particulate matter or discolouration is identified.

DOSING TABLE – PREPARATION OF THE SOLUTION FOR INFUSION IN ADULTS

Dose (mg)	Number of vials	Volume to be withdrawn from the 250 mL bag/bottle for intravenous infusion (mL)	Volume of water for injections to be added to each vial (mL)	Total volume of reconstituted solution to be added to the intravenous infusion bag/bottle (mL)	Total infusion volume (mL)	Final concentration of solution for infusion (mg/mL)
400	2	20	9.5	20*	250	1.6
200	1	10	9.5	10	250	0.8

* 10 mL from each of the two vials, 20 mL in total.

Any unused medicinal product or waste material should be disposed of in accordance with national requirements.

Authorisation no.

68394 (Swissmedic)

Packs

Pack containing 1 vial [A]

Marketing authorisation holder

Mundipharma Medical Company, Hamilton/Bermuda, Basel branch

Date of revision of the text

January 2026