Approved Professional Information for Medicines for Human Use:

MYCIBACT IV

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

MYCIBACT IV 500 mg powder for solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains azithromycin dihydrate equivalent to 500 mg of azithromycin, which after reconstitution results in a 100 mg/mL azithromycin solution. The concentrate should be further diluted to 1 mg/mL or 2 mg/mL.

Sugar free.

Contains 114 mg (4,96 mmol) sodium per vial.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for solution for infusion. A white to off-white lyophilised powder. The reconstituted solution is clear and colourless, free of undissolved particles.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

MYCIBACT IV is indicated for the treatment of community acquired pneumonia caused by susceptible organisms, including *Legionella pneumophila,* in patients who require initial intravenous therapy.

The safety and efficacy of MYCIBACT IV for the treatment of infections in children has not been established.

4.2 Posology and method of administration

Posology

For more severe infections, the recommended dose of MYCIBACT IV for the treatment of adult patients with community acquired pneumonia requiring hospitalisation due to the indicated organisms is 500 mg as a single daily dose by the intravenous route for at least two days. Intravenous therapy should be followed by azithromycin by the oral route as a single daily dose of 500 mg to complete a 7 to 10 day course of therapy. The timing of the conversion to oral therapy should be done at the discretion of the medical practitioner and in accordance with clinical response.

Special populations

Elderly population

No dosage adjustment is necessary in elderly patients requiring MYCIBACT IV therapy. Elderly patients may be more susceptible to development of Torsade de Pointes dysrhythmia than younger patients (see section 4.4).

Use in children

The safety and effectiveness of MYCIBACT IV for the treatment of infections in children has not been established.

Method of administration

MYCIBACT IV after reconstitution and dilution is for administration by intravenous infusion only.

MYCIBACT IV should not be given as a bolus or as an intramuscular injection.

The infusate concentration and rate of infusion for azithromycin powder for solution for infusion should be either 1 mg/mL over 3 hours or 2 mg/mL over 1 hour.

For instructions for preparation or reconstitution, see section 6.6.

4.3 Contraindications

MYCIBACT IV is contraindicated in patients with a known hypersensitivity to azithromycin, erythromycin or any of the macrolide antibiotics, or to any of the excipients of MYCIBACT IV.

Because of the theoretical possibility of ergotism, MYCIBACT IV and ergot derivatives should not be co-administered.

Use in hepatic impairment

As the liver is the principal route of excretion of MYCIBACT IV, it should not be prescribed in patients with hepatic disease.

4.4 Special warnings and precautions for use

Hypersensitivity

Rare serious allergic reactions including angioedema and anaphylaxis (rarely fatal), dermatologic reactions including acute generalised exanthematous pustulosis (AGEP),Stevens Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) (rarely fatal) and medicine reaction with eosinophilia and systemic symptoms (DRESS) have been reported. Some of these reactions with

azithromycin have resulted in recurrent symptoms and required a longer period of observation and treatment. If an allergic reaction occurs MYCIBACT IV should be discontinued, and appropriate therapy should be instituted. Medical practitioner should be aware that reappearance of the allergic symptoms may occur when symptomatic therapy is discontinued.

Hepatotoxicity

Since the liver is the principal route of elimination for azithromycin, the use of MYCIBACT IV should not be prescribed in patients with hepatic disease (see section 4.3). Cases of fulminant hepatitis potentially leading to life-threatening liver failure have been reported with azithromycin (see section 4.8). Some patients may have had pre-existing hepatic disease or may have been taking other hepatotoxic medicines.

In case of signs and symptoms of liver dysfunction, such as rapid developing asthenia associated with jaundice, dark urine, bleeding tendency or hepatic encephalopathy, liver function tests/ investigations should be performed immediately. MYCIBACT IV administration should be stopped if liver dysfunction has emerged.

Ergot derivatives

In patients receiving ergotamine derivatives, ergotism has been precipitated by co-administration of some macrolide antibiotics. There are no data concerning the possibility of an interaction between ergot and azithromycin. However, because of the theoretical possibility of ergotism, MYCIBACT IV and ergot derivatives should not be co-administrated (see section 4.3).

Prolongation of the QT interval

Prolonged cardiac repolarisation and QT interval, imparting a risk of developing cardiac dysrhythmia and torsades de pointes, have been seen in treatment with other macrolides. A similar effect with azithromycin cannot be completely ruled out in patients at increased risk for prolonged cardiac repolarisation (see Section 4.8); therefore, caution is required when treating patients:

• With congenital or documented QT prolongation

• Currently receiving treatment with other active medicines known to prolong QT interval such as antidysrhythmics of classes Ia and III, cisapride and terfenadine

• With electrolyte disturbance, particularly in case of hypokalaemia and hypomagnesemia

• With clinically relevant bradycardia, cardiac dysrhythmia or severe cardiac insufficiency.

Superinfection

Observation for signs of superinfection with non-susceptible organisms including fungi is recommended.

***Clostridium difficile* associated diarrhoea**

Clostridium difficile associated diarrhoea (Pseudomembranous colitis - CDAD) has been reported with azithromycin, and may range in severity from mild diarrhoea to fatal colitis. Treatment with antibiotics alters the normal flora of the colon allowing an overgrowth of *C. difficile*. Strains of *C. difficile* producing hypertoxin A and B contribute to the development of CDAD. Hypertoxin producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. Therefore, CDAD must be considered in patients who present with diarrhoea during or subsequent to the administration of any antibiotics. Careful medical history is

necessary since CDAD has been reported to occur over two months after the administration of antibacterial. Discontinuation of therapy with azithromycin and the administration of specific treatment for *C. difficile* should be considered.

Streptococcal infections

Penicillin is usually the first choice for treatment of pharyngitis/tonsillitis due to *Streptococcus pyogenes* and also for prophylaxis of acute rheumatic fever. Azithromycin is in general effective against streptococcus in the oropharynx, but no data are available that demonstrate the efficacy of azithromycin in preventing acute rheumatic fever.

Renal impairment

In patients with severe renal impairment (GFR < 10 mL /min) a 33 % increase in systemic exposure to azithromycin was observed (see Section 5.2). Acute renal failure and interstitial nephritis have been reported (see section 4.8).

Myasthenia gravis

Exacerbations of the symptoms of myasthenia gravis and new onset of myasthenia syndrome have been reported in patients receiving azithromycin therapy. Safety and efficacy of azithromycin intravenous infusion for treatment of infections in children have not been established.

General

Safety and efficacy for prevention or treatment of MAC in children have not been established.

Azithromycin (azithromycin as powder for solution for infusion) should be reconstituted and diluted according to the instructions and should be administered

as an intravenous infusion over at least 60 minutes. It should not be administered as an intravenous bolus or an intramuscular injection (see sections 4.2 and 6.6).
This medicine contains 114 mg (4,96 mmol) sodium per vial, equivalent to approximately 5,7 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

Paediatric population

The efficacy and safety of azithromycin as powder for solution for infusion for the treatment of infections in children and adolescents has not been established.

4.5 Interaction with other medicines and other forms of interaction

Cetirizine

In healthy volunteers, co-administration of a 5-day regimen of azithromycin with cetirizine 20 mg at steady state resulted in no pharmacokinetic interaction and no significant changes in the QT interval.

Didanosine (Dideoxyinosine)

Co-administration of 1200 mg/day azithromycin with 400 mg/day didanosine in six HIV positive subjects did not appear to affect the steady-state pharmacokinetics of didanosine as compared to placebo.

Digoxin and colchicine

Concomitant administration of macrolide antibiotics, including azithromycin, with P-glycoprotein substrates such as digoxin and colchicine, has been reported to result in increased serum levels of the P-glycoprotein substrate. Therefore, if azithromycin and P-glycoprotein substrates such as digoxin are administered

concomitantly, the possibility of elevated serum digoxin concentrations should be considered. Clinical monitoring, and possibly serum digoxin levels, during treatment with azithromycin and after its discontinuation are necessary.

Ergot derivatives *(Ergotamine)***:** Due to the theoretical possibility of ergotism, the concurrent use of azithromycin with ergot derivatives is not recommended (See Section 4.4).

Zidovudine: Single 1000 mg doses and multiple 1200 mg or 600 mg doses of azithromycin had little effect on the plasma pharmacokinetics or urinary excretion of zidovudine or its glucuronide metabolite. However, administration of azithromycin increased the concentrations of phosphorylated zidovudine, the clinically active metabolite, in peripheral blood mononuclear cells. The clinical significance of this finding is unclear, but it may be of benefit to patients.

Azithromycin does not interact significantly with the hepatic cytochrome P450 system. It is not believed to undergo the pharmacokinetic drug interactions as seen with erythromycin and other macrolides. Hepatic cytochrome P450 induction or inactivation via cytochrome-metabolite complex does not occur with azithromycin.

Atorvastatin: Co-administration of atorvastatin (10 mg daily) and azithromycin (500 mg daily) did not alter the plasma concentrations of atorvastatin (based on a HMG CoA-reductase inhibition assay)

Carbamazepine: In a pharmacokinetic interaction study in healthy volunteers, no significant effect was observed on the plasma levels of carbamazepine or its active metabolite in patients receiving concomitant azithromycin.

Cimetidine: In a pharmacokinetic study investigating the effects of a single dose of cimetidine, given 2 hours before azithromycin, on the pharmacokinetics of azithromycin, no alteration of azithromycin pharmacokinetics was seen.

Warfarin: In a pharmacokinetic interaction study, azithromycin did not alter the anticoagulant effect of a single 15 mg dose of warfarin administered to healthy volunteers. There have been reports received in the post-marketing period of potentiated anticoagulation subsequent to co-administration of azithromycin and warfarin. Although a causal relationship has not been established, consideration should be given to the frequency of monitoring prothrombin time when azithromycin is used in patients receiving warfarin.

Ciclosporin: In a pharmacokinetic study with healthy volunteers that were administered a 500 mg/day oral dose of azithromycin for 3 days and were then administered a single 10 mg/kg oral dose of ciclosporin, the resulting ciclosporin C_{max} and AUC were found to be significantly elevated (by 24 % and 21 % respectively), however no significant changes were seen in AUC_{0-5}. Consequently, caution should be exercised before considering concurrent administration of these medicines. If co-administration of these medicine is necessary, ciclosporin levels should be monitored and the dose adjusted accordingly.

Efavirenz: Co-administration of a single dose of 600 mg azithromycin and 400 mg efavirenz daily for 7 days did not result in any clinically significant pharmacokinetic interactions.

Fluconazole: Co-administration of a single dose of 1200 mg azithromycin did not alter the pharmacokinetics of a single dose of 800 mg fluconazole. Total exposure and half-life of azithromycin were unchanged by the coadministration of fluconazole, however, a clinically insignificant decrease in C_{max} (18 %) of azithromycin was observed.

Indinavir: Co-administration of a single dose of 1200 mg azithromycin had no statistically significant effect on the pharmacokinetics of indinavir administered as 800 mg three times daily for 5 days.

Methylprednisolone: In a pharmacokinetic interaction study in healthy volunteers, azithromycin had no significant effect on the pharmacokinetics of methylprednisolone.

Nelfinavir: Co-administration of azithromycin (1200 mg) and nelfinavir at steady state (750 mg three times daily) resulted in increased azithromycin concentrations. No clinically significant adverse effects were observed, and no dose adjustment was required.

Midazolam: In healthy volunteers, co-administration of azithromycin 500 mg/day for 3 days did not cause clinically significant changes in the pharmacokinetics and pharmacodynamics of a single 15 mg dose of midazolam.

Rifabutin: Co-administration of azithromycin and rifabutin did not affect the serum concentrations of either medicine. Neutropenia was observed in subjects receiving concomitant treatment of azithromycin and rifabutin. Although neutropenia has been associated with the use of rifabutin, a causal relationship to combination with azithromycin has not been established (see Section 4.8).

Sildenafil: In normal healthy male volunteers, there was no evidence of an effect of azithromycin (500 mg daily for 3 days) on the AUC and C_{max}, of sildenafil or its major circulating metabolite.

Terfenadine: Pharmacokinetic studies have reported no evidence of an interaction between azithromycin and terfenadine. There have been rare cases reported where the possibility of such an interaction could not be entirely excluded; however, there was no specific evidence that such an interaction had occurred.

Theophylline: There is no evidence of a clinically significant pharmacokinetic interaction when azithromycin and theophylline are co-administered to healthy volunteers.

Triazolam: In healthy volunteers, co-administration of azithromycin 500 mg on Day 1 and 250 mg on Day 2 with 0,125 mg triazolam on Day 2 had no significant effect on any of the pharmacokinetic variables for triazolam compared to triazolam and placebo.

Trimethoprim/sulfamethoxazole: Co-administration of trimethoprim/sulfamethoxazole DS (160 mg/800 mg) for 7 days with azithromycin 1200 mg on Day 7 had no significant effect on peak concentrations, total exposure or urinary excretion of either trimethoprim or sulfamethoxazole. Azithromycin serum concentrations were similar to those seen in other studies.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no adequate data from the use of azithromycin in pregnant women. In reproduction toxicity studies in animals, azithromycin was shown to pass the placenta, but no teratogenic effects were observed. The safety of azithromycin has not been confirmed with regard to the use of the azithromycin active substance during pregnancy. Therefore, Azithromycin, MYCIBACT IV should only be used during pregnancy if definitely indicated.

Breastfeeding

Azithromycin passes into breast milk. Because it is not known whether azithromycin may have adverse effects on the breast-fed infant, nursing should be discontinued during treatment with MYCIBACT IV. Among other things diarrhoea, fungus infection of the mucous membrane as well as sensitisation is possible in the nursed infant. It is recommended to discard the milk during treatment and up until 2 days after discontinuation of treatment. Nursing may be resumed thereafter.

Fertility

Animal data do not suggest an effect of the treatment of azithromycin on male and female fertility. Human data are lacking.

4.7 Effects on ability to drive and use machines

MYCIBACT IV may cause side effects such as dizziness and visual impairment (see section 4.8), which should be taken into consideration on the ability to drive or operate machinery.

4.8 Undesirable effects

System Organ Class	Frequency		
	Frequent	**Less Frequent**	**Not known**
Infections and infestations	.	Candidiasis, oral candidiasis, vaginal infection	Pseudomembranous colitis
Blood and lymphatic system disorders		Leukopenia, neutropenia	Thrombocytopenia, haemolytic anaemia
Immune system disorders		Angioedema, hypersensitivity	Anaphylactic reaction (See Section 4.4)
Metabolism and nutrition disorders	Anorexia		
Psychiatric disorders		Nervousness, Agitation	Aggression, anxiety
Nervous system disorders	Dizziness, headache, paraesthesia, dysgeusia	Hypoaesthesia, somnolence, insomnia	Syncope, convulsion, psychomotor hyperactivity, anosmia, ageusia, parosmia, myasthenia gravis (See Section 4.4)
Eye disorders	Visual impairment		Abnormal vision

Ear and labyrinth disorders	Deafness	Impaired hearing, tinnitus, vertigo	
Cardiac disorders		Palpitations.	Torsades de pointes (See Section 4.4), arrhythmia (See Section 4.4) including ventricular tachycardia
Vascular disorders			Hypotension
Gastrointestinal disorders	Diarrhoea, abdominal pain, nausea, flatulence, Vomiting, dyspepsia	Gastritis, constipation	Pancreatitis, tongue discolouration
Hepatobiliary disorders	Abnormal liver function	Hepatic function abnormal	Hepatic failure (See Section 4.4)**, hepatitis, fulminant, hepatic necrosis, jaundice cholestatic.
Skin and subcutaneous tissue disorders	Pruritis, rash, oedema	Stevens-Johnson syndrome (SJS), photosensitivity reaction, urticaria, Acute Generalised Exanthematous Pustulosis (AGEP), Drug reaction with	Toxic epidermal necrolysis (TEN), erythema multiforme

		eosinophilia and systemic symptoms (DRESS)	
Musculoskeletal and connective tissue disorders	Arthralgia		
Renal and urinary disorders			Acute renal failure, interstitial nephritis,
General disorders and administration site conditions	Pain and inflammation on the local injection site*		General disorders and administration site conditions
Investigations	Decreased lymphocyte count, increased eosinophil count, decreased blood bicarbonate	Increased Aspartate aminotransferase, increased alanine aminotransferase, increased blood bilirubin, increased blood urea, increased blood creatinine, abnormal blood potassium	Electrocardiogram QT prolonged (See Section 4.4)

* have been reported with the intravenous administration of azithromycin.
** which has rarely resulted in death

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via the “6.04 Adverse Drug Reaction Reporting Form”, found online under SAHPRA’s publications:
https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Adverse events experienced in higher than recommended doses were similar to those seen at normal doses. The typical symptoms of an overdose with macrolide antibiotics include loss of hearing, severe nausea, vomiting and diarrhoea. In the event of overdose,
general symptomatic treatment and supportive measures are indicated as required.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological Classification/ Category and Class: A.20.1.1 Broad and medium spectrum antibiotics.
Pharmacotherapeutic group: Antibacterial for systemic use, Macrolides,
ATC Code: J01FA10

Mechanism of action

Azithromycin is a macrolide antibiotic belonging to the azalide group. The molecule is constructed by adding a nitrogen atom to the lactone ring of erythromycin A. The mechanism of action of azithromycin is based upon the

suppression of bacterial protein synthesis by means of binding to the ribosomal 50s sub-unit and inhibition of peptide translocation.

Mechanism of resistance

There are two dominant genes that determine the resistance of isolates of *Streptococcus pneumoniae* and *Streptococcus pyogenes*: mef and erm. The mef gene encodes a flow pump that mediates resistance to macrolides 14- and 15-only. The mef gene has also been described in a variety of other species. The erm gene codes for a 23S-rRNA methyltransferase that adds methyl groups to adenine 2058 of 23S rRNA (numbering system of *E. coli* rRNA).

The methylated nucleotide is located in a domain V and is thought to interact with the lincosamides and streptogramin B, in addition to macrolides, resulting in a phenotype known as MLSB resistance. Genes erm (B) and erm (A) are clinical isolates of *S. pneumoniae* and *S. pyogenes*.

The pump AcrAB-TolC of *Haemophilus influenzae* is responsible for the innate MIC values higher for macrolides.

In clinical isolates, mutations in 23S rRNA, specifically in nucleotides 2057 – 2059 or 2611 in domain V, or mutations in ribosomal protein L4 or L22, are rare.

A complete cross resistance exists among erythromycin, azithromycin, other macrolides and lincosamides for *Streptococcus pneumoniae*, beta-haemolytic streptococci of group A, Enterococcus *spp.* and *Staphylococcus aureus*, including methicillin resistant *Staphylococcus aureus* (MRSA). Penicillin susceptible *Streptococcus pneumoniae* are more likely to be susceptible to azithromycin than are penicillin resistant strains of *Streptococcus pneumoniae*. Methicillin resistant *Staphylococcus aureus* (MRSA) is less likely to be susceptible to azithromycin than methicillin susceptible *Staphylococcus aureus* (MSSA).

Species for which acquired resistance may be a problem:

Aerobic Gram-positive microorganisms

Streptococcus pneumoniae penicillin-intermediate and penicillin-resistant.

Inherently resistant organisms:

Aerobic Gram-positive microorganisms

Enterococcus faecalis

Staphylococci MRSA, MRSE (Methicillin-resistant staphylococci have a very high prevalence of acquired resistance to macrolides and have been placed here because they are rarely susceptible to azithromycin.)

Anaerobic microorganisms:

Bacteroides fragilis group.

5.2 Pharmacokinetic properties

Absorption

In patients hospitalised with community acquired pneumonia treated with a single daily intravenous infusion of 500 mg azithromycin, over one hour, in a solution with a concentration of 2 mg/mL, for 2 to 5 days, the mean C_{max} ±S.D achieved was of 3,63 ±1,60 µg/mL, while the trough levels concentration at 24 hours was 0,20 ± 0,15 µg/mL and the AUC_{24} was 9,60 ± 4,80 µg.h/mL. The Mean Cmax, trough levels concentration at 24 hours and AUC_{24} values were of 1,14 ± 0,14 µg/mL, 0,18 ± 0,02 µg/mL and 8,03 ± 0,86 µg.h/mL, respectively, in normal volunteers receiving intravenous infusion of 500 mg azithromycin at a concentration of 1mg/mL, for 3 hours.

Distribution

In animal tests, high concentrations of azithromycin have been found in phagocytes. It has also been established that during active phagocytosis higher

concentrations of azithromycin are released from inactive phagocytes. In animal models this results in high concentrations of azithromycin being delivered to the site of infection.

In pharmacokinetic studies it has been demonstrated that the concentrations of azithromycin measured in tissues are noticeably higher (as much as 50 times than those measured in plasma), which indicates that the medicine strongly binds to tissues.

Concentrations in target tissues such as lung, tonsil, and prostate exceed the MIC90 for likely pathogen after a single dose of 500 mg. High azithromycin concentrations were detected in gynaecological tissue 96 hours after a single dose of 500 mg azithromycin.

Biotransformation/Elimination

In a multiple-dose study in 12 normal volunteers using a 500 mg (1 mg/mL) one-hour intravenous dosage regimen for five days, the amount of administered azithromycin dose excreted in urine in 24 hours was about 11 % after the 1st dose and 14 % after the 5th dose. These values are higher than the reported 6 % as being excreted unchanged in urine after oral administration of azithromycin. Particularly high concentrations of unchanged azithromycin have been found in human bile. Also in bile, ten metabolites were detected, which were formed through N- and O- demethylation, hydroxylation of desosamine and aglycone rings and cleavage of cladinose conjugate. Comparison of the results of liquid chromatography and microbiological analyses carried has shown that the metabolites do not contribute to azithromycin microbiological activity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Citric acid anhydrous
- Sodium hydroxide

6.2 Incompatibilities

Azithromycin IV reconstituted solution may be diluted using the instructions and compatible infusion solutions indicated in Section 6.6.

This medicine must not be mixed with other medicine except those mentioned in Section 6.6.

Other intravenous substances, additives or medicines should not be added to Azithromycin or infused simultaneously through the same intravenous line.

6.3 Shelf life

36 months.

Concentrated solution after reconstitution (according to the instructions):

The reconstituted solution of Azithromycin lyophilized powder for infusion 500 mg/vial is stable for 24 hours when stored at room temperature (below 30 °C).

Additionally, the final infusion solutions of Azithromycin lyophilized powder for infusion 500 mg/vial, are stable for 24 hours when stored at room temperature (below 30 °C) and for 72 hours when stored at refrigerator (2 to 8) °C.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at (2 to 8) °C., unless reconstitution / dilution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

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 Section 6.3.

6.5 Nature and contents of container

MYCIBACT IV powder for solution for infusion 500 mg/vial is supplied in an uncoloured glass type I single dose vial with a grey bromobutyl rubber stopper and sealed with an aluminium/plastic flip-off cap with green plastic subcap, Each vial is packaged in a cardboard box.

6.6 Special precautions for disposal and other handling

Azithromycin as powder for solution for infusion is supplied in single dose vials.

Preparation of the solution for intravenous administration is as follows:

Reconstitution

Prepare the initial solution of azithromycin powder for solution for infusion by adding 4,8 mL of sterilised Water for Injections to the 500 mg vial and shaking the vial until all of the medicine is dissolved. It is recommended that a standard 5 mL (non-automated) syringe be used to ensure that the exact amount of 4,8 mL of sterilised Water for Injections is dispensed. Each mL of reconstituted solution contains 100 mg azithromycin.

Parenteral administration medicine should be inspected visually for particulate suspension prior to administration. If particulate suspension is evident in reconstituted fluids, the medicine should be discarded.

Dilute this solution further prior to administration as instructed below.

Dilution

To provide azithromycin over a concentration range of 1,0 – 2,0 mg/mL, transfer 5 mL of the 100 mg/mL azithromycin solution into the appropriate amount of any of the diluents listed below.

Final Infusion Solution Concentration (mg/mL)	**Amount of diluent (mL)**
1,0 mg/mL	500 mL
2,0 mg/mL	250 mL

The reconstituted solution can be diluted with:

Normal Saline (0,9 % sodium chloride)

½ Normal Saline (0,45 % sodium chloride)

5 % Dextrose in Water

Lactated Ringer's Solution

5 % Dextrose in ½ Normal Saline (0,45 % sodium chloride) with 20 mEq KCl

5 % Dextrose in lactated Ringer's Solution

5 % Dextrose in ⅓ Normal Saline (0,3 % sodium chloride)

5 % Dextrose in ½ Normal Saline (0,45 % sodium chloride)

It is recommended that a 500 mg dose of azithromycin powder for solution for infusion, diluted as above, be infused over a period of not less than 60 minutes.

The reconstituted medicine is chemically and physically stable during 24 hours, when stored below 30 °C. Diluted solutions, prepared according to the instructions, are chemically and physically stable for 24 hours at or below 30 °C, or for 7 days if stored under refrigeration (2 °C- 8 °C). From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 °C to 8 °C, unless the

reconstitution/dilution has taken place in controlled and validated aseptic conditions.

7. HOLDER OF CERTIFICATE OF REGISTRATION

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8. REGISTRATION NUMBER

53/20.1.1/0193

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

15 August 2023

10. DATE OF REVISION OF THE TEXT