SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

NOVAZITH SUSPENSION (200 mg/5ml) Powder for Oral Suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml of NOVAZITH SUSPENSION contains azithromycin dihydrate equivalent to azithromycin 200 mg.

Excipients with known effect: contains 3,89 g sucrose per 5 ml.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for oral suspension

Dry powder: White to off-white, granular powder.

Reconstituted suspension: Pale to dark pink flavoured suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Children: 1 year and over (under 45 kg)

NOVAZITH SUSPENSION is indicated for pharyngitis/tonsillitis and otitis media caused by susceptible organisms.

Adults and children over 45 kg:

NOVAZITH SUSPENSION is indicated for mild to moderate infections caused by susceptible organisms; in lower respiratory tract infections including bronchitis due to *Haemophilus influenzae*, *Moraxella catarrhalis*, *Streptococcus pneumoniae* or *Staphylococcus aureus* and pneumonia due to *Streptococcus pneumoniae* or *Haemophilus influenzae*; uncomplicated skin and soft tissue infections; sinusitis due to *Haemophilus influenzae*, *Streptococcus pneumoniae* or *Staphylococcus aureus*; and as an alternative to first line therapy of pharyngitis/tonsillitis.

4.2 Posology and method of administration

Posology

NOVAZITH SUSPENSION powder for oral suspension should be administered as a single daily dose.

NOVAZITH SUSPENSION should be administered to children using the 10 ml oral dosing syringe. NOVAZITH SUSPENSION can be taken with food.

Use in children: 1 year and older

The total dose in children is 30 mg/kg which should be given as a single daily dose of 10 mg/kg for 3 days according to the following guidance:

< 15 kg: 10 mg/kg once daily on days 1 - 3.

15-25 kg: 200 mg (5 ml) once daily on days 1 - 3.

26-35 kg: 300 mg (7,5 ml) once daily on days 1 - 3.

36-45 kg: 400 mg (10 ml) once daily on days 1 - 3.

> 45 kg: Dose as per adults (Azithromycin solid dosage form Professional Information).

Method of administration

NOVAZITH SUSPENSION is for oral administration only.

See reconstitution of suspension: section 6.6.

4.3 Contraindications

- Hypersensitivity to azithromycin, erythromycin or to any of the macrolide antibiotics or to any of the excipients listed in section 6.1.
- Because of the theoretical possibility of ergotism, NOVAZITH SUSPENSION and ergot derivatives should not be co-administered.

Use in hepatic impairment

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

Use in children under 1 year of age

The safety and efficacy of NOVAZITH SUSPENSION in children less than 1 year have not been established.

4.4 Special warnings and precautions for use

Hypersensitivity

Serious allergic reactions, including angioedema and anaphylaxis and dermatologic reactions including Stevens-Johnson syndrome, Acute Generalised Exanthemateous Pustulosis (AGEP), Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) and toxic epidermal necrolysis have been reported. Some of these reactions with NOVAZITH SUSPENSION have resulted in recurrent symptoms and required a longer period of observation and treatment.

If an allergic reaction occurs, NOVAZITH SUSPENSION should be discontinued and appropriate therapy should be instituted. Medical practitioners to 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 NOVAZITH SUSPENSION should be undertaken with caution in patients with hepatic disease (see section 4.3).

Abnormal liver function, hepatitis, cholestatic jaundice, hepatic necrosis, and hepatic failure, some of which resulted in death, have been reported. Discontinue NOVAZITH SUSPENSION immediately if signs and/or symptoms of hepatitis occur.

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. NOVAZITH SUSPENSION administration should be stopped if liver dysfunction has emerged.

Ergot derivatives

In patients receiving ergot derivatives, ergotism has been precipitated by co-administration of some macrolide antibiotics. There is no data concerning the possibility of an interaction between ergot and NOVAZITH SUSPENSION. However, because of the theoretical possibility of ergotism, NOVAZITH SUSPENSION 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 Torsade de Pointes, have been seen in treatment with other macrolides including NOVAZITH SUSPENSION (see section 4.8). Prescribers should specifically consider the risk of QT prolongation, which can be fatal in at-risk groups including:

- Patients with congenital or documented QT prolongation
- Patients currently receiving treatment with other active substance known to prolong QT interval such as antidysrhythmics of Classes IA and III; antipsychotic agents; antidepressants; and fluoroquinolones
- Patients with electrolyte disturbance, particularly in case of hypokalaemia and hypomagnesaemia
- Patients with clinically relevant bradycardia, cardiac dysrhythmia or cardiac insufficiency.
- Elderly patients: elderly patients may be more susceptible to medicine-associated effects on the QT interval

Superinfection

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

Pseudomembranous colitis

Pseudomembranous colitis has been reported and may range in severity from mild to life threatening. Therefore, it is important to consider this diagnosis in patients with diarrhoea subsequent to administration of NOVAZITH SUSPENSION.

Clostridium difficile associated diarrhoea

Clostridium difficile associated diarrhoea (CDAD) due to overgrowth of *Clostridium difficile* in the gut, has been reported with the use of NOVAZITH SUSPENSION, and may range in severity from mild diarrhoea to fatal colitis.

If CDAD is suspected or confirmed, ongoing NOVAZITH SUSPENSION use should be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of *Clostridium difficile*, and surgical evaluation should be instituted as clinically indicated.

Renal impairment

In patients with a creatine clearance < 30, a 33 % increase in systemic exposure to NOVAZITH SUSPENSION 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 (see section 4.8).

Diabetes

Caution in diabetic patients: 5 ml of reconstituted suspension contains 3,89 g of sucrose.

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take NOVAZITH SUSPENSION.

Use in children under 1 year of age:

The safety and efficacy of oral NOVAZITH SUSPENSION preparations in children less than 1 year have not been established.

4.5 Interaction with other medicines and other forms of interaction

Ergot derivatives:

Because of the theoretical possibility of ergotism, NOVAZITH SUSPENSION and ergot derivatives should not be co-administered (see section 4.3 and section 4.4).

Cetirizine:

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

Azithromycin does not interact significantly with the hepatic cytochrome P450 system. It is not believed to be associated with the pharmacokinetic medicine interactions seen with erythromycin. Hepatic cytochrome P450 induction or inactivation via cytochrome-metabolite complex does not occur with azithromycin.

Pharmacokinetic studies have been conducted between azithromycin and the following medicines known to undergo significant cytochrome P450 mediated metabolism:

Atorvastatin:

Co-administration of atorvastatin (10 mg daily) and azithromycin (500 mg daily) did not alter the plasma concentrations of atorvastatin (based on an HMG CoA-reductase inhibition assay). However, post-marketing cases of rhabdomyolysis in patients receiving azithromycin with statins have been reported.

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 1 200 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 co-administration of fluconazole, however, a clinically insignificant decrease in C_{max} (18 %) of azithromycin was observed.

Indinavir:

Co-administration of a single dose of 1 200 mg azithromycin had no statistically significant effect on the pharmacokinetics of indinavir administered as 800 mg three times daily for 5 days.

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 dose of 15 mg midazolam.

Nelfinavir:

Co-administration of azithromycin (1 200 mg) and nelfinavir at steady state (750 mg three times daily) resulted in increased azithromycin concentrations. No clinically significant adverse effects were observed and although a dose adjustment of NOVAZITH SUSPENSION is not recommended when administered in combination with nelfinavir, close monitoring for known side effects of NOVAZITH SUSPENSION is warranted.

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.

Triazolam:

In 14 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 1 200mg 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.

Special administration advised with the following:

Antacids:

In a pharmacokinetic study investigating the effects of simultaneous administration of antacid with azithromycin, no effect on overall bioavailability was seen, although peak serum concentrations were reduced by approximately 24 %. In patients receiving both NOVAZITH SUSPENSION and antacids, the medicines should not be taken simultaneously. NOVAZITH SUSPENSION should be taken at least 1 hour before or 2 hours after an antacid. Administration of oral antacids is not expected to affect the disposition of azithromycin given intravenously.

Cimetidine:

A single dose of cimetidine administered 2 hours before NOVAZITH SUSPENSION had no effect on the pharmacokinetics of NOVAZITH SUSPENSION.

No pharmacokinetic interactions were reported in studies of NOVAZITH SUSPENSION co-administered with:

Carbamazepine, methylprednisolone, didanosine (dideoxyinosine), theophylline, rifabutin, however co-administration of NOVAZITH SUSPENSION and *rifabutin* was associated with the development of neutropenia.

A causal relationship to its combination with NOVAZITH SUSPENSION has not been established (see section 4.8) and *zidovudine* single 1 000 mg doses and multiple 1 200 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.

Special precautionary monitoring is advised with the following:

Ciclosporin:

In a pharmacokinetic study with healthy volunteers who 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_{0-5} were found to be significantly elevated (C_{max} increase by 24 % and AUC_{0-5} was 5 107 and 4 210 ngh/mL with and without azithromycin, respectively, $p \leq 0.05$). Consequently, caution should be exercised before co-administration of these two medicines. If co-administration is necessary, ciclosporin levels should be monitored and the dose adjusted accordingly.

P-glycoprotein substrates:

Concomitant administration of NOVAZITH SUSPENSION with P-glycoprotein substrates such as digoxin or dabigatran has been reported to result in increased serum levels of the P-glycoprotein substrate. Therefore, if NOVAZITH SUSPENSION and P-glycoprotein substrates such as digoxin or dabigatran are administered concomitantly, the possibility of elevated serum medicine concentrations should be considered. Clinical monitoring, and serum monitoring of digoxin levels, during treatment with NOVAZITH SUSPENSION and after its discontinuation are necessary.

Some of the macrolide antibiotics have been reported to impair the metabolism of digoxin (in the gut) in some patients. Therefore, in patients receiving concomitant NOVAZITH SUSPENSION, a related azalide antibiotic, and digoxin the possibility of raised digoxin levels should be borne in mind.

Warfarin:

In a pharmacokinetic interaction study, azithromycin did not alter the anticoagulant effect of a single dose of 15 mg warfarin administered to healthy volunteers. However, 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 NOVAZITH SUSPENSION is used in patients receiving coumarin-type oral anticoagulants.

4.6 Fertility, pregnancy and lactation

The safety and efficacy of NOVAZITH SUSPENSION in pregnancy and lactation have not been established.

Pregnancy

Animal reproduction studies have been performed at doses up to moderately maternally toxic dose concentrations. In these studies, no evidence of harm to the foetus due to azithromycin was found. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, NOVAZITH SUSPENSION should be used during pregnancy only if clearly needed.

Lactation

Azithromycin has been reported to be secreted into human breast milk, but there are no adequate and well-controlled clinical studies in nursing women that have characterised the pharmacokinetics of azithromycin excretion into human breast milk.

NOVAZITH SUSPENSION should only be used in lactating women where adequate alternatives are not available.

4.7 Effects on ability to drive and use machines

Side effects such as dizziness, convulsions, vertigo, somnolence, and syncope have been reported with usage of NOVAZITH SUSPENSION. These side effects may affect a patient’s ability to drive or operate machinery.

4.8 Undesirable effects

The following undesirable effect have been reported.

System organ class	Frequency	Side effect
Infections and infestations	*Less frequent*	Candidiasis, oral candidiasis, vaginal infection, pneumonia, fungal infection, pharyngitis, gastroenteritis, respiratory disorder, rhinitis.
	Frequency unknown	Pseudomembranous colitis (see section 4.4)
Blood and lymphatic system disorders	*Less frequent*	Leukopenia, neutropenia, eosinophilia
	Frequency unknown	Thrombocytopenia, haemolytic anaemia
Immune system disorders	*Less frequent*	Angioedema, hypersensitivity
	Frequency unknown	Anaphylactic reaction (see section 4.4)
Metabolism and nutrition disorders	*Less frequent*	Anorexia
Psychiatric disorders	*Less frequent*	Nervousness, agitation, insomnia
	Frequency unknown	Aggression, anxiety, delirium, hallucination
Nervous system disorders	*Frequent*	Headache
	Less frequent	Dizziness, somnolence, paraesthesia, dysgeusia
	Frequency unknown	Syncope, convulsion, psychomotor hyperactivity, anosmia, hypoesthesia, Myasthenia gravis (see section 4.4)
Eye disorders	*Frequency unknown*	Visual impairment, blurred vision
Ear and labyrinth disorders	*Less frequent*	Ear disorder, vertigo
	Frequency unknown	Hearing impairment including deafness and/or tinnitus
Cardiac disorders	*Less frequent*	Palpitations

	Frequency unknown	Torsades de pointes (see section 4.4), dysrhythmia (see section 4.4) including ventricular tachycardia, Electrocardiogram QT prolonged (see section 4.4)
Vascular disorders	*Less frequent*	Hot flush
	Frequency unknown	Hypotension
Respiratory, thoracic and mediastinal disorders	*Less frequent*	Dyspnoea, Epistaxis
Gastrointestinal disorders	*Frequent*	Diarrhoea, abdominal pain, nausea, vomiting
	Less frequent	Gastritis, constipation, flatulence, dyspepsia, dysphagia, abdominal distension, dry mouth, eructation, mouth ulceration, salivary hypersecretion
	Frequency unknown	Pancreatitis, tongue discolouration
Hepato-biliary disorders	*Less frequent*	Hepatic function abnormal, jaundice cholestatic
	Frequency unknown	Hepatic failure (see section 4.4), which has rarely resulted in death, hepatitis fulminant, hepatic necrosis
Skin and subcutaneous tissue disorders	*Less frequent*	Rash, pruritus, dermatitis, dry skin, hyperhidrosis, photosensitivity reaction, urticaria, acute Generalised Exanthematous Pustulosis (AGEP)[*§], Drug reaction with eosinophilia and systemic symptoms (DRESS)[*§]
	Frequency unknown	Stevens-Johnson syndrome, Toxic Epidermal Necrolysis (TEN), erythema multiforme
Musculoskeletal, connective tissue disorders	*Less frequent*	Osteoarthritis, myalgia, back pain, neck pain
	Frequency unknown	Arthralgia
Renal and urinary disorders	*Less frequent*	Dysuria, renal pain
	Frequency unknown	Acute renal failure, interstitial nephritis

Reproductive system and breast disorders	*Less frequent*	Metrorrhagia, testicular disorder
General disorders and administration site conditions	*Less frequent*	Chest pain, oedema, malaise, asthenia, fatigue, face oedema, pyrexia, pain, peripheral oedema
Investigations	*Frequent*	Lymphocyte count decreased, eosinophil count increased, blood bicarbonate decreased, basophils increased, monocytes increased, neutrophils increased
	Less frequent	Aspartate aminotransferase increased, alanine aminotransferase increased, blood bilirubin increased, blood urea increased, blood creatinine increased, blood potassium abnormal, blood alkaline phosphatase increased, chloride increased, glucose increased, platelets increased, haematocrit decreased, bicarbonate increased, abnormal sodium

* ADR identified post-marketing

§ ADR frequency represented by the estimated upper limit of the 95 % confidence interval calculated using the "Rule of 3".

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 providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions 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 hearing loss, severe nausea, vomiting and diarrhoea. General supportive measures are indicated.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antibacterials for systemic use. ATC code: J01FA10

Mode of action

Azithromycin is an azalide, a subclass of the macrolide antibiotics. Chemically it is derived by insertion of a nitrogen atom into the lactone ring of erythromycin A. The chemical name of azithromycin is 9-deoxy-9a-aza-9a-methyl-9a-homoerythromycin A. The molecular weight is 749,0.

Azithromycin binds to the 23S rRNA of the 50S ribosomal subunit. It blocks protein synthesis by inhibiting the transpeptidation/translocation step of protein synthesis and by inhibiting the assembly of the 50S ribosomal subunit.

Cardiac electrophysiology

QTc interval-prolongation was studied in a randomised, placebo-controlled parallel trial in 116 healthy subjects who received either chloroquine (1 000 mg) alone or in combination with azithromycin (500 mg, 1 000 mg, and 1 500 mg once daily). Co-administration of azithromycin significantly increased the QTc interval in a dose- and concentration-dependent manner. In comparison to chloroquine alone, the maximum mean (95 % upper confidence bound) increases in QTcF were 5 (10) ms, 7 (12) ms and 9 (14) ms with the co-administration of 500 mg, 1 000 mg and 1 500 mg azithromycin, respectively.

Efflux pumps occur in a number of bacteria, including Gram-negatives, such as *Haemophilus influenzae* (where they may determine intrinsically higher MICs) and staphylococci. In streptococci and enterococci, an efflux

pump that recognises 14- and 15-membered macrolides (which include, respectively, erythromycin and azithromycin) is encoded by *mef*(A) genes.

Mechanism of resistance

Azithromycin demonstrates cross-resistance with erythromycin-resistant Gram-positive organisms. Ribosomal modifications determine cross-resistance with other classes of antibiotics whose ribosomal binding sites overlap that of the macrolides: the lincosamides (including clindamycin), and the streptogramins B (which include, for example, the quinupristin component of quinupristin/dalfopristin). A decrease in macrolide susceptibility over time has been noted in particular in *Streptococcus pneumoniae* and *Staphylococcus aureus*, and has also been observed in *Viridans streptococci* and in *Streptococcus agalactiae*.

Azithromycin has *in vitro* activity against:

- Aerobic and facultative Gram-positive bacteria (erythromycin-susceptible organisms)
- Aerobic and facultative Gram-negative bacteria

In vitro resistance to azithromycin:

Azithromycin-resistant organisms are encountered relatively frequently among aerobic and facultative Gram-positive bacteria, in particular among methicillin-resistant *Staphylococcus aureus* (MRSA) and penicillin-resistant *Streptococcus pneumoniae* (PRSP)

Pseudomonas spp. and most *Enterobacteriaceae* are inherently resistant to azithromycin, although azithromycin has been used to treat *Salmonella enterica*, *Pneumocystis jirovecii* and *Toxoplasma gondii* infections.

In vitro sensitivity does not necessarily imply *in vivo* efficacy.

5.2 Pharmacokinetic properties

Absorption:

Following oral administration in humans, azithromycin is widely distributed throughout the body; bioavailability is approximately 37 %. No significant decrease in bioavailability was observed when azithromycin was administered with a meal. The time taken to peak plasma levels is 2 to 3 hours.

Distribution:

Kinetic studies of variable times ranging from hours to days after oral intake have shown markedly higher azithromycin levels in tissue than in plasma (up to 50 times the maximum observed concentration in plasma) indicating that the medicine is highly tissue bound. Concentrations in target tissues such as lung, tonsil and prostate exceed the MIC90 for likely pathogens after a single dose of 500 mg.

Elimination:

Plasma terminal elimination half-life closely reflects the tissue depletion half-life of 2 to 4 days.

Biliary excretion of azithromycin is a major route of elimination for unchanged medicine following oral administration. Very high concentrations of unchanged medicine have been found in human bile, together with 10 metabolites, formed by N- and O-demethylation, by hydroxylation of the desosamine and aglycone rings, and by cleavage of the cladinose conjugate. Comparison of HPLC and microbiological assays in tissues suggests that metabolites play no part in the microbiological activity of azithromycin.

Pharmacokinetics in special patient groups:

Renal impairment:

The pharmacokinetics of azithromycin in adult patients with mild-to-moderate renal impairment (GFR 10 – 80 ml/min) were not affected following a single 1 g dose of immediate release azithromycin. Statistically significant differences in AUC_{0-120} (8,8 mg x hr/ml vs. 11,7 mg x hr/ml), C_{max} (1,0 mg/ml vs. 1,6 mg/ml) and CLr (2,3 mL/min/kg vs. 0,2 ml/min/kg) were observed between the group with severe renal impairment (GFR < 10 ml/min) and the group with normal renal function.

Hepatic impairment:

In patients with mild (Class A) to moderate (Class B) hepatic impairment, there is no evidence of a marked change in serum pharmacokinetics of azithromycin compared to those with normal hepatic function. The urinary clearance of azithromycin appears to increase in these patients, perhaps to compensate for reduced hepatic clearance. Azithromycin has not been studied and should not be used in patients with severe hepatic impairment.

Elderly:

Elderly volunteers (> 65 years) had slightly higher AUC values than in young volunteers (< 40 years) after a 5-day regimen, but these are not considered clinically significant, and hence no dose adjustment is recommended.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydroxypropyl cellulose

Sucrose

Tribasic sodium phosphate anhydrous

Xanthum Gum

Art Cherry flavour IHS

Art Ripe Banana FL SD IHS

FD&C Red No. 40 IHS

6.2 Incompatibilities

Not applicable

6.3 Shelf life

NOVAZITH SUSPENSION powder for oral suspension: 2 years

Once reconstituted with water, NOVAZITH SUSPENSION has a shelf life of 5 days.

6.4 Special precautions for storage

For dry powder: Store at or below 25 °C.

For reconstitution suspension: The reconstitution suspension should be stored at or below 25 °C and any unused suspension should be discarded after 5 days. No refrigeration required.

6.5 Nature and contents of container

NOVAZITH SUSPENSION 15 ml: White opaque round 30 ml HDPE container with 28 mm neck finish closed with 28 mm white opaque polypropylene child resistant closure with wad having induction sealing liner.

NOVAZITH SUSPENSION 30 ml: White opaque round 60 ml HDPE container with 28 mm neck finish closed with 28 mm white opaque polypropylene child resistant closure with wad having induction sealing liner.

Plastic syringe: contains plunger, barrel, tip cap and adaptor. Printing with measuring marks up to 10 ml with 0,2 ml graduation.

NOVAZITH SUSPENSION (powder or oral suspension) HDPE bottles shall be further packed in an outer carton with patient information leaflet and plastic syringe.

6.6 Special precautions for disposal and other handling

Reconstituting instructions for NOVAZITH SUSPENSION powder for oral suspension for 15 ml and 30 ml bottles:

The table below indicates the volume of water to be used for constitution:

Amount of water to be added	Total deliverable volume (azithromycin content)	Azithromycin concentration after reconstitution
9 ml	15 ml (600 mg)	200 mg/5 ml

15 ml	30 ml (1 200 mg)	200 mg/5 ml

Shake well before each use. Oversized bottle provides shake space. Keep tightly closed. After mixing store below 25 °C (no refrigeration required) and discard any unused suspension after 5 days.

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

7. HOLDER OF CERTIFICATE OF REGISTRATION

Novagen Pharma (Pty) Ltd

100 Sovereign Drive

Route 21 Corporate Park

Nellmapius Drive

Irene

Pretoria

0157

8. REGISTRATION NUMBER

51/A20.1.1/0587

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

03 November 2020

10. DATE OF REVISION OF THE TEXT

Not applicable