

NAME OF THE VETERINARY MEDICINAL PRODUCT

Rx Spectrum® Azitromicina

2. PHARMACEUTICAL PRESENTATION

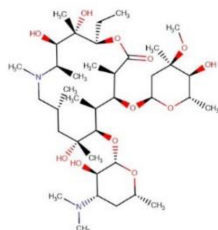
Powder for oral suspension

3. FORMULA

Once reconstituted, each ml contains:

Azithromycin dihydrate	40 mg
Vehicle q.s.	1ml

4. STRUCTURAL FORMULA



5. THERAPEUTIC INDICATIONS

Broad-spectrum antimicrobial, for the treatment of respiratory (upper and lower respiratory tract), otorhinolaryngological, dermatological, stomatological, urogenital, digestive and osteoarticular infections caused by microorganisms susceptible to the active ingredient of the formula (Matiello, 2001; Sumano *et al.*, 2019).

6. SPECTRUM

Azithromycin is active against:

- **Gram positive aerobes:** *Staphylococcus* sp., *Streptococcus* sp., *Corynebacterium* sp., *Listeria* sp.
- **Gram-negative aerobes:** *Haemophilus* sp., *Pasteurella* sp., *Bordetella* sp., *Bartonella* sp., *Campylobacter* sp.
- **Anaerobes:** *Bacteroides* sp., *Clostridium* sp. and *Fusobacterium* sp.
- **Protozoa:** *Toxoplasma* sp., *Cryptosporidium* sp., *Cystoisospora* sp., *Isospora* sp.
- **Other organisms:** *Borrelia* sp., *Chlamydia* sp., *Mycoplasma* sp., *Mycobacterium* sp., *Ureaplasma* sp., *Listeria* sp. (Brook *et al.*, 2013; BSAVA, 2017; Grayson, 2010; Maddisson, 2008; Marin, 2016; Matiello, 2001; Plumb, 2018; Wibe, 2015).

7. SPECIES

Canine and Feline(Plumb, 2018).

8. APPLICATION METHOD

Oral (Plumb, 2018).

9. DOSAGE

General dosage:

10 mg/kg (2.2 lb) of body weight daily for 3 to 5 days (Plumb, 2018).

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Canine and feline: administer 1 ml (40 mg) per 4 kg (9 lb) of body weight for 3 to 5 days.

To eliminate coccidia, it is recommended to administer two doses of 30 mg per kg (2.2 lb) of body weight every 48 hours.

For the treatment of chlamydiosis, it is recommended to administer a dose of 10 mg per kg (2.2 lb) of body weight every 24 hours for 15 days, followed by 5 mg per kg (2.2 lb.) of body weight every 24 hours for 7 days, and then 5 mg per kg (2.2 lb.) of body weight every 48 hours for 14 days.

The dosage may be adjusted at the discretion of the Veterinarian.

10. MECHANISM OF ACTION

Like other macrolide antimicrobials, azithromycin inhibits protein synthesis by binding to the 50S ribosome of susceptible bacteria, blocking the translocation of amino acids from the acyl-tRNA to the growing peptide chain. It is considered to be a bacteriostatic antimicrobial. In addition, azithromycin has multiple immunomodulatory effects, which probably contribute to a good therapeutic response in infections. These effects include enhanced neutrophil degranulation and apoptosis, inhibition of inflammatory cytokine production, and improved macrophage functions. It also exhibits a post-antibiotic effect lasting at least 8 hours (Papich, 2016; Plumb, 2018; Sumano *et al.*, 2015).

11. PHARMACOKINETICS

After oral administration, it is rapidly absorbed and widely distributed throughout the body (except to cerebrospinal fluid). It has a bioavailability of 97% in dogs and 58% in cats. It binds to plasma proteins from 7 to 51%. Tissue fibroblasts act as the natural "reservoir" for the drug *in vivo*, enabling its efficient transfer to phagocytes where azithromycin concentrates, facilitating its delivery to specific sites of infection. Tissue concentrations are up to 100 times higher than plasma concentrations and 200 to 300 times higher in

leukocytes. Its half-life in dogs is more than 90 h and in cats from 13 to 72 h. It presents an enterohepatic cycle and follows a first-pass effect. It is primarily eliminated through feces and, to a lesser extent, through urine. (Sumano *et al.*, 2015; Sumano *et al.*, 2019).

12. WARNINGS

It should not be administered to patients with hypersensitivity to azithromycin or other macrolide antimicrobials (erythromycin). Caution should be exercised in patients with a history of arrhythmias, liver failure and/or biliary dysfunction (Plumb, 2018; Koch *et al.*, 2012).

Once reconstituted, keep refrigerated for a maximum of 10 days, after this time the product should be discarded.

Incorrect use of this product may cause bacterial resistance.

13. ADVERSE REACTIONS

Vomiting, diarrhea, anorexia, abdominal pain, cholestatic hepatitis, stomatitis and glossitis may be observed (Koch *et al.*, 2012; BSAVA, 2017).

14. OVERDOSAGE

Vomiting, diarrhea and gastrointestinal pain have been reported in cases of acute oral overdose (Plumb, 2018).

15. DRUG-DRUG INTERACTIONS

Azithromycin, unlike erythromycin, does not inhibit the hepatic microsomal enzyme CYP3A4 (formerly known as cytochrome P450 IIIA4), which reduces the possibility of drug interactions.

Oral antacids (magnesium and aluminum based) may reduce the absorption of azithromycin, it is recommended to take azithromycin at least one hour before or two hours after the antacid.

There is antagonism with other macrolides, chloramphenicol and lincosamides, due to competition for the same binding site.

Azithromycin can elevate serum levels of cyclosporine, methylprednisolone, digoxin and theophylline, since macrolide antibiotics interfere with their metabolism.

The anticoagulant effect of warfarin is increased by concomitant administration of azithromycin.

No significant effects on plasma levels of carbamazepine or its active metabolite were detected in patients receiving concomitant azithromycin.

Patients administered diuretics such as spironolactone could suffer hyperkalemia if azithromycin is administered.

The concomitant administration of cisapride and azithromycin may increase QT interval prolongation, ventricular arrhythmias, and torsades de pointes, as macrolides interfere with the metabolism of cisapride.

Concomitant use of macrolides with ketoconazole is not recommended because azithromycin levels may decrease (BSAVA, 2017; Costa, 1997; Plumb, 2018; Koch *et al.*, 2012).

16. INTERACTIONS WITH LABORATORY TESTS

It can cause an increase in liver enzymes (Koch *et al.*, 2012).

17. USE DURING GESTATION AND/OR NURSING

Safety during these physiological stages has not been established, so its use is only recommended when clearly

necessary (Plumb, 2018).

18. PRECAUTIONS

Store in a cool, dry place away from direct sunlight and/or heat.

Keep out of reach of children and pets. Product for exclusive use in Veterinary Medicine.

19. EXPIRATION PERIOD

Expiration Period of the veterinary drug product as packaged for sale: 24 months.

20. HOLDER OF THE REGISTRY

HOLLAND DE MEXICO SA DE CV

Calle 21 Este. No 12, Col. Civac

Jiutepec, Morelos, CP 62578

21. REGISTRATION NUMBER

Q-4196-176

22. PROHIBITION OF SALE, DISTRIBUTION AND/OR USE

Prescription required.

Consult your veterinarian.

Shake before use

23. PRESENTATION

Box with bottle/powder for suspension 30 mL (1.01 fl oz).

24. REFERENCES

- 24.1 BSAVA. Small Animal Formulary. 9th. Zenith Media, 2017.
- 24.2 Costa H. Useful drug interactions in dermatology. *Dermatol. Peru* 1997; 7 (1):35-7
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- 24.12 Sumano *et al.* Manual of Clinical Pharmacology for Small Species. 7th ed. Mexico, 2019.
- 24.13 Sumano *et al.* Veterinary Pharmacology. Fourth ed. Mexico, 2015.
- 24.14 Wiebe J. Drug Therapy for Infectious Diseases of the Dog and Cat. Wiley BlackWell,^{1st} ed, India, 2015.