1.3 Product Information

1.3.1 Summary of product characteristics (SmPC)

1. 3.1.1 Name of the medicinal product: PAXTEREX AZITHROMYCIN
(Azithromycin Tablets USP 500mg)

1.3. 1.2 Qualitative and quantitative composition:

Each Film Coated Tablet Contains:
Azithromycin Dihydrate Equivalent to Azithromycin USP (500 mg)
Approved Colour Used. (-)
Excipients (QS)

Sr. No.	Name of Ingredient	Specification	Label Claim	Over-ages added (In %)	Quantity/ Tablet in mg	Reason for Function
a)	**Dry Mixing**					
1.	Azithromycin dihydrate	USP	Azithromycin dihydrate equivalent to Azithromycin 500mg	NA	524.00	Medicament
2.	Calcium hydrogen phosphate dihydrate	BP	NA	NA	23.42	Diluent
3.	Lactose monohydrate	BP	NA	NA	15.00	Diluent
4.	Croscarmellose sodium	BP	NA	NA	5.96	Disintegrant
5.	Povidone (K 30)	BP	NA	NA	26.00	Disintegrant
b)	**Binder Preparation**					
6.	Maize starch	BP	NA	NA	35.00	Binder
7.	Methyl hydroxybenzoate	BP	NA	NA	0.42	Preservative
8.	Propyl hydroxybenzoate	BP	NA	NA	0.22	Preservative
9.	Purified water	BP	NA	NA	--	Vehicle
c)	**Lubrication**					
10.	Sodium lauryl sulfate	BP	NA	NA	2.98	Lubricant
11.	Magnesium stearate	BP	NA	NA	7.00	Lubricant
12.	Croscarmellose sodium	BP	NA	NA	20.00	Disintegrant
	Average weight of uncoated tablet (in mg)				**660.000**	
d)	**Film Coating**					
13.	Hypromellose (15 CPS)	BP	NA	NA	5.60	Film Former
14.	Macrogol-6000	BP	NA	NA	0.40	Plasticizer
15.	Titanium dioxide	BP	NA	NA	1.00	Colour
16.	Purified talc	BP	NA	NA	3.00	Antiadherant
17.	Purified water	BP	NA	NA	--	Vehicle
	Average weight of film coated tablet (in mg)				**670.000**	

1. 3.1.3 Pharmaceutical form: Film coated Tablet

Description: White coloured, capsule shaped, biconvex, film coated tablet breakline on one side and plain on other side.

1.3.1.4 Clinical Particulars

1.3.1.4.1 Therapeutic indications:

PAXTEREX AZITHROMYCIN (Azithromycin Tablets USP 500mg) can be applied for the treatment of the following infections, when caused by microorganisms sensitive to azithromycin:

- acute bacterial sinusitis
- acute bacterial otitis media
- pharyngitis, tonsillitis
- acute exacerbation of chronic bronchitis
- mild to moderately severe community acquired pneumonia
- skin and soft tissue infections
- uncomplicated Chlamydia trachomatis urethritis and cervicitis

1.3.1.4.2 Posology and method of administration

Posology

Adults

In uncomplicated Chlamydia trachomatis urethritis and cervicitis the dose is 1000 mg as a single oral dose.

For all other indications the dose is 1500 mg, to be administered as 500 mg per day for three consecutive days. As an alternative the same total dose (1500 mg) can also be administered over a period of five days with 500 mg on the first day and 250 mg on the second to the fifth day.

Elderly people

The same dose as in adult patients is used for elderly people. Since older people can be patients with ongoing proarrhythmic conditions a particular caution is recommended due to the risk of developing cardiac arrhythmia and torsades de pointes.

Paediatric population

Azithromycin tablets should only be administered to children weighing more than 45 kg when normal adult dose should be used. For children under 45 kg other pharmaceutical forms of azithromycine, e.g. suspensions, may be used.

In patients with renal impairment: No dose adjustment is necessary in patients with mild to moderate renal impairment (GFR 10-80 ml/min).

In patients with hepatic impairment: A dose adjustment is not necessary for patients with mild to moderately impaired liver function.

Method of administration

Azithromycin Tablets should be given as a single daily dose. The tablets may be taken with food.

1.3.1.4.3 Contraindications

Hypersensitivity to the active substance, erythromycin, any macrolide or ketolide antibiotic, soya lecithin or to any of the excipients listed in section 1.3.1.6.1

1.3.1.4.4 Special warnings and precautions for use

Hypersensitivity

As with erythromycin and other macrolides, rare serious allergic reactions including angioneurotic oedema and anaphylaxis (rarely fatal), dermatologic reactions including acute generalised exanthematous pustulosis (AGEP), Stevens Johnson syndrome (SJS), toxic epidermal necrolysis

Lactation

Azithromycin is excreted in breast milk. Because of the long half-life, accumulation in the milk is possible. Information available from published literature indicates that, in short-term use, this does not lead to clinically relevant quantities in the milk. No serious side effects have been observed by azithromycin in breast-fed children.

A decision should be taken whether breastfeeding is discontinued or that treatment with azithromycin is discontinued/initiated or not, taking into account the benefit of breastfeeding for the child and the benefit of treatment for the woman.

1.3.1.4.7 Effects on the ability to drive and use machines

There is no evidence to suggest that azithromycin may have an effect: on a patient's ability to drive or operate machinery. Visual impairment and vision blurred may have an effect on a patient's ability to drive or operate machinery.

1.3.1.4.8 Undesirable effects

The more common side effects of **PAXTEREX AZITHROMYCIN** (Azithromycin Tablets USP 500mg) can include Diarrhoea, nausea, stomach pain, vomiting.

Serious side effects can include:

• Liver problems. Symptoms can include: tiredness or weakness, loss of appetite, pain in your upper stomach, dark urine, yellowing of your skin or the whites of your eyes.

• QT prolongation. This can cause fast or irregular heart rhythm

• Allergic reactions. Symptoms can include: trouble breathing, swelling of your face, lips, tongue, or throat, hives

• Severe skin reactions, such as Stevens-Johnson syndrome, acute generalized exanthematous pustulosis (AGEP), or toxic epidermal necrolysis, which can cause symptoms such as red, blistering skin or skin sloughing (shedding dead skin cells)

• Infantile hypertrophic pyloric stenosis (in newborns). Symptoms can include: vomiting after eating, irritability with feeding, lack of weight gain.

1.3.1.4.9 Overdoses

Adverse events experienced in higher than recommended doses were similar to those seen at normal doses. In the event of overdosage general symptomatic and general supportive measures are indicated as required.

Symptoms

The typical symptoms of an overdose with macrolide antibiotics include reversible loss of hearing, severe nausea, vomiting and diarrhoea.

Treatment

In the event of overdose the administration of medicinal charcoal and general symptomatic treatment and supportive measures are indicated as required.

1.3.1.5 Pharmacological properties

1.3.1.5.1 Pharmacodynamic properties

General properties

Pharmacotherapeutic group: antibacterials for systemic use; macrolids; azithromycin, ATC code: J01FA10

Mode of action:

Azithromycin is an azalide, a sub-class of the macrolid antibiotics. By binding to the 50S-ribosomal sub-unit, azithromycin avoids the translocation of peptide chains from one side of the

ribosome to the other. As a consequence of this, RNA-dependent protein synthesis in sensitive organisms is prevented.

PK/PD relationship

For azithromycin the AUC/MIC is the major PK/PD parameter correlating best with the efficacy of azithromycin.

Following the assessment of studies conducted in children, the use of azithromycin is not recommended for the treatment of malaria, neither as monotherapy nor combined with chloroquine or artemisinin based drugs, as non-inferiority to anti-malarial drugs recommended in the treatment of uncomplicated malaria was not established.

Mechanism of resistance:

Resistance to azithromycin may be inherent or acquired. There are three main mechanisms of resistance in bacteria: target site alteration, alteration in antibiotic transport and modification of the antibiotic.

Complete cross resistance exists among *Streptococcus pneumoniae*, betahaemolytic streptococcus of group A, *Enterococcus faecalis* and *Staphylococcus aureus*, including methicillin resistant *S. aureus* (MRSA) to erythromycin, azithromycin, other macrolides and lincosamides.

1.3.1.5.2 Pharmacokinetic properties

Absorption: After oral administration the bioavailability of azithromycin is approximately 37%. Peak plasma levels are reached after 2-3 hours (C_{max} after a single dose of 500 mg orally was approximately 0.4 mg/l).

Distribution: Kinetic studies have shown markedly higher azithromycin levels in tissue than in plasma (up to 50 times the maximum observed concentration in plasma) indicating that the active substance is heavily tissue bound (steady state distribution volume of approximately 31 l/kg). Concentrations in target tissues such as lung, tonsil, and prostate exceed the MIC_{90} for likely pathogens after a single dose of 500 mg.

In experimental in vitro and in vivo studies azithromycin accumulates in the phagocytes, freeing is stimulated by active phagocytosis. In animal studies this process appeared to contribute to the accumulation of azithromycin in the tissue.

In serum the protein binding of azithromycin is variable and depending on the serum concentration varies from 50% in 0.05 mg/l to 12% in 0.5 mg/l.

Metabolism: The identified metabolites (formed by N- and O- demethylising, by hydroxylising of the desosamine and aglycone rings, and by the splitting of the cladinose conjugate) are microbiologically inactive.

Excretion: Plasma terminal elimination half-life closely reflects the tissue depletion half-life of 2 to 4 days. About 12% of an intravenously administered dose is excreted in the urine unchanged over a period of 3 days; the majority in the first 24 hours. Biliary excretion of azithromycin, predominantly in unchanged form, is a major route of elimination.

1.3.1.5.3 Preclinical safety Data:

In high-dose animal studies, giving active substance concentrations 40 fold higher than those expected in clinical practice, azithromycin has been noted to cause reversible phospholipidosis, generally without discernible toxicological consequences. There is no evidence that this is of relevance to the normal use of azithromycin in humans.

Carcinogenic potential:

Long-term studies in animals have not been performed to evaluate carcinogenic potential.

Mutagenic potential:

Azithromycin has shown no mutagenic potential in standard laboratory tests: mouse lymphoma assay, human lymphocyte clastogenic assay, and mouse bone marrow clastogenic assay.

Reproductive toxicity:

No teratogenic effects were observed in animal studies of embryotoxicity in mice and rats. In rats, azithromycin doses of 100 and 200 mg/kg bodyweight/day led to mild retardations in foetal ossification and in maternal weight gain. In peri-/postnatal studies in rats, mild retardations following treatment with 50 mg/kg/day azithromycin and above were observed.

1.3.1.6 Pharmaceutical particulars

1.3.1.6.1 List of excipients
Calcium hydrogen phosphate dihydrate, Lactose monohydrate, Croscarmellose sodium, Maize starch, Povidone (K 30), Methyl hydroxybenzoate, Propyl hydroxybenzoate, Sodium Lauryl sulfate, Magnesium stearate, Hypromellose (15 CPS), Purified talc, Titanium dioxide, Macrogol-6000, Purified Water.

1.3.1.6.2 Incompatibilities
Not applicable

1.3.1.6.3 Shelf life
36 months

1.3.1.6.4 Special precautions for storage
Store below 30°C in a dry & dark place.
Keep all medicines out of reach of children.

1.3.1.6.5 Nature and contents of container
Primary packing: 10 Tablets in an ALU-ALU blister.
Secondary packing: 1 Blister is packed in an inner carton along with leaflet.
Tertiary packing: 10 Inner cartons are packed in an outer carton. Shrink individual outer carton. Such 100 Shrinks are packed in a 5 Ply shipper sealed with BOPP tape & strap with strapping roll.

1.3.1.6.5 Special precautions for disposal and other handling
None.

1.3.1.7 Applicant / Manufacturer

Applicant

Applicant name and address	**M/s. MANKIND LIFESCIENCES LTD.** No 2, Aggrey Road, Fegge Onitsha, Anambra State.
Contact person's phone number	
Contact person's email	

Manufacturer

Manufacturer name and address	**M/s. IMPULSE PHARMA PVT. LTD.** J-201, J-202/1 , MIDC Tarapur, Boisar, Dist. Palghar - 401506, Maharashtra State, India.
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