SUMMARY OF PRODUCT CHARACTERISTICS

AGYCIN

(AZITHROMYCIN FOR ORAL SUSPENSION USP 40 MG / ML)

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

Agycin (Azithromycin for oral suspension USP 40 mg / ml)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml suspension after reconstitution contains:

Azithromycin (as dihydrate) USP equivalent to

Azithromycin anhydrous …… 40 mg

Excipients …… q.s.

Detail excipients are mentioned in Section 6.1

3. PHARMACEUTICAL FORM

Powder for oral suspension

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Azithromycin powder for oral suspension is indicated for the treatment of the following infections, when caused by microorganisms sensitive to azithromycin (see section 4.4 and 5.1):

− Acute bacterial otitis media

− Pharyngitis, tonsillitis

− Acute bacterial exacerbation of chronic obstructive pulmonary diseases

– Community Acquired Pneumonia

− Urethritis, Cervicitis

- Uncomplicated skin and skin structure infections

Considerations should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

Children and adolescents (< 18 years)

The total dosage in children aged 1 year and older is 30 mg/kg administered as 10 mg/kg once daily for three days, or over a period of five days starting with a single dose of 10 mg/kg on the first day, followed by doses of 5 mg/kg per day for the following 4 days. There are limited data on use in children younger than 1 year.

Body Weight	**Day -1**	**Day -2**	**Day - 3**
15 Kg to 25 Kg	5 ml	5 ml	5 ml
26 Kg to 35 Kg	7.5 ml	7.5 ml	7.5 ml
36 Kg to 45 Kg	10 ml	10 ml	10 ml

Patients with renal impairment:

No dose adjustment is necessary in patients with mild to moderate renal impairment (GFR 10-80 ml/min) (see section 4.4).

Patients with hepatic impairment:

A dose adjustment is not necessary for patients with mild to moderately impaired liver function (see section 4.4).

Method of administration

Before use the powder should be reconstituted with water into a white to off white coloured, homogenous suspension, see section 6.6. After reconstitution the drug can be administered using a PE/PP syringe for oral use.

After taking the suspension a bitter after-taste can be avoided by drinking fruit juice directly after swallowing. Azithromycin powder for oral suspension should be given in a single daily dosage. The suspension may be taken together with food.

4.3 Contraindications

The use of this product is contraindicated in patients with hypersensitivity to azithromycin, erythromycin, any macrolide or ketolide antibiotic, or to any of the excipients listed in section 6.1 (see also section 4.4).

4.4 Special warnings and special precautions for use

As with erythromycin and other macrolides, rare serious allergic reactions, including angiooedema and anaphylaxis (rarely fatal), have been reported. Some of these reactions with azithromycin have resulted in recurrent symptoms and required a longer period of observation and treatment.

Since liver is the principal route of elimination for azithromycin, the use of azithromycin should be undertaken with caution in patients with significant hepatic disease. 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 medicinal products.

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. Azithromycin administration should be stopped if liver dysfunction has emerged.

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 ergotamine derivatives and azithromycin. However, because of the theoretical possibility of ergotism, azithromycin and ergot derivatives should not be co-administered (see section 4.5).

As with any antibiotic preparation, observation for signs of superinfection with non- susceptible organisms, including fungi is recommended.

Clostridium difficile associated diarrhoea (CDAD) has been reported with the use of nearly all antibacterial agents, including azithromycin, and may range in severity from mild diarrhoea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C. difficile*.

C. difficile produces toxins A and B which 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. CDAD must be considered in all patients who present with diarrhoea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antimicrobial agents.

In patients with severe renal impairment (GFR < 10 ml/min) a 33% increase in systemic exposure to azithromycin was observed (see section 5.2).

Prolonged cardiac repolarisation and QT interval, imparting a risk of developing cardiac arrhythmia 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 acquired QT prolongation.
- Currently receiving treatment with other active substances known to prolong QT interval such as antiarrhythmic of classes IA and III, cisapride and terfenadine.
- With electrolyte disturbance, particularly in cases of hypokalaemia and hypomagnesaemia
- With clinically relevant bradycardia, cardiac arrhythmia or severe cardiac insufficiency.

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).

Safety and efficacy for the prevention or treatment of MAC (*Mycobacterium avium* complex) in children have not been established.

The following should be considered before prescribing azithromycin:

Azithromycin powder for oral solution is not suitable for treatment of severe infections where a high concentration of the antibiotic in the blood is rapidly needed.

Azithromycin is not the first choice for the empiric treatment of infections in areas where the prevalence of resistant isolates is 10% or more (see section 5.1).

In areas with a high incidence of erythromycin A resistance, it is especially important to take into consideration the evolution of the pattern of susceptibility to azithromycin and other antibiotics.

As for other macrolides, high resistance rates of *Streptococcus pneumoniae* (> 30 %) have been reported for azithromycin in some European countries (see section 5.1). This should be taken into account when treating infections caused by *Streptococcus pneumoniae*.

Pharyngitis/ tonsillitis

Azithromycin is not the substance of first choice for the treatment of pharyngitis and tonsillitis caused by *Streptococcus pyogenes*. For this and for the prophylaxis of acute rheumatic fever penicillin is the treatment of first choice.

Sinusitis

Often, azithromycin is not the substance of first choice for the treatment of sinusitis.

Acute otitis media

Often, azithromycin is not the substance of first choice for the treatment of acute otitis media.

Skin and soft tissue infections

The main causative agent of soft tissue infections, *Staphylococcus aureus*, is frequently resistant to azithromycin. Therefore, susceptibility testing is considered a precondition for treatment of soft tissue infections with azithromycin.

Sexually transmitted disease

In case of sexually transmitted diseases a concomitant infection by *T. palladium* should be excluded.

Azithromycin 200mg/5 ml contain aspartame which is a source of phenylalanine. It may be harmful for people with phenylketonuria.

4.5 Interaction with other FPPs and other forms of interaction

Antacids:

In a pharmacokinetic study investigating the effects of simultaneous administration of antacids and azithromycin, no effect on the total bio-availability was seen, although the peak serum concentrations were reduced by approximately 25%. Azithromycin must be taken at least 1 hour before or 2 hours after antacids.

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.

Didanosins (Dideoxyinosine):

Co-administration of 1,200 mg/day azithromycin with 400 mg/day didanosine in 6 HIV-positive subjects did not appear to affect the steady-state pharmacokinetics of didanosine as compared with placebo.

Digoxin:

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

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.

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.

Ergotamine derivatives:

Due to the theoretical possibility of ergotism, the concurrent use of azithromycin with ergot derivatives is not recommended (see section 4.4).

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

Astemizole, alfentanil

There are no known data on interactions with astemizole or alfentanil. Caution is advised in the co-administration of these medicines with Azithromycin because of the known enhancing effect of these medicines when used concurrently with the macrolid antibiotic erythromycin.

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.

Cisapride

Cisapride is metabolized in the liver by the enzyme CYP 3A4. Because macrolides inhibit this enzyme, concomitant administration of cisapride may cause the increase of QT interval prolongation, ventricular arrhythmias and torsades de pointes.

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.

Coumarin-Type Oral Anticoagulants:

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 coumarin-type oral anticoagulants. 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 coumarin-type oral anticoagulants.

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 cyclosporin, the resulting cyclosporin C_{max} and AUC_{0-5} were found to be significantly elevated. Consequently, caution should be exercised before considering concurrent administration of these drugs. If co-administration of these drugs is necessary, cyclosporin levels should be monitored and the dose adjusted accordingly.

Efavirenz:

Co-administration of a 600 mg single dose of 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.

Methylprednisolone:

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

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.

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 no dose adjustment is required.

Rifabutin:

Co-administration of azithromycin and rifabutin did not affect the serum concentrations of either drug.

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. As interactions of other macrolides

with theophylline have been reported, alertness to signs that indicate a rise in theophylline levels is advised.

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 1,200 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 Pregnancy and lactation

Not applicable as the product is intended for paediatric use.

4.7 Effects on 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. When performing these functions, account should be taken of the occurrence of the adverse effects of dizziness and convulsions.

4.8 Undesirable effects

The table below lists the adverse reactions identified through clinical trial experience and post-marketing surveillance by system organ class and frequency. Adverse reactions identified from post-marketing experience are included in italics. The frequency grouping is defined using the following convention:

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); very rare (< 1/10,000); not known (cannot be estimated from the available data).

Within each frequency group, undesirable effects are listed in order of decreasing seriousness.

Adverse reactions possibly or probably related to azithromycin based on clinical trial experience and post-marketing surveillance:

System Organ Class	Frequency	Adverse reaction
Infections and infestations	Uncommon	Candidiasis, oral candidiasis, vaginal infection
	Not known	*Pseudomembranous colitis* (see section 4.4)
Blood and lymphatic system disorders	Common	Lymphocyte count decreased, eosinophil count increased
	Uncommon	Leukopenia, neutropenia
	Rare	Thrombocytopenia, haemolytic anaemia
Immune system disorders	Uncommon	Angioedema, hypersensitivity
	Not known	*Anaphylactic reaction* (see section 4.4)
Metabolism and nutrition disorders	Common	Anorexia
Psychiatric disorders	Uncommon	Nervousness
	Rare	Agitation, depersonalisation
	Not known	*Aggression, anxiety*
Nervous system disorders	Common	Dizziness, headache, paraesthesia, dysgeusia
	Uncommon	Hypoaesthesia, somnolence, insomnia
	Not known	*Syncope, convulsion, psychomotor hyperactivity, anosmia, ageusia, parosmia, myasthenia gravis (see section 4.4).*
Eye disorders	Common	Visual impairment
Ear and labyrinth disorders	Common	Deafness
	Uncommon	Hearing impaired, tinnitus

System Organ Class	Frequency	Adverse reaction
	Rare	Vertigo
Cardiac disorders	Uncommon	Palpitations
	Not known	*Torsades de pointes* (see section 4.4), *arrhythmia* (see section 4.4) *including ventricular tachycardia, electrocardiogram QT prolonged* (see section 4.4)
Vascular disorders	Not known	*Hypotension*
Gastrointestinal disorders	Very common	Diarrhoea, abdominal pain, nausea, flatulence
	Common	Vomiting, dyspepsia
	Uncommon	Gastritis, constipation
	Not known	*Pancreatitis, tongue discolouration*
Hepatobiliary disorders	Uncommon	Hepatitis, aspartate aminotransferase increased, alanine aminotransferase increased, blood bilirubine increased
	Rare	Hepatic function abnormal
	Not known	*Hepatic failure (see section 4.4)*, hepatitis fulminant, hepatic necrosis, jaundice cholestatic*
Skin and subcutaneous tissue disorders	Common	Rash, pruritus
	Uncommon	Steven-Johnson syndrome, photosensitivity reaction, urticaria
	Not known	*Toxic epidermal necrolysis, erythema multiforme*
Musculoskeletal and connective tissue disorders	Common	Arthralgia
Renal and urinary	Uncommon	Blood urea increased

System Organ Class	Frequency	Adverse reaction
disorders	Rare	Renal failure acute, nephritis interstitial
General disorders and administration site conditions	Common	Fatigue
	Uncommon	Chest pain, oedema, malaise, asthenia
Investigations	Common	Blood bicarbonate decreased
	Uncommon	Blood creatinine increased, blood potassium abnormal

* Which has rarely resulted in death

4.9 Overdose

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

General properties

Antibacterial for systemic use; macrolides; azithromycin, ATC code: J01FA10

Mode of action

Azithromycin is an azalide, a sub-class of the macrolide 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.

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.

Breakpoints

EUCAST (European Committee on Antimicrobial Susceptibility Testing)

Pathogens	**susceptible (mg/l)**	**resistant (mg/l)**
Staphylococcus spp.	≤ 1	> 2
Streptococcus spp. (Group A, B, C, G)	≤ 0.25	> 0.5
Streptococcus pneumoniae	≤ 0.25	> 0.5
Haemophilus influenzae	≤ 0.125	> 4
Moraxella catarrhalis	≤ 0.5	> 0.5
Neisseria gonorrhoeae	≤ 0.25	> 0.5

Susceptibility

The prevalence of acquired resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

prevalence of resistance is equal to or greater than 10% in at least one country in the European Union.

Table of susceptibility

Commonly susceptible species
Aerobic Gram-negative microorganisms
*Haemophilus influenzae**
*Moraxella catarrhalis**
Other microorganisms
Chlamydophila pneumoniae
Chlamydia trachomatis
Legionella pneumophila
Mycobacterium avium
*Mycoplasma pneumonia**
Species for which acquired resistance may be a problem
Aerobic Gram-positive microorganisms
*Staphylococcus aureus **
Streptococcus agalactiae
*Streptococcus pneumoniae**
*Streptococcus pyogenes**
Other microorganisms
Ureaplasma urealyticum
Inherently resistant organisms

Commonly susceptible species
Aerobic Gram-positive microorganisms
Staphylococcus aureus – methicillin resistant and erythromycin resistant strains
Streptococcus pneumoniae – penicillin resistant strains
Aerobic Gram-negative microorganisms
Escherichia coli
Pseudomonas aeruginosa
Klebsiella spp.
Anaerobic Gram-negative microorganisms
Bacteroides fragilis-group

* Clinical effectiveness is demonstrated by sensitive isolated organisms for approved clinical indications.

5.2 Pharmacokinetic properties

Absorption

The biological availability of azithromycin after oral administration is approximately 37%. Peak plasma levels are achieved 2-3 hours after taking the medicinal product.

Distribution

After oral administration, azithromycin is distributed throughout the entire body. Pharmacokinetic studies have shown clearly higher azithromycin levels in the tissues than in the plasma (up to 50 times the maximum observed concentration in plasma). This indicates that the substance is bound in the tissues in considerable quantities.

Concentrations in the infected tissues, such as lungs, tonsil and prostate are higher than the MRC90 of the most frequently occurring pathogens after a single dose of 500 mg.

The protein binding of azithromycin in serum is variable and varies, depending on the serum concentration, from 52% at 0.05 mg/l to 12% at 0.5 mg/l. The steady state distribution volume is 31.1 l/kg.

Elimination

The terminal plasma-elimination half-life closely follows the tissue depletion half-life from 2 to 4 days.

Approximately 12% of an intravenously administered dose of azithromycin is, over a period of 3 days, excreted unchanged in the urine. High concentrations of unchanged azithromycin were found in human bile. In this, ten metabolites were also detected (formed by N- and O-desmethylation, by hydroxylation of the desosamin and aglycon rings and by splitting the cladinose conjugate). A comparison of fluid chromatography and microbiological assessment methods shows that the metabolites are microbiologically inactive.

In animal models high concentrations of azithromycin were found in phagocytes. Also it has been shown that during active phagocytosis higher concentrations of azithromycin are released than during inactive phagocytosis. In animal models this process was shown to contribute to the accumulation of azithromycin in infectious tissue.

Pharmacokinetics in special populations

Renal insufficiency

Following a single oral dose of azithromycin 1 g, mean C_{max} and AUC_{0-120} increased by 5.1% and 4.2% respectively, in subjects with mild to moderate renal impairment (glomerular filtration rate of 10-80 ml/min) compared with normal renal function (GFR > 80 ml/min). In subjects with severe renal impairment, the mean C_{max} and AUC_{0-120} increased 61% and 33% respectively compared to normal.

Hepatic insufficiency

In patients with mild to moderate hepatic impairment, there is no evidence of a marked change in serum pharmacokinetics of azithromycin compared to normal hepatic function. In these patients, urinary recovery of azithromycin appears to increase perhaps to compensate for reduced hepatic clearance.

Elderly

The pharmacokinetics of azithromycin in elderly men was similar to that of young adults; however, in elderly women, although higher peak concentrations (increased by 30-50%) were observed, no significant accumulation occurred.

Infants, toddlers, children and adolescents

Pharmacokinetics have been studied in children aged 4 months – 15 years taking capsules, granules or suspension.. At 10 mg/kg on day 1 followed by 5 mg/kg on days 2-5, the C_{max} achieved is slightly lower than adults with 224 ug/l in children aged 0.6-5 years and after 3 days dosing and 383 ug/l in those aged 6-15 years. The $t_{1/2}$ of 36 h in the older children was within the expected range for adults.

5.3 Preclinical safety data

In animal tests in which the dosages used amounted to 40 times the clinical therapeutic dosages, azithromycin was found to have caused reversible phospholipidosis, but as a rule no true toxicological consequences were observed which were associated with this. The relevance of this finding to humans receiving azithromycin in accordance with the recommendations is unknown. Electrophysiological investigations have shown that azithromycin prolongs the QT interval.

Mutagenic potential:

There was no evidence of a potential for genetic and chromosome mutations in *in-vivo* and *in-vitro* test models.

Reproductive toxicity:

In embryotoxicity studies in mice and rats no teratogenic effects were observed. In rats, azithromycin dosages of 100 and 200 mg/kg bodyweight/day led to slight retardations in fetal ossification and in maternal weight gain. In peri-/postnatal studies in rats, slight retardations in physical development and delay in reflex development were observed following treatment with 50 mg/kg/day azithromycin and above.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Kyron T-112 BN

Sucrose

Aspartame

Powdarome Peppermint premium

Xanthan Gum

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 Months (2 Years)

6.4 Special precautions for storage

Store in dry place, below 30°C. protect from light.

The reconstituted mixture should be stored in a refrigerator (2°C to 8°C).

6.5 Nature and contents of container

6.75 g of powder filled in 15 ml HDPE bottle. Each bottle is packed in Monocarton along with leaflet.

6.6 Instructions for use and handling and disposal

Not Applicable

7. MARKETING AUTHORISATION HOLDER

BLISS GVS PHARMA LIMITED,

102, Hyde Park, Saki-Vihar road,

Andheri (East) Mumbai 400 072,

INDIA