SUMMARY OF PRODUCT CHARACTERISTICS

LONART 20/120
Artemether 20 mg and Lumefantrine 120 mg Oral powder for Suspension.

1. NAME OF THE MEDICINAL PRODUCT
LONART 20/120

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each sachet contains 20 mg artemether and 120 mg lumefantrine.
For full list of excipients refer section 6.1.

3. PHARMACEUTICAL FORM
Sachet

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
LONART 20/120 is indicated for the treatment of acute uncomplicated *Plasmodium falciparum.* Malaria in children only.
Consideration should be given to official guidance regarding the appropriate use of antimalarial agents.

4.2 Posology and method of administration
Sachet for oral administration.
To increase absorption, LONART 20/120 should be taken with food or a milky drink. If patients are unable to tolerate food, LONART 20/120 should be administered, but the systemic exposure may be reduced. Patients who vomit within 1 hour of taking the medication should repeat the dose. For administration to small children and infants, LONART 20/120 is not suitable.

Adults and children weighing 35 kg and above
A course of treatment comprises six doses' Sachets i.e., total of 6 Sachets, given over a period of 60 hours as follows: the first dose of one Sachet, given at the time of initial diagnosis, should be followed by five further doses of one Sachet given at 8, 24, 36, 48 and 60 hours thereafter.

4.3 Contraindications
LONART 20/120 is contraindicated in:
- Patients with known hypersensitivity to the active substances or to any of the excipients.
- Patients with severe malaria according to WHO definition*.
- Patients who are taking any drug which is metabolized by the cytochrome enzyme. CYP2D6 (e.g., metoprolol, imipramine, amitryptyline, clomipramine).
- Patients with a family history of sudden death or of congenital prolongation of the QTc interval on electrocardiograms, or with any other clinical condition known to prolong the QTc interval.
- Patients taking drugs that are known to prolong the QTc interval (proarrythmic). These drugs include:
  - antiarrhythmics of classes IA and III,
  - neuroleptics, antidepressive agents,
  - certain antibiotics including some agents of the following classes: macrolides, fluoroquinolones, imidazole and triazole antifungal agents,
  - certain non-sedating antihistamines (terfenadine, astemizole),
  - cisapride
  - flecainide

- Patients with a history of symptomatic cardiac arrythmias or with clinically relevant bradycardia or with congestive cardiac failure accompanied by reduced left ventricle ejection fraction.
  - Patients with disturbances of electrolyte balance e.g., hypokalemia or hypomagnesemia.
- Patients taking drugs that are strong inducers of CYP3A4 such as rifampin, carbamazepine, phenytoin, St. John's wort (*Hypericum perforatum*).

(*Presence of one or more of the following clinical or laboratory features:

Clinical manifestation: Prostration; impaired consciousness or unarousable coma; failure to feed; deep breathing, respiratory distress (acidotic breathing); multiple convulsions; circulatory collapse or shock; pulmonary edema (radiological); abnormal bleeding; clinical jaundice; hemoglobinuria.

Laboratory test: Severe normocytic anemia; hemoglobinuria; hypoglycemia; metabolic acidosis; renal impairment; hyperlactatemia; hyperparasitemia)

4.4 Special warnings and precautions for use.

LONART 20/120 must not be used in the first trimester of pregnancy in situations where other suitable and effective antimalarials are available. LONART 20/120 has not been evaluated for the treatment of severe malaria, including cases of cerebral malaria or other severe manifestations such as pulmonary oedema or renal failure. Due to limited data on safety and efficacy, LONART 20/120 should not be given concurrently with any other antimalarial agent unless there is no other treatment option. If a patient deteriorates whilst taking LONART 20/120, alternative treatment for malaria should be started without delay. In such cases, monitoring of the ECG is recommended and steps should be taken to correct any electrolyte disturbances.The long elimination half-life of lumefantrine must be considered when administering quinine in patients previously treated with LONART 20/120. If quinine is given after LONART 20/120, close monitoring of the ECG is advised. LONART 20/120 is not indicated and has not been evaluated for prophylaxis. LONART 20/120should be used cautiously in patients on ARTs since decreased artemether, DHA, and/or lumefantrine concentrations may result in a decrease of antimalarial efficacy of LONART 20/120 Like other antimalarials (e.g., halofantrine, quinine and quinidine) LONART 20/120 has the potential to cause QT prolongation. Caution is recommended when combining LONART 20/120 with drugs exhibiting variable patterns of inhibition, moderate induction, or competition for CYP3A4 as the therapeutic effects of some drugs could be altered. Drugs that have a mixed inhibitory/induction effect on CYP3A4, especially anti-retroviral drugs such as HIV protease inhibitors and non- nucleoside reverse transcriptase inhibitors should be used with caution in patients taking LONART 20/120 Caution is recommended when combining LONART 20/120 with hormonal contraceptives. LONART20/120 may reduce the effectiveness of hormonal contraceptives. Therefore, patients using oral, transdermal patch, or other systemic hormonal

contraceptives should be advised to use an additional non-hormonal method of birth control for about one month Patients who remain averse to food during treatment should be closely monitored as the risk of recrudescence may be greater.In patients with severe hepatic impairment, a clinically relevant increase of exposure to artemether and lumefantrine and/or their metabolites cannot be ruled out. Therefore, caution should be exercised in dosing patients with severe hepatic impairment.

Renal impairment

No specific studies have been carried out in this group of patients. There is no significant renal excretion of lumefantrine, artemether and Dihydroartemisinin in studies conducted in healthy volunteers and clinical experience is limited. No dose adjustment for the use of LONART 20/120 in patients with renal impairment is recommended. Caution is advised when administering LONART 20/120 to patients with severe renal impairment. In these patients, ECG and blood potassium monitoring is advised.

Hepatic impairment

No specific studies have been carried out in this group of patients. No dose adjustment is. recommended for patients with mild to moderate hepatic impairment. Caution is advised when administering LONART 20/120 to patients with severe hepatic impairment. In these patients, ECG and blood potassium monitoring is advised.

Elderly

There is no information suggesting that the dosage in patients over 65 years of age should, be different than in younger adults.

New infections

Data for a limited number of patients in a malaria endemic area show that new infections, can be treated with a second course of LONART 20/120. In the absence of carcinogenicity study data, and due to lack of clinical experience, more than two courses of LONART 20/120 cannot be recommended.

4.5 Interaction with other medicinal products and other forms of interaction

Contraindications of concomitant use

Interaction with drugs that are known to prolong the QTc interval:

LONART 20/120 is contraindicated with concomitant use of drugs (they may cause prolonged QTc interval and Torsade de Pointes) such as: antiarrhythmics of classes IA and III, neuroleptics and antidepressant agents, certain antibiotics including some agents of the following classes: macrolides, fluoroquinolones, imidazole, and triazole antifungal agents, certain non-sedating antihistaminics (terfenadine, astemizole), cisapride, flecainide.

Interaction with drugs metabolized by CYP2D6:

Lumefantrine was found to inhibit CYP2D6 in vitro. This may be of clinical,relevance for compounds with a low therapeutic index. Co-administration of LONART 20/120with drugs that are metabolised by this iso-enzyme is contraindicated (e.g., neuroleptics, metoprolol, and tricyclic antidepressants such as imipramine, amitriptyline, clomipramine) is contraindicated.

Interaction with strong inducers of CYP3A4 such as rifampin

Oral administration of rifampin (600 mg daily), a strong CYP3A4 inducer, with LONART 20/120 Sachets (6-dose regimen over 3 days) in six HIV-1 and tuberculosis coinfected adults without malaria resulted in significant decreases in exposure to artemether (89%), DHA (85%) and lumefantrine (68%) when compared to exposure values after LONART 20/120 alone. Concomitant use of strong inducers of CYP3A4 such as rifampin, carbamazepine, phenytoin, St. John's Wort is contraindicated with LONART 20/120Inducers should not be administered at least one month after LONART 20/120administration, unless critical to use as judged by the prescriber.

Concomitant use not recommended.

Interaction with other antimalarial drugs

Data on safety and efficacy are limited, and LONART 20/120should therefore not be given concurrently with other antimalarials unless there is no other treatment option

If LONART 20/120is given following administration of mefloquine or quinine, close monitoring of food intake (for mefloquine) or of the ECG (for quinine) is advised. The long elimination half-life of lumefantrine must be taken into account when administering quinine in patients previously treated with LONART 20/120. In patients previously treated with halofantrine, LONART 20/120should not be administered earlier than one month after the last halofantrine dose

Mefloquine

A drug interaction study with LONART 20/120in man involved administration of a 6-dose regimen over 60 hours in healthy volunteers which was commenced at 12 hours after completion of a 3-dose regimen of mefloquine or placebo. Plasma mefloquine concentrations from the time of addition of LONART 20/120were not affected compared with a group which received mefloquine followed by placebo.

Pre-treatment with mefloquine had no effect on plasma concentrations of artemether or the artemether/dihydroartemisinin ratio but there was a significant reduction in plasma levels of lumefantrine, possibly due to lower absorption secondary to a mefloquine-induced decrease in bile production. Patients should be encouraged to eat at dosing times to compensate for the decrease in bioavailability.

Quinine

A drug interaction study in healthy male volunteers showed that the plasma concentrations

of lumefantrine and quinine were not affected when i.v. quinine (10 mg/kg BW over 2 hours) was given sequentially 2 hours after the last (sixth) dose of LONART 20/120 (so as to produce concurrent plasma peak levels of lumefantrine and quinine). Plasma concentrations of artemether and dihydroartemisinin (DHA) appeared to be lower. In this study, administration of LONART 20/120to 14 subjects had no effect on QTc interval. Infusion of quinine alone in 14 other subjects caused a transient prolongation of QTc interval, which was consistent with the known cardiotoxicity of quinine. This effect was slightly, but significantly, greater when quinine was infused after LONART 20/120in 14 additional subjects. It would thus appear that the inherent risk of QTc prolongation associated with i.v. quinine was enhanced by prior administration of LONART 20/120.

Concomitant use requiring caution Interactions

affecting the use of LONART 20/120

Interaction with CYP3A4 inhibitors

Both artemether and lumefantrine are metabolised predominantly by the cytochrome enzyme CYP3A4, but do not inhibit this enzyme at therapeutic concentrations. **Ketoconazole**

The concurrent oral administration of ketoconazole with LONART 20/120led to a modest increase (≤ 2-fold) in artemether, DHA, and lumefantrine exposure in healthy adult subjects. This increase in exposure to the antimalarial combination was not associated withincreased side effects or changes in electrocardiographic parameters. Based on this study, dose adjustment of LONART 20/120is considered unnecessary in falciparum malaria patients when administered in association with ketoconazole or other potent CYP3A4 inhibitors. LONART 20/120 should be used cautiously with drugs that inhibit CYP3A4 and are contraindicated with drugs which additionally are known to prolong QTc, due to potential for increased concentrations of lumefantrine which could lead to QT prolongation.

Grapefruit juice

Administration of artemether with grapefruit juice in healthy adult subjects resulted in an approximately two fold increase in systemic exposure to the parent drug. Grapefruit juice should be used cautiously during LONART 20/120treatment.

Interaction with weak to moderate inducers of CYP3A4

When LONART 20/120is co-administered with moderate inducers of CYP3A4, it may result in decreased concentrations of artemether and/or lumefantrine and loss of antimalarial efficacy

Interaction with anti-retroviral drugs such as protease inhibitors and non-nucleoside reverse transcriptase inhibitors

Both artemether and lumefantrine are metabolized by CYP3A4. Anti-retroviral drugs (ARTs), such as protease inhibitors and non-nucleoside reverse transcriptase inhibitors, are known to have variable patterns of inhibition, induction or competition for CYP3A4. LONART 20/120should be used cautiously in patients on ARTs since decreased artemether, DHA, and/or lumefantrine concentrations may result in a decrease of antimalarial efficacy of LUFANTER, and increased lumefantrine concentrations may cause QT prolongation Lopinavir/ ritonavir In a clinical study in healthy volunteers, lopinavir/ritonavir decreased the systemic exposures to artemether and DHA by approximately 40% but increased the exposure to lumefantrine by approximately 2.3- fold. Exposures to lopinavir/ritonavir were not significantly affected by concomitant use of LONART 20/120.

Nevirapine

In a clinical study in HIV-infected adults, nevirapine significantly reduced the median Cmax and AUC of artemether by approximately 61% and 72%, respectively and reduced the median Cmax and AUC of dihydroartemisinin by approximately 45% and 37%, respectively. Lumefantrine Cmax and AUC were non-significantly reduced by nevirapine. Artemether/lumefantrine reduced the median Cmax and AUC of nevirapine by approximately 43% and 46% respectively.Efavirenz decreased the exposures to artemether, DHA, and lumefantrine by approximately 50%, 45%, and 20%, respectively. Exposures to efavirenz were not significantly affected by concomitant use of LONART 20/120

Interactions resulting in effects of LONART 20/120on other drugs

Interaction with drugs metabolized by CYP450 enzymes.

When LONART 20/120is co-administered with substrates of CYP3A4 it may result in decreased concentrations of the substrate and potential loss of substrate efficacy. Studies in humans have demonstrated that artemisinins have some capacity to induce CYP3A4 and CYP2C19 and inhibit CYP2D6 and CYP1A2. Although the magnitude of the changes was generally low it is possible that these effects could alter the therapeutic response of drugs that are predominantly metabolised by these enzymes

Interaction with hormonal contraceptives: In vitro, the metabolism of ethinyl estradiol and levonorgestrel was not induced by artemether, DHA, or lumefantrine. However, artemether has been reported to weakly induce, in humans, the activity of CYP2C19, CYP2B6, and CYP3A.

Therefore, LONART 20/120may potentially reduce the effectiveness of hormonal contraceptives. Patients using oral, transdermal patch, or other systemic hormonal contraceptives should be advised to use an additional nonhormonal method of birth control for about one month

Drug-food/drink interactions

LONART 20/120should be taken with food or drinks rich in fat such as milk as the absorption of both artemether and lumefantrine is increased.

Grapefruit juice should be used cautiously during LONART 20/120treatment.

4.6 Fertility, pregnancy, and lactation

Pregnancy

There is insufficient data from the use of artemether and lumefantrine in pregnant women. Based on animal data, LONART 20/120 is suspected to cause serious birth defects when administered during the first trimester of pregnancy. Reproductive studies with artemether have shown evidence of post-implantation losses and teratogenicity in rats and rabbits. Other artemisinin derivatives have also demonstrated teratogenic potential with an increased risk during early gestation Safety data from an observational pregnancy study of approximately 500 pregnant women who were exposed to LONART 20/120 (including a third of patients who were exposed in the first trimester), and published data of another over 500 pregnant women who were exposed to artemether- lumefantrine (including over 50 patients who were exposed in the first trimester), as well as published data of over 1,000 pregnant women who were exposed to artemisinin derivatives, did not show an increase in adverse pregnancy outcomes or teratogenic effects over background rates. LONART 20/120 treatment must not be used during the first trimester of pregnancy in situations where other suitable and effective antimalarials are available. However, it should not be withheld in life-threatening situations, where no other effective antimalarials are available. During the second and third trimester, treatment should only be considered if the expected benefit to the mother outweighs the risk to the foetus.

Women of childbearing potential

Women using oral, transdermal patch, or other systemic hormonal contraceptives should, be advised to use an additional non-hormonal method of birth control for about one month.

Lactation

Animal data suggest excretion into breast milk, but no data are available in humans. Women taking LONART 20/120 should not breast-feed during their treatment. Due to the long elimination half-life of lumefantrine (2 to 6 days), it is recommended that breast-feeding

should not resume until at least one week after the last dose of LONART 20/120unless potential benefits to the mother and child outweigh the risks of LONART 20/120treatment.

Fertility

There is no information on the effects of LONART 20/120on human fertility.

4.7 Effects on ability to drive and use machines.

Patients receiving LONART 20/120should be warned that dizziness or fatigue/asthenia may occur in which case they should not drive or use machines.

4.8 Undesirable effects

The safety of LONART 20/120 has been evaluated in 20 clinical trials with more than 3500.patients. A total of 1810 adults and adolescents above 12 years of age as well as 1788 infants and children of 12 years of age and below have received LONART 20/120 in clinical trials. Adverse reactions reported from clinical studies and post-marketing experience are listed below according to system organ class. Adverse reactions are ranked under headings of frequency using the MedDRA frequency convention: Very common (≥1/10), Common (≥1/100 to <1/10), ncommon (≥1/1,000 to<1/100), Rare (≥1/10,000 to <1/1,000), Very rare (<1/10,000) and not known (cannot be estimated from available data).

Table 1: Frequency of Undesirable effect

	Adults and adolescents above 12 years of age	**Infants and children of 12 years of age and below (incidence estimates)**
Immune system disorders		
Hypersensitivity	Not known	Rare
Metabolism and nutrition disorders		
Decreased appetite	Very common	Very common (16.8 %)
Psychiatric disorders		
Sleep disorders	Very common	Common (6.4 %)
Insomnia	Common	Uncommon
Nervous system disorders		
Headache	Very common	Very common (17.1 %)
Dizziness	Very common	Common (5.5 %)
Paraesthesia	Common	--
Ataxia, hypoaesthesia	Uncommon	--
Somnolence	Uncommon	Uncommon
Clonus	Common	Uncommon
Cardiac disorders		
Palpitations	Very common	Common (1.8 %)
Electrocardiogram QT	Common	Common (5.3 %)
Respiratory, thoracic, and mediastinal disorders		
Cough	Common	Very common (22.7 %)
Gastrointestinal disorders		
Vomiting	Very common	Very common (20.2 %)
Abdominal pain	Very common	Very common (12.1 %)

Nausea	Very common	Common (6.5 %)
Diarrhoea	Common	Common (8.4 %)
Hepatobiliary disorders		
Liver function tests increased	Uncommon	Common (4.1 %)
Skin and subcutaneous tissue disorders		
Rash	Common	Common (2.7 %)
Pruritus	Common	Uncommon
Urticaria	Uncommon	Uncommon
Angioedema*	Not known	Not known
Musculoskeletal and connective tissue disorders		
Arthralgia	Very common	Common (2.1 %)
Myalgia	Very common	Common (2.2 %)
General disorders and administration site conditions		
Asthenia	Very common	Common (5.2 %)
Fatigue	Very common	Common (9.2 %)
Gait disturbance	Common	--

*: These adverse reactions were reported during post-marketing experience. Because these spontaneously reported events are from a population of uncertain size, it is difficult to estimate their frequency.

4.9 Overdose

In cases of suspected overdosage symptomatic and supportive therapy should be given as appropriate, which should include ECG and blood potassium monitoring.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties.

LONART 20/120 comprises a fixed ratio of 1:6 parts of artemether and lumefantrine, respectively. The site of antiparasitic action of both components is the food vacuole of the malarial parasite, where they are thought to interfere with the conversion of haem, a toxic intermediate produced during haemoglobin breakdown, to the nontoxic haemozoin, malaria pigment. Lumefantrine is thought to interfere with the polymerisation process, while artemether generates reactive metabolites as a result of the interaction between its peroxide bridge and haem iron. Both artemether and lumefantrine have a secondary action involving inhibition of nucleic acid- and protein synthesis within the malarial parasite.

5.2 Pharmacokinetic properties

Pharmacokinetic characterisation of LONART 20/120 is limited by the lack of an intravenous formulation, and the very high inter-and intra-subject variability of artemether and lumefantrine plasma concentrations and derived pharmacokinetic parameters (AUC, Cmax).

Absorption

Artemether is absorbed rapidly and dihydroartemisinin, the active metabolite of artemether, appears rapidly in the systemic circulation with peak plasma concentrations of both compounds reached about 2 hours after dosing. Mean Cmax and AUC values of artemether ranged between 60.0-104 ng/mL and 146-338 ng·h/mL, respectively, in fed healthy adults after a single dose of LUFANTER, 80 mg artemether/480 mg lumefantrine. Mean Cmax and AUC values of dihydroartemisinin ranged between 49.7-104 ng/mL and 169-308 ng·h/mL, respectively. Absorption of lumefantrine, a highly lipophilic compound, starts after a lag-time of up to 2 hours, with peak plasma concentration (mean between 5.10- 9.80 µg/mL) about 6-8 hours after dosing. Mean AUC values of lumefantrine ranged between 108 and 243 µg·h/mL. Food enhances the absorption of both artemether and lumefantrine: in healthy volunteers the relative bioavailability of artemether was increased more than two-fold, and that of lumefantrine sixteen-fold compared with fasted conditions when LONART 20/120 was taken after a high-fat meal. Food has also been shown to increase the absorption of lumefantrine in patients with malaria, although to a lesser extent (approximately two-fold), most probably due to the lower fat content of the food ingested by acutely ill patients. The food interaction data indicate that absorption of lumefantrine under fasted conditions is very poor (assuming 100% absorption after a high-fat meal, the amount absorbed under fasted conditions would be <10% of the dose). Patients should therefore be encouraged to take the medication with a normal diet as soon as food can be tolerated.

Distribution

Artemether and lumefantrine are both highly bound to human serum proteins *in vitro* (95.4% and 99.7%, respectively). Dihydroartemisinin is also bound to human serum proteins (47-76%).

Metabolism

Artemether is rapidly and extensively metabolised (substantial first-pass metabolism) both *in vitro* and in humans. Human liver microsomes metabolise artemether to the biologically active main metabolite dihydroartemisinin (demethylation), predominantly through the isoenzyme CYP3A4/5. This metabolite has also been detected in humans *in vivo*. Dihydroartemisinin is further converted to inactive metabolites. The pharmacokinetics of artemether in adults is time-dependent. During repeated administration of LONART 20/120 , plasma artemether levels decreased significantly, while levels of the active metabolite (dihydroartemisinin) increased, although not to a statistically significant degree. The ratio of day 3/day 1 AUC for artemether was between 0.19 and 0.44, and was between 1.06 and2.50 for dihydroartemisinin.

This suggests that there was induction of the enzyme responsible for the metabolism of artemether. Artemether and dihydroartemisinin were reported to have a mild inducing effect on CYP3A4 activity.Lumefantrine is N-debutylated, mainly by CYP3A4, in human liver microsomes. *In vivo* in animals (dogs and rats), glucuronidation of lumefantrine takes place directly and after oxidative biotransformation. In humans, the exposure to lumefantrine increases with repeated administration of LONART 20/120over the 3-day treatment period, consistent with the slow elimination of the compound. Systemic exposure to the metabolite desbutyl- lumefantrine, for which the *in vitro* antiparasitic effect is 5 to 8-fold higher than that for lumefantrine, was less than 1% of the exposure to the parent drug. Desbutyl-lumefantrine data is not available specifically for an African population. *In vitro,* lumefantrine significantly inhibits the activity of CYP2D6 at therapeutic plasma concentrations.

Elimination

Artemether and dihydroartemisinin are rapidly cleared from plasma with a terminal half- life of about 2 hours. Lumefantrine is eliminated very slowly with an elimination half-life of 2 to 6 days. Demographic characteristics such as sex and weight appear to have no clinically relevant effects on the pharmacokinetics of LONART 20/120. Limited urinary excretion data are available for humans. In 16 healthy volunteers, neither lumefantrine nor artemether was found in urine after administration of LONART 20/120, and only traces of dihydroartemisinin were detected (urinary excretion of dihydroartemisinin amounted to less than 0.01% of the artemether dose).

Dose proportionality

No specific dose proportionality studies were performed. Limited data suggest a dose-proportional increase of systemic exposure to lumefantrine when doubling the LONART 20/120dose. No conclusive data is available for artemether.

Bioavailability/bioequivalence studies

Systemic exposure to lumefantrine, artemether and dihydroartemisinin was similar following administration of LONART 20/120as dispersible Sachets and crushed Sachets in healthy adults.Systemic exposure to lumefantrine was similar following administration of LONART 20/120and intact Sachets in healthy adults. However, exposure to artemether and dihydroartemisinin was significantly lower (by 20-35%) for the dispersible than for the intact Sachet. These findings are not considered to be clinically relevant for the use of the dispersible Sachets in the paediatric population since adequate efficacy of LONART 20/120dispersible Sachets was demonstrated in this population. The dispersible Sachet is not recommended for use in adults.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate (Pharmatose 200 M), Croscarmellose sodium, Hypromellose (HPMC E6 LV), Polysorbate 80, Sucrose, Sucralose, Quinoline Yellow, Microcrystalline cellulose PH 101, Powdarome Orange 4153

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Store in dry place, below 30°C. Keep out of reach of children.

6.5 Nature and contents of container

Sachetof Aluminum/Polyester/LDPE foil
Packs of 6 sachets.

6.6 Special precautions for disposal and other handling

After successful treatment the remaining Sachets should be discarded or returned to the pharmacist.

7. MARKETING AUTHORISATION HOLDER

Bliss GVS Pharma Ltd., 102, Hyde Park, Saki Vihar Road, Andheri (East),Mumbai - 400 072.