SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

MALAPHAR for Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 mL ampoule contains:

Artemether 80 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Sterile Colourless or Yellowish clear oily solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

MALAPHAR Injection is indicated for the treatment of malaria caused by all forms of Plasmodium including severe malaria caused by multiple drug resistant strains of P. falciparum.

4.2 Posology and method of administration

MALAPHAR is administered by intramuscular injection.

Dosage information

Starting dose: 240 mg administered as two consecutive subcutaneous injections of 120 mg each

Maintenance dose–(monthly): 80 mg administered as one subcutaneous injection

Your doctor will decide on the site of injection, how much of the medicine and how many injections you will receive depending on the condition being treated and its severity. Your doctor will inject you with the lowest dose for the shortest possible time to get effective relief of your symptoms.

MALAPHAR contain artemether as an active and administered intramuscularly, most commonly used in the case of sever malaria, such as cerebral malaria, and also in patient showing gastrointestional problems.

Loading Dose for Adults and Children: 3.2 mg/kg body weight administered as a single intramuscular injection on the first day.

Maintenance Dose for Adults and Children: 1.6 mg/kg/day

administered as intramuscular injection once a day during the following four (04) days.

Administration for Children: For children, the dose should be chosen as follows:

AGE (Year)	WEIGHT	TOTAL DOSE	DAY1	DAY 2-5
< 1	< 8 Kg	75 mg	25 mg	12.5 mg
1-3	8 - 12.5 Kg	120 mg	40 mg	20 mg
3-6	12.5 - 17.5 Kg	150 mg	50 mg	25 mg
6-9	17.5 - 25 Kg	240 mg	80 mg	40 mg
9-12	25- 32 Kg	300 mg	100 mg	50 mg
12 - 16	32-47 Kg	360 mg	120 mg	60 mg

The dose for children should decrease or increase on the basis of individual weight or under Doctor's prescription.
Maintenance treatment can also be continued by oral Artemisinin-based combination therapies (ACT) if the patient's conditions does not require injections.
The drug is given by intramuscular injection in the gluteal muscle or the quadriceps. Combination of other drugs in the same syringe should be avoided. Aseptic conditions must be respected when injecting Artemether.

Note: A full course therapy of five d a ys is essential i n order to avoid recrudescence
In case of severe malaria it may be necessary to increase the loading dose and to prolong treatment for seven (07) days if parasitaemia is not cleared during the first few days.

4.3 Contraindications

MALAPHAR Injection is contraindicated in patients hypersensitive to the active substance (this has not been seen so far) or to any of the excipients.

Hepatic impairment

Patients with known or suspected hepatic disorder have not been included in long-term clinical trials with degarelix. Mild, transient increases in ALT and AST have been seen, these were not accompanied by a rise in bilirubin or clinical symptoms. Monitoring of liver function in patients with known or suspected hepatic disorder is advised during treatment. The pharmacokinetics of degarelix has been investigated after single intravenous administration in subjects with mild to moderate hepatic impairment.

Renal impairment

Degarelix has not been studied in patients with severe renal impairment and caution is therefore warranted.

Hypersensitivity

Degarelix has not been studied in patients with a history of severe untreated asthma, anaphylactic reactions or severe urticaria or angioedema.

Changes in bone density

Decreased bone density has been reported in the medical literature in men who have had orchiectomy or who have been treated with a GnRH agonist. It can be anticipated that long periods of testosterone suppression in men will have effects on bone density. Bone density has not been measured during treatment with degarelix.

Glucose tolerance

A reduction in glucose tolerance has been observed in men who have had orchiectomy or who have been treated with a GnRH agonist. Development or aggravation of diabetes may occur; therefore, diabetic patients may require more frequent monitoring of blood glucose when receiving androgen deprivation therapy. The effect of degarelix on insulin and glucose levels has not been studied.

Cardiovascular disease

Cardiovascular disease such as stroke and myocardial infarction has been reported in the medical literature in patients with androgen deprivation therapy. Therefore, all cardiovascular risk factors should be taken into account.

4.4 Special warnings and precautions for use

In cerebral malaria and complicated malaria, general supporting therapy is usually required.

4.5 Interaction with other medicinal products and other forms of interaction

No formal drug-drug interaction studies have been performed.

4.6 Fertility, pregnancy and lactation

Pregnancy and breast-feeding

There is no relevant indication for use of MALAPHAR in

women.

Fertility

MALAPHAR may inhibit male fertility as long as the testosterone due to

suppression.

4.7 Effects on ability to drive and use machines

MALAPHAR has no or negligible influence on the ability to drive and use machines. Fatigue and dizziness are common adverse reactions that might influence the ability to drive and use machines.

4.8 Undesirable effects

At the therapeutic dose (700 mg) there are virtually no side effects. There are reports on laboratory abnormalities i.e. a decrease in reticulocytes count, an increase in transaminase and ECG changes (Sinus Bradycardia). However, these are transient. At high doses, transient abdominal pain, diarrhoea and tinnitus can occur.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

4.9 Overdose

There is no experience with the effects of an acute overdose. In the event of an overdose the patient should be monitored and appropriate supportive treatment should be given, if considered necessary.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antimalarial, artemisinin derivative.

Artemether is an artemisinin derivative. It is metabolised in the body to the active metabolite dihydroartemisinin.

Artemether acts against the erythrocytic stages of *Plasmodium falciparum* by inhibiting nucleic acid and protein synthesis.

Artemether has a rapid onset of action and is rapidly cleared from the body. It is considered to provide rapid symptomatic relief by reducing the number of malarial parasites.

Artemether is commonly administered in combination with lumefantrine for improved antimalarial efficacy. Lumefantrine has a substantially longer half-life and is believed to clear residual parasites.

Mechanism of action

The precise mechanism of action of artemisinin derivatives has not been fully established.

One proposed mechanism is that artemisinin derivatives inhibit antioxidant and metabolic enzymes, resulting in oxidative and metabolic stress within the parasite. Pathways involving glutathione and glucose metabolism may be affected, resulting in cellular lesions and reduced parasite growth.

Another proposed mechanism suggests that artemisinin derivatives exert their parasiticidal action through inhibition of PfATP6. PfATP6 is an enzyme involved in the regulation of cellular calcium concentrations. Its malfunction may result in intracellular calcium accumulation and subsequent cell death.

5.2 Pharmacokinetic properties

Artemether is rapidly hydrolysed to the active metabolite dihydroartemisinin.

Artemether is highly protein bound, with approximately 95.4% protein binding.

Artemether is metabolised primarily by hepatic CYP3A4/5 enzymes.

Both artemether and its active metabolite are rapidly eliminated.

The elimination half-life following intramuscular administration is approximately **4–11 hours**.

5.3 Preclinical safety data

Toxicity

Animal studies of acute toxicity have reported the following LD50 values for artemether:

- Mice: 895 mg/kg following a single intragastric administration.
- Mice: 296 mg/kg following a single intramuscular injection.
- Rats: 597 mg/kg following a single intramuscular injection.

Carcinogenicity

Carcinogenicity studies with artemether have not been conducted.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Butylated Hydroxy Anisole (BHA) BP
- Butylated Hydroxy Toluene (BHT) BP
- Ethyl Oleate BP

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life: 3 years.

6.4 Special precautions for storage

Store in dry place, below

30°C. Protect from light.

Keep out of reach of children.

6.5 Nature and contents of container

10 Ampoules are kept in hip tray and packed within monocarton along with pack insert, Such 10 monocarton is packed in PVC/PE shrink wrap. (10 x 1 x 10).
or

Box of 10x 1 ml ampoules of 1ml containing: Artemether 80mg/1ml.

6.6 Special precautions for disposal and other handling

The instructions for reconstitution must be followed carefully.

7. MARKETING AUTHORISATION HOLDER

Sai Pharmaceuticals Limited
Unit C1, Whitefield Place,
28 School Lane,
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MANUFACTURER

Indasi Lifescience Pvt. Ltd.
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8. MARKETING AUTHORISATION NUMBER(S)

H2021/CTD8109/16404

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

2021 September 23

10. DATE OF REVISION OF THE TEXT

2021 September 23