SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

MALOXINE, scored tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Sulfadoxine .....500 mg
Pyrimethamine ..... 25 mg
For one scored tablet

Excipients
For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Scored tablet

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Maloxine is indicated for:

- Intermittent prevention of malaria in pregnant women during the 2nd and 3rd trimesters of pregnancy.
- Treatment of acute, uncomplicated *P. falciparum* : Maloxine in combination with artesunate is recommended by WHO.

4.2. Posology and method of administration

For oral use, single dose.
Tablets should be swallowed with a glass of water, without chewing them. The usual dosage is as follows:

Intermittent prevention of malaria in pregnant women :
3 tablets as a single dose to be taken twice, up to 3 times during pregnancy from the 2nd semester of pregnancy. The last dose must be taken not later than 30 days before the expected date of delivery.

Treatment of uncomplicated malaria:
Target dosage: sulfadoxine 25 mg/ pyrimethamine 1.25 mg/kg as a single dose in combination with artesunate 4 mg/kg once daily during 3 days;

4.3. Contraindications

Maloxine is contraindicated in the following cases:

- Known hypersensitivity to sulfonamides or pyrimethamine or any other ingredient
- Severe hepatic or renal insufficiencies (except when no alternative treatment is available).
- History of hepatitis due to sulfadoxine or pyrimethamine intake.

4.4. Special warnings and precautions for use

Skin reactions, blood disorders or marrow failure (angina, oral ulcers) require immediate and definitive discontinuation of the treatment (see section 4.8).
Due to cumulated risk of bone marrow toxicity, Maloxine should not be associated with other anti-folinic nor drugs containing pyrimethamine.

4.5. Interaction with other medicinal products and other forms of interaction

Interactions related to pyrimethamine

Special precautions with the following drugs

+ Didanosine
Decrease in pyrimethamine digestive absorption due to an increased stomach pH (antacid contained in the DDI tablet).
Whenever possible, a 2 hours interval should be respected between pyrimethamine and didanosine administrations.

+ Trimethoprim (alone or in association)
Megaloblastic anaemia, particularly when both substances are administered at a high dosage (folic acid deficiency due to the association of two 2-4 diaminopyrimidine compounds).
Frequent haemogram monitoring and association with a folinic acid treatment (regular IM or IV injections).

+ Zidovudine
Increase in haematologic toxicity by dihydrofolate reductase inhibition. Frequent haemogram monitoring is required.

Interactions related to sulfadoxine

Special precautions with the following drugs

+ Methotrexate
Increase in haematologic methotrexate toxicity (increase in free methotrexate plasma concentration due to displacement from plasmatic proteins by some sulfonamides). Level of free methotrexate should be monitored and dosage should be adapted during and after treatment with Maloxine.

4.6. Pregnancy and lactation

Pregnancy
The use during pregnancy involves a specific prenatal monitoring.

Lactation
Both pyrimethamine and sulfadoxine pass into breast milk, this medicine must therefore not be used during breastfeeding.

4.7. Effects on ability to drive and use machines

Not applicable.

4.8. Undesirable effects

- Rare gastro-intestinal disorders

- Signs of skin allergic reactions: rash, itching, exceptionally severe reactions, including Stevens-Johnson and Lyell syndromes.
- Blood disorders (megaloblastic anaemia, leukopenia, agranulocytosis, thrombopenia), which require treatment discontinuation and a possible IM or IV folinic acid administration.
- Renal disorders: some cases of renal function alterations have been reported with sulfonamides.
- Hepatic function disorders: rare cases of transaminase level increase and hepatitis have been reported

Skin reactions or blood disorders require an immediate and definitive discontinuation of the treatment.

4.9. Overdose

High doses of pyrimethamine are potentially fatal. Prominent symptoms of overdose are anorexia, vomiting and seizures. Induction of emesis or gastric lavage is of value if undertaken within a few hours after ingestion. Convulsions may be controlled with parenteral diazepam.
Blood dyscrasia that may be induced by large doses of pyrimethamine should be treated with folinic acid.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

ANTIMALARIAL combining an ANTIFOLINIC SULFONAMIDE and an ANTIFOLINIC DIAMINOPYRIMIDINE.
(**P: Parasitology**)

The association has a schizonticide activity by inhibiting the metabolism of folic acid (it blocks the dihydrofolate reductase) needed by the haematozoa to grow.
Maloxine may also be effective against strains of *P. falciparum* resistant to other antimalarial drugs.
However, some trains of *Plasmodium falciparum* are resistant to the association.
The efficacy of sulfonamides against *Plasmodium ovale* and *Plasmodium vivax* is weak.

5.2. Pharmacokinetic properties

Both pyrimethamine and sulfadoxine are well absorbed after oral administration.
Half-life is about 4 days for pyrimethamine and about 8 days for sulfadoxine.
Both pyrimethamine and sulfadoxine are excreted mostly via the kidneys; pyrimethamine is partly eliminated as metabolites.

5.3. Preclinical safety data

Not available

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients
Maize starch, sodium methyl hydroxybenzoate (E219), sodium propyl hydroxybenzoate (E217), talc, magnesium stearate, carmellose sodium.

6.2. Incompatibilities
Not applicable.

6.3. Shelf-life
3 years.

6.4. Special precautions for storage
Store in the original package, protect from heat, light and moisture.

6.5. Nature and contents of container
Maloxine is available in pouches of 3 scored tablets in alu/alu strips.

6.6. Special precautions for disposal and other handlings
No special requirements.

7. MARKETING AUTHORISATION HOLDER

Exphar s.a.
Zoning Industriel de Nivelles Sud, Zone II,
Avenue Thomas Edison 105
1402 Thines, Belgium

8. CATEGORY OF DISTRIBUTION

☐ Over-the counter medicine ☒ Prescription only medicine

9. MANUFACTURER

Gracure Pharmaceuticals Ltd.,
E-1105, Industrial Area, Phase-III,
Bhiwadi, Dist. Alwar (Raj.) INDIA
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10. UPDATE DATE

08/2016