1.3.1

Summary Of Product Characteristics (SPC)

1.3.1 Product information for health professionals

1.3.1.1 Invented Name of the Medicinal Product

RELUDRINE

Proguanil Tablets BP 100 mg

1.3.1.2 Strength

Each uncoated tablet contains:

Proguanil Hydrochloride BP…….100 mg

Excipient……QS

1.3.1.3 Dosage Form

Oral Solid Dosage Form (Uncoated Tablet)

1.3.1.4 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each uncoated tablet contains:

Proguanil Hydrochloride BP…….100 mg

Excipient……QS

1.3.1.5 PHARMACEUTICAL FORM

White coloured round shaped biconvex uncoated tablets embossed coloured R/D on one round side shaped and other biconvex side is plain uncoated tablets

1.3.1.6 CLINICAL PARTICULARS

1.3.1.6.1Therapeutic indications

RELUDRINE is an effective antimalarial agent. It is recommended for the prevention and suppression of malaria.

1.3.1.6.2 POSOLOGY AND METHOD OF ADMINISTRATION

Oral use

Non-immune subjects entering a malarious area are advised to begin treatment with RELUDRINE 1 week before, or if this is not possible, then at least 2 days before entering the malarious area. The daily

dose of RELUDRINE should be continued throughout exposure to risk and for 4 weeks after leaving the area.

Adults:

Two tablets (200 mg) daily.

Paediatric population:

Under 1 year:	1/4 tablet (25 mg) daily
1 to 4 years:	1/2 tablet (50 mg) daily
5 to 8 years:	1 tablet (100 mg) daily
9 to 14 years:	1 1/2 tablets (150 mg) daily
Over 14 years:	Adult dose daily

The daily dose is best taken with water, after food, at the same time each day.

Provided the tablet fragment gives the minimum amount specified, precise accuracy in children's dosage is not essential since the drug possesses a wide safety margin.

For a young child, the dose may be administered crushed and mixed with milk, honey or jam.

Older people: There are no special dosage recommendations for the elderly, but it may be advisable to monitor elderly patients so that optimum dosage can be individually determined.

Renal Impairment: Based on a theoretical model derived from a single dose pharmacokinetic study, the following guidance is given for adults with renal impairment.

Creatinine clearance (ml/min 1.73 m^2)	**Dosage**
≥ 60	200 mg once daily (standard dose)
20 to 59	100 mg once daily
10 to 19	50 mg every second day
< 10	50 mg once weekly

The grade of renal impairment and/or the serum creatinine concentration may be approximately equated to creatinine clearance levels as indicated below.

Creatinine clearance (ml/min/1.73 m^2)	**Approx* serum creatinine (micromol/1)**	**Renal Impairment Grade (arbitrarily divided for dosage purposes)**
≥ 60	-	-
20 to 59	150 to 300	Mild
10 to 19	300 to 700	Moderate
< 10	> 700	Severe

*Serum creatinine concentration is only an approximate guide to renal function unless corrected for age, weight and sex.

1.3.1.6.3 CONTRAINDICATIONS

Hypersensitivity to the active substance or any of the excipients.

1.3.1.6.4 WARNING AND PRECAUTIONS

Renal Impairment:

Haematological changes in patients with severe renal impairment have been reported.

RELUDRINE should be used with caution in patients with severe renal impairment.

In any locality where drug-resistant malaria is known or suspected, it is essential to take local medical advice on what prophylactic regimen is appropriate. Prophylactic use of RELUDRINE alone may not be sufficient.

1.3.1.6.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

Antacids

Antacids may reduce the absorption of proguanil, so should be taken at least 2-3 hours apart.

Anticoagulants

Proguanil can potentiate the anticoagulant effect of warfarin and related anticoagulants through a possible interference with their metabolic pathways. Caution is advised when initiating or withdrawing malaria prophylaxis with RELUDRINE in patients on continuous treatment with anticoagulants.

Live oral typhoid vaccination (Ty21a strain)

Proguanil should be stopped 3 days before and should not be started until 3 days after receiving live oral typhoid vaccination (Ty21a strain).

Boosted protease-inhibitors

When given with boosted protease-inhibitors, reduction in proguanil exposure has been observed. This combination should be avoided when possible.

1.3.1.6.6 PREGNANCY AND LACTATION

Pregnancy: There are limited data available from the use of proguanil in pregnant women.

RELUDRINE should not be used during pregnancy unless, in the judgement of the physician, potential benefit outweighs the risk.

Malaria in pregnant women increases the risk of maternal death, miscarriage, still-birth and low birth weight with the associated risk of neonatal death. Although travel to malarious areas should be avoided during pregnancy, if this is unavoidable effective prophylaxis is therefore strongly advised in pregnant women.

Proguanil is a dihydrofolate reductase inhibitor and adequate folate supplements should be given to pregnant women taking proguanil.

Lactation: Although RELUDRINE is excreted in breast milk, the amount is insufficient to confer any benefit on the infant. Separate chemoprophylaxis for the infant is required.

1.3.1.6.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

There is no evidence to suggest that RELUDRINE causes sedation or is likely to affect concentration.

1.3.1.6.8 UNDESIRABLE EFFECTS

Undesirable effects are listed by MedDRA System Organ Classes.

Assessment of undesirable effects is based on the following frequency groupings:

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

System Organ Class	Undesirable Effect and Frequency
Blood and lymphatic system disorders	*Not known* Haematological changes such as aplastic anaemia, anaemia megaloblastic and pancytopenia
Immune system disorders	*Not known* Hypersensitivity, including urticaria, angioedema Vasculitis
Gastrointestinal disorders	*Not known* Gastric disorder, including diarrhoea and constipation* Mouth ulceration Stomatitis
Hepatobiliary disorders	*Not known* Cholestasis
Skin and subcutaneous tissue disorders	*Not known* Skin reactions such as skin exfoliation, rash, pruritus and alopecia**
General disorders and administration site conditions	*Not known* Pyrexia

* usually subsides as treatment is continued.

**reversible alopecia

1.3.1.6.9 OVERDOSE

The following effects have been reported in cases of overdosage:

Haematuria, renal irritation, epigastric discomfort and vomiting. There is no specific antidote and symptoms should be treated as they arise.

Consider activated charcoal in patients who have ingested 30 mg/kg or more within 1 hour. Check urea and electrolytes (U&Es), liver function test (LFTs) and full blood count (FBC) in all patients. Check FBC again 3 days and again one week after the overdose or in case any new symptoms appear.

1.3.1.7 PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antiprotozoals, Antimalarials

ATC code: P01BB01

Proguanil is an antimalarial drug and dihydrofolate reductase inhibitor. It acts like the other antifolate antimalarials by interfering with the folic-folinic acid systems and thus exerts its effect mainly at the time the nucleus is dividing. Since its activity is dependent on its metabolism, proguanil has a slow schizonticidal effect in the blood. It also has some schizonticidal activity in the tissues.

Proguanil is effective against the exoerythrocytic forms of some strains of plasmodium falciparum but it has little or no activity against the exoerythrocytic forms of p. Vivax. It has a marked sporonticidal effect against some strains of p falciparum; it does not kill the gametocytes, but renders them non-infective for the mosquito while the drug is present in the blood. Malaria parasites in the red blood cells are killed more rapidly by chloroquine or quinine than by proguanil, which is therefore not the best drug to use for the treatment of acute malaria.

Soon after proguanil was introduced, it was observed that the drug was inactive as an inhibitor of the in vitro growth of p. Gallinaceum and p. Cynomolgi, but that sera from dosed monkeys were active against p. Cynomolgi in vitro. These findings suggested that proguanil was activated in vivo.

Since that time it has been accepted by most investigators in this field that cycloguanil is the active metabolite of proguanil and that parent compound is inactive per se.

Cycloguanil acts by binding to the enzyme dihydrofolate reductase in the malaria parasite. The effect of this action is to prevent the completion of schizogony. This is seen in the asexual blood stages as an arrest of maturation of the developing schizonts and an accumulation of large, abnormal looking trophozoites.

Proguanil is highly active against the primary exoerythocytic forms of p. Falciparum and it has a fleeting inhibiting action on those of p. Vivax. Proguanil is therefore a valuable drug for causal prophylaxis in falciparum malaria.

Pharmacokinetic properties

Absorption: Rapid, reaching a peak at 3 to 4 hours. The active metabolite (cycloguanil) peaks somewhat later (4 to 9 hours).

Half-life: The half-life of proguanil is 14 to 20 hours, whilst cycloguanil has a half-life of the order of 20 hours. Accumulation during repeated dosing is therefore limited, steady-state being reached within approximately 3 days.

Metabolism: Transformation of proguanil into cycloguanil is associated with cytochrome P450, CYP 2C19, activity. A smaller part of the transformation of proguanil into cycloguanil is probably catalysed by CYP 3A4.

Elimination: Elimination occurs both in the faeces and, principally, in the urine.

In the event of a daily dose being missed, the blood levels fall rapidly but total disappearance of the drug only occurs 3 to 5 days after stopping treatment.

Preclinical safety data

Proguanil is a drug on which extensive clinical experience has been obtained. All relevant information for the prescriber is provided elsewhere in the Summary of Product Characteristics.

1.3.1.8. PHARMACEUTICAL PARTICULARS

1.3.1.8.1 List of excipients

Sr. No.	Name of Ingredients	Specification
01.	Maize Starch	BP
02.	Microcrystalline Cellulose	BP
0.3	Sodium Starch Glycolate	BP
04.	Poly Vinyl Pyrolidone	BP
05.	Sodium Methyl Paraben	BP
06.	Sodium Propyl Paraben	BP
07	Sodium Lauryl Sulphate	BP
08	Purified Talc	BP
09	Magnesium Stearate	BP
10	Colloidal Silicon dioxide	BP
11	Cross Carmellose Sodium	BP
12	Glycerin	BP

1.3.1.8.2 Incompatibilities:

None stated.

1.3.1.8.3 Shelf life:

3 years

1.3.1.8.4 Special precautions for storage:

Store below 30°C and protected from moisture.

1.3.1.8.5 Nature and contents of container:

10 Tablets in one Blister Such 10 Blister in a outer carton. Such 5 cartons should be shrink Wrapped. Such20 shink should be packed in a shipper.

1.3.1.8.6 Special precautions for disposal and other Special handling:

No special requirements.

Any unused product or waste material should be disposed of in accordance with local requirements.

1.3.1.9 Marketed by:

M/S. REALS PHARMACEUTICALS LIMITED.,
PLOT 1, ALHAJI JUNAID DOSUNMU,
CBD, ALAUSA, IKEJA,
LAGOS, NIGERIA.,

1.3.1.10 Manufactured by:

MCW HEALTHCARE PVT LTD.
236, Sector – E, Industrial Area,
Sanwer Road, Indore (M.P)