1. Name of product

Piramal Dry Powder for Oral Suspension

Dihydroartemisinin; Piperaquine Phosphate 80 mg/80 mL; 640 mg/80 mL

2. Qualitative and quantitative composition

Each 80 ml of reconstituted suspension contains:

Dihydroartemisinin 80 mg

Piperaquine Phosphate 640 mg

Excipients Q.S.

For a full list of excipients, refer section 6.1

3. Pharmaceutical form

Powder for oral suspension

4. Clinical particulars

4.1 Therapeutic indications

Treatment of clinical attacks of Malaria caused by P. falciparum, P, Vivax and P. malariae

4.2 Posology and method of administration

Dihydroartemisinin and Piperaquine Phosphate Tablets should be administered once daily over three consecutive days taken orally with water and without food. Each dose should be taken not less than 3 hours after the last food intake and no food should be taken within 3 hours after each dose. Patients should follow doctor's instruction.

4.3 Contraindication

The product is not recommended for use in women during the first 3 months of pregnancy.

4.4 Special warnings and precautions for use

Do not exceed the stated dosage.

4.5 Interaction with other medical products and other forms of interaction

Dihydroartemisinin and Piperaquine Phosphate Tablets is contraindicated in patients already taking other medicinal products that are known to prolong the QTc interval due to the risk of a pharmacodynamic interaction leading to an additive effect on the QTc interval.

4.6 Pregnancy and lactation

There are insufficient data on the use of dihydroartemisinin and piperaquine in pregnant women, however, Dihydroartemisinin and Piperaquine Phosphate Tablets should not be used during the first trimester of pregnancy.

Animal data suggest excretion of piperaquine into breast milk but no data are available in humans. Women taking Dihydroartemisinin and Piperaquine Phosphate Tablets should not breast-feed during their treatment.

4.7 Effects on ability to drive and use machines

Patients should know that mild dizziness, vertigo, headache, nausea, vomiting and abdominal discomfort may occur, and so should stop driving and operating machinery during the treatment.

4.8 Undesirable effects

1. Nausea or vomiting may occur occasionally with incidence of less than 6%

2. No noticeable side effect of Dihydroartenisinin is reported. The Dihydroartemisinin would, for certain individuals, bring effects of greater or lesser severity: for example, a reversible reduction in reticulocyte counts.

3. Possible side-effect of PQP include mild dizziness, vertigo, headache, nausea, vomiting and abdominal discomfort. Reversible leucopenia was infrequently reported; dyspnea and palpitations were also reported but not further specified.

4.9 Overdose

In cases of suspected overdose, symptomatic and supportive therapy should be given as appropriate, including ECG monitoring because of the possibility of QTc interval prolongation.

5. Pharmacological properties

5.1 Pharmacodynamic properties

This product is a compound preparation composed of dihydroartemisinin and piperaquine phosphate.

Dihydroartemisinin is a derivative of artemisinin and the active substance of artemisinin.

It has a strong killing effect on plasmodium anasexuals, and can quickly kill the plasmodium, thereby controlling symptoms. Drug resistance breeding experiments show that Plasmodium is not easily resistant to dihydroartemisinin.

Piperaquine phosphate is a 4-aminoquinoline antimalarial drug. Its antimalarial effect is similar to that of chloroquine. It affects the ultrastructure of plasmodium schizont in the red stage, and can mainly swell the trophozoite food bubble membrane and mitochondria, leading to its physiological The function is destroyed, thereby killing the malaria parasite. Piperquine phosphate has no cross-resistance to chloroquine.

In vitro pharmacodynamic studies have shown that the combined use of dihydroartemisinin and piperaquine phosphate has a synergistic effect and can delay the development of resistance to malaria parasites.

5.2 Pharmacokinetic properties

Mode of action of Dihydroartemisinin:

Dihydroartemisinin mainly interferes with the membrane structures of trophozoites (erythrocytic asexual forms), i.e. whorled food vacuole membrane, distended mitochondria, swollen unclear membranes, dissociation of ribosomes from endoplasmic reticulum leading to cytoplasmic

vacuolization and autophagocytosis- In addition, biochemical depression of protein synthesis and nucleic acid synthesis are exhibited.

Upon oral administration Dihydroartemisin is rapidly absorbed and maximum blood concentration attained 1 hour afterwards, with a half-life of about 4 hours. It is widely distributed in the liver, kidneys and bile. Approximately 80% is excreted through the urine and feces within 24 hrs after administration It is metabolized to two inactive metabolites, deoxydihydroartemisinin and dihydroxydihydroartemisinin.

Mode of action of Piperaquine Phosphate:

Experimental results show that PQP interferes with physiological function of the food vacuole membrane of the trophozoites leading to autophagocytosis of the parasites. It has no marked effect on the ring forms, immature or mature schizonts and the male or female gametocytes. Upon oral administration about 80-90% is absorbed within 24 hrs.

It is widely distributed in the body mainly in the liver, kidneys, lungs and spleen. About 25% of the total dose is partitioned in the liver within 8 hrs of intake. Elimination is very slow with the half-life of about 9.4 days. It is excreted through bile by hepatoenteral circulation.

5.3 Preclinical safety data

Dihydroartemisinin:

Genetic toxicity: The results of Ames test, CHL chromosome aberration test, and micronucleus test were all negative.

Reproductive toxicity: It has embryotoxic effects on pregnant mice, which can increase embryo absorption in a dose-dependent manner; no teratogenic effects are seen.

Piperaquine phosphate:

Repeated administration toxicity: Beagle dogs were given oral administration once a week, 100mg/Kg for 14 weeks, or 25mg/Kg for 26 weeks, the liver was found to be the main target organ for toxicity.

Genotoxicity: Ames test, bone marrow cell chromosome analysis and sister chromatid exchange rate (SCE) test results were all negative.

Reproductive toxicity: no embryo toxicity and teratogenic effects have been found in animal experiments.

Dihydroartemisinin and piperaquine phosphate are used in combination, which is additive in toxicity and has no toxic effect.

6. Pharmaceutical particulars

6.1 List of excipients

Sucrose

Micro crystalline cellulose

Xanthan Gum

Methyl Paraben

Propyl Paraben

Fumed silica

Citric Acid

Strawberry Flavour

Aspartame

Erythrosine Colour

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store in a cool and dry place below 30°C. Protect from light. Keep out of reach of children

6.5 Nature and contents of container

1 x 80 ml

6.6 Special precautions for disposal and other handing

For the treatment of children and infants, the Dihydroartemisinin and Piperaquine Phosphate Powder for oral suspension should be prescribed. The prescriber and pharmacist should instruct the parent or care giver on the posology for their child and that a variable number of Dihydroartemisinin and Piperaquine Phosphate Powder for oral suspension (depending on the child's body weight) will be requested for the full treatment. Therefore, the whole pack may not be used. After successful treatment the remaining Dihydroartemisinin and Piperaquine Phosphate Powder for oral suspension should be discarded or returned to the pharmacist

7. Marketing authorization holder

Emzor Pharmaceutical Industries Limited

Flowergate Mixed Development Scheme,Km 1 Sagamu/Benin Expressway, Sagamu, Ogun State

8. Marketing authorization number(s)

N/A

9. Date of first authorization/renewal of authorization

N/A

10. Date of revision of text

N/A