EMA/3102/2016
EMEA/H/W/002319

EPAR summary for the public

Pyramax

pyronaridine tetraphosphate / artesunate

This is a summary of the European public assessment report (EPAR) for Pyramax. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion on the medicine and its recommendations on the conditions of use for Pyramax.

What is Pyramax?

Pyramax is a medicine that contains the active substances pyronaridine tetraphosphate and artesunate. It is available as tablets (180 mg/60 mg) and as granules (60 mg/20 mg in each sachet).

What is Pyramax used for?

Pyramax is used to treat uncomplicated malaria, caused by two types of malaria parasites, *Plasmodium falciparum* and *Plasmodium vivax*. 'Uncomplicated' means the disease does not involve severe, life-threatening symptoms. Pyramax tablets are used for adults and children weighing 20 kg or more and the granules are used for babies and children weighing between 5 and 20 kg.

The medicine can only be obtained with a prescription.

How is Pyramax used?

Pyramax is taken once a day for three days. The daily dose depends on the patient's weight, and for tablets it ranges from one tablet a day for patients weighing between 20 and 24 kg to four tablets a day for patients over 65 kg.

Pyramax granules suspended in water are used for babies and children weighing from 5 kg to under 20 kg. The dose ranges from one sachet a day for babies and children weighing between 5 and under 8 kg to three sachets a day for children weighing between 15 and under 20 kg. For more information on how to use Pyramax, see the summary of product characteristics (SmPC).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

How does Pyramax work?

Malaria is an infectious disease caused by *Plasmodium* parasites and spread through the bite of an infected mosquito.

The active substances in Pyramax act against *P. falciparum and P.vivax* species of the parasite. Artesunate is a derivative of the naturally occurring substance artemisinin. Although the exact way in which artemisinin antimalarials work is not fully understood, it is thought that they could work by forming toxic substances called 'free radicals' inside the parasite or by damaging calcium pumps that are important for the parasite to thrive.

Pyronaridine is thought to work by blocking a step in the parasite's metabolism needed for its survival in the patient's red blood cells.

How has Pyramax been studied?

There were three main studies in patients with uncomplicated *P. falciparum* malaria. Two studies, conducted in Africa and Asia, involved a total 2,543 adults and children weighing 20 kg and over and compared Pyramax tablets with other artemisinin combinations (artesunate plus mefloquine or artemether-lumefantrine). A third study, conducted in Africa and the Philippines using Pyramax granules involved a total of 535 children weighing between 5 kg and 25 kg compared Pyramax to artemether-lumefantrine.

One further main study involving a total of 456 adults and children weighing 20 kg and over was conducted in uncomplicated *P. vivax* malaria. This study, which was took place in Asia, compared Pyramax with chloroquine, a medicine widely used to treat *P. vivax* malaria.

Finally, another study compared Pyramax with artemether-lumefantrine for treating malaria that recurred over two malarial seasons. It involved a total of 1,686 West African patients, of which 393 patients taking Pyramax weighed between 5 and 20 kg.

The main measures of effectiveness were based on the number of patients whose blood was cleared of the malaria parasites, excluding those patients who got new infection during study.

What benefit has Pyramax shown during the studies?

Pyramax was effective in treating *P. falciparum* and *P. vivax* malaria, on average clearing parasites from the blood within one or two days.

Pyramax was also as effective as the comparator medicines in patients who were evaluated. Excluding patients with new infections, around 95% of patients treated with Pyramax in one *P. falciparum* study and 98% in another had no *P. falciparum* parasites in their blood after 42 days compared with around 97% and 99% seen with the comparator medicines. In addition, 94% of patients in the study of small children had no P. *falciparum* parasites in their blood after 42 days compared with 96% of the patients taking the comparator.

In uncomplicated *P. vivax* malaria, around 97% of patients taking Pyramax were cleared of *P. vivax* parasites after 28 days compared with 97% of patients treated with chloroquine.

Pyramax was also effective in the additional study in patients treated again when malaria recurred.

What is the risk associated with Pyramax?

The most common side effects with Pyramax (seen in between 1 and 10 patients in 100) were headache, abnormal levels of white blood cells, anaemia (low red blood cell counts), increased platelet

count, vomiting, abdominal pain (stomach ache), bradycardia (slow heart rate), increased levels of liver enzymes, and hypoglycaemia (low blood glucose levels). For the full list of all side effects reported with Pyramax, see the package leaflet.

Pyramax must not be used in patients with severe kidney problems. It must also not be taken by patients with severe liver disease or those with signs or symptoms of liver problems such as nausea, abdominal pain and yellowing of the eyes and skin (jaundice).

Why has Pyramax been approved?

The CHMP noted that the World Health Organization recommends that artemisinin be used in combination with other medicines to reduce the risk of the parasites developing resistance.

Pyramax has been shown in clinical studies to be as effective as two other artemisinin combinations in treating the most dangerous parasite, *P. falciparum*, and as effective as chloroquine in treating *P. vivax.* With regard to the risks, the main concern was related to increases in levels of liver enzymes seen in some patients. To minimise the risk to the liver, Pyramax should not be used in patients with severe liver disease or in those with signs or symptoms of liver problems.

What measures are being taken to ensure the safe and effective use of Pyramax?

A risk management plan has been developed to ensure that Pyramax is used as safely as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Pyramax, including the appropriate precautions to be followed by healthcare professionals and patients.

Other information about Pyramax

The CHMP gave a positive scientific opinion on Pyramax on 16 February 2012. This opinion was given as part of its cooperation with the World Health Organization, whereby the CHMP provides opinions on medicines that are not intended for use in the EU but are needed to prevent or treat diseases of major public interest around the world.

The full EPAR for Pyramax can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/Medicines for use outside the EU. For more information about treatment with Pyramax, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 01-2016.