EMA/350999/2017
EMEA/H/C/000943

EPAR summary for the public

Kuvan

sapropterin dihydrochloride

This is a summary of the European public assessment report (EPAR) for Kuvan. It explains how the Agency assessed the medicine to recommend its authorisation in the EU and its conditions of use. It is not intended to provide practical advice on how to use Kuvan.

For practical information about using Kuvan, patients should read the package leaflet or contact their doctor or pharmacist.

What is Kuvan and what is it used for?

Kuvan is a medicine that is used to treat high blood levels of phenylalanine in adults and children of all ages with the genetic disorders phenylketonuria (PKU) or tetrahydrobiopterin (BH4) deficiency.

Patients with these disorders cannot process the amino acid phenylalanine from dietary protein, and as a result the amino acid builds up in the blood to abnormally high levels, causing problems in the nervous system.

Because the number of patients with conditions leading to high phenylalanine levels is low, the conditions are considered 'rare', and Kuvan was designated an 'orphan medicine' (a medicine used in rare diseases) on 8 June 2004.

Kuvan contains the active substance sapropterin dihydrochloride.

How is Kuvan used?

Kuvan is available as soluble tablets (100 mg) or as powder (100 or 500 mg), to be dissolved in water and drunk. Kuvan can only be obtained with a prescription and treatment must be started and supervised by a doctor who has experience in treating PKU and BH4 deficiency. It is important that patients continue with a diet low in phenylalanine and protein when taking Kuvan, and intake of phenylalanine and protein must be monitored and adjusted to make sure that blood phenylalanine levels and nutritional balance are controlled. Kuvan is intended for long-term use.

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The starting dose of Kuvan depends on the patient's weight. The dose is then adjusted depending on blood levels of amino acids including phenylalanine. Kuvan is taken with a meal at the same time every day, preferably in the morning. For some patients with BH4 deficiency, the dose may need to be divided into two or three doses over the course of the day to get the best effect.

A satisfactory response is defined as a reduction in blood phenylalanine levels of at least 30% or to a level determined by the doctor. If this has been achieved after one month, the patient is classified as a 'responder' and can continue taking Kuvan.

How does Kuvan work?

The high levels of phenylalanine in the blood are due to a problem with the breakdown of phenylalanine through the enzyme 'phenylalanine hydroxylase'. Patients with PKU have defective versions of the enzyme, and patients with BH4 deficiency have low levels of BH4, a 'cofactor' that this enzyme needs to work properly.

The active substance in Kuvan, sapropterin dihydrochloride, is a synthetic copy of BH4. In PKU, it works by enhancing the activity of the defective enzyme, while in BH4 deficiency it replaces the missing cofactor. These actions help restore the ability of the enzyme to convert phenylalanine into tyrosine, thereby reducing phenylalanine levels in the blood.

What benefits of Kuvan have been shown in studies?

In PKU treatment, a main study compared the reductions in blood phenylalanine in 88 patients treated with either Kuvan or placebo (a dummy treatment). Two other studies in 101 patients looked at how effective Kuvan was at allowing the patients to consume foods containing phenylalanine while keeping blood phenylalanine at target levels (i.e. phenylalanine tolerance).

Kuvan was more effective than placebo at reducing blood phenylalanine levels in patients with PKU, achieving a reduction of 236 micromoles per litre after 6 weeks compared with an increase of 3 micromoles per litre seen with placebo. In addition Kuvan allowed patients with PKU who were not on a restricted diet to increase their daily phenylalanine intake by 17.5 mg per kg body weight after 10 weeks compared with 3.3 mg/kg with placebo. When Kuvan plus diet restriction was compared with diet restriction alone, the average daily phenylalanine intake that was tolerated after 26 weeks was 81 mg/kg in the Kuvan group and 50 mg/kg in the group on diet restriction alone.

For the treatment of BH4 deficiency, which is a very rare condition, the company presented results of three studies from the published literature in which some patients were treated with sapropterin for an average of 15.5 months. In these studies, patients showed an improvement in blood phenylalanine levels and other markers of the disease when they were taking the medicine.

Studies with Kuvan involved adults and children of all ages.

What are the risks associated with Kuvan?

The most common side effects with Kuvan (seen in more than 1 patient in 10) are headache and rhinorrhoea (runny nose).

For the full list of all side effects and restrictions with Kuvan, see the package leaflet.

Why is Kuvan approved?

The Agency decided that Kuvan's benefits are greater than its risks and recommended that it be given marketing authorisation.

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

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Kuvan have been included in the summary of product characteristics and the package leaflet.

Other information about Kuvan

The European Commission granted a marketing authorisation valid throughout the European Union for Kuvan on 2 December 2008.

The summary of opinion of the Committee for Orphan Medicinal Products for Kuvan can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/Rare disease designations.

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

This summary was last updated in 07-2017.