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EPAR summary for the public

Zonegran

zonisamide

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

What is Zonegran?

Zonegran is a medicine that contains the active substance zonisamide. It is available as capsules (25, 50 and 100 mg) and orodispersible tablets (25, 50, 100 and 300 mg). Orodispersible tablets are tablets that dissolve in the mouth.

What is Zonegran used for?

Zonegran is used to treat patients with partial seizures (epileptic fits starting in one part of the brain), including those who have secondary generalisation (where the seizure subsequently spreads to the whole brain). It is used on its own in newly diagnosed adults and as an 'add-on' therapy in adults and children aged 6 years and above already receiving other antiepilepsy medicines.

The medicine can only be obtained with a prescription.

How is Zonegran used?

When Zonegran is used on its own in newly diagnosed adults, the recommended starting dose is 100 mg once a day for two weeks, which may be increased by 100 mg at intervals of two weeks. The usual maintenance dose is 300 mg a day.

When Zonegran is used as an 'add-on' to existing treatment in adults, the recommended starting dose is 25 mg twice a day. After one week the dose may be increased to 50 mg twice a day and then further increased in steps of 100 mg every week, depending on the patient's response. Zonegran can be given once or twice a day after an appropriate dose is reached. The usual maintenance dose is between 300 and 500 mg a day.

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When Zonegran is used as an 'add-on' to existing treatment in children aged 6 years and above, the dose depends on body weight; the recommended starting dose is 1 mg per kg of body weight daily. After one or two weeks, the daily dose may be increased in steps of 1 mg per kg every one or two weeks until an appropriate dose is reached. The total dose must not exceed 500 mg a day.

Dose increases may need to be made less frequently in patients with liver or kidney problems or those taking certain other medicines. Before stopping Zonegran, the dose should be decreased gradually. For further information, see the package leaflet.

How does Zonegran work?

The active substance in Zonegran, zonisamide, is an anti-epileptic. Epileptic fits are caused by abnormal electrical activity in the brain. Zonisamide works by blocking specific pores on the surface of nerve cells called sodium channels and calcium channels. These channels transmit electrical impulses between nerve cells. By blocking these channels, zonisamide prevents the nerve cells from synchronising their activity and prevents abnormal electrical activity spreading through the brain. This reduces the chances of an epileptic fit. Zonegran also acts on the neurotransmitter gamma-aminobutyric acid (GABA, a chemical that allows nerve cells to communicate with each other). This may help to stabilise electrical activity in the brain.

How has Zonegran been studied?

Zonegran used on its own was compared with carbamazepine, another anti-epileptic medicine, in a main study involving 583 adults newly diagnosed with partial epilepsy. The main measure of effectiveness was the proportion of patients who were seizure-free for a period of six months.

Two other main studies, one involving 351 adults and one involving 207 children (between 6 and 17 years old), looked at Zonegran as an add-on to existing treatment. These studies compared Zonegran with placebo (a dummy treatment). In the study involving adults, the main measure of effectiveness was the change in the frequency of partial seizures between the 12 weeks before treatment started and the 18-week period when a stable dose was used. In the study in children, the main measure of effectiveness was the proportion of patients in whom the number of seizures was at least halved between the 8 weeks before treatment started and the 12-week period when a stable dose was used.

What benefit has Zonegran shown during the studies?

Zonegran used on its own was shown to be beneficial in adults with partial seizures: 69.4% of patients on Zonegran were seizure-free for six months. The percentage of patients on carbamazepine who were seizure-free for six months was 74.7%.

Zonegran was more effective than placebo at reducing the frequency of seizures when used as an 'add-on' to existing treatment. Adults taking 500 mg Zonegran per day had an average reduction in seizure frequency of 51%, compared with 16% in those taking placebo. In children, the number of seizures was at least halved in 50% of the patients taking Zonegran, compared with 31% of those taking placebo.

What is the risk associated with Zonegran?

The most common side effects with Zonegran (seen in more than 1 patient in 10) are loss of appetite, agitation, irritability, confusion, depression, ataxia (an inability to co-ordinate muscle movements), dizziness, memory impairment, somnolence (sleepiness), diplopia (double vision) and decreased blood bicarbonate levels; although the safety profile is similar in children and adults, some side effects are

reported more frequently in children than in adults. Zonegran can cause heatstroke and de-hydration, particularly in children, and these need to be treated promptly. Severe rashes have occurred in patients taking Zonegran, including cases of Stevens-Johnson syndrome (a severe, life-threatening type of allergic reaction affecting the skin and mucous membranes). For the full list of all side effects reported with Zonegran, see the package leaflet.

Zonegran must not be used in people who are hypersensitive (allergic) to zonisamide, to any of the other ingredients, or to sulphonamides (such as some antibiotics).

Why has Zonegran been approved?

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

Other information about Zonegran:

The European Commission granted a marketing authorisation valid throughout the European Union for Zonegran on 10 March 2005.

The full EPAR for Zonegran 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 Zonegran, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

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