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EPAR summary for the public

Zontivity

vorapaxar

This is a summary of the European public assessment report (EPAR) for Zontivity. 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 Zontivity.

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

What is Zontivity and what is it used for?

Zontivity is a medicine used to reduce the occurrence of atherothrombotic events (problems caused by blood clots and hardening of the arteries) such as heart attacks or strokes in adult patients who have already had a heart attack or who have peripheral arterial disease (problem with blood flow in the arteries) with symptoms. It is given in combination with aspirin (acetylsalicylic acid) and where appropriate with a third medicine, clopidogrel, both of which also help prevent atherothrombotic events.

Zontivity contains the active substance vorapaxar.

How is Zontivity used?

Zontivity is available as tablets (2 mg) and can only be obtained with a prescription. The recommended dose is one tablet once a day.

For patients who have had a heart attack, treatment with Zontivity should start from 2 weeks after and preferably within one year of the occurrence of the heart attack. There are limited data on the use of Zontivity for longer than 2 years; therefore, after 2 years of treatment, the benefits and risks of Zontivity should be re-evaluated in individual patients by the treating doctor. It is given in combination with aspirin and where appropriate, clopidogrel.

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For patients with peripheral arterial disease, treatment with Zontivity may be started at any time. It is given in combination with either aspirin or, where appropriate, with clopidogrel.

How does Zontivity work?

Heart attacks and some types of strokes result from blood clots in arteries. The active substance in Zontivity, vorapaxar, is an inhibitor of platelet aggregation. This means that it helps to prevent blood clots from forming. When the blood clots, components in the blood called platelets stick together. Vorapaxar blocks the PAR-1 receptors (known as 'thrombin receptors') on the surface of the platelets. Thrombin is one of the substances involved in the clotting process, and when it attaches to the PAR-1 receptor it causes the platelets to become 'sticky', helping the blood clot to form. Blocking the PAR-1 receptor stops the platelets becoming sticky, reducing the risk of a blood clot forming and helping to prevent a stroke or heart attack.

What benefits of Zontivity have been shown in studies?

Zontivity was compared with placebo (a dummy treatment) in a main study involving over 26,000 adults who had had a heart attack or other atherothrombotic event or who had peripheral arterial disease. Nearly all patients also took aspirin and/or another medicine to prevent atherothrombotic events, and were treated for at least a year. The main measure of effectiveness was based on the number of patients having an 'event' such as a heart attack or stroke, or dying from cardiovascular disease (problems affecting the heart and blood vessels).

Zontivity was more effective than placebo at reducing the occurrence of atherothrombotic events. Overall, 9.5% of patients (1,259 out of 13,225 patients) taking Zontivity had an atherothrombotic event compared with 10.7% (1,417 out of 13,224 patients) of patients taking placebo. The benefits of Zontivity were clearest in a group of 16,897 patients who had had a heart attack, but had no history of stroke or transient ischaemic attack (so-called 'mini stroke'). In this group, 8.5% of patients (719 out of 8,458 patients) treated with Zontivity had an atherothrombotic event, compared with 10.3% of patients (867 out of 8,439 patients) on placebo.

Among patients with peripheral arterial disease, 10.9% (177 out of 1,622 patients) taking Zontivity had an atherothrombotic event compared with 12.5% (206 out of 1,651 patients) of patients taking placebo.

What are the risks associated with Zontivity?

The most common side effect with Zontivity (which may affect up to 1 in 10 people) is bleeding, particularly nosebleed. For the full list of all side effects, see the package leaflet.

Zontivity must not be used in patients who have had a stroke or mini stroke. It must also not be used in patients who have had intracranial haemorrhage (bleeding in the brain) or who are actively bleeding, nor in patients with severely reduced liver function. Zontivity must not be used together with prasugrel or ticagrelor, two other medicines that help to prevent platelets from sticking together. For the full list of restrictions, see the package leaflet.

Why is Zontivity approved?

The Agency's Committee for Medicinal Products for Human Use (CHMP) decided that Zontivity's benefits are greater than its risks and recommended that it be approved for use in the EU. The medicine has been shown to be beneficial in reducing the number of atherothrombotic events in patients who had had a heart attack. In patients with peripheral arterial disease, the data showed a

benefit for patients taking Zontivity, although the number of atherothrombotic events reported during the main study was not large enough to enable conclusive results. However, as patients with peripheral arterial disease have a high risk of atherothrombotic events and the treatment options for prevention of these events are limited, the CHMP considered that Zontivity's benefits are greater than its risks for this condition.

Regarding Zontivity's safety profile, the CHMP was concerned about the risk of bleeding in patients taking Zontivity on top of their standard therapy, particularly serious bleeding which was more frequent in patients with a history of stroke. It therefore considered it appropriate to restrict the use to patients who have not had a stroke.

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

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

Other information about Zontivity

The European Commission granted a marketing authorisation valid throughout the European Union for Zontivity on 19 January 2015.

The full EPAR and risk management plan summary for Zontivity 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 Zontivity, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 07-2016.