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EPAR summary for the public

Clopidogrel Zentiva[1]

clopidogrel

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

What is Clopidogrel Zentiva?

Clopidogrel Zentiva is a medicine that contains the active substance clopidogrel. It is available as pink tablets (round: 75 mg; oblong: 300 mg).

What is Clopidogrel Zentiva used for?

Clopidogrel Zentiva is used to prevent problems caused by blood clots in adults who have:

- recently had a myocardial infarction (heart attack). Clopidogrel Zentiva can be started between a few days and 35 days after the attack;
- recently had an ischaemic stroke (stroke caused by failure of the blood supply to part of the brain). Clopidogrel Zentiva can be started between seven days and six months after the stroke;
- peripheral arterial disease (problems with blood flow in the arteries);
- a condition known as 'acute coronary syndrome', when it should be given with aspirin (another medicine that prevents blood clots). Acute coronary syndrome is a group of heart problems that include heart attacks and unstable angina (a severe type of chest pain). Some of these patients have had a stent inserted (a short tube) placed in an artery to prevent it from closing up.
- atrial fibrillation (irregular rapid contractions of the upper chambers of the heart), when it should be given with aspirin. It is used in those patients who have at least one risk factor for vascular

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events such as a heart attack or stroke, cannot take vitamin K antagonists (other medicines that prevent blood clots) and are at low risk of bleeding.

The medicine can only be obtained with a prescription.

How is Clopidogrel Zentiva used?

The standard dose of Clopidogrel Zentiva is one 75-mg tablet once a day. In acute coronary syndrome, treatment generally starts with a loading dose of one 300-mg tablet or four 75-mg tablets. This is then followed by the standard 75-mg dose once a day for at least four weeks (in 'ST segment elevation' myocardial infarction) or for up to 12 months (in unstable angina or 'non-Q-wave' myocardial infarction). In acute coronary syndrome and atrial fibrillation, Clopidogrel Zentiva is used together with aspirin, the dose of which should not be higher than 100 mg.

Clopidogrel Zentiva is converted into its active form in the body. For genetic reasons, some patients may not be able to convert Clopidogrel Zentiva as effectively as others, which could reduce their response to the medicine. The best dose to use in these patients has not yet been determined.

How does Clopidogrel Zentiva work?

The active substance in Clopidogrel Zentiva, clopidogrel, is an inhibitor of platelet aggregation. This means that it helps to prevent blood clots from forming. When the blood clots, this is due to special cells in the blood called platelets aggregating (sticking together). Clopidogrel stops the platelets aggregating by blocking a substance called ADP from attaching to a special receptor on their surface. This stops the platelets becoming 'sticky', reducing the risk of a blood clot forming and helping to prevent another heart attack or stroke.

How has Clopidogrel Zentiva been studied?

Clopidogrel Zentiva has been compared with aspirin in a study called CAPRIE including around 19,000 patients who had recently had a heart attack or ischaemic stroke, or who had established peripheral arterial disease. The main measure of effectiveness was how many patients experienced a new 'ischaemic event' (heart attack, ischaemic stroke or death) over one to three years.

In acute coronary syndrome, Clopidogrel Zentiva has been compared with placebo (a dummy treatment) in one study involving over 12,000 patients with non-ST segment elevation, 2,172 of whom had a stent inserted during the study (CURE study, lasting up to a year). Clopidogrel Zentiva has also been compared with placebo in two studies involving patients with ST segment elevation: CLARITY, which involved over 3,000 patients and lasted for up to eight days; and COMMIT, which involved almost 46,000 patients and in which the patients received Clopidogrel Zentiva with or without metoprolol (another medicine used for heart problems or high blood pressure) for up to four weeks. In the studies of acute coronary syndrome, all of the patients also took aspirin and the main measure of effectiveness was the number of patients who experienced an 'event' such as a blocked artery, another heart attack or death during the study.

In atrial fibrillation, Clopidogrel Zentiva has been compared with placebo (both taken together with aspirin) in one main study involving around 7,500 patients who had at least one risk factor for vascular events and who could not take vitamin K antagonist therapy. The patients were treated for an average of three years, and the main measure of effectiveness was the number of patients who experienced an 'event' such as a heart attack, ischaemic stroke or death.

What benefit has Clopidogrel Zentiva shown during the studies?

Clopidogrel Zentiva was more effective than aspirin at preventing new ischaemic events. In CAPRIE, there were 939 events in the Clopidogrel Zentiva group, and 1,020 in the aspirin group. This corresponds to a relative reduction in risk of 9% compared with aspirin. This means that fewer patients will have new ischaemic events if they receive Clopidogrel Zentiva than if they receive aspirin. In other words, about 10 patients in 1,000 will avoid having a new ischaemic event two years after starting Clopidogrel Zentiva instead of aspirin.

In non-ST segment elevation acute coronary syndrome, the overall relative reduction in the risk of an event compared with placebo was 20%. There was also a reduction in the patients who had a stent inserted. In ST segment elevation myocardial infarction, fewer patients on Clopidogrel Zentiva had events than patients on placebo (262 against 377 in the CLARITY study, and 2,121 against 2,310 in the COMMIT study). This showed that Clopidogrel Zentiva reduces the risk of an event.

In the study in atrial fibrillation patients, Clopidogrel Zentiva taken together with aspirin reduced the risk of new events by 11% compared with placebo taken with aspirin, with the largest reduction (28%) seen for stroke.

What is the risk associated with Clopidogrel Zentiva?

The most common side effects with Clopidogrel Zentiva (seen in between 1 and 10 patients in 100) are haematoma (a collection of blood under the skin), epistaxis (nosebleeds), gastrointestinal haemorrhage (bleeding in the stomach or gut), diarrhoea, abdominal pain (stomach ache), dyspepsia (heartburn), bruising and bleeding where the skin is punctured. For the full list of all side effects reported with Clopidogrel Zentiva, see the Package Leaflet.

Clopidogrel Zentiva should not be used in people who may be hypersensitive (allergic) to clopidogrel or any of the other ingredients. It must not be used in patients who have severe liver disease or a disease that may cause bleeding such as a stomach ulcer or bleeding in the brain.

Why has Clopidogrel Zentiva been approved?

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

Other information about Clopidogrel Zentiva

The European Commission granted a marketing authorisation valid throughout the European Union for Clopidogrel Winthrop on 16 July 2008. This authorisation was based on the authorisation granted to Plavix in 1998 ('informed consent'). The name of the medicine was changed to Clopidogrel Zentiva on 23 August 2011.

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

This summary was last updated in 11-2011.