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EPAR summary for the public

Dafiro HCT

amlodipine / valsartan / hydrochlorothiazide

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

What is Dafiro HCT?

Dafiro HCT is a medicine that contains three active substances, amlodipine, valsartan and hydrochlorothiazide. It is available as tablets containing amlodipine, valsartan and hydrochlorothiazide in the following amounts: 5/160/12.5 mg, 10/160/12.5 mg, 5/160/25 mg; 10/160/25 mg and 10/320/25 mg.

What is Dafiro HCT used for?

Dafiro HCT is used to treat essential hypertension (high blood pressure) in adults whose blood pressure is already adequately controlled with a combination of amlodipine, valsartan and hydrochlorothiazide. 'Essential' means that the hypertension has no obvious cause.

The medicine can only be obtained with a prescription.

How is Dafiro HCT used?

Dafiro HCT is taken by mouth as one tablet once a day, at the same time of the day and preferably in the morning. The dose of Dafiro HCT to be used is the same as the doses of three individual active substances that the patient was taking before. The daily dose of Dafiro HCT should not exceed 10 mg of amlodipine, 320 mg of valsartan and 25 mg of hydrochlorothiazide.

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How does Dafiro HCT work?

The three active substances in Dafiro HCT are anti-hypertensive medicines that are already in use in the European Union (EU).

Amlodipine is a 'calcium channel blocker'. It blocks special channels on the surface of cells called calcium channels, through which calcium ions normally enter the cells. When calcium ions enter the cells in the muscles of blood vessel walls, this causes contraction. By reducing the flow of calcium into the cells, amlodipine prevents the cells from contracting and helps the blood vessel walls to relax and widen, thereby reducing blood pressure.

Valsartan is an 'angiotensin II receptor antagonist', which means that it blocks the action of a body hormone called angiotensin II. Angiotensin II is a powerful vasoconstrictor (a substance that narrows blood vessels). By blocking the receptors to which angiotensin II normally attaches, valsartan stops the hormone having an effect, allowing the blood vessels to widen and blood pressure to reduce.

Hydrochlorothiazide is a diuretic. It works by increasing urine output, reducing the volume of fluid in the blood and lowering the blood pressure.

The combination of the three active substances has an additive effect, reducing the blood pressure more than the individual medicines alone. By lowering the blood pressure, the risks associated with high blood pressure, such as having a stroke, are reduced.

How has Dafiro HCT been studied?

Because the combination of the three active substances has been in use for a number of years, the company presented studies showing that the tablet containing all three substances is absorbed in the body in the same way as the separate tablets.

In addition, one main study was carried out in 2,271 patients with moderate to severe hypertension with the highest strength of Dafiro HCT (320 mg valsartan, 10 mg amlodipine and 25 mg hydrochlorothiazide). Patients received either Dafiro HCT or one of the three combinations containing only two of the active substances for eight weeks. The main measure of effectiveness was the average change in the blood pressure.

What benefit has Dafiro HCT shown during the studies?

Treatment with the highest strength of Dafiro HCT was more effective at treating hypertension than dual combinations containing any of the two active substances. The average reduction in blood pressure was around 39.7/24.7 mmHg in patients taking Dafiro HCT compared with 32/19.7 mmHg, 33.5/21.5 mmHg and 31.5/19.5 mmHg in patients taking valsartan/hydrochlorothiazide, valsartan/amlodipine and hydrochlorothiazide/amlodipine combinations, respectively.

What is the risk associated with Dafiro HCT?

The most common side effects with Dafiro HCT (seen in between 1 and 10 patients in 100) are hypokalaemia (low blood potassium levels), dizziness, headache, hypotension (low blood pressure), dyspepsia (heartburn), pollakiuria (abnormally frequent urination), fatigue (tiredness) and oedema (fluid retention). For the full list of all side effects reported with Dafiro HCT, see the package leaflet.

Dafiro HCT must not be used in people who are hypersensitive (allergic) to the active substances, to other sulfonamides, to dihydropyridine derivatives or to any of the other ingredients in Dafiro HCT. It must not be used in women who are more than three months pregnant. It must also not be used in patients who have liver or bile problems (such as jaundice), severe kidney problems, anuria (a

condition in which a patient cannot make or pass urine) or in patients undergoing dialysis (a blood clearance technique). Finally, Dafiro HCT must not be used in patients with hypokalaemia (low blood potassium levels), hyponatraemia (low blood sodium levels) and hypercalcaemia (high blood calcium levels) that do not respond to treatment and in patients with hyperuricaemia (high blood levels of uric acid) that causes symptoms.

Dafiro HCT must also not be used in combination with aliskiren-containing medicines (also used to treat essential hypertension) in patients with type 2 diabetes or in patients with moderate or severe kidney impairment.

Why has Dafiro HCT been approved?

The CHMP noted that patients already taking the three active substances would be more likely to comply with their treatment if prescribed Dafiro HCT which combines the three substances in a single tablet. The main study showed the benefit of the highest strength of Dafiro HCT in lowering the blood pressure. For all doses, Dafiro HCT also met requirements to prove that it was comparable to the combinations of the individual active substances taken separately. The CHMP therefore decided that Dafiro HCT's benefits are greater than its risks and recommended that it be given marketing authorisation.

Other information about Dafiro HCT

The European Commission granted a marketing authorisation valid throughout the European Union for Dafiro HCT on 4 November 2009.

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

This summary was last updated in 09-2013.