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EPAR summary for the public

Jalra

vildagliptin

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

What is Jalra?

Jalra is a medicine that contains the active substance vildagliptin. It is available as tablets (50 mg).

What is Jalra used for?

Jalra is used to treat type 2 diabetes mellitus. It can be used in the following ways:

- on its own (monotherapy) in patients whose diabetes is not sufficiently controlled by diet and exercise and who cannot take metformin;
- together with metformin, a thiazolidinedione or a sulphonylurea (dual therapy) when the patient's diabetes is insufficiently controlled by this other medicine taken alone, but it is only used in combination with a sulphonylurea in patients who cannot take metformin;
- together with a sulphonylurea and metformin (triple therapy) in patients whose diabetes is not sufficiently controlled by these medicines plus diet and exercise;
- together with insulin (with or without metformin) in patients whose diabetes is not sufficiently controlled by diet and exercise plus a stable dose of insulin.

The medicine can only be obtained with a prescription.

How is Jalra used?

In adults, the recommended dose of Jalra is:

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- one tablet in the morning and another in the evening (100 mg per day), when used alone, with metformin, with a thiazolidinedione, with metformin plus a sulphonylurea, or with insulin (with or without metformin);
- one tablet in the morning (50 mg per day) when taken with a sulphonylurea. A lower dose of the sulphonylurea may also be considered to reduce the risk of hypoglycaemia (low blood glucose levels).

The daily dose should not exceed two tablets (100 mg).

Jalra is not recommended for patients who have moderate or severe problems with their kidneys, including those on haemodialysis (a blood clearance technique) with end-stage renal disease. Jalra is not recommended for patients with liver problems.

How does Jalra work?

Type 2 diabetes is a disease in which the pancreas does not make enough insulin to control the level of glucose (sugar) in the blood or when the body is unable to use insulin effectively. The active substance in Jalra, vildagliptin, is a dipeptidyl peptidase 4 (DPP-4) inhibitor. It works by blocking the breakdown of 'incretin' hormones in the body. These hormones are released after a meal and stimulate the pancreas to produce insulin. By increasing levels of incretin hormones in the blood, vildagliptin stimulates the pancreas to produce more insulin when blood glucose levels are high. Vildagliptin does not work when the blood glucose is low. Vildagliptin also reduces the amount of glucose made by the liver, by increasing insulin levels and decreasing the levels of the hormone glucagon. Together, these processes reduce blood glucose levels and help to control type 2 diabetes.

How has Jalra been studied?

Jalra has been studied in eleven main studies involving a total of over 5,000 patients with type 2 diabetes and insufficient control of blood glucose levels.

Five of these studies looked at the effects of Jalra taken alone in a total of 3,644 patients, comparing it with placebo (a dummy treatment), metformin, rosiglitazone (a thiazolidinedione) or or gliclazide (a sulphonylurea).

Four studies compared the effects of Jalra, taken at doses of 50 or 100 mg a day for 24 weeks, with those of placebo, when used as an add-on to existing treatment with metformin (544 patients), pioglitazone (a thiazolidinedione, 463 patients), glimepiride (a sulphonylurea, 515 patients) or insulin (296 patients).

A further study compared Jalra with placebo as an add-on treatment in 318 patients who were already taking metformin and glimepiride.

A further study compared Jalra with placebo as an add-on treatment in 449 patients who were already taking a stable dose of long-acting insulin. Some of the patients were also taking metformin.

In all studies, the main measure of effectiveness was the change in blood levels of a substance called glycosylated haemoglobin (HbA1c), which gives an indication of how well blood glucose is controlled.

What benefit has Jalra shown during the studies?

Jalra used on its own was effective at reducing levels of HbA1c, but was less effective than the comparator medicines. In the study comparing Jalra with metformin, significantly better results were

seen with metformin: a reduction in HbA1c of 1.5 percentage points after 52 weeks compared with a reduction of around 1 percentage point in patients treated with Jalra.

When used as an add-on to existing treatment for type 2 diabetes, Jalra was more effective than placebo in reducing HbA1c levels. With metformin and with pioglitazone, the 100 mg daily dose was more effective than the 50 mg daily dose, with a reduction in HbA1c levels of between 0.8 and 1.0 percentage points. In combination with glimepiride, both 50 mg and 100 mg daily doses caused a reduction of around 0.6 percentage points. In contrast, patients adding placebo to their existing treatment showed smaller changes in HbA1c levels, ranging from a fall of 0.3 to a rise of 0.2 percentage points.

In combination with metformin and glimepiride, 50 mg Jalra taken twice a day reduced HbA1c levels by 1 percentage point, compared with a reduction of 0.3 percentage points in patients taking placebo.

In the study involving 296 patients taking insulin, adding Jalra caused a greater reduction in HbA1c levels than adding placebo, but the size of this effect was small possibly due to the fact that the study included long-term patients who were less likely to show improvement.. However, in another study involving 449 patients taking insulin, the size of this effect was significant. Patients taking Jalra in addition to insulin, with or without metformin, had a reduction in HbA1c levels of 0.77 percentage points, compared with 0.05 percentage points in patients taking placebo in addition to insulin.

What is the risk associated with Jalra?

The most common side effect with Jalra (seen in between 1 and 10 patients in 100) is dizziness. For the full list of all side effects reported with Jalra, including side effects occurring when Jalra is taken with other antidiabetes medicines, see the package leaflet.

Jalra must not be used in people who are hypersensitive (allergic) to vildagliptin or any of the other ingredients. Its use in patients with heart disease should be limited to patients with mild disease.

Because vildagliptin has been associated with liver problems, patients should have tests to check their liver function before treatment with Jalra and at regular intervals during treatment.

Why has Jalra been approved?

The CHMP noted that Jalra was effective as an add-on to metformin, a thiazolidinedione or a sulphonylurea (dual therapy), a sulphonylurea and metformin (triple therapy) or insulin with or without metformin, and concluded that the benefits of the add-on treatment outweigh the risks.

The CHMP also considered the use of Jalra on its own and concluded that it was effective in reducing blood glucose but was less effective than metformin. Jalra should therefore be used only in patients for whom metformin is inappropriate either because of side effects occurring with metformin or because they have a condition that makes metformin unsuitable for them.

Other information about Jalra

The European Commission granted a marketing authorisation valid throughout the European Union for Jalra on 19 November 2008.

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

This summary was last updated in 11-2012.