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## EPAR summary for the public

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# Janumet

sitagliptin / metformin hydrochloride

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

## What is Janumet?

Janumet is a medicine that contains two active substances, sitagliptin and metformin hydrochloride. It is available as tablets (50 mg sitagliptin / 850 mg metformin hydrochloride; and 50 mg sitagliptin / 1,000 mg metformin hydrochloride).

## What is Janumet used for?

Janumet is used in patients with type 2 diabetes to improve the control of blood glucose (sugar) levels. It is used in addition to diet and exercise in the following ways:

- in patients who are not satisfactorily controlled on metformin (an antidiabetes medicine) used on its own;
- in patients who are already taking a combination of sitagliptin and metformin as separate tablets;
- in combination with a sulphonylurea, a PPAR-gamma agonist such as a thiazolidinedione, or insulin (other types of antidiabetes medicine) in patients who are not satisfactorily controlled on this medicine and metformin.

The medicine can only be obtained with a prescription.



## How is Janumet used?

Janumet is taken twice a day. The strength of tablet to use depends on the dose of the other antidiabetes medicines that the patient was taking before. If Janumet is taken with a sulphonylurea or insulin, the dose of the sulphonylurea or insulin may need to be lowered, to avoid hypoglycaemia (low blood sugar levels).

The maximum dose of sitagliptin is 100 mg a day. Janumet should be taken with food to avoid any stomach problems caused by metformin.

## How does Janumet work?

Type 2 diabetes is a disease in which the pancreas does not make enough insulin to control the level of glucose in the blood or when the body is unable to use insulin effectively. The active substances in Janumet, sitagliptin and metformin hydrochloride, each have a different mode of action.

Sitagliptin 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 the levels of incretin hormones in the blood, sitagliptin stimulates the pancreas to produce more insulin when blood glucose levels are high. Sitagliptin does not work when the blood glucose is low. Sitagliptin also reduces the amount of glucose made by the liver, by increasing insulin levels and decreasing the levels of the hormone glucagon. Sitagliptin has been authorised in the European Union (EU) as Januvia and Xelvia since 2007, and as Tesavel since 2008.

Metformin works mainly by inhibiting glucose production and reducing its absorption in the gut. Metformin has been available in the EU since the 1950s.

As a result of the action of both active substances, blood glucose levels are reduced and this helps to control type 2 diabetes.

## How has Janumet been studied?

Sitagliptin on its own as Januvia/Xelvia/Tesavel can be used with metformin, and with both metformin and a sulphonylurea, in type 2 diabetes patients. The company presented the results of three studies of Januvia/Xelvia to support the use of Janumet in patients who were not satisfactorily controlled on their existing metformin treatment. Two of the studies looked at sitagliptin as an add-on to metformin: the first compared it with placebo (a dummy treatment) in 701 patients, and the second compared it with glipizide (a sulphonylurea) in 1,172 patients. The third study compared sitagliptin with placebo, when used as an add-on to glimepiride (another sulphonylurea), with or without metformin, in 441 patients.

The results of three further studies were used to support the use of Janumet. The first included 1,091 patients who were not satisfactorily controlled on diet and exercise alone and compared the effect of Janumet with that of metformin or sitagliptin alone. The second included 278 patients who were not satisfactorily controlled on the combination of metformin and rosiglitazone (a PPAR-gamma agonist) and compared the effects of adding sitagliptin or placebo. The third included 641 patients who were not satisfactorily controlled on a stable dose of insulin, three-quarters of whom were also taking metformin. This study also compared the effects of adding sitagliptin or placebo.

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

The company carried out additional studies to show that the active substances in Janumet are absorbed by the body in the same way as the two medicines given separately.

### **What benefit has Janumet shown during the studies?**

Janumet was more effective than metformin alone. Adding 100 mg sitagliptin to metformin reduced HbA1c levels by 0.67% (from around 8.0%) after 24 weeks, compared with a fall of 0.02% in the patients adding placebo. The effectiveness of adding sitagliptin to metformin was similar to that of adding glipizide. In the study in which sitagliptin was added to glimepiride and metformin, the levels of HbA1c were reduced by 0.59% after 24 weeks, compared with an increase of 0.30% in the patients adding placebo.

In the first of the three further studies, Janumet was more effective than metformin or sitagliptin alone. In the second, HbA1c levels were reduced by 1.03% after 18 weeks in patients adding sitagliptin to metformin and rosiglitazone, compared with a fall of 0.31% in those adding placebo. Finally, they were reduced by 0.59% after 24 weeks in patients adding sitagliptin to insulin, compared with a fall of 0.03% in those adding placebo. There was no difference in this effect between the patients also taking metformin and those not taking it.

### **What is the risk associated with Janumet?**

The most common side effect with Janumet (seen in between 1 and 10 patients in 100) is nausea (feeling sick). For the full list of all side effects reported with Janumet, see the package leaflet.

Janumet must not be used in people who are hypersensitive (allergic) to sitagliptin, metformin or any of the other ingredients. It must not be used in patients who have diabetic ketoacidosis or pre-coma (dangerous conditions that can occur in diabetes), problems with the kidneys or liver, conditions that may affect the kidneys, or a disease that causes a reduced supply of oxygen to the tissues such as failure of the heart or lungs or a recent heart attack. It must also not be used in patients who consume excessive amounts of alcohol or are alcoholic, or in women who are breast-feeding. For the full list of restrictions, see the package leaflet.

### **Why has Janumet been approved?**

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

### **Other information about Janumet**

The European Commission granted a marketing authorisation valid throughout the EU for Janumet on 16 July 2008.

The full EPAR for Janumet can be found on the Agency's website: [ema.europa.eu/Find/medicine/Human\\_medicines/European\\_public\\_assessment\\_reports](http://ema.europa.eu/Find/medicine/Human_medicines/European_public_assessment_reports). For more information about treatment with Janumet, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

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