17 November 2011
EMA/897336/2011
EMEA/H/C/002394
EMEA/H/C/002519
EMEA/H/C/002520
EMEA/H/C/002521

Questions and answers

Withdrawal of the marketing authorisation application for Janacti (sitagliptin/pioglitazone) and related names

On 7 November 2011 Merck Sharp & Dohme Ltd. officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a marketing authorisation for Janacti and related names, for the treatment of type 2 diabetes.

What is Janacti?

Janacti is a medicine that contains two active substances, sitagliptin and pioglitazone. It was to be available as tablets (100 mg sitagliptin and 30 mg pioglitazone; 100 mg sitagliptin and 45 mg pioglitazone).

What was Janacti expected to be used for?

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

- in patients who are already taking a combination of sitagliptin and pioglitazone as separate tablets;
- in patients who are not satisfactorily controlled on pioglitazone used on its own and at the maximum possible dose;
- in patients who are not satisfactorily controlled on pioglitazone and metformin (another anti-diabetes medicine) used together and at the maximum possible dose.

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How is Janacti expected to 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 Janacti, sitagliptin and pioglitazone, each have a different mode of action and have been available as separate medicines in the European Union (EU) for the treatment of diabetes for a number of years.

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 level 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 Xelevia since 2007, as Tesavel since 2008, and as Ristaben since 2010.

Pioglitazone makes cells (in body fat, muscle and the liver) more sensitive to insulin, which means that the body makes better use of the insulin it produces. Pioglitazone on its own has been authorised in the EU under the name Actos since 2000.

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

What did the company present to support its application?

Because pioglitazone and sitagliptin are already used in authorised medicines in the EU, the company presented data obtained from earlier studies, from new studies and from the published literature.

Three studies of sitagliptin were used to support the use of Janacti in type 2 diabetes. Two of the studies compared sitagliptin with placebo in patients who were also taking pioglitazone with or without metformin. A third study compared sitagliptin and pioglitazone with pioglitazone alone.

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

The company also presented the results of new studies carried out to investigate whether the levels of the active substances in the blood were the same in people taking Janacti as in people taking sitagliptin and pioglitazone as separate tablets.

How far into the evaluation was the application when it was withdrawn?

The application was withdrawn before 'day 120'. This means that the CHMP was still evaluating the initial documentation provided by the company.

What was the recommendation of the CHMP at that time?

As the CHMP was evaluating the initial documentation provided by the company, it had not yet made any recommendations.

What were the reasons given by the company for withdrawing the application?

The letter from the company notifying the Agency of the withdrawal of the application is available under the tab ‘All documents’.