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EPAR summary for the public

Incresync

alogliptin / pioglitazone

This is a summary of the European public assessment report (EPAR) for Incresync. It explains how the Agency assessed the medicine to recommend its authorisation in the EU and its conditions of use. It is not intended to provide practical advice on how to use Incresync.

For practical information about using Incresync, patients should read the package leaflet or contact their doctor or pharmacist.

What is Incresync and what is it used for?

Incresync is a diabetes medicine containing the active substances alogliptin and pioglitazone. It is used as an addition to diet and exercise in adults with type 2 diabetes to improve the control of blood glucose (sugar) levels:

- in patients who are not satisfactorily controlled with pioglitazone alone, and who cannot be treated with metformin (another diabetes medicine);
- together with metformin, in patients who are not satisfactorily controlled with a combination of pioglitazone and metformin.

Incresync can also be used as a replacement tablet (supplying both alogliptin and pioglitazone) in patients who are already being treated with alogliptin and pioglitazone given separately.

How is Incresync used?

Incresync is available as tablets (12.5 or 25 mg alogliptin and 30 mg pioglitazone; 12.5 or 25 mg alogliptin and 45 mg pioglitazone) and can only be obtained with a prescription. It is taken by mouth once daily. The choice of tablet strength to start with depends on the patient's current treatment. If patients were previously taking pioglitazone alone, the strength of Incresync that provides the same dose of pioglitazone should be used. If patients are also taking metformin, lower doses of metformin or pioglitazone may need to be given to reduce the risk of hypoglycaemia (low blood sugar levels). If patients were previously taking pioglitazone and alogliptin separately, Incresync should be used in a

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strength that continues to provide the same doses. The dose should be lowered in patients with moderately reduced kidney function. For further information, see the summary of product characteristics (also part of the EPAR).

How does Incresync 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 Incresync, alogliptin and pioglitazone, work in different ways to help correct this.

Alogliptin 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 blocking the breakdown of Incretin hormones in the blood, alogliptin prolongs their action in stimulating the pancreas to produce more insulin when blood glucose levels are high. Alogliptin does not work when the blood glucose is low. Alogliptin 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. Alogliptin is licensed in the EU as Vipidia.

Pioglitazone makes cells (fat, muscle and liver) more sensitive to insulin, which means that the body makes better use of the insulin it produces. Pioglitazone is authorised in the EU as Actos and associated names.

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

What benefits of Incresync have been shown in studies?

Incresync has been studied in two main studies involving 1,296 patients with type-2 diabetes that was not well controlled by previous treatment. One of the studies compared the effects of alogliptin with placebo (a dummy treatment) when used as an add-on to existing treatment with pioglitazone (the same combination as in Incresync), with or without metformin or another diabetes medicine. In the other study the effects of adding alogliptin to existing treatment with pioglitazone and metformin was compared with increasing the doses of pioglitazone. In both studies, the main measure of effectiveness was the change in the level of glycosylated haemoglobin (HbA1c), which is the percentage of haemoglobin in the blood that has glucose attached. HbA1c levels give an indication of how well the blood glucose is controlled. HbA1c levels were measured after 26 weeks in the first study and 52 weeks in the second study.

Both studies showed that the combination of active substances in Incresync could produce a small but clinically relevant improvement in HbA1c. When added to pioglitazone, the improvement was a fall of 0.47% at a dose of alogliptin of 12.5 mg, and 0.61% for alogliptin 25 mg. Incresync was at least as effective as pioglitazone and metformin in reducing HbA1c.

What are the risks associated with Incresync?

The most common side effects with Incresync (which may affect up to 1 in 10 people) are upper respiratory tract infections (colds), sinusitis, headache, nausea (feeling sick), dyspepsia (heartburn), abdominal pain (tummy ache), pruritus (itching), myalgia (muscle pain), peripheral oedema (swelling in arms and legs) and weight gain. For the full list of all side effects reported with Incresync, see the package leaflet.

Incresync must not be used in patients who are hypersensitive (allergic) to the active substances or any of the ingredients or who have had serious allergic reactions to any dipeptidyl-peptidase-4 (DPP 4) inhibitor. It must also not be used in patients who have or have ever had heart failure or bladder cancer, those with reduced liver function, diabetic ketoacidosis (a serious condition that can occur in diabetes), or blood in the urine that has not been properly investigated. For the full list of restrictions, see the package leaflet.

Why is Incresync approved?

The Agency's Committee for Medicinal Products for Human Use (CHMP) concluded that Incresync's benefits are greater than its risks and recommended that it be approved for use in the EU. The CHMP considered that adding alogliptin to existing treatment with pioglitazone with or without metformin had shown to produce modest but clinically relevant improvements in HbA1c. The CHMP therefore considered that the combination of alogliptin and pioglitazone in Incresync is of benefit to patients. Regarding safety, Incresync's safety profile was consistent with that seen with the individual components.

What measures are being taken to ensure the safe and effective use of Incresync?

A risk management plan has been developed to ensure that Incresync is used as safely as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Incresync, including the appropriate precautions to be followed by healthcare professionals and patients.

In addition, the company that markets Incresync will produce educational materials for doctors prescribing the medicine, which will cover the possible risk of heart failure and bladder cancer with treatments that contain pioglitazone, the criteria for selecting patients and the need to review treatment regularly and stop treatment if patients are no longer benefiting.

Other information about Incresync

The European Commission granted a marketing authorisation valid throughout the European Union for Incresync on 19 September 2013.

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

This summary was last updated in 08-2013.