25 July 2013
EMA/CHMP/229752/2013
Committee for Medicinal Products for Human Use (CHMP)

Summary of opinion[1] (initial authorisation)

Incresync

alogliptin/pioglitazone

On 25 July 2013, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a marketing authorisation for Incresync, 12.5 mg / 45 mg, 12.5 mg / 30 mg, 25 mg / 45 mg and 25 mg / 30 mg, film-coated tablet intended for the treatment of type 2 diabetes mellitus. The applicant for this medicinal product is Takeda Pharma A/S. They may request a re-examination of any CHMP opinion, provided they notify the European Medicines Agency in writing of their intention within 15 days of receipt of the opinion.

The active substances of Incresync are alogliptin/pioglitazone (A10BD09), a combination of two blood glucose-lowering products: alogliptin is a dipeptidyl peptidase 4 (DPP 4) inhibitor which reduces the cleavage and inactivation of the active (intact) form of the incretin hormones glucagon-like peptide 1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP), producing an elevation of incretin concentrations that leads to an enhancement of glucose-dependent insulin secretion and a reduction in glucagon release. Pioglitazone is a thiazolidinedione and acts via activation of a specific nuclear receptor (peroxisome proliferator activated receptor gamma) leading to increased insulin sensitivity of liver, fat and skeletal muscle cells.

The benefit of Incresync is its effect on glycaemic control in patients with type 2 diabetes when used in combination with metformin or in patients inadequately controlled on pioglitazone alone. The most common side effects of alogliptin as add-on therapy to pioglitazone are upper respiratory tract infections, sinusitis, headache, nausea, dyspepsia, abdominal pain, pruritus, myalgia, peripheral oedema and weight increase.

Pioglitazone can cause fluid retention, which may exacerbate or precipitate heart failure. Cases of bladder cancer were reported more frequently in a meta-analysis of controlled clinical trials with pioglitazone, and available epidemiological data suggests a small increased risk of bladder cancer in diabetic patients treated with pioglitazone.

A pharmacovigilance plan for Incresync will be implemented as part of the marketing authorisation.

[1] Summaries of positive opinion are published without prejudice to the Commission decision, which will normally be issued 67 days from adoption of the opinion.

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The approved indication is: "Incresync is indicated as a second or third line treatment in adult patients aged 18 years and older with type 2 diabetes mellitus:

- as an adjunct to diet and exercise to improve glycaemic control in adult patients (particularly overweight patients) inadequately controlled on pioglitazone alone, and for whom metformin is inappropriate due to contraindications or intolerance.
- in combination with metformin (i.e. triple combination therapy) as an adjunct to diet and exercise to improve glycaemic control in adult patients (particularly overweight patients) inadequately controlled on their maximal tolerated dose of metformin and pioglitazone.

In addition, Incresync can be used to replace separate tablets of alogliptin and pioglitazone in those adult patients aged 18 years and older with type 2 diabetes mellitus already being treated with this combination.

After initiation of therapy with Incresync, patients should be reviewed after 3 to 6 months to assess adequacy of response to treatment (e.g. reduction in HbA1c). In patients who fail to show an adequate response, Incresync should be discontinued. In light of potential risks with prolonged pioglitazone therapy, prescribers should confirm at subsequent routine reviews that the benefit of Incresync is maintained (see section 4.4)."

Detailed recommendations for the use of this product will be described in the summary of product characteristics (SmPC), which will be published in the European public assessment report (EPAR) and made available in all official European Union languages after the marketing authorisation has been granted by the European Commission.

The CHMP, on the basis of quality, safety and efficacy data submitted, considers there to be a favourable benefit-to-risk balance for Incresync and therefore recommends the granting of the marketing authorisation.