21 November 2013
EMA/CHMP/703245/2013
Committee for Medicinal Products for Human Use (CHMP)

Summary of opinion[1] (initial authorisation)

Xigduo

dapagliflozin/metformin

On 21 November 2013, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a marketing authorisation for the medicinal product Xigduo, 5 mg/850 mg and 5 mg/1,000 mg film-coated tablets intended for the treatment of type 2 diabetes mellitus in adults. The applicant for this medicinal product is Bristol-Myers Squibb/AstraZeneca EEIG. 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 substance of Xigduo is dapagliflozin/metformin, a combination of oral blood glucose lowering drugs (A10BD15).

Dapagliflozin is a highly potent selective and reversible inhibitor of sodium-glucose co-transporter 2 (SGLT2), the predominant transporter responsible for reabsorption of glucose from the glomerular filtrate back into the circulation, that improves fasting and post-prandial plasma glucose levels by reducing renal glucose reabsorption leading to urinary glucose excretion.

Metformin is a biguanide with antihyperglycaemic effects, lowering both basal and postprandial plasma glucose. It does not stimulate insulin secretion and, therefore, does not produce hypoglycaemia. It is thought to act via various mechanisms, including decreasing hepatic glucose production, decreasing intestinal absorption of glucose, and improving insulin sensitivity by increasing peripheral glucose uptake and utilisation.

Xigduo combines these two glucose-lowering agents with complementary and distinct mechanisms of action.

The benefits with Xigduo are its ability to improve the glycaemic control through reduction of blood glucose levels in patients inadequately controlled by metformin alone. The most common side effects are hypoglycaemia, nausea, vomiting, diarrhoea, abdominal pain, loss of appetite, vulvovaginitis, balanitis and related genital infections, urinary tract infection, dysuria and polyuria.

[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.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7<sector fax>
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

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

The approved indication is:

"Xigduo is indicated in adults aged 18 years and older with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycaemic control

• in patients inadequately controlled on their maximally tolerated dose of metformin alone

• in combination with other glucose lowering medicinal products, including insulin, in patients inadequately controlled with metformin and these medicinal products (see sections 4.4, 4.5 and 5.1 for available data on different combinations)

• in patients already being treated with the combination of dapagliflozin and metformin as separate tablets".

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 Xigduo and therefore recommends the granting of the marketing authorisation.