European Medicines Agency
Pre-Authorisation Evaluation of Medicines for Human Use

London, 25 September 2008
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COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE
SUMMARY OF POSITIVE OPINION*
for
ZOMARIST

International Nonproprietary Name (INN): ***vildagliptin / metformin hydrochloride***

On 25 September 2008 the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion,** recommending to grant a marketing authorisation for the medicinal product Zomarist 50 mg/850 mg and 50 mg/1000 mg, film-coated tablet intended for treatment of type 2 diabetes mellitus. The applicant for this medicinal product is Novartis Europharm Ltd.

The active substance of Zomarist is vildagliptin and metformin hydrochloride, a combination of oral blood glucose lowering drugs (A10BD08). Vildagliptin is a dipeptidyl peptidase-4 (DPP-4) inhibitor. DPP-4 inhibition reduces the cleavage and inactivation of the active (intact) form of the incretin hormones, including GLP-1 (glucagon-like peptide 1) and GIP (glucose-dependent insulinotropic polypeptide), producing an elevation of incretin concentrations that lead to enhancement of glucose-dependent insulin secretion and a reduction in glucagon release, thus contributing to the maintenance of glucose homeostasis. Metformin is a biguanide and has an antihyperglycaemic effect. It is thought to act via various mechanisms, including inhibition of gluconeogenesis in the liver, a delay in intestinal glucose absorption, and an increase in insulin sensitivity and glucose uptake in some target tissues. Zomarist combines these two antidiabetic agents with complementary mechanisms of action.

The benefits with Zomarist include a clinically relevant and significant reduction of blood glucose levels compared to placebo, a neutral effect on weight, and a presumed improvement of compliance by use of two antidiabetic agents in one tablet. The most common side effects when taking Zomarist are tremor, headache, dizziness, nausea and hypoglycaemia. When vildagliptin is used as monotherapy the following adverse reactions are observed: dizziness, headache, constipation, arthralgia, hypoglycaemia, upper respiratory tract infection, nasopharyngitis and peripheral oedema. Furthermore, the following adverse reactions for metformin are known: decrease of vitamin B_{12} absorption and lactic acidosis, metallic taste, nausea, vomiting, diarrhoea, abdominal pain and loss of appetite, liver function test abnormalities or hepatitis and skin reactions as erythema, pruritus and urticaria.

A pharmacovigilance plan for Zomarist, as for all medicinal products, will be implemented as part of the marketing authorisation.

The approved indication is: “Zomarist is indicated in the treatment of type 2 diabetes mellitus patients who are unable to achieve sufficient glycaemic control at their maximally tolerated dose of oral metformin alone or who are already treated with the combination of vildagliptin and metformin as separate tablets.”

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* Summaries of positive opinion are published without prejudice to the Commission Decision, which will normally be issued within 67 days from adoption of the Opinion.

** Applicants may request a re-examination of any CHMP opinion, provided they notify the EMEA in writing of their intention to request a re-examination within 15 days of receipt of the opinion.

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Detailed recommendations for the use of this product will be described in the Summary of Product Characteristics (SPC) which will be published in the European Public Assessment Report (EPAR) and will be 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 of the reference product Eucreas, considers that there is a favourable benefit-risk balance for Zomarist and therefore recommends the granting of the marketing authorisation.