European Medicines Agency

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QUESTIONS AND ANSWERS ON THE WITHDRAWAL OF THE APPLICATION FOR A CHANGE TO THE MARKETING AUTHORISATION
for
NOVONORM/PRANDIN

International non-proprietary name (INN): ***repaglinide***

On 12 October 2006, Novo Nordisk A/S officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a change to the marketing authorisation for NovoNorm/Prandin, to add the use of NovoNorm/Prandin in combination with a thiazolidinedione for the treatment of type 2 diabetes.

What is NovoNorm/Prandin?
NovoNorm/Prandin is an antidiabetic medicine. It is available as tablets containing 0.5 mg, 1 mg and 2 mg of the active substance repaglinide.
NovoNorm/Prandin is authorised for use in patients who have non insulin-dependent diabetes (type 2 diabetes). It is used together with diet and exercise. It can be used on its own to lower blood glucose (sugar) in patients whose hyperglycaemia (high blood glucose) cannot be controlled by diet, weight reduction and exercise. NovoNorm/Prandin may also be used with metformin (another anti-diabetes medicine) in patients with type 2 diabetes who are not satisfactorily controlled on metformin alone.

What was NovoNorm/Prandin expected to be used for?
NovoNorm/Prandin was to be used for the treatment of type 2 diabetes in combination with a thiazolidinedione (another type of anti-diabetes medicine) such as rosiglitazone or pioglitazone, in patients whose blood sugar levels could not be controlled by a thiazolidinedione taken alone.

How does NovoNorm/Prandin 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. NovoNorm/Prandin helps the pancreas to produce more insulin at mealtimes and is used to control type 2 diabetes. Type 2 diabetes is also known as non-insulin-dependent diabetes mellitus or maturity onset diabetes.

What documentation did the company present to support its application to the CHMP?
The company presented information on 2 clinical studies, involving 498 patients with type 2 diabetes. The studies compared the effects of NovoNorm/Prandin combined with either rosiglitazone or pioglitazone, compared to the medicines taken alone. Both studies included patients whose blood sugar levels were not controlled satisfactorily with a sulphonylurea or metformin (other antidiabetic medicines). The studies measured the level of a substance in the blood (glycosylated haemoglobin, HbA1c) after 24 weeks of treatment. HbA1c gives an indication of how well the blood glucose is controlled.

How far into the evaluation was the application when it was withdrawn?
The application was at day 175 when the company withdrew. After the CHMP had assessed the responses from the company to a list of questions, there were still some unresolved issues outstanding.

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The CHMP may take 90 days or more to adopt an opinion after it has received an application for a change to a marketing authorisation. Following the CHMP's opinion, it usually takes around 6 weeks for the European Commission to update the licence.

What was the recommendation of the CHMP at that time?
Based on the review of the data submitted for this variation and the company's response to the CHMP list of questions at the time of the withdrawal, the CHMP had some concerns and was of the provisional opinion that NovoNorm/Prandin in combination with a thiazolidinedione could not have been approved for the treatment of type 2 diabetes.

What were the concerns of the CHMP at the time of the withdrawal?
The major concern of the CHMP was that the studies presented by the company did not support the requested change in the marketing authorisation, as the patients treated in the studies had not been treated with the highest permitted dose of either rosiglitazone or pioglitazone before entering the studies. Consequently, they could not be regarded as having failed treatment with thiazolidinediones. In addition, the CHMP was concerned that the studies did not compare NovoNorm/Prandin with a thiazolidinedione to a combination of a thiazolidinedione with sulphonylurea, which is an approved treatment for patients who have failed to respond to a thiazolidinedione taken alone.
Therefore, at the time of the withdrawal, the CHMP's view was that a benefit of NovoNorm/Prandin in combination with a thiazolidinedione had not been sufficiently demonstrated and any benefits did not outweigh the identified risks.

What were the reasons given by the company to withdraw the application?
The letter from the company notifying the EMEA of the withdrawal of the application is available here.

What are the consequences of the withdrawal for patients undergoing clinical trials with NovoNorm/Prandin?
The withdrawal has no consequences for patients currently included in clinical trials with NovoNorm/Prandin. If you are in a clinical trial and need more information about your treatment, contact the doctor who is giving it to you.

What is happening with NovoNorm/Prandin used in its current indications?
There are no consequences for NovoNorm/Prandin's use in the indications for which it is already authorised, where the known benefit and risk remain unchanged.