European Medicines Agency

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QUESTIONS AND ANSWERS ON THE WITHDRAWAL OF THE MARKETING APPLICATION for SYNORDIA

International non-proprietary name (INN): ***fenofibrate/metformin hydrochloride***

On 7 December 2006, Fournier Laboratories Ireland Ltd officially notified the Committee for Medicinal Products for Human Use (CHMP) that they wish to withdraw their application for a marketing authorisation for Synordia, for the improvement of glycaemic control and dyslipidaemia in patients with type 2 diabetes.

What is Synordia?
Synordia is a medicine containing the active substances fenofibrate and metformin hydrochloride. The tablets contain 80 mg fenofibrate and 500 mg metformin, 80 mg fenofibrate and 850 mg metformin, or 54 mg fenofibrate and 850 mg metformin.

What was Synordia expected to be used for?
Synordia was to be used to improve levels of sugar and fat in the blood of patients with type 2 diabetes, along with changes to diet and exercise. It was intended for use in patients who require both fenofibrate and metformin, and whose condition had already been stabilised by taking these two medicines separately.

How is Synordia expected to work?
Type 2 diabetes is a disease in which the pancreas does not make enough insulin to control the level of glucose (sugar) in the blood. Patients with type 2 diabetes often have dyslipidaemia (abnormal levels of fat in the blood), such as low levels of high-density lipoprotein (HDL or 'good') cholesterol and high levels of triglycerides.
The active substances in Synordia, fenofibrate and metformin, are both well-known medicines: fenofibrate is a serum lipid reducing agent that has been available in the European Union since 1975, and metformin hydrochloride is an anti-diabetic medicine that has been available since 1959. They are combined into one tablet in Synordia in order to reduce the number of tablets the patients need to take every day. It was hoped that this would make it easier for patients to stick to their treatment.
Fenofibrate can help to correct blood fat levels by activating a receptor within cells called 'peroxisome proliferator activated receptor (PPAR) alpha'. This receptor is normally involved in controlling levels of fat in the body. By activating this receptor, the medicine increases levels of HDL cholesterol and decreases levels of triglycerides and other types of fat.
Metformin reduces elevated blood glucose levels. It works mainly by inhibiting glucose production and reducing its absorption in the gut.
As a result of the action of both substances, the blood fat and glucose levels were expected to improve.

What documentation did the company present to support its application to the CHMP?
The company presented the results of 2 main studies including 1065 patients. Both studies compared the effects of various doses of fenofibrate and metformin taken as separate medicines. The doses were the same as the 3 doses available in Synordia tablets.
The first study included 382 patients with type 2 diabetes and high blood triglyceride levels who were already being treated with metformin. It examined the effect of adding fenofibrate to the patients'

7 Westferry Circus, Canary Wharf, London E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 75 23 71 29
E-mail: mail@emea.europa.eu http://www.emea.europa.eu

existing treatment. The main measure of effectiveness was the change in blood triglyceride levels after 12 weeks.
The second study examined the effects of a combination of the 2 active substances in 683 patients with abnormal levels of glucose or fat in the blood. Around half of the patients in this study had type 2 diabetes. The main measure of effectiveness was the proportion of patients whose blood glucose and fat levels had returned to within the normal range after 12 weeks of treatment.

How far into the evaluation was the application when it was withdrawn?
The application was at day 113 when the company withdrew.
The CHMP was evaluating the initial documentation provided by the company.
The CHMP normally takes up to 210 days to evaluate a new application. Based on the review of the initial documentation, the CHMP prepares a list of questions at day 120, which is sent to the company. Once the company has supplied responses to the questions, the CHMP reviews them and may, before giving an opinion, ask any remaining questions at day 180. Following the CHMP's opinion, it usually takes around 2 months for the European Commission to grant a licence.

What was the recommendation of the CHMP at that time?
The CHMP was evaluating the initial documentation provided by the company and had not yet made any recommendations.

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 Synordia?
The company informed the CHMP that there are no consequences for patients currently included in clinical trials of Synordia. If you are in a clinical trial and need more information about your treatment, contact the doctor who is giving it to you.