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Questions and answers on the withdrawal of medicines containing benfluorex

The European Medicines Agency has completed a review of the safety and effectiveness of benfluorex. The Agency's Committee for Medicinal Products for Human Use (CHMP) has concluded that the benefits of benfluorex no longer outweigh its risks, and that all marketing authorisations for medicines containing benfluorex should be revoked throughout the European Union (EU).

The review was carried out under an 'Article 107' procedure[1].

What is benfluorex?

Benfluorex was used as an add-on treatment in patients with diabetes who are overweight. It was used in combination with an appropriate diet.

Benfluorex works by making the cells more sensitive to insulin, which means that the body makes better use of the insulin it produces and the blood glucose is reduced. It also has an effect on the liver by increasing the production of glycogen (the storage form of glucose in the liver). This has been known to make patients feel less hungry (appetite suppressant).

Medicines containing benfluorex were first authorised in 1974. At the time of this review,they were available as tablets containing 150 mg benfluorex hydrochloride in France and Portugal[2] under the following invented names, Mediator, Benfluorex Mylan and Benfluorex Qualimed.

Why was benfluorex reviewed?

Since its marketing authorisation, the safety of benfluorex has been reviewed several times. In 2007, a re-assessment of the benefit–risk balance led to the withdrawal of the indication for the use in patients with high blood levels of triglycerides, a type of fat. In November 2009, following several reports of cardiac valvulopathy (thickening of the heart valves) and pulmonary arterial hypertension (high blood pressure in the artery that leads from the heart to the lungs), the French medicines regulatory authority carried out a review of the safety of benfluorex and decided to suspend its marketing authorisation. As a result, benfluorex-containing medicines were taken off the market in France.

[1] Article 107 of Directive 2001/83/EC as amended.
[2] Benfluorex-containing products are also authorised but not marketed in Cyprus and Luxemburg.

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Shortly after, as a precautionary measure, the Portuguese medicines regulatory authority also decided to recall these medicines from the market.

As required by Article 107, the French authority informed the CHMP of its action so that the Committee could prepare an opinion on whether the marketing authorisations for products containing benfluorex should be maintained, changed, suspended or revoked across the EU.

Which data has the CHMP reviewed?

The CHMP has reviewed available information on the safety and efficacy of benfluorex-containing medicines, particularly data on the associated risk of heart valve diseases and pulmonary arterial hypertension. The review included information provided by the market leader from clinical trials, information published in scientific journals, and 'spontaneous reports' of side effects from patients to the companies that make the medicines or health authorities.

What are the conclusions of the CHMP?

The CHMP noted that the available data show that the effect of benfluorex in the treatment of diabetes is only limited. In addition, there is risk of valve diseases with the use of benfluorex, which was confirmed in a new study conducted in October 2009. Therefore, on the basis of the evaluation of these data and the scientific discussion within the Committee, the CHMP concluded that the benefits of benfluorex-containing medicines do not outweigh their risks, and therefore recommended that the marketing authorisation of these medicines be revoked.

What are the recommendations for patients and prescribers?

- Patients who are currently treated with benfluorex-containing medicines should, when convenient, make an appointment with their doctor to change their prescription.
- Doctors should stop prescribing benfluorex. Alternative treatments should be used as appropriate, based on each patient's symptoms and risk profile.
- Patients who have been treated with these medicines in the past should mention this to their doctor, who will look for the signs and symptoms of heart valve disease.
- Patients who have any questions should speak to their doctor or pharmacist.

The European Commission issued a decision on 14 June 2010.

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