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PRAC recommends modified-release paracetamol be removed from market

Overdose complex and difficult to manage with modified-release products

Following a review, the European Medicines Agency's experts in medicines safety have recommended that modified- or prolonged-release paracetamol products (designed to release paracetamol slowly over a longer period than the usual immediate-release products) should be suspended from marketing. This is in view of the risks to patients from the complex way these medicines release paracetamol into the body after an overdose.

The review of modified-release paracetamol has been carried out by EMA's Pharmacovigilance Risk Assessment Committee (PRAC), following a request from the Swedish medicines authority, the Medical Products Agency, which had noted problems in managing overdose with such a product since marketing approval. The PRAC evaluated published studies and reports of overdose with these medicines, consulted experts in the management of poisoning and assessed how overdose with paracetamol is managed in the EU and other parts of the world.

Experience has shown that in overdose (particularly at high doses), because of the way the paracetamol in modified-release products is released in the body, the usual treatment procedures developed for immediate-release products are not appropriate. If doctors are not aware modified-release paracetamol has been taken, which affects decisions such as when and for how long to give an antidote, overdose might result in severe liver damage or death. In modified-release products that also contain the painkiller tramadol this could be complicated further because of the additional effects of overdose with tramadol.

In many cases, it may not be known whether an overdose of paracetamol involves immediate-release or modified-release products, making it difficult to decide what type of management is needed. The Committee could not identify means to minimise the risk to patients, or a feasible and standardised way to adapt the management of paracetamol overdose across the EU to allow for treatment of cases that involve modified-release preparations. It concluded on balance that the risk following overdose with these medicines outweighs the advantage of having a longer-acting preparation. The Committee therefore recommended that marketing of modified-release paracetamol medicines should be suspended. Immediate-release paracetamol products, which are not affected by this review, will continue to be available as before.

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As the medicines involved are all authorised by national procedures, the PRAC recommendations will now be sent to the CMDh which will adopt a position.[1]

When used appropriately and in recommended doses the benefits of paracetamol outweigh its risks. It remains important that patients seek medical advice quickly if they have taken, or think they may have taken, more than the recommended amount of any paracetamol-containing product. Patients should also consult a healthcare professional if they have any other concerns about their medication.

More about the medicine

Paracetamol is a medicine that has been widely used for many years to relieve pain and fever in adults and children. Paracetamol-containing immediate-release products have been authorised in all EU Member States but are not included in this review.

Products covered by this review contain paracetamol for modified-release and are intended to be taken by mouth and have a longer action. They are available in Belgium, Denmark, Finland, Luxembourg, Portugal, Romania, and Sweden under various names including Alvedon 665 mg, Panadol Artro, Panadol Extend, Panadol Retard 8 hours, Panodil 665 mg, Paratabs Retard and Pinex Retard. Modified-release medicines containing paracetamol with the opioid painkiller tramadol are available under the names Diliban Retard or Doreta in Bulgaria, Czech Republic, Estonia, Hungary, Iceland, Latvia, Lithuania, Poland, Portugal, Romania, Slovakia, Slovenia and Spain, and these medicines are also covered by this review.

More about the procedure

The review of modified-release paracetamol was initiated on 30 June 2016 at the request of Sweden, under Article 31 of Directive 2001/83/EC.

The review has been carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which has made a set of recommendations. The PRAC recommendations will now be sent to Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), which will adopt a position. The CMDh is a body representing EU Member States as well as Iceland, Liechtenstein and Norway. It is responsible for ensuring harmonised safety standards for medicines authorised via national procedures across the EU.

[1] The companies concerned by this review have the right to request the PRAC to re-examine its recommendations before they are sent to CMDh