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# Review of terlipressin medicines started

EMA has started a review of medicines that contain terlipressin. These medicines are authorised in several EU countries to treat kidney problems in people with advanced liver disease (hepatorenal syndrome; HRS), as well as bleeding from enlarged veins in the passage between the mouth and the stomach (the oesophagus) and certain forms of bleeding associated with surgery.

EMA's safety committee (PRAC) started this review due to safety concerns about results from a large clinical trial[1] involving patients with a form of HRS where kidney function declines rapidly. The results suggest that patients who were treated with terlipressin were more likely to experience and die from respiratory disorders within 90 days after the first dose than those who were given placebo (a dummy treatment). Respiratory disorders, such as respiratory failure (severe breathing difficulties), are a known risk of these medicines. However, the frequency of respiratory failure seen in this study (10%) was higher than reported in the product information, where it is listed as uncommon (i.e., affecting up to 1% of patients).

As a result of these concerns, the Danish medicines agency requested a review of the safety of terlipressin medicines in the context of their benefits when used to treat HRS. At present, this review does not cover the use of terlipressin for the treatment of bleeding, since no new information on safety concerns has emerged for these uses. While the review is ongoing, terlipressin can continue to be used for these indications as well as for the treatment of HRS, according to the authorised product information.

EMA will communicate PRAC's recommendations once the review has concluded.

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**More about the medicine**

Terlipressin is a vasopressin analogue. This means that it works in the same way as the natural hormone vasopressin to cause narrowing of certain blood vessels in the body, in particular those that supply the abdominal organs. In patients with HRS, increased blood pressure in the liver due to liver failure leads to widening of these blood vessels. This causes an imbalance in the blood circulation, resulting in poor blood supply to the kidneys. By narrowing the blood vessels that supply the

[1] Wong F, et al. Terlipressin plus albumin for the treatment of type 1 hepatorenal syndrome. N Engl J Med. 2021 Mar 4;384(9):818-828. doi: 10.1056/NEJMoa2008290

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abdominal organs, terlipressin helps to restore blood flow to the kidneys, thereby improving kidney function.

Terlipressin is available as a solution and a powder for solution - both for intravenous use.

Terlipressin-containing medicines are available in the majority of EU member states and under a variety of names including Glypressin, Terlipressin Acetate and Variquel.

**More about the procedure**

The review of terlipressin has been initiated at the request of Denmark, under Article 31 of Directive 2001/83/EC.

The review is being carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which will make a set of recommendations. As terlipressin-containing medicines are all authorised nationally, the PRAC recommendations will be forwarded to the 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.