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EMA concludes review of anxiety medicine Stresam (etifoxine)

On 27 January 2022, EMA's human medicines committee (CHMP) finalised its review of Stresam (etifoxine) and concluded that the medicine can continue to be used for the treatment of anxiety disorders, but it must not be used in patients who previously had severe skin reactions or severe liver problems after taking etifoxine.

During the review, the CHMP assessed all available data on the benefits and risks of Stresam, including the results of a study (AMETIS) on the efficacy of etifoxine in treating adjustment disorders with anxiety (where people have difficulty coping with stressful events). The Committee also assessed safety data from clinical studies and post-marketing experience.

EMA concluded that Stresam can continue to be used for the treatment of anxiety disorders in some patients, but restrictions on its use have been put in place to minimise the risk of very rare but serious side effects that may occur with etifoxine. The medicine must not be used in patients who experienced severe skin reactions (including DRESS syndrome, Stevens Johnson syndrome and generalised exfoliative dermatitis) or severe liver damage (severe hepatitis or cytolytic hepatitis) with previous etifoxine treatment, and treatment must be stopped if signs of skin reactions or liver problems appear. In patients at risk of liver problems, liver function tests should be performed before starting treatment and around one month after treatment has started. In addition, the company that markets Stresam will have to conduct a study to further characterise the effects of etifoxine in patients with anxiety.

The product information for Stresam will be updated to include the above recommendations.

Information for patients

- Stresam (etifoxine) can continue to be used for the treatment of anxiety disorders.
- Stresam must not be used in patients who had serious skin reactions or liver damage following previous treatment with etifoxine.
- Patients should stop taking the medicine and seek urgent medical attention if they experience:
  - severe skin or allergic reactions;
  - jaundice (yellowing of the skin and eyes), vomiting, tiredness, abdominal (belly) pain - these could be signs of severe liver problems;
  - watery diarrhoea.

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- If you are at risk of developing liver problems, your doctor will do some tests to check your liver function before starting Stresam and around one month after you start treatment.
- If you are taking Stresam and have any questions or concerns, speak to your doctor or pharmacist.

Information for healthcare professionals

- Very rare cases of severe dermatological reactions (including DRESS syndrome, Stevens Johnson Syndrome (SJS) and generalised exfoliative dermatitis) and severe cytolytic hepatitis have been reported in patients treated with Stresam.
- Stresam is now contraindicated in patients who had severe dermatological reactions or severe cases of hepatitis or cytolytic hepatitis during previous treatment with etifoxine.
- Patients should be instructed to stop taking Stresam and seek urgent medical care if they experience:
  - severe skin or allergic reactions;
  - jaundice, vomiting, tiredness, abdominal pain, which can be indicative of severe liver problems;
  - watery diarrhoea.
- In patients with risk factors for hepatic disorders (such as elderly patients, patients with medical history of previous viral hepatitis or other conditions), liver function tests should be performed before starting Stresam and around one month after treatment initiation.
- Few cases of lymphocytic colitis have been reported with the use of Stresam. Appropriate examinations should be considered in case of watery diarrhoea during treatment.

A letter summarising the above recommendations will be sent in due course to healthcare professionals prescribing, dispensing or administering the medicine.

More about the medicine

Stresam is authorised in France, Malta, Bulgaria and Romania for the treatment of anxiety disorders. The medicine contains the active substance etifoxine. The exact way etifoxine works is not fully understood, but it is known to attach to the same targets (receptors) on nerve cells as GABA (gamma-amino butyric acid). GABA is a neurotransmitter (a chemical that nerve cells use to communicate) that blocks certain brain signals. Etifoxine mimics the effect of GABA both directly and indirectly, leading to a calming effect that helps to control the symptoms associated with anxiety.

Stresam is available as capsules that are taken daily for a few days up to a number of weeks.

In 2014, the French medicines agency put in place risk minimisation measures (update to the product information and a letter to healthcare professionals) to mitigate the risk of certain side effects identified at that time. The company was also asked to perform additional studies, including the AMETIS study.

More about the procedure

The review of Stresam was initiated in June 2021 at the request of France, under Article 31 of Directive 2001/83/EC.

The review was carried out by the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which adopted the Agency's opinion. The CHMP opinion was forwarded to the European Commission, which issued a final legally binding decision applicable in all EU Member States on 24 March 2022.