# Direct Healthcare Professional Communication

June 2022

**Severe dermatological reactions and cytolytic hepatitis with etifoxine, 50 mg capsules (Stresam® and generics, etifoxine): new contraindications, warnings and precautions for use**

*Information for general practitioners, psychiatrists and pharmacists.*

Dear Healthcare professionals,

BIOCODEX company, in agreement with the European Medicines Agency (EMA), would like to inform you about the update of the marketing authorization of Stresam® and its generics, regarding the contraindications, warnings and precautions for use, and undesirable effects. This modification follows the re-evaluation, by the European Medicines Agency (EMA), of the benefit-risk balance of Stresam® which remains favourable.

## Summary

- **Etifoxine is now contraindicated in patients who had severe dermatological reactions or severe cases of hepatitis or cytolytic hepatitis during previous treatment with etifoxine.**

- **Healthcare professionals should inform the patients to stop taking etifoxine and seek urgent medical care if they experience the following undesirable effects:**
  - **severe skin or allergic reactions;**
  - **jaundice, vomiting, tiredness, and abdominal pain, which can be indicative of severe liver problems;**
  - **watery diarrhoea.**

- **In patients with risk factors for hepatic disorders, liver function tests should be performed before starting etifoxine and after treatment initiation.**

### Further information

The analysis of pharmacovigilance data confirms the risk of very rare but serious adverse reactions such as severe dermatological reactions, severe hepatic disorders, lymphocytic colitis and metrorrhagia, which may occur during treatment with etifoxine.

Etifoxine is now contraindicated in patients who had severe dermatological reactions such as drug reaction with eosinophilia and systemic symptoms (DRESS syndrome),

Stevens-Johnson Syndrome (SJS) and generalized exfoliative dermatitis, or severe cases of hepatitis or cytolytic hepatitis during previous treatment with etifoxine.

**Skin toxicity** induced by etifoxine usually has an onset ranging from a few days to one (1) month of treatment, depending on the reactions. The outcomes of these skin reactions are mostly favourable after etifoxine withdrawal and no fatal outcome due to severe cutaneous adverse reactions has been reported with etifoxine.
Thus,

- **Patients should be aware of this risk of skin toxicity;**
- **The occurrence of cutaneous signs and symptoms should be closely monitored;**
- **In case of skin toxicity with etifoxine, the medicinal product should be immediately discontinued and never reintroduced.**

**Hepatic disorders** induced by etifoxine usually have an onset ranging from two (2) weeks and one (1) month of treatment. Hepatic disorders can be asymptomatic and detected only through specific laboratory tests. Caution should be taken in patients with risk factors for hepatic disorders such as elderly patients, patients with a medical history of previous viral hepatitis or any other conditions identified on an individual basis by the practitioner. **In patients with risk factors for hepatic disorders:**

- **liver function tests should be performed before starting etifoxine and around one (1) month after treatment initiation**;
- **In case of liver toxicity with etifoxine, the treatment should be immediately discontinued and never reintroduced.**

Since marketing authorization, rare cases of lymphocytic colitis have been reported with the use of etifoxine. **Appropriate examinations should be considered in case of watery diarrhoea in patients treated with etifoxine. In case of watery diarrhoea with etifoxine, the medicinal product should be immediately discontinued**.

**Call for reporting**

Suspected Adverse Drug Reactions (side effects) or medication errors may be reported using the Medicines Authority ADR reporting form available online at www.medicinesauthority.gov.mt/adrportal and sent to Pharmacovigilance Section at Post-Licensing Directorate, Medicines Authority**,** Sir Temi Zammit Buildings, Malta Life Sciences Park, San Gwann SGN, Malta, or sent by email to: postlicensing.medicinesauthority@gov.mt.

Suspected Adverse Drug Reactions (side effects) or medication errors may be reported to the Pharmacovigilance Unit at Medina Healthcare Ltd. (Malta) Mr Josie Cachia (RPPV) +35699862709 or Ms Rodianne Galea Bondin (Deputy RPPV) +35699320419 or to Biocodex (Marketing Authorization Holder, France) at vigilance@biocodex.fr.

**Company contact points**

If you have any questions or require further information, you can contact the Pharmacovigilance Unit at Medina Healthcare Ltd. (Malta) Mr Josie Cachia (RPPV) +35699862709 or Ms Rodianne Galea Bondin (Deputy RPPV) +35699320419.