Core Safety Profile

Active substance: Tianeptine
Pharmaceutical form(s)/strength: coated tablet
P-RMS: FR/H/PSUR/0068/001
Date of FAR: 13.03.2014
4.3. Contra-indications

- Association with MAO inhibitors
  There should be an interval of two weeks between the end of treatment with a MAO inhibitor and the beginning of treatment with tianeptine, and at least 24 hours is required when replacing tianeptine with a MAOI.

- Hypersensitivity to the active substance or to any of the excipients.

4.4. Special warnings and precautions for use

- Suicide/suicidal thoughts or clinical worsening: Depression is associated with an increased risk of suicidal thoughts, self-harming and suicidality (suicidal behaviour). This risk persists until a significant remission has been obtained. Clinical improvement may not be obtained until after several weeks of treatment, and so patients must be closely monitored until this improvement has been achieved. Clinical experience shows that the risk of suicide can increase during the very early stages of recovery. Patients with a history of suicidal behaviour or expressing significant suicidal thoughts before starting the treatment face a higher risk of the onset of suicidal thoughts or suicidal behaviour, and must be closely monitored during treatment. A meta-analysis of placebo-controlled clinical trials of the use of antidepressants in adults displaying psychiatric disorders has revealed an increase in the risk of suicidal behaviour in patients under 25 years of age who were being treated with antidepressants compared to those receiving a placebo. Careful monitoring of patients, and particularly of high-risk patients, must accompany use of this medication, particularly at the beginning of treatment and at times of dose changes.
  The patients (and their family and friends) must be alerted to the need to monitor for the onset of clinical worsening, the appearance of suicidal thoughts/behaviour or any abnormal change of behaviour, and to seek medical advice immediately if such symptoms present.

- As with any psychotropic drug, the intake of alcohol should be avoided during the treatment with tianeptine.

- If general anaesthesia is necessary, the anaesthetist should be informed of the treatment, and the drug stopped 24 or 48 hours prior to surgery.

- In an emergency, surgery may be performed without an intervening wash-out period; peroperative monitoring should be performed.

- As with all psychotropic agents, if the treatment is to be interrupted the dosage should be gradually reduced over a period of 7 to 14 days.

- If there is a history of drug dependence or alcohol dependence, the patients must be kept under very close surveillance in order to avoid any increase in dosage.

- Do not exceed the recommended doses.

- Due to the sucrose content, this medicinal product is contraindicated for patients with fructose intolerance, glucose and galactose malabsorption syndrome or sucrase-isomaltase deficiency (rare inherited diseases).

- Use in children and adolescents: Tianeptine is not recommended in the treatment of depression in patients under 18 years of age since safety and efficacy of tianeptine have not been established in this age group. In clinical trials among children and adolescents treated with other antidepressants, suicide-
related behaviour (suicide attempt and suicidal thoughts), and hostility (predominantly aggression, oppositional behaviour and anger) were more frequently observed compared to those treated with placebo.

4.5. Interactions with other medicinal products and other forms of interactions

UNADVISABLE COMBINATIONS

- With irreversible MAO inhibitors (iproniazide)
Risk of cardiovascular collapse or paroxysmal hypertension, hyperthermia, convulsions, death.

4.6. Fertility, pregnancy and lactation

- Pregnancy:
It is preferable to maintain a balanced maternal psychic equilibrium throughout pregnancy. If medical treatment is necessary to ensure this balance, treatment should be initiated or continued at the necessary dose throughout pregnancy and if possible as monotherapy.

Animal trials are reassuring but clinical data is still insufficient.
In consideration of this data, it is preferable not to use tianeptine during pregnancy whatever the term. If initiation or continuation of treatment with tianeptine proves to be vital during pregnancy, the pharmacological profile of the molecule should be taken into account when monitoring the newborn baby.

- Breast feeding:
Tricyclic antidepressants are excreted in into breast milk, and thus breast feeding is not recommended during treatment.

4.7. Effects on ability to drive and use machines

Some patients may experience diminished alertness. The attention of drivers and machine-operators should thus be drawn to the risk of somnolence with this product.

4.8. Undesirable effects

The following undesirable effects have been observed during treatment with tianeptine and ranked under the following frequency:
Very common (> 1/10) ; common (> 1/100 to <1/10) ; uncommon (> 1/1,000 to < 1/100) ; rare (> 1/10,000 to <1/1,000) ; very rare (> 1/100,000 to <1/10,000), not known (cannot be estimated from the available data).

- Metabolism and nutrition disorders:
Common: Anorexia
Not known: Hyponatremia

- Psychiatric disorders:
Common: Nightmare
Uncommon: Drug abuse and dependence, in particular in subjects less than 50 years old with a history of alcohol or drug dependence.
Not known:
  • Cases of suicidal thought or behaviour have been reported during treatment with tianeptine or shortly after discontinuation (see section 4.4).
  • Confusional state, hallucination

- **Nervous system disorders:**
  Common: Insomnia, somnolence, dizziness, headache, lipothymia, tremor.
  Not known: Extrapyramidal disorder, dyskinesia.

- **Cardiac disorders:**
  Common: Tachycardia, extrasystoles, chest pain.

- **Vascular disorders:**
  Common: Hot flush

- **Respiratory disorders:**
  Common: Dyspnoea

- **Gastrointestinal disorders:**
  Common: Gastralgia, abdominal pain, dry mouth, nausea, vomiting, constipation, flatulence.

- **Skin disorders:**
  Uncommon: Maculopapular or erythematous rash, pruritus, urticaria.
  Unknown: Acne, dermatitis bullous in exceptional cases.

- **Musculoskeletal disorders:**
  Common: Myalgia, lumbar pain.

- **General disorders:**
  Common: Asthenia, lump feeling in throat.

- **Hepato-biliary disorders:**
  Not known: Increased liver enzymes, hepatitis that can, in exceptional cases, be severe.

### 4.9. Overdose

In all cases, stop treatment and monitor the patient closely.

- Gastric lavage
- Cardiopulmonary, metabolic and renal monitoring
- Symptomatic treatment of any clinical manifestations, especially assisted ventilation and correction of metabolic and renal disorders.