

SUMMARY OF PRODUCT CHARACTERISTICS**STABLON****INN : Tianeptine****1. NAME OF THE MEDICINAL PRODUCT**

Stablon 12.5 mg, coated-tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Tianeptine (INN) Sodium salt 12.5 mg

Excipients : q.s. for one coated tablet.

3. PHARMACEUTICAL FORM

Coated-tablet

4. CLINICAL PARTICULARS**4.1. THERAPEUTIC INDICATIONS**

Major depressive episodes (i.e. typical).

4.2. POSOLOGY AND METHOD OF ADMINISTRATION

The recommended dosage is 1 tablet (12.5 mg) three times a day (morning, midday and evening) at the beginning of the main meals.

In chronic alcoholics, whether cirrhotic or not, no alteration of dosage is necessary.

In subjects aged over 70 years, and in subjects with renal insufficiency, the dosage should be restricted to 2 tablets per day.

4.3. CONTRA-INDICATIONS

- Children under 15 years old.
- Association with MAOIs.
- A wash-out period of two weeks is necessary between treatment with MAOIs and treatment with tianeptine. A wash-out period of only 24 hours is required when replacing tianeptine with an MAOI.

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 those 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.

If general anaesthesia is necessary, the anaesthetist should be informed of the treatment, and the drug discontinued 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).

4.5. INTERACTIONS WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

Combination that are inadvisable

- + With non-selective MAOIs : risk of cardiovascular collapse or paroxysmal hypertension, hyperthermia, convulsions, death.
- + With mianserine : because of its antagonistic effect in the experimental model

4.6. 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 by tianeptine proves to be vital during pregnancy, the pharmacological profile of the molecule should be taken into account when monitoring the newborn baby.

Lactation :

Tricyclic antidepressants are excreted 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 drowsiness with this product.

4.8. UNDESIRABLE EFFECTS

Rare:

- epigastric pain, abdominal pain, dry mouth, anorexia, nausea, vomiting, constipation, flatulence,
- insomnia, drowsiness, nightmares, asthenia,
- tachycardia, extrasystoles, precordial pain,
- vertigo, headache, lipothymia, tremor, hot flushes,
- respiratory discomfort, lump in the throat,
- myalgia, lumbagos,
- abuse, dependence, in particular in subjects under 50 years of age with a history of drug dependence or alcohol dependence.

Cases of suicidal thoughts or behaviour have been reported during STABLON treatment or shortly after its discontinuation (see § 4.4.).

4.9. OVERDOSAGE

In all cases, stop treatment and keep the patient under close surveillance.

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

5. PHARMACOLOGICAL PROPERTIES

5.1. PHARMACODYNAMIC PROPERTIES

ANTI-DEPRESSANT

Tianeptine is an antidepressant :

In animals, Tianeptine has the following properties:

- Tianeptine increases the spontaneous activity of pyramidal cells in the hippocampus and accelerates their recovery after functional inhibition,
- Tianeptine increases the rate of serotonin re-uptake by neurons in the cortex and hippocampus.

In man, Tianeptine is characterized by :

- an action on mood disturbances giving it an intermediate position in the bipolar classification between sedative antidepressants and stimulant antidepressants,
- marked action on somatic complaints, especially gastrointestinal complaints related to anxiety and mood disturbances.

Moreover, Tianeptine has no effect on :

- sleep and alertness,
- the cholinergic system (no anticholinergic symptoms).

5.2. PHARMACOKINETICS PROPERTIES

Gastrointestinal absorption is rapid and complete.

Distribution is rapid, and is associated with a high level of protein binding (approximately 94%). The molecule is extensively metabolised in the liver by the processes of beta-oxidation and N-demethylation.

The elimination of tianeptine is characterised by a short terminal half life of 2½h, with essentially renal excretion of the metabolites.

In elderly subjects : pharmacokinetics studies performed in chronically treated elderly patients (aged over 70 years) demonstrated an increase of one hour in the elimination half-life.

In subjects with hepatic insufficiency : studies have shown that the effects of chronic alcoholism on the pharmacokinetic parameters are negligible, even when the alcoholism is associated with cirrhosis of the liver.

In subjects with renal insufficiency : studies have shown an increase of one hour in the elimination half-life.