

SUMMARY OF PRODUCT CHARACTERISTICS

1. TRADE NAME OF THE MEDICINAL PRODUCT

Triptafen 25mg/2mg Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Actives

Amitriptyline Hydrochloride 25.0 mg

Perphenazine 2.0 mg

Also contains

Lactose 49.5 mg

Sucrose 66 mg

Butyl hydroxybenzoate 0.0313mg

Tartrazine (E102) 0.0019mg

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Coated tablet (Tablet)

Round, pink, biconvex, sugar-coated tablets engraved on one side with Evans/ 1D.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Triptafen tablets are indicated for the treatment of depression associated with anxiety, psychosomatic disorders, withdrawal syndrome in chronic alcoholism.

4.2 Posology and Method of Administration

One tablet orally three times daily with a further tablet at night if necessary.

Failure to respond within four weeks is an indication to review treatment. In all cases treatment should not continue beyond three months without reassessment.

Triptafen preparations are not suitable for administration to children under fourteen years of age.

4.3 Contra-indications

Glaucoma, urinary retention, concurrent administration of other antidepressant drugs particularly monoamine oxidase inhibitors. No triptafen preparation should be given to patients with leucopenia, or in association with drugs liable to cause bone marrow depression. Acute recovery from myocardial infarction, cardiac arrhythmias, lactation and breast feeding. Hypersensitivity to dibenzazepines, phenothiazines or to any component of the product.

Patients with rare hereditary of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.4 Special Warnings and Special Precautions for Use

Persistent oral dyskinesia has been reported occasionally, particularly in elderly female patients after long term treatment with potent phenothiazine drugs including perphenazine. Consequently, Triptafen should be used with caution in elderly patients. Caution is also advised in patients with epilepsy and impaired liver function.

Amitriptyline should not be used in the treatment of children and adolescents under the age of 18 years. Studies in depression in this age group did not show a beneficial effect for tricyclic antidepressants. Studies with other classes of antidepressants such as monoamine-oxidase inhibitors (e.g. tranylcypromine, phenelzine), selective serotonin re-uptake inhibitors (e.g. citalopram, fluoxetine), other antidepressant drugs (e.g. flupentixol, mirtazapine) have shown a risk of suicidality, self-harm and hostility related to these compounds. This risk cannot be excluded with amitriptyline. In addition, amitriptyline is associated with a risk of cardiovascular adverse events in all age groups. Furthermore, long term safety data in children and adolescents concerning growth, maturation and cognitive and behavioural development are not available (see also section 4.8 Undesirable effects and section 4.9 Overdose). Caution in patients with cardiovascular disease or family history of QT prolongation. Avoid concomitant antipsychotics.

Suicide/suicidal thoughts or clinical worsening

Depression is associated with an increased risk of suicidal thoughts, self harm and suicide (suicide-related events). This risk persists until significant remission occurs. As improvement may not occur during the first few weeks or more of treatment, patients should be closely monitored until such improvement occurs. It is general clinical experience that the risk of suicide may increase in the early stages of recovery.

Other psychiatric conditions for which Triptafen is prescribed can also be associated with an increased risk of suicide-related events. In addition, these conditions may be co-morbid with major depressive disorder. The same precautions observed when treating patients with major depressive disorder should therefore be observed when treating patients with other psychiatric disorders

Patients with a history of suicide-related events, or those exhibiting a significant degree of suicidal ideation prior to commencement of treatment are known to be at greater risk of suicidal thoughts or suicide attempts, and should receive careful monitoring during treatment. A meta-analysis of placebo-controlled clinical trials of antidepressant drugs in adult patients with psychiatric disorders showed an increased risk of suicidal behaviour with antidepressants compared to placebo in patients less than 25 years old.

Close supervision of patients and in particular those at high risk should accompany drug therapy especially in early treatment and following dose changes. Patients (and caregivers of patients) should be alerted about the need to monitor for any clinical worsening, suicidal behaviour or thoughts and unusual changes in behaviour and to seek medical advice immediately if these symptoms present.

4.5 Interactions with Other medicinal products and other forms of Interaction

Triptafen should not be given in conjunction with monoamine oxidase inhibitors. Because of the persistent action of monoamine oxidase inhibitors an interval of at least fourteen days should be allowed to elapse between administration of a monoamine oxidase inhibitor and the introduction of triptafen. Concomitant administration with anti-hypertensives of the guanethidine type or methyl dopa may

inhibit their effects, while use with drugs having an anti-cholinergic action, sympathomimetics, ethchlorvynol, central nervous system depressants including alcohol, thyroid hormone therapy will potentiate their effects. Concurrent use with agents with a potential for bone marrow depression should be avoided. Barbiturates increase the metabolism of Triptafen whilst quinidine and cimetidine inhibit metabolism. Ritonavir may possibly increase plasma concentration of tricyclic antidepressants such as amitriptyline. Plasma levels of amitriptyline can be reduced by St. John Wort. Monitor for evidence of reduced antidepressant efficacy if the two are given together. Avoid concomitant QT prolonging drugs, drugs causing electrolyte imbalance & metabolic inhibitors (CYP_) where known.

4.6 Pregnancy and Lactation

Unless there are compelling reasons, this preparation should not be used during pregnancy, especially during the first and last trimesters. There is inadequate evidence of safety of Triptafen. The drug has been shown to cross the placenta and is excreted in breast milk.

4.7 Effects on Ability to Drive and Use Machines

Triptafen may give rise to drowsiness and occasionally blurred vision. Patients receiving this medication should not drive or operate machinery.

4.8 Undesirable Effects

Cases of suicidal ideation and suicidal behaviours have been reported during Triptafen therapy or early after treatment discontinuation (see section 4.4)

Amitriptyline may give rise to dryness of the mouth, and occasionally tachycardia. Perphenazine may cause a slight fall in blood pressure, and in addition tremor extrapyramidal side-effects have been reported. Idiosyncratic side effects, such as pruritus, nausea, diarrhoea and ingestion may occur. Also confusion, hypomania, paraesthesia, anticholinergic effects, bone marrow depression, hepatic dysfunction, headache and convulsions may be associated with this drug.

Perphenazine being a phenothiazine, may be associated with the following effects: ECG changes with prolongation of QT interval and T wave changes, cardiac arrest & Torsades de pointes. There have been rare occurrences of cases of serious arrhythmias, including tachycardia and fibrillation, ventricular arrhythmias – VF, VT, which have also occurred after overdosage. Sudden, unexpected and unexplained deaths have been reported in hospitalised psychotic patients receiving phenothiazines. Care should be taken on reducing dose or discontinuing treatment.

4.9 Overdose

Gastric lavage should be performed as soon as possible. If convulsions occur or threaten they should be controlled with standard methods, but barbiturates should be avoided. In severe cases haemodialysis may be performed if practicable.

It is recommended that patients who have taken an overdose of Triptafen should be observed for at least 48 hours even if symptoms are not severe.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Amitriptyline hydrochloride is a tricyclic antidepressant which does not inhibit monoamine oxidase. Its action is believed to be related to its ability to block the re-uptake of released monoamines into the pre-synaptic nerve endings. It has anticholinergic effects and sedative properties.

Perphenazine is a phenothiazine, which blocks dopamine receptors in the central nervous system.

5.2 **Pharmacokinetic Properties**

Amitriptyline Hydrochloride

Absorption – Readily absorbed after oral administration.

Distribution – Rapidly taken up by the tissues, may be secreted in milk.

Metabolic Reactions - Demethylation, hydroxylation, and conjugation with glucuronic acid together with some N-oxide formation. The metabolites formed include nortriptyline, didesmethylamitriptyline, their conjugates and their 10-hydroxy derivatives, and amitriptyline N-oxide.

Excretion – about 90% of an intravenous dose is excreted in the urine, 1-5% is excreted unchanged in the faeces.

Perphenazine

Absorption – Readily absorbed from the gastro-intestinal tract.

Distribution – Widely distributed throughout the body and readily crosses the placenta.

Metabolic reactions – Extensively metabolised by sulphoxidation, demethylation, hydroxylation, N-oxidation, glucuronic acid conjugation, and possibly ring fission.

Excretion – 20-70% is excreted in the urine, very little being changed. About 5% of a dose is excreted in the faeces.

5.3 **Preclinical safety data**

6. **PHARMACEUTICAL PARTICULARS**

6.1 **List of Excipients**

Tablet Core

Lactose

Magnesium stearate

Starch maize special

Starch maize pregelatinised.

Tablet Coat

Acacia

Gelatin

Butyl hydroxybenzoate

Calcium phosphate

Calcium sulphate dihydrate

Tartrazine ariavit 311840

Erythrosine ariavit 311807

Sugar

Mineral water

Opaglos aqueous AG-7350 (containing white beeswax, carnauba wax, polysorbate 20 and sorbic acid E200).

Opacode black (Shellac glaze, Iron oxide black (E172), Propylene glycol (E1520)).

6.2 Incompatibilities

Not applicable

6.3 Shelf-life

3 years

6.4 Special Precautions for Storage

This medicinal product does not require any special storage conditions.

6.5 Nature and Contents of Containers

Cardboard carton containing 10 strips of 10 tablets packed in aluminium foil.

6.6 Instructions for Use/Handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Goldshield Pharmaceuticals Limited

NLA Tower,

12-16 Addiscombe Road,

Croydon,

Surrey,

CR0 0XT

UK

8. MARKETING AUTHORISATION HOLDER

PA 899/27/1

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

Date of first authorisation: 7th July 1998

Date of last renewal: 7th July 2003

10. DATE OF REVISION OF THE TEXT

May 2009