

# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Stelazine 1mg/5ml Syrup

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml of syrup contains 1 mg of trifluoperazine as trifluoperazine hydrochloride.

Excipients: Each 5ml of syrup contains 0.01mg sunset yellow (E110) and 1.76ml sorbitol liquid (E420).

For a full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Syrup

A clear, yellow, solution with a peach aroma.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

In the management of anxiety states, and psychoses, and as an anti-emetic.

### 4.2 Posology and method of administration

#### Oral Administration:

#### Low Dosage Requirements

##### Adults:

The usual total daily dosage is 2 to 6mg in divided doses.

##### Children: Aged 6 to 12 years:

The usual total daily dosage is 1 to 4mg in divided doses.

#### High Dosage Requirements

##### Adults:

The usual total daily dosage is 5 to 25mg in divided doses.

##### Children: Aged 6 to 12 years:

The usual total daily dosage is 5mg in divided doses.

##### The Elderly:

Reduce the starting dose in elderly or frail patients by at least half.

### 4.3 Contraindications

Do not use 'Stelazine' in patients with coma particularly if associated with other central nervous system depressants. Do not use 'Stelazine' in patients with existing blood dyscrasias, or known liver damage, or in those hypersensitive to trifluoperazine, related compounds, or any of the excipients. Patients with uncontrolled cardiac decompensation should not be given 'Stelazine'.

### 4.4 Special warnings and precautions for use

'Stelazine' should be discontinued at the first sign of clinical symptoms of tardive dyskinesia and Neuroleptic Malignant Syndrome.

Patients on long-term phenothiazine therapy require regular and careful surveillance with particular attention to tardive dyskinesia and possible eye changes, blood dyscrasias, liver dysfunction, and myocardial conduction defects, particularly if other concurrently administered drugs have potential effects on these systems.

Care should be taken when treating elderly patients and the initial dosage should be reduced. Such patients can be especially sensitive, particularly to extrapyramidal and hypotensive effects. Patients with cardiovascular disease including arrhythmias should also be treated with caution. Because 'Stelazine' may increase activity, care should be taken in patients with angina pectoris. If an increase in pain is noted, the drug should be discontinued.

Patients who have demonstrated bone marrow suppression or jaundice with a phenothiazine should not be re-exposed to 'Stelazine' (or any trifluoperazine) unless in the judgement of the physician the potential effects of treatment outweigh the possible hazard.

In patients with Parkinson's disease, symptoms may be worsened, and the effects of levodopa reversed. Since phenothiazines may lower the convulsive threshold, patients with epilepsy should be treated with caution and metrizamide avoided.

Although 'Stelazine' has minimal anticholinergic activity, this should be borne in mind when treating patients with narrow angle glaucoma, myasthenia gravis or prostatic hypertrophy.

Nausea and vomiting as a sign of organic disease may be masked by the antiemetic action of 'Stelazine'.

An approximately 3-fold increased risk of cerebrovascular adverse events have been seen in randomised placebo controlled clinical trials in the dementia population with some atypical antipsychotics. The mechanism for this increased risk is not known. Stelazine should be used with caution in patients with risk factors for stroke

Caution should be used in patients with cardiovascular disease or family history of QT prolongation. Concomitant use of neuroleptics should be avoided.

Cases of venous thromboembolism (VTE) have been reported with antipsychotic drugs. Since patients treated with antipsychotics often present with acquired risk factors for VTE, all possible risk factors for VTE should be identified before and during treatment with Stelazine and preventive measures undertaken.

Acute withdrawal symptoms including nausea, vomiting and insomnia have been described after abrupt cessation of antipsychotic drugs. Recurrence of psychotic symptoms may also occur, and the emergence of involuntary movement disorders (such as akathisia, dystonia and dyskinesia) has been reported. Therefore, a gradual withdrawal is advisable.

Phenothiazines should be used with particular care in the presence of extremes of temperature since they may affect body temperature control.

Increased mortality in elderly people with Dementia:

Data from two large observational studies showed that elderly people with dementia who are treated with antipsychotics are at a small increased risk of death as compared to those who are not treated. There are insufficient data to give a firm estimate of the precise magnitude of the risk and the cause of the increased risk is not known.

Stelazine is not licensed for the treatment of dementia-related behavioural disturbances.

The excipient sorbitol liquid may have a mild laxative effect.

Sunset yellow may cause allergic reactions.

#### **4.5 Interaction with other medicinal products and other forms of interactions**

Potentiation may occur if antipsychotic drugs are combined with CNS depressants such as alcohol, hypnotics, anaesthetics and strong analgesics, or with antihypertensives or other drugs with hypotensive activity, anticholinergics or antidepressants.

Phenothiazines may antagonise the action of guanethidine and levodopa. Trifluoperazine may aggravate Parkinsonism and antagonise the action of levodopa. They may lower the convulsive threshold. Hence patients with epilepsy should be treated with caution.

Serum levels of phenothiazines can be reduced to non-therapeutic concentrations by concurrent administration of lithium.

Desferrioxamine should not be used in combination with 'Stelazine', since prolonged unconsciousness has occurred after combination with the related prochlorperazine.

Trifluoperazine may diminish the effect of oral anticoagulants.

Severe extrapyramidal side-effects or neurotoxicity have been observed in patients concurrently treated with lithium and trifluoperazine. Sleep walking has been described in some patients taking phenothiazines and lithium

Antacids can reduce the absorption of phenothiazines.

Phenothiazines increase the risk of ventricular arrhythmias when given with drugs which prolong the Q-T interval, drugs causing electrolyte imbalances.

#### **4.6 Fertility, pregnancy and lactation**

Trifluoperazine has been available since 1958. There are some animal studies that indicate a teratogenic effect, but results are conflicting. There is no clinical evidence (including follow-up surveys in over 800 women who had taken low-dosage Trifluoperazine during pregnancy) to indicate that trifluoperazine has a teratogenic effect in man. Nevertheless, drug treatment should be avoided in pregnancy unless essential, especially during the first trimester.

Neonates exposed to antipsychotics (including Trifluoperazine) during the third trimester of pregnancy are at risk of adverse reactions including extrapyramidal and/or withdrawal symptoms that may vary in severity and duration following delivery. There have been reports of agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress, or feeding disorder. Consequently, newborns should be monitored carefully.

Trifluoperazine passes into the milk of lactating dogs. Breast feeding should only be allowed at the discretion of the physician.

#### **4.7 Effects on ability to drive and use machines**

Stelazine may cause side effects including drowsiness, dizziness and visual disturbances which interfere with the ability to drive and operate machinery. Do not drive or use machines when you first start to take this medicine until you are certain that you are not getting these side effects.

#### 4.8 Undesirable effects

Lassitude, drowsiness, dizziness, transient restlessness, insomnia, dry mouth, blurred vision, muscular weakness, anorexia, mild postural hypotension, skin reactions including photosensitivity reactions, weight gain, oedema and confusion may occasionally occur. Tachycardia, constipation, urinary hesitancy and retention, and hyperpyrexia have been reported very rarely. Adverse reactions tend to be dose-related and to disappear.

Hyperprolactinaemia may occur at higher dosages with associated effects such as galactorrhoea or amenorrhoea; certain hormone-dependant breast neoplasms may be affected.

Phenothiazines can produce ECG changes with prolongation of the QT interval and T-wave changes; ventricular arrhythmias (VF, VT (rare)), sudden unexplained deaths; cardiac arrest and Torsades de pointes have been reported.

Such effects are rare with 'Stelazine'. In some patients, especially non-psychotic patients, 'Stelazine' even at low dosage may cause unpleasant symptoms of being dulled or, paradoxically, of being agitated. Extrapyramidal symptoms are rare at oral daily dosages of 6 mg or less; they are considerably more common at higher dosage levels. These symptoms include parkinsonism; akathisia, with motor restlessness and difficulty in sitting still; and acute dystonia or dyskinesia, which may occur early in treatment and may present with torticollis, facial grimacing, trismus, tongue protrusion and abnormal eye movements including oculogyric crises. Such reactions may often be controlled by reducing the dosage or by stopping medication. In more severe dystonic reactions, an anticholinergic antiparkinsonism drug should be given.

Tardive dyskinesia of the facial muscles, sometimes with involuntary movements of the extremities, has occurred in some patients on long-term, high-dosage and, more rarely, low-dosage phenothiazine therapy, including 'Stelazine'. Symptoms may appear for the first time either during or after a course of treatment; they may become worse when treatment is stopped. The symptoms may persist for many months or even years, and while they gradually disappear in some patients, they appear to be permanent in others.

Patients have most commonly been elderly, with organic brain damage. Particular caution should be observed in treating such patients. Periodic gradual reduction of dosage to reveal persisting dyskinesia has been suggested, so that treatment may be stopped if necessary. If tardive dyskinesia occurs, trifluoperazine should be discontinued. Anticholinergic antiparkinsonism agents may aggravate the condition. Since the occurrence of tardive dyskinesia may be related to length of treatment and dosage, Trifluoperazine should be given for as short a time and at as low a dosage as possible.

The neuroleptic malignant syndrome is a rare but occasionally fatal complication of treatment with neuroleptic drugs, and is characterised by hyperpyrexia, muscle rigidity, altered consciousness and autonomic instability. Intensive symptomatic treatment, following discontinuation of 'Stelazine', should include cooling. Intravenous dantrolene has been suggested for muscle rigidity.

Mild cholestatic jaundice and blood dyscrasias such as agranulocytosis, pancytopenia, leucopenia and thrombocytopenia have been reported very rarely.

Signs of persistent infection should be investigated.

Very rare cases of skin pigmentation and lenticular opacities have been reported with Stelazine'.

Cases of venous thromboembolism, including cases of pulmonary embolism and cases of deep vein thrombosis have been reported with antipsychotic drugs- Frequency unknown.

Withdrawal reactions have been reported in association with antipsychotic drugs (see 4.4).

Pregnancy, puerperium and perinatal conditions-Drug withdrawal syndrome neonatal (see 4.6) –Frequency not known.

#### Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via  
HPRA Pharmacovigilance,

Earlsfort Terrace,  
IRL - Dublin 2;  
Tel: +353 1 6764971; Fax: +353 1 6762517;  
Website: [www.hpra.ie](http://www.hpra.ie); E-mail: [medsafety@hpra.ie](mailto:medsafety@hpra.ie).

## 4.9 Overdose

Signs and symptoms will be predominantly extrapyramidal; hypotension may occur. Treatment consists of gastric lavage together with supportive and symptomatic measures.

Do not induce vomiting. Extrapyramidal symptoms may be treated with an anticholinergic antiparkinsonism drug. Treat hypotension with fluid replacement; if severe or persistent, noradrenaline may be considered. Adrenaline is contraindicated.

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

The product is a piperazine phenothiazine tranquilliser with potent antipsychotic, anxiolytic and antiemetic activity, and a pharmacological profile of moderate sedative and hypotensive properties, and fairly pronounced tendency to cause extrapyramidal reactions.

### 5.2 Pharmacokinetic properties

A phenothiazine well absorbed but with extensive first pass metabolism. Distribution is wide and elimination of metabolites and drug occurs in bile and urine.

### 5.3 Preclinical safety data

None available.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Saccharin Sodium (E954)  
Sodium Benzoate (E211)  
Citric Acid Anhydrous (E330)  
Sodium Citrate (E331)  
Sorbitol liquid (non-crystallising) (E420)  
Quinoline Yellow (E104)  
Sunset Yellow (E110)  
Peach Flavour  
Purified water

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

12 months  
Diluted syrup: 4 weeks. Discard any unused diluted syrup.

### 6.4 Special precautions for storage

Do not store above 25°C. Store in the original container to protect from light.  
For storage of the diluted product, see section 6.3. and protect from light.

## **6.5 Nature and contents of container**

Amber glass bottles, with plastic screw caps or polypropylene screw caps or roll-on metal screw-caps, containing 200 ml solution.

Not all pack sizes may be marketed.

## **6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product**

If it is necessary to dilute 'Stelazine' 1mg/5ml Syrup, use Sorbitol liquid (non- crystallizing)

## **7 MARKETING AUTHORISATION HOLDER**

Amdipharm Limited  
Temple Chambers  
3 Burlington Road  
Dublin 4

Ireland

## **8 MARKETING AUTHORISATION NUMBER**

PA1142/037/003

## **9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 01April 1997

Date of last renewal: 01 April 2007

## **10 DATE OF REVISION OF THE TEXT**

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