

**IRISH MEDICINES BOARD ACTS 1995 AND 2006**

**MEDICINAL PRODUCTS(CONTROL OF PLACING ON THE MARKET)REGULATIONS,2007**

**(S.I. No.540 of 2007)**

**PPA0465/238/001**

Case No: 2068098

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

**PCO Manufacturing Limited**

**Unit 10, Ashbourne Business Park, Rath, Ashbourne, Co. Meath, Ireland**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

**Stemetil 5mg Tablets**

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **14/08/2009**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

## Part II

### Summary of Product Characteristics

#### 1 NAME OF THE MEDICINAL PRODUCT

Stemetil 5mg Tablets

#### 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 5mg of prochlorperazine maleate.

Excipients: also include lactose monohydrate.

For a full list of excipients, see section 6.1.

#### 3 PHARMACEUTICAL FORM

Tablet

*Product imported from the UK:*

Off-white to pale cream coloured circular tablets approximately 6.4mm in diameter and 3.2mm thick: not mottled or speckled. Smooth almost matt biconvex surfaces, one face impressed 'STEMETIL' around a centrally impressed '5'; reverse face plain.

#### 4 CLINICAL PARTICULARS

##### 4.1 Therapeutic Indications

Stemetil tablets are recommended in the management of acute vertigo such as is associated with Meniere's syndrome, nausea and vomiting, migraine and anxiety states. The course of treatment should not normally exceed 2 weeks duration.

In the management of phobias, schizophrenia, acute mania, and similar psychotic reactions.

##### 4.2 Posology and method of administration

The route of administration is oral

Recommended Dosage:

Adults:

For the management of Meniere's syndrome, nausea and vomiting: -

The usual total daily dosage is 10-40mg in divided doses

In schizophrenia and other psychotic disorders:

The usual total daily dosage is 75-100mg in divided doses.

Elderly:

Stemetil should be used cautiously in the elderly owing to their susceptibility to drugs acting centrally on the nervous system. There is an increased risk of drug-induced Parkinsonism in the elderly particularly after prolonged use therefore a lower initial dosage is recommended. Care should also be taken not to confuse the adverse effects of Stemetil, e.g. orthostatic hypotension, with effects due to the underlying disorder.

Children : Not recommended for use in children.

### 4.3 Contraindications

- Use in patients with a known hypersensitivity to the active ingredient.
- Use in patients with impaired liver function

### 4.4 Special warnings and precautions for use

- Phenothiazines should only be used with great caution in patients with a history of jaundice.
- Patients receiving phenothiazines over a prolonged period require regular and careful surveillance with particular attention to potential for inducing eye changes, effects on haemopoiesis, liver dysfunction, myocardial conduction effects, particularly if other concurrently administered drugs also have potential effects on these systems.
- Prolonged administration of any phenothiazine may result in persistent or tardive dyskinesias, particularly in the elderly.
- Use of phenothiazines at high (relative or absolute) doses may induce extrapyramidal side-effects, dyskinesia, akathisia, dystonia. These are likely to be particularly severe in children.
- Neuroleptic malignant syndrome: The syndrome may occur with the use of any neuroleptic agent. Symptoms include clouding of consciousness, rigidity and other extrapyramidal effects, and autonomic dysfunction, most importantly hyperpyrexia. Treatment involves the immediate cessation of neuroleptic therapy and symptomatic management as appropriate.
- Phenothiazines should only be used with great caution in patients with coronary insufficiency, cardiovascular disorders which may predispose to prolongation of the QT interval.
- As with other neuroleptics, very rare cases of QT-interval prolongation have been reported with Stemetil.
- Cases of QT prolongation, possibly dose related have been reported with neuroleptic drugs. This effect can increase the risk of serious ventricular disorders such as torsades de pointes. As a precaution before administration of Prochlorperazine, it is recommended if possible, to eliminate the risk factors for cardiac rhythm disturbances:
  - Brachycardia <55 beats per minute
  - Hypokalaemia
  - Congenial or aquired QT prolongation
  - Ongoing treatments with drugs which can result in brachycardia (<55 beats/minute), hypokalemia, slowed intracardiac conduction, QT prolongation (*See section 4.5, Interaction with other medicinal products and other forms of interactions*).

Except in emergencies, it is recommended that an ECG be preformed as part of the initial evaluation of patients due to receive treatment with a neuroleptic drug.

There have been isolated reports of sudden death with phenothiazines with possible causes of a cardiac origin.

- Avoid concomitant prescription of other antipsychotics.

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

Stroke: in randomised clinical trials versus placebo performed in a population of elderly patients with dementia and treated with certain atypical antipsychotic drugs, a 3-fold increase of the risk of cerebrovascular events has been observed. The mechanism of such risk increase is not known. An increase in the risk with other antipsychotic drugs or other populations of patients cannot be excluded. Nozinan should be used with caution in patients with stroke risk factors.

### 4.5 Interaction with other medicinal products and other forms of interaction

The concomitant administration of this product with other medications such as central nervous system depressants (including alcohol and anaesthetics), or antihypertensives or anticholinergics will result in accentuation of their effect while potentiation of action will also occur with monoamine oxidase inhibitors, antidepressants and analgesics. Concomitant drugs which could induce prolongation of the QT interval or torsade de pointes (*see section 4.4, Special warnings and precautions for use*)

- Bradycardia-inducing medications such as beta-blockers, bradycardia-inducing calcium channel blockers such as diltiazem and verapamil, clonidine; digitalis.

- Medications which induce electrolyte imbalance, in particular those causing hypokalaemia ( such as hypokalaemic diuretics, stimulant laxatives, IV amphotericin B , glucocorticoids, tetracosactides). Electrolyte imbalance should be corrected.
- Class Ia antiarrhythmic agents such as quinidine, disopyramide.
- Class III antiarrhythmic agents such as amiodarone, sotalol.
- Other medications such as pimozone, sultopride, haloperidol, imipramine antidepressants, lithium, cisapride, thioridazine, IV erythromycin, IV vincamine, halofantrine, pentamidine, sparfloxacin.

Simultaneous administration of prochlorperazine and desferrioxamine has been observed to induce a transient metabolic encephalopathy characterised by loss of consciousness for 48-72 hours.

## 4.6 Pregnancy and lactation

Phenothiazines should only be used during pregnancy if considered essential by the physician. The drug is excreted in breast milk and breast feeding should cease during therapy.

## 4.7 Effects on ability to drive and use machines

Phenothiazines may induce drowsiness. Persons taking these drugs should not drive or operate machinery unless the drug has been shown not to interfere with physical or mental ability.

## 4.8 Undesirable effects

Side effects include dizziness, dry mouth, nasal stuffiness and agitation, QT interval prolongation may occur. Phenothiazines may induce contact allergic reactions on handling.

QT interval prolongation and of ventricular arrhythmias such as torsade de pointes, ventricular tachycardia, which may result in ventricular fibrillation or cardiac arrest.

There have been isolated reports of sudden death, with possible causes of cardiac origin (*see section 4.4, Special warnings and precautions for use*), as well as cases of unexplained sudden death, in patients receiving neuroleptic phenothiazines.

## 4.9 Overdose

Symptoms of phenothiazine overdosage include drowsiness or loss of consciousness, hypotension, tachycardia, E.C.G. changes, ventricular arrhythmias and hypothermia. Severe extra-pyramidal dyskinesias may occur. If the patient is seen sufficiently soon (up to 6 hours) after ingestion of a toxic dose, gastric lavage may be attempted. Pharmacological induction of emesis is unlikely to be of any use. Activated charcoal should be given. There is no specific antidote. Treatment is supportive.

Generalised vasodilatation may result in circulatory collapse; raising the patient's legs may suffice, in severe cases, volume expansion by intravenous fluids maybe needed; infusion fluids should be warmed before administration in order not to aggravate hypothermia.

Positive inotropic agents such as dopamine may be tried if fluid replacement is insufficient to correct the circulatory collapse. Peripheral vasoconstrictor agents are not generally recommended; avoid the use of adrenaline.

Ventricular or supraventricular tachy-arrhythmias usually respond to restoration of normal body temperature and correction of circulatory or metabolic disturbances. If persistent or life threatening, appropriate anti-arrhythmic therapy may be considered. Avoid lignocaine and, as far as possible, long acting anti-arrhythmic drugs.

Pronounced central nervous system depression requires airway maintenance or, in extreme circumstances, assisted respiration. Severe dystonic reactions usually respond to procyclidine (5-10 mg) or orphenadrine (20-40 mg) administered intramuscularly or intravenously. Convulsions should be treated with intravenous diazepam.

Neuroleptic malignant syndrome should be treated with cooling. Dantrolene sodium may be tried.

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Stemetil is a potent phenothiazine neuroleptic.

### 5.2 Pharmacokinetic properties

Potent phenothiazine neuroleptic with anti-emetic properties with an elimination  $t_{1/2}$  of approximately 6-12 hours depending on the route and formulation.

### 5.3 Preclinical safety data

Not relevant.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Lactose monohydrate  
Maize starch  
Silicon dioxide (E551)  
Magnesium stearate

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf Life

The shelf-life expiry date of this product is the date shown on the container and outer package of the product on the market in the country of origin.

### 6.4 Special precautions for storage

Do not store above 30°C.  
Store in the original container in order to protect from light.

### 6.5 Nature and contents of container

PVdC coated uPVC/Aluminium foil blisters of 28 tablets in an over-labelled outer carton.  
Pack size: 84 tablets.

### 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

No special requirements.

**7 Parallel Product Authorisation Holder**

PCO Manufacturing  
Unit 10 Ashbourne Business Park  
Rath  
Ashbourne  
County Meath  
Ireland

**8 Parallel Product Authorisation Number**

PPA0465/238/001

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

Date of first authorisation: 14th August 2009

**10 DATE OF REVISION OF THE TEXT**