SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Muscinil

Procyclidine Tablets 5mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 5.0mg of procyclidine hydrochloride.

Excipient(s) with known effect

Anhydrous lactose 173.4mg

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet
Each white, convex tablet is marked with a “PR5” on one side and a breakline on the reverse side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

- Parkinsonism of arteriosclerotic, idiopathic and post-encephalitic origin.
- Control of neuroleptic drug-induced extrapyramidal symptoms, such as pseudo-parkinsonism, akathisia and acute dystonic reactions.

4.2 Posology and method of administration

The dosage must be determined according to the needs of individual patients.

Adults:

Initially 2.5 mg three times daily and increased by 2.5 – 5 mg per day at intervals of two to three days, until symptomatic relief is obtained without side-effects, usually between 20 mg and 30 mg daily. The daily dose should be in 3 or 4 divided doses and taken after meals.

Daily doses of up to 60 mg have occasionally been required. Arteriosclerotic patients generally require less than post-encephalitic patients. In some patients who cannot tolerate a too rapid increase in dosage it is advisable to make the increase

at longer intervals.

Procyclidine may be combined with levodopa or amantadine in patients who are inadequately controlled on a single agent.

In drug-induced extrapyramidal syndromes treatment should begin with 2.5 mg three times daily, increasing to the optimum daily dosage which is usually 10 mg to 20 mg in divided doses. After 3 to 4 months (and periodically thereafter, in long-term therapy), treatment should be stopped and the patient observed for recurrence of the symptoms.

Abrupt cessation of treatment must be avoided.

Elderly:

The elderly are more sensitive to anticholinergics and a reduced dose may be required.

Paediatric population

Not recommended.

Method of administration

For oral use.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Procyclidine is also contra-indicated in patients with the following conditions:

- Untreated urinary retention
- Angle-closure (narrow angle) glaucoma
- Gastro-intestinal obstruction
- Prostatic hypertrophy

4.4 Special warnings and precautions for use

As with all anticholinergics the benefit/risk ratio should be assessed when prescribing procyclidine in patients with existing angle-closure (narrow angle) glaucoma or those considered to be predisposed to glaucoma. Also use with caution in patients with obstructive disease of the gastrointestinal tract, cardiac disorders, cardiovascular disease, hepatic and renal impairment, and those with urinary symptoms associated with prostatic hypertrophy.

In a proportion of patients undergoing neuroleptic treatment, tardive dyskinesias will occur. While anticholinergic agents do not cause this syndrome, when given in combination with neuroleptics they may exacerbate the symptoms of tardive dyskinesia or reduce the threshold at which these symptoms appear in predisposed

patients. In such individuals subsequent adjustment of neuroleptic therapy or reduction in anticholinergic treatment should be considered.

Patients with mental disorders occasionally experience a precipitation of a psychotic episode when procyclidine is administered for the treatment of the extrapyramidal side effects of neuroleptics.

Elderly patients, especially those on high doses of anticholinergics, may be more susceptible to the adverse events associated with such therapy. Specifically, the elderly patient may be particularly vulnerable to central nervous system disturbances such as confusion, impairment of cognitive function and memory, disorientation and hallucinations. These effects are usually reversible on reduction or discontinuation of anticholinergic therapy.

There is no specific information available concerning the use of procyclidine hydrochloride in patients with impaired renal or hepatic function. However, since procyclidine is metabolised in the liver and excreted via the urine, care should be exercised when administering procyclidine to patients with impairment of renal or hepatic function.

Caution: procyclidine may be liable to abuse; it may produce a euphoric effect. Although the cases of abuse are rare, physicians should exercise caution in prescribing procyclidine to patients with symptoms that may not be genuine. Transition to or from procyclidine therapy should be gradual otherwise symptoms may be aggravated.

Contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

A proportion of patients undergoing treatment with neuroleptics agents will develop tardive dyskinesia. If these patients are receiving concurrent treatment with procyclidine their susceptibility to tardive dyskinesia may be increased. Should this syndrome occur adjustment of the neuroleptic therapy is indicated.

The concomitant use of procyclidine with some neuroleptics for the treatment of extrapyramidal symptoms has been associated with a reduction in neuroleptic plasma concentrations. However, this reduction is unlikely to be associated with a significant reduction in clinical effect.

The anticholinergic action of procyclidine may be increased by agents having anticholinergic activity, e.g. tricyclic and related antidepressants (e.g. amitriptyline) and MAOI's, clozapine, phenothiazines (e.g. thioridazine), antihistamines, amantadine, memantine, disopyramide and nefopam.

The use of drugs with cholinergic properties, such as tacrine, may reduce the therapeutic response to procyclidine. Furthermore, drugs with anticholinergic properties may antagonise the effect of parasympathomimetic agents.

Anticholinergics, including procyclidine, may reduce the efficacy of levodopa by increasing gastric emptying time, resulting in enhanced gastric degradation.

Procyclidine may potentiate the vagolytic effects of quinidine.

The absorption of ketoconazole may be reduced by concomitant administration of procyclidine (anticholinergics).

Exposure to high environmental temperature and humidity in association with phenothiazine/anticholinergic drug regimen has rarely resulted in hyperpyrexia.

Antimuscarinics antagonise the gastro-intestinal effects of cisapride, metoclopramide and domperidone and the effects of parasympathomimetics.

There may be reduced effect of sublingual nitrates due to failure to dissolve under the tongue because of a dry mouth.

Daily administration of paroxetine increases significantly the plasma levels of procyclidine. If anticholinergic effects are seen, the dose of procyclidine should be reduced.

4.6 Pregnancy and lactation

Pregnancy

The safety of using procyclidine during pregnancy has not been established. However, extensive clinical use has not given any evidence that it in any way compromises the normal course of pregnancy.

Nevertheless, as with all drugs, use should be considered only when the expected clinical benefit of treatment for the mother outweighs any possible risk to the developing foetus.

Lactation

No data are available on the excretion of procyclidine in human breast milk.

4.7 Effects on ability to drive and use machines

Drowsiness is not a problem but the occurrence of tardive dyskinesia in susceptible patients, and also of blurred vision, dizziness, mental confusion, impaired cognition and memory, disorientation and hallucinations in patients on higher dosage, could affect their ability to drive or operate machinery. Therefore, if affected, patients should be advised no to drive or operate machinery.

4.8 Undesirable effects

Frequencies displayed use the following convention: 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 (<1/10,000), not known (cannot be estimated form the available data).

The most commonly reported side effects are those due to the anticholinergic properties of procyclidine, and are generally reversible on reduction of dosage.

The following undesirable effects have been observed:

Psychiatric disorders:

Uncommon: Agitation, anxiety, nervousness, confusion, disorientation, hallucinations

Rare: Psychotic disorder

These effects are more likely to occur at higher doses, and in the elderly (see section 4.4).

There is the potential for drug abuse (see section 4.4).

Nervous system disorders:

Uncommon: Dizziness, impaired cognition, memory impairment, especially at higher doses and in the elderly.

Frequency unknown: Exacerbation of tardive dyskinesia (see section 4.4)

Eye disorders:

Common: Blurred vision

Gastrointestinal disorders;

Common: Dry mouth, constipation

Uncommon: Nausea, vomiting, gingivitis

Skin and subcutaneous disorders:

Uncommon: Rash

Renal and urinary disorders:

Common: Urinary retention

Cardiac disorders:

Not known: tachycardia

The main undesirable effects are those to be expected from any anticholinergic agent – these are generally reversible on reducing the dosage.

With high doses of Procyclidine dizziness, mental confusion, excitement, impaired cognition and memory, disorientation, anxiety, agitation, insomnia and hallucinations may occur.

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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Symptoms and signs:

Reports of overdosage are relatively rare. Symptoms of overdosage include stimulant effects such as are agitation, restlessness, mental confusion, visual and auditory hallucinations and severe sleeplessness lasting up to 24 hours or more. Mood disturbance is likely. Most subjects are euphoric but the occasional patient may be anxious and aggressive. The pupils are widely dilated and unreactive to light. In recorded cases, the disorientation has lasted 1 to 4 days and ended in recuperative sleep.

Signs of central nervous system depression including somnolence, reduced consciousness and occasionally coma have been reported, usually following very large overdoses.

Tachycardia has also been reported in cases of procyclidine overdose.

Management:

If procyclidine has been ingested within the previous hour or two (or possibly longer in view of its likely effects on gastric motility), then activated charcoal should be used to reduce absorption. Gastric lavage should only be considered if clinically appropriate. Other active measures such as the use of cholinergic agents or haemodialysis are extremely unlikely to be of clinical value, although if convulsions occur they should be controlled by injections of diazepam.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anticholinergic agents; tertiary amines

ATC Code: N04AA04

Procyclidine is a synthetic anticholinergic agent that blocks the excitatory effects of acetylcholine at the muscarinic receptor.

Idiopathic Parkinson’s disease is thought to result from degeneration of neurones in the substantia nigra whose axons project and inhibit cells in the corpus striatum. Blockade by neuroleptic drugs of the dopamine released by these terminals produces a similar clinical picture. The cell bodies in the corpus striatum also receive cholinergic innervation which is excitatory.

It acts centrally by inhibition of the cholinergic input to neurones in the corpus striatum that is one of the causes of the Parkinsonian syndrome.

Procyclidine is particularly effective in the alleviation of rigidity. Tremor, akinesia, speech and writing difficulties, gait, sialorrhea and drooling, sweating, oculogyric crises and depressed mood are also beneficially influenced.

5.2 Pharmacokinetic properties

Procyclidine is rapidly and completely absorbed from the gastro-intestinal tract. Peak plasma concentrations occur 1 to 2 hours post-dose in fasting subjects. Presystemic metabolism reduces the systemic bioavailability to approximately 75%. The compound is lipid soluble such that penetration of the blood-brain barrier is likely and inferred from its central actions.

Only small amounts are excreted unchanged in the urine. The mean elimination half-life following oral administration is approximately 12.6 hours. Plasma clearance is approximately 67.5 $ml.min^{-1}$. The volume of distribution (after oral or intravenous dosing) is about 1 $L.kg^{-1}$. Procyclidine is moderately protein-bound in plasma.

5.3 Preclinical safety data

Not applicable

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Anhydrous lactose

Maize starch

Magnesium stearate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

Shelf life in the product as Packaged for Sale

36 months when stored in proposed market packs.

Shelf life after dilution of reconstitution according to directions

Not applicable

Shelf life after first opening the container

Not applicable

6.4 Special precautions for storage

Do not store above 25°C. Store in the original container.

6.5 Nature and contents of container

Polypropylene “securitainers” with polyethylene, tamper-evident caps, containing 28, 84, 100, 500, 2000 or 5000 tablets.

6.6 Special precautions for disposal

Not applicable

7 MARKETING AUTHORISATION HOLDER

Strides Pharma UK Ltd
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Metro Centre
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WD18 9SS, UK
Trading as: Co-pharma

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15th June 2008

10 DATE OF REVISION OF THE TEXT

27/04/2018