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.

For 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 mg per day 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.

Children:

Not recommended.

4.3 Contraindications

Procyclidine is contra-indicated in patients with a known sensitivity to the ingredients in the tablets and those with the following conditions:

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

4.4 Special warnings and precautions for use

As with all anticholinergics such as procyclidine, cautious prescribing is indicated in patients with existing angle-closure glaucoma or those considered to be predisposed to glaucoma. Caution is also required in patients predisposed to obstructive disease of the gastro-intestinal tract, 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.

Procyclidine tablets should not be withdrawn abruptly as rebound Parkinsonian symptoms may occur.

As with other anticholinergic drugs, procyclidine has the potential to be abused. Although abuse cases are rare, caution should be exercised in prescribing procyclidine to patients whose symptoms may not be genuine.

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

4.5 Interaction with other medicinal products and other forms of interaction

Monoamine oxidase inhibitors or drugs with anticholinergic properties, eg., amantadine, memantine disopyramide, antihistamines, phenothiazines (eg., thioridazine), clozapine, tricyclic and related antidepressants (eg., amitriptyline) and nefopam may increase the anticholinergic activity of procyclidine.

The use of drugs with cholinergic properties, eg., tacrine, may reduce the therapeutic response to procyclidine.

Drugs with anticholinergic properties such as procyclidine may antagonise the effect of parasympathomimetic agents.

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.

Procyclidine may decrease salivation causing dry mouth, and may therefore reduce the absorption and the therapeutic effect of sublingual or buccal tablets (e.g. nitrates).

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

The anticholinergic effect of procyclidine on gastrointestinal motility may antagonise the gastrointestinal effects of domperidone and metoclopramide.

Procyclidine may potentiate the vagolytic effects of quinidine.

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

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

Daily administration of paroxetine increases significantly the plasma levels of procyclidine, possibly resulting in increased anticholinergic effects. If these become apparent, 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

Adverse events of a neurological character eg., blurred vision, dizziness, confusion and disorientation have been reported with procyclidine. Therefore, if affected, patients should be advised not to drive or operate machinery.

4.8 Undesirable effects

Adverse reactions are listed by estimated frequency: common (>1/100, <1/10); uncommon (>1/1,000, <1/100); rare (>1/10,000, <1/1,000); very rare (<1/10,000)

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

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.

4.9 Overdose

Symptoms:

Reports of overdosage are relatively rare. Symptoms of overdosage are agitation, restlessness and confusion with severe sleeplessness lasting up to 24 hours or more. Visual and occasionally auditory hallucinations are 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

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

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

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WD18 9SS, UK

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15th June 2008

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20.05.2016