SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Procyclidine 5mg Tablets

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 extra-pyramidal 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.

Adult:
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.
In general, younger patients or those with postencephalitic parkinsonism may require higher doses for a therapeutic response than older patients and those with arteriosclerotic parkinsonism.
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. The tablets may be better tolerated if taken with a meal.

4.3 Contraindications

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

- Untreated urinary retention
- Angle closure (narrow angle) glaucoma
- Gastro intestinal obstruction
- prostatic hypertrophy or in patients with known hypersensitivity to any of the ingredients

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 cardiac disorders, cardiovascular disease, hepatic and renal impairment.

In a proportion of patients undergoing neuroleptic treatment, tardive dyskinesias will occur. While anticholinergics 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 anticholinergics 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 extra-pyramidal 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 patient with impaired renal or hepatic function. However, since procyclidine is metabolized 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 Parkinsonism symptoms may occur.

As with other anticholinergic drugs, procyclidine has the potential to be abused, it may produce euphoric effect. Although abuse cases are rare, caution should be exercised in prescribing procyclidine to patients whose symptoms 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, 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

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.

Monoamine oxidase inhibitors or drugs with anti-cholinergic properties, e.g., amantadine, memantine disopyramide, antihistamines, phenothiazines (e.g., thioridazine), clozapine, tricyclic and related antidepressants (e.g., amitriptyline) and nefopam, may increase the anticholinergics activity of procyclidine.

The use of drugs with cholinergic properties., e.g., 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 neuroleptic for the treatment of extra pyramidal symptoms has been associated with a reduction in neuropleptic 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 tablet (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 cisapride, 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 Fertility, 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.

Breast-feeding

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. Adverse events of a neurological character e.g., 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. 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), 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.

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

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

Immune system disorders:
Not known: hypersensitivity

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

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. 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.

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anticholinergic drug, ATC code: N04AA04.

Procyclidine is a synthetic anticholinergic agent that blocks the excitatory effects of acetylcholine at the muscarinic receptor. The control of symptoms is exerted by its central action on the cell bodies of the corpus striatum.

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.

Relief of the Parkinsonian syndrome can be achieved, either by potentiation of the dopaminergic system or blockade of the cholinergic input by anticholinergics. It is by a central action of this latter type by which procyclidine exerts its effect.

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

Procyclidone 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 and intravenous 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 1λ.kg-^{1}. Procyclidine is moderately protein-bound in plasma.

No detailed information is available on the metabolic fate of procyclidine but very little of the parent compound is excreted in the urine unchanged. When given orally about one fifth of the dose is known to be metabolised in the liver, principally by cytochrome P450 and then conjugated with glucuronic acid. This conjugate has been detected in the urine.

5.3 Preclinical safety data

Fertility:
A three generation study in rats dosed at 40mg/kg/day via the diet before and during pregnancy showed only that the number of viable pups was slightly decreased from the second mating. No other parameters were affected.

Teratogenicity:
No teratogenic effects were seen in rats dosed subcutaneously with 10, 30 or 100mg/kg/day on days 8 to 16 of pregnancy. Maternal bodyweight gain was reduced at doses of 30 or 100mg/kg/day, and a 10% reduction in foetal weight was seen at 100mg/kg/day.

Mutagenicity:
Procyclidine was not genotoxic in in vitro bacterial mutation or mouse lymphoma assays.

Carcinogenicity:
There are no data on the carcinogenic potential of procyclidine hydrochloride

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 and Reconstitution According to Directions

Not applicable.

Shelf Life After 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.

White opaque PVC/PVdC/aluminium blisters: 28 tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Not applicable.

7 MARKETING AUTHORISATION HOLDER

SPECIAL CONCEPT DEVELOPMENT (UK) LIMITED T/A RX FARMA,

UNITS 1-7 COLONIAL WAY,

WATFORD, HERTFORDSHIRE,

WD24 4YR

UNITED KINGDOM

8 MARKETING AUTHORISATION NUMBER(S)

PL 36722/0059

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

24/03/2025

10 DATE OF REVISION OF THE TEXT

27/07/2025