

1. NAME OF THE MEDICINAL PRODUCT

Procyclidine Rosemont 2.5mg/5ml Oral Solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Procyclidine Hydrochloride 2.5mg/5ml

Excipient(s) with known effect:

Benzyl Alcohol 0.26mg/5ml

Ethanol 0.05mg/5ml

Liquid Maltitol (E965) 2.73g/5ml

Methyl Parahydroxybenzoate (E218) 6.0mg/5ml

Propyl Parahydroxybenzoate (E216) 1.5mg/5ml

Propylene Glycol (E1520) 113mg/5ml

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Solution for oral administration

4.1. Therapeutic indications

Procyclidine is indicated in all forms of Parkinson's disease: idiopathic (paralysis agitans), postencephalitic and arteriosclerotic.

Symptoms often responding well to Procyclidine include: rigidity, akinesia, tremor, speech and writing difficulties, gait, sialorrhoea and drooling, sweating, oculogyric crises and depressed mood.

Procyclidine is also used to control troublesome extrapyramidal symptoms induced by neuroleptic drugs including pseudo-parkinsonism, acute dystonic reactions and akathisia.

4.2. Posology and method of administration

For oral administration only.

Adults:

The variation in optimum dosage from one patient to another should be taken into consideration by the physician. Treatment is usually started at 2.5mg three times a day, increasing by 2.5 – 5mg daily at intervals of two to three days until the optimum clinical response is achieved. The usual maximum total daily dose is 30mg. However, at the discretion of the attending physician where appropriate this total may be as high as 60mg.

The daily dosage used in the control of neuroleptic-induced extrapyramidal symptoms is usually not more than 20mg daily. After a period of 3-4 months Procyclidine

Rosemont should be stopped and the patient observed to see if the neuroleptic-induced extrapyramidal symptoms recur. Cessation of treatment periodically is to be recommended even in patients who appear to require the drug for longer periods. Avoid abrupt discontinuation of treatment.

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

Children:

Not recommended for use in children.

Use in the Elderly:

Elderly patients are more sensitive to anticholinergics, and a reduced dose may be required.

4.3. Contraindications

Procyclidine is contra-indicated in individuals with known hypersensitivity to any component of the preparation, untreated urinary retention, closed angle glaucoma and gastro-intestinal obstruction.

4.4. Special warnings and precautions for use

As with all anticholinergics such as procyclidine, cautious prescribing is indicated in patients pre-disposed to glaucoma or with existing angle-closure (narrow angle) glaucoma, obstructive disease of the gastro-intestinal tract 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 reduce the threshold at which the dyskinesias appear in patients pre-disposed to the abnormality. In such individuals, subsequent adjustment of neuroleptic therapy or reduction in anti-cholinergic 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 (see Undesirable Effects). 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 impairment of 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 should not be withdrawn abruptly as rebound parkinsonian symptoms may occur.

Abuse

Procyclidine, along with other anticholinergic drugs, has the potential to be abused. Although the cases of abuse are rare, physicians should exercise caution in prescribing Procyclidine to patients with symptoms that may not be genuine.

Excipient Warnings

- Benzyl Alcohol – This medicine contains 0.26mg benzyl alcohol in each 5ml. Benzyl alcohol may cause allergic reactions. High volumes should be used with caution and only if necessary, especially in subjects with liver or kidney impairment because of the risk of accumulation and toxicity (metabolic acidosis).
- Ethanol – This medicine contain 0.05mg of alcohol (ethanol) in each 5ml. The amount in 5ml of this medicine is equivalent to less than 1ml beer and 1ml wine. The small amount of alcohol in this medicine will not have any noticeable effects.
- Liquid Maltitol (E965) - Patients with rare hereditary problems of fructose intolerance should not take this medicine.
- Methyl and Propyl parahydroxybenzoates (E218 and E216) – May cause allergic reactions (possibly delayed).
- Propylene Glycol (E1520) - This medicine contains 113mg of propylene glycol in each 5ml.
- Sodium – This medicine contains less than 1 mmol sodium (23mg) per 5ml, that is to say essentially ‘sodium-free’.

4.5. Interactions with other medicinal products and other forms of interaction

Monoamine oxidase inhibitors or drugs with anticholinergic properties, such as amantadine, memantine, antihistamines, phenothiazines, and tricyclic antidepressants and related antidepressants, clozapine, disopyramide and nefopam, may increase the anticholinergic action of procyclidine.

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 parasympathetic 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.

Drugs with anticholinergic properties may decrease salivation causing dry mouth and, in theory, may reduce the absorption and therefore the therapeutic effect of sublingual or buccal nitrate tablets.

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

The effect of anticholinergics such as procyclidine may antagonise the gastrointestinal effects of domperidone and metoclopramide.

Procyclidine may potentiate the vagolytic effects of quinidine.

Anticholinergics may reduce the absorption of ketoconazole.

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

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. Fertility, pregnancy and lactation

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. No data are available on the excretion of this drug in breast milk.

4.7. Effects on ability to drive and use machines

Adverse events of a neurological character such as 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

The main side effects are those to be expected from any anticholinergic agent. Dry mouth, blurring of vision, urinary retention and constipation are most commonly recorded. Nausea, vomiting, gingivitis, nervousness and rash have been reported occasionally. The unwanted anticholinergic effects are easily reversed by reducing the dosage.

At higher doses, dizziness, mental confusion, impaired cognition and memory, disorientation, anxiety, agitation and hallucinations may occur.

Rarely the development of psychotic-like symptoms have been reported in association with procyclidine.

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 professional are asked to report any suspected adverse reactions via the national reporting system listed.

United Kingdom

Yellow Card Scheme.

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

4.9. Overdose

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 CNS depression including somnolence, reduced consciousness, and occasionally coma have been reported usually following very large overdoses.

Tachycardia has also been reported in association with cases of procyclidine overdose.

If procyclidine has been ingested within the previous hour or two (or possibly longer in view of its likely effects on gastric motility) 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

Procyclidine is a synthetic anticholinergic agent, which blocks the excitatory effects of acetyl choline at the muscarinic receptor.

Idiopathic Parkinson's disease is now 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 produce 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 that procyclidine exerts its effect.

5.2. Pharmacokinetic properties

Procyclidine is adequately absorbed from the gastro-intestinal tract and disappears rapidly from the tissues. After both oral and IV dosing the mean values for volume of

distribution, total body clearance and plasma elimination half-life of procyclidine were of the order of 1 litre/Kg, 68ml/min and 12 hours respectively.

5.3. Preclinical safety data

None known.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Citric acid monohydrate (E330), sodium citrate (E331), methyl hydroxybenzoate (E218), propyl hydroxybenzoate (E216), propylene glycol (E1520), liquid maltitol (E965), grape flavour 545419E (contains propylene glycol), blackcurrant flavour (contains **pulegone**, benzyl alcohol, ethanol, and propylene glycol) and purified water.

6.2 Incompatibilities

None known.

6.3. Shelf life

24 months

6.4. Special precautions for storage

Store at or below 25°C

6.5. Nature and contents of container

Bottles: Amber (Type III) glass

Closures: HDPE, EPE wadded, tamper evident, child resistant.

Capacity: 150ml

6.6. Special precautions for disposal and other handling

Keep out of the sight and reach of children

7 MARKETING AUTHORISATION HOLDER

Rosemont Pharmaceuticals Ltd
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Yorkdale Industrial Park
Braithwaite Street
Leeds

LS11 9XE
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 0427/0082

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

4.10.91 / 31.10.96

10 DATE OF REVISION OF THE TEXT

29/06/2023