

NEW ZEALAND DATA SHEET

1. KEMADRIN™ Tablets (procyclidine hydrochloride 5 mg tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient: procyclidine hydrochloride 5mg

White, round, biconvex tablets, one face with a break line and coded KT above the break line and 05 below the break line, with a score line on the other face.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

KEMADRIN is indicated for the treatment of all forms of Parkinson's disease: idiopathic (paralysis agitans), postencephalitic and arteriosclerotic.

KEMADRIN is efficacious in the relief of parkinsonian symptoms. It is particularly effective in the alleviation of rigidity. Tremor, akinesia, speech and writing difficulties, gait, sialorrhoea and drooling, sweating, oculogyric crises and depressed mood are also beneficially influenced.

KEMADRIN is also indicated for the control of extrapyramidal symptoms induced by neuroleptic drugs including pseudo-parkinsonism, acute dystonic reactions and akathisia.

4.2 Dose and method of administration

The variation in optimum dosage from one patient to another should be taken into consideration by the physician.

Dosage in adults

Parkinson's disease

Treatment is usually started at 2.5mg procyclidine three times per day, increasing by 2.5 to 5mg per day at intervals of two or three days until the optimum clinical response is achieved.

The usual maintenance dose to achieve optimal response is 15 to 30mg procyclidine per day. Addition of a fourth dose before retiring has been seen to be beneficial in some patients. Doses up to 60mg procyclidine have been well tolerated, and at the discretion of the attending physician dosing to this level may be appropriate.

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.

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

Neuroleptic-induced extrapyramidal symptoms

Treatment is usually initiated at 2.5mg procyclidine three times per day increasing by 2.5mg daily until symptoms are relieved.

The effective maintenance dose is usually 10 to 30mg procyclidine per day.

After a period of 3 to 4 months of therapy, KEMADRIN should be withdrawn and the patient observed to see whether the neuroleptic-induced extra-pyramidal symptoms recur. If this is the case KEMADRIN should be reintroduced to avoid debilitating extra-pyramidal symptoms.

Cessation of treatment periodically is to be recommended even in patients who appear to require the drug for longer periods.

Dosage in children

Safety and efficacy have not been established in the paediatric age group; therefore, the use of KEMADRIN in this age group requires that the potential benefits be weighed against the possible risk to the child.

Dosage in the Elderly

Elderly patients may be more susceptible than younger adults to the anticholinergic effects of KEMADRIN and a reduced dosage may be required (See Special Warnings and Special Precautions for Use).

Administration

Pharmacokinetic studies have indicated that the mean plasma elimination half life of KEMADRIN is sufficient to allow twice daily administration. Oral administration may be better tolerated if associated with a meal.

4.3 Contraindications

KEMADRIN is contraindicated in individuals with known hypersensitivity to any component of the preparation.

4.4 Special warnings and precautions for use

As with all anticholinergics the benefit/risk ratio should be assessed when prescribing KEMADRIN in patients with existing angle-closure (narrow angle) glaucoma or those considered to be predisposed to glaucoma. Cautious prescribing is also indicated in patients predisposed to 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 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 (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 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.

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

Abuse

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

4.5 Interaction with Other Medicaments and Other Forms of Interaction

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

The use of drugs with cholinergic properties, such as tacrine, may reduce the therapeutic response to KEMADRIN.

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.

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 cisapride, 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

Fertility and Embryo-Foetal Development

In studies in rats, procyclidine did not affect fertility or cause foetal abnormalities.

Pregnancy

The safety of using KEMADRIN 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 medicines, 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 information is available on the passage of procyclidine into human breast milk following administration of KEMADRIN.

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. A clinical study reported several patients on neuroleptic therapy that had considerably less fatigue and more energy and drive when transferred from other anticholinergic agents to KEMADRIN.

4.8 Undesirable effects

For this preparation there is no modern clinical documentation which can be used as support for determining the frequency of adverse reactions.

Psychiatric disorders	Uncommon ($\geq 1/1000$ and $< 1/100$)	Agitation, anxiety, nervousness, confusion, disorientation, hallucinations.
	Rare ($< 1/1000$)	Psychotic disorder
Nervous system disorders	Uncommon ($\geq 1/1000$ and $< 1/100$)	Dizziness, memory impairment, impaired cognition
Eye disorders	Common ($\geq 1/100$)	Blurred vision
Gastrointestinal disorders	Common ($\geq 1/100$)	Dry mouth, constipation
	Uncommon ($\geq 1/1000$ and $< 1/100$)	Nausea, vomiting, gingivitis
Skin and subcutaneous tissue disorders	Uncommon ($\geq 1/1000$ and $< 1/100$)	Rash
Renal and urinary disorders	Common ($\geq 1/100$)	Urinary retention

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, impaired cognition and memory, disorientation, anxiety, agitation and hallucinations may occur.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions <https://nzphvc.otago.ac.nz/reporting/>

4.9 Overdose

Symptoms and signs

Symptoms of overdosage include stimulant effects such as agitation, restlessness and confusion with severe sleeplessness lasting up to 24 hours or more. Visual and auditory hallucinations have been reported. 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 a 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 KEMADRIN overdose.

Treatment

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. Further management should be as clinically indicated or as recommended by the national poisons centre, where available.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Procyclidine is a synthetic anticholinergic agent which 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. 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.

5.2 Pharmacokinetic Properties

Procyclidine is adequately absorbed from the gastro-intestinal tract with a bioavailability of 75% and disappears rapidly from the tissues.

The relatively low clearance of 68mL/min represents a predominantly metabolic change with a small first pass effect. The mean plasma disappearance half-life after both oral and intravenous administration is approximately 12 hours.

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

Mutagenicity

No data are available regarding the mutagenic potential of procyclidine hydrochloride.

Carcinogenicity

There are no data on the carcinogenic potential of procyclidine hydrochloride.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

None

6.2 Incompatibilities

None

6.3 Shelf Life

5 years

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and Contents of Container

KEMADRIN tablets are supplied in bottles of 100 tablets.

6.6 Special precautions for disposal

None

7. MEDICINE SCHEDULE

Prescription Only Medicine.

8. SPONSOR

Pharmacy Retailing Pty Ltd
t/a Healthcare Logistics
58 Richard Pearse Drive
Airport Oaks
Auckland
New Zealand

9. DATE OF FIRST APPROVAL

18 October 2006

10. DATE OF REVISION OF THE TEXT

April 2019

KEMADRIN™ is a trade mark of Aspen

SUMMARY TABLE OF CHANGES

Section Changed	Summary of New Information
Format of Data sheet	As per new SPC-style format