Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Kemadrin 5mg/ml Solution for Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Injection containing 5 mg/ml (10 mg/2 ml) Procyclidine Hydrochloride.

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Solution for injection
Clear colourless solution.

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.

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

Kemadrin is used to control troublesome extra-pyramidal symptoms induced by neuroleptic drugs including pseudo-parkinsonism, acute dystonic reactions and akathisia.

4.2 Posology and method of administration

Administration:
Kemadrin injection is administered by intravenous injection.

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 2.5mg daily until the level of optimal control is reached.

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.

In general, young and postencephalitic patients may require a somewhat higher dosage than older patients and those with arteriosclerosis.

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, Kemadrin 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.

4.3 Contraindications

Tardive dyskinesias.

4.4 Special warnings and precautions for use

As with all anticholinergics such as Kemadrin, cautious prescribing is indicated in the elderly, in patients either predisposed to glaucoma or with existing angle-closure (narrow angle) glaucoma, obstructive disease of the gastro-intestinal tract including pyloric stenosis and paralytic ileus, with urinary symptoms associated with prostatic hypertrophy and in patients with disorders characterised by tachycardia, e.g. thyrotoxicosis.

In a proportion of patients undergoing neuroleptic treatment, tardive dyskinesias will occur. While anti-cholinergic agents do not cause or control this syndrome, when given in combination with neuroleptics they may reduce the threshold at which dyskinesias appear in patients predisposed to this abnormality. In such individuals subsequent adjustment of neuroleptic therapy is indicated.

In rare instances, Kemadrin administered for the treatment of neuroleptic induced symptoms was associated with an apparent worsening of the patient's state.

Dosage should only be introduced gradually. Sudden withdrawal of the product should be avoided.

High dosage may induce dizziness, mental confusion and hallucinations.

4.5 Interaction with other medicinal products and other forms of interaction

The anticholinergic effects of this product may be increased by concomitant use of amantadine, antihistamines, phenothiazines, butyrophenones, antidepressants.

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

4.6 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 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 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.

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

The main undesirable effects are those to be expected from any anticholinergics 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.

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) then gastric lavage is probably indicated. 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 which blocks the excitatory effects of acetylcholine 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 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 and disappears rapidly from the tissues. It has an elimination half-life of 12 hours. After intravenous administration it acts within 5 to 20 minutes with a duration of up to 4 hours. No information is available on its metabolic fate and excretion.

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

Lactic acid
Water for injections

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

Unopened: 5 years.
Opened: For immediate use. Discard any unused solution.

6.4 Special precautions for storage

Do not store above 25°C. Discard any unused solution from opened ampoules.

6.5 Nature and contents of container

Type I (2ml), clear, neutral glass ampoules. Packs contain 5 x 2ml ampoules.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

GlaxoSmithKline (Ireland) Limited
Stonemasons Way
Rathfarnham
Dublin 16

8 MARKETING AUTHORISATION NUMBER

PA 1077/60/2

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