PATIENT INFORMATION LEAFLET

PROCYCLIDINE HYDROCHLORIDE 5 mg/ml Solution for Injection

Please read all of this leaflet carefully before taking your medicine.

• Keep this leaflet. You may need to read it again.
• If you have any further questions, ask your doctor or pharmacist.
• This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
• If any of the side effects become serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

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1. What is PROCYCLIDINE Injection and what is it used for?

What is PROCYCLIDINE Injection?
PROCYCLIDINE Injection belongs to a group of medicines called anticholinergics. Anticholinergics block the effects of a substance called acetylcholine in your body.

What is PROCYCLIDINE Injection used for?
PROCYCLIDINE Injection is used to treat and relieve the symptoms of Parkinson’s disease such as stiff muscles, paralysis, tremor, difficulties with speech, writing and walking, overproduction of saliva and dribbling, sweating, uncontrolled eye movements and depression.

Some tranquillisers have side-effects like the symptoms of Parkinson’s disease and they can also cause restlessness and abnormal head and body movements. PROCYCLIDINE Injection is also sometimes used to control these side effects.

2. Before you are given PROCYCLIDINE Injection

Do not use PROCYCLIDINE Injection:
Your doctor may decide that you should not be given PROCYCLIDINE Injection if any of the points listed below applies to you:
• Have you ever had an allergy (rash, itching, and shortness of breath) to procyclidine or lactic acid?

Special precautions to be taken:
Your doctor may decide to take special precautions when giving you PROCYCLIDINE Injection if any of the points listed below applies to you:
• Do you experience uncontrolled movements of the face and tongue (tardive dyskinesia)?
• Do you suffer from glaucoma (eye disease caused by too much pressure within the eye)?
• If you are a man, do you suffer from an enlarged prostate gland?
• Do you often suffer from stomach cramps, abdominal pains or constipation?
• Do you suffer from kidney or liver disease?
If any of the above applies to you talk to your doctor or pharmacist.

Taking other medicines
Always tell your doctor if you are taking any other medicines because taking some medicines together can be harmful. Remember that the doctor at the hospital may not have been informed if you have recently begun a course of treatment for another illness.

Are you taking any of the following drugs?
• Tranquillisers (e.g. thioridazine)
• Tricyclic and related antidepressants (e.g. amitriptyline)
• Monoamine oxidase inhibitors, otherwise known as MAOIs (used for depressive illness)
• Amantadine (used for parkinsonism and viral infections)
• Antihistamines (used to treat allergies)
• Ketoconazole (used as antifungals)
• Tacrine, memantine, phenothiazines and neuroleptics (medicines used to treat mental health problems including Alzheimer’s disease and dementia)
• Clozapine (used for schizophrenia)
• Quinidine and disopyramide (used for arrhythmias - too fast, too slow or irregular heart beat)
• Nefopam (used for moderate pain)
• Metoclopramide, cisapride and domperidone (used for gastro-intestinal disorders)
• Levodopa (used for parkinsonism)
• Nitrate tablets that dissolve in the mouth (used for angina attacks)

If any of the above applies to you talk to your doctor or pharmacist.

Pregnancy and breast feeding
If you are pregnant, trying to become pregnant or breastfeeding, PROCYCLIDINE Injection will only be given to you if your doctor considers the benefit of treatment outweighs the risk to the developing baby or new born baby.

Driving and using machines
PROCYCLIDINE Injection can cause blurred vision and at higher doses, dizziness, confusion and hallucinations may occur. If you are affected in this way, do NOT drive or operate machinery while you are receiving PROCYCLIDINE 5 mg/ml Solution for Injection.

3. How will you be given PROCYCLIDINE Injection

Important:
PROCYCLIDINE Injection will be given to you as an injection into a vein (intravenously) or muscle (intramuscularly). Your doctor will decide on a dose of PROCYCLIDINE Injection which is right for you.

Adults:
intravenous injection:
• The usual starting dose is 2.5mg, three times a day, intravenously. Your doctor may then increase this by 2.5mg to 5mg daily, every two or three days, until the desired effect is seen. This is known as the maintenance dose.

Intravenous injection:
Adults:
• The usual starting dose is 2.5mg, three times a day, intravenously. Your doctor may then increase this by 2.5mg to 5mg daily, every two or three days, until the desired effect is seen. This is known as the maintenance dose.

Intramuscular injection:
Adults:
• The usual starting dose is 2.5mg, three times a day, intramuscularly. Your doctor may then increase this by 2.5mg to 5mg daily, every two or three days, until the desired effect is seen. This is known as the maintenance dose.
• The usual total daily maintenance dose is 15 to 30mg, however, in certain cases your doctor may decide to prescribe more (up to a maximum of 60mg).
• Although the dose is usually taken three times a day, your doctor may give you a fourth dose before bedtime.
• If PROCYCLIDINE Injection is being used to control the side-effects of another drug, then the usual maximum daily dose is 30mg.
• Your doctor may decide to stop PROCYCLIDINE Injection after 3 or 4 months to see if the side-effects return.
• Given intravenously, a 5mg to 10mg dose of PROCYCLIDINE may relieve abnormal head and body movements within 5 to 10 minutes. Occasionally, a higher dose is needed and may take up to half an hour to bring relief.

Intramuscular injection:
• PROCYCLIDINE Injection may be given intramuscularly in doses of 5 to 10mg; this may be repeated after 20 minutes, up to a daily maximum of 20mg.

Elderly:
Your doctor may decide to use a lower dose than the above.

Children:
PROCYCLIDINE Injection is not usually recommended for use in children. However, in certain cases your doctor may decide that PROCYCLIDINE Injection is required.

Treatment with PROCYCLIDINE Injection should not be stopped suddenly.

If you think you have been given too much PROCYCLIDINE Injection or if someone else takes your medicine by mistake, tell a doctor or nurse immediately.

Symptoms of overdose: Agitation, restlessness, confusion, sleeplessness lasting up to 24 hours or more, hallucinations, euphoria, anxiousness, aggressiveness, dilation of pupils and increased heart beat.

Tell your doctor or healthcare professional if you have any of these side effects so that he/she can give appropriate treatment. If you have already left the medical premises, contact your nearest hospital, doctor or pharmacist.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme (Website: www.mhra.gov.uk/yellowcard). By reporting side effects, you can help provide more information on the safety of this medicine.

5. Storing PROCYCLIDINE Injection
Keep out of the reach and sight of children.
Do not use PROCYCLIDINE Injection after the expiry date on the carton. The expiry date refers to the last day of that month.
PROCYCLIDINE Injection should be stored below 25 °C.

6. Further information
What PROCYCLIDINE Injection contains:
The active substance is PROCYCLIDINE HYDROCHLORIDE 5 mg in each 1 ml of solution.
The solution for injection also contains lactic acid and water for injections.
Contents of the pack: PROCYCLIDINE Injection is supplied in cartons of five, 2 ml ampoules. Each ampoule contains 10 mg of procyclidine hydrochloride.
Marketing authorisation holder:
Auden Mckenzie (Pharma Division) Ltd. Mckenzie House, Bury Street, Ruislip, Middlesex, HA4 7TL
Manufacturer:
Rotexmedica GmbH Arzneimittelwerk Bunsenstrasse 4, Trittau, Schleswig-Holstein, 22946, Germany.
This leaflet was last approved in May 2015.
For information in large print, on tape, on CD or in Braille, phone 01895 627 420.

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2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Procyclidine Hydrochloride BP 5mg per ml (10mg in each 2ml ampoule)

3. PHARMACEUTICAL FORM

Solution for injection

4. CLINICAL PARTICULARS

4.1. Therapeutic Indications

Procyclidine is indicated for the treatment and symptomatic relief of all forms of Parkinson's disease e.g., idiopathic (paralytic) akinasia, postencephalitic and arteriosclerotic disease.

Procyclidine is also used to control troublesome extra-pyramidal symptoms induced by neuroleptics including Phenothiazine, acute dystonic reactions and akathisia.

4.2. Posology 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 three times per day, increasing by 2.5 to 5mg daily 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.

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

Neuroleptic induced extra-pyramidal symptoms:-

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

The effective maintenance dose is usually 10 to 30 mg procyclidine per day. After a period of 3 to 4 months of therapy, Procyclidine should be withdrawn and the patient observed to see whether the neuroleptic-induced extra-pyramidal symptoms recur.

If this is the case Procyclidine should be reintroduced to avoid destabilising extra-pyramidal symptoms. Cessation of treatment periodically is to be recommended even in patients who appear to require the drug for longer periods.

Procyclidine Injection may be given intramuscularly in doses of 5 to 10mg, repeated after 20 minutes if necessary, up to a daily maximum of 20mg procyclidine.

In acute torsion dystonia and parkynsonian dystonias, doses of 5 to 10mg procyclidine intravenously are frequently effective within 5 to 10 minutes. Occasionally, patients may need more than 10 mg procyclidine, and may require up to half an hour to obtain relief.

Dosage in children:-

The use of in Procyclidine this age group is not recommended.

Dosage in Elderly:-

Elderly patients may be more susceptible than younger adults to the anticholinergic effects of Procyclidine 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 Procyclidine is sufficient to allow twice daily administration orally or intravenously, if more convenient.

Oral administration may be better tolerated if associated with a meal.

4.3. Contra-Indications

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 Special Precautions For Use

As with all anticholinergics the benefit/risk ratio should be assessed when prescribing in Procyclidine 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 dyskinesia 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 psychiatric 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 (See ADVERSE EVENTS). 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, 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 to Procyclidine patients with symptoms that may not be genuine.

4.5 Interaction with other medicinal products and other forms of interaction

Monoamine oxidase inhibitors or drugs with anticholinergic properties, such as amantadine, memantine, antihistaminics, phentolamine, trimipramine and related antidepressants, cisapride, 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 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.

Drugs with anticholinergic properties may decrease saliva loss 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 cisapride, domperidone and metoclopramide.

Procyclidine may potentiate the vagal effects of quinidine.

Anticholinergics may reduce the absorption of ketanserine.

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

Daily administration of paracetamol increases significantly the plasma levels of procyclidine. If anticholinergic effects are seen, 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 information is available on the passage of procyclidine into human breast milk following administration of Procyclidine.

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.

The main undesirable effects are those to be expected from any anticholinergic agent these are generally reversible on reducing the dose.

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

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.

Procyclidine is particularly effective in the alleviation of rigidity. Tremor, akinesia, speech and writing difficulties, gait, akathisia and drooling, sweating, oculogyric crises and depressed mood are also beneficially influenced.

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 relative low clearance of 68 ml/min represents a predominantly metabolic change with a small first pass effect. The mean plasma elimination half-life after 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. Pre-clinical Safety Data

Fertility:-
A three generation study in rats dosed at 40 mg/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 100 mg/kg/day on days 8 to 16 of pregnancy. Maternal bodyweight gain was reduced at doses of 30 or 100 mg/kg/day, and a 10% reduction in foetal weight was seen at 100 mg/kg/day.

Mutagenicity:-
No data is available regarding the mutagenic potential of procyclidine hydrochloride.

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

6. Pharmaceutical Particulars

6.1. List of Excipients

Lactic acid 10μg
Lactic acid for pH 3.9 to 4.5 (quantity not fixed)
Lactic acid 10μg
Water for Injections to 2ml
Lactic acid for pH 3.9 to 4.5 (quantity not fixed)
P450 and then conjugated with glucuronic acid. This conjugate has been detected in the urine.

6.2. Incompatibilities

None known.

6.3. Shelf Life

5 years.

6.4. Special Precautions for Storage

Store below 25°C

6.5. Nature and Contents of Container

2ml Neutral glass ampoules

6.6. Instructions for Use, Handling and Disposal

No special instructions

7. Marketing authorisation holder

Auden Mckenzie (Pharma Division) Ltd
Mckenzie House, Bury Street, Ruislip, Middlesex, HA4 7TL, UK

8. MARKETING AUTHORIZATION NUMBER

PL 17507/0047

9. DATE OF FIRST AUTHORISATION/

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18/05/2015

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