PROFESSIONAL INFORMATION FOR DETRUNORM® XL

SCHEDULING STATUS:

S3

PROPRIETARY NAME (and dosage form):

DETRUNORM® XL (Modified release Capsules)

COMPOSITION:

Each capsule contains 30 mg propiverine hydrochloride.

List of excipients: Citric acid (anhydrous), Povidone (K-value: 25), Lactose monohydrate, Talc, Triethylcitrate, Magnesium stearate, Methacrylic acid – methyl methacrylate copolymer (1:1) (Eudragit L®), Methacrylic acid – methyl methacrylate copolymer (1:2) (Eudragit S®), Ammonio methacrylate copolymer type A (Eudagrit RL®), Ammonio methacrylate copolymer type B (Eudagrit RS®) Gelatin, Titanium dioxide E171, Red iron oxide E 172, Yellow iron oxide E 172

Contains sugar-lactose monohydrate

PHARMACOLOGICAL CLASSIFICATION:

A.5.4 Medicines affecting autonomic functions Cholinolytics (Anticholinergics)

PHARMACOLOGICAL ACTION:

Propiverine hydrochloride is an anticholinergic with spasmolytic activities, caused by inhibition of calcium influx

Pharmacodynamic properties

In animal models propiverine hydrochloride causes a dose dependent decrease of the intravesical pressure and an increase in bladder capacity.

The effect is based on the sum of the pharmacological properties of propiverine and its three active metabolites.

Pharmacokinetic properties

Distribution

Propiverine is extensively metabolised pre-systemically.

The calculated volume of distribution (after 10 mg, 20 mg respectively) of approximately 253 l (125 – 473 l) indicates, that a large amount of available propiverine is distributed to peripheral compartments.

The protein binding is around 90% for the parent substance and around 60% for the principal active metabolite.

Metabolism

Propiverine hydrochloride has a high first pass effect. The main metabolite, the N-oxide of propiverine, is found in the blood at a concentration which exceeds that of the parent substance. Two other active metabolites can be detected qualitatively.

Excretion

The elimination of propiverine and its metabolites takes place via the urine (less than 20% of the dose administered), bile and faeces.

The effect of food and other medicines on bioavailability of DETRUNORM® XL has not been studied

INDICATIONS

The treatment of urinary incontinence, in unstable bladder conditions, including neurogenic bladder.

CONTRA-INDICATIONS

DETRUNORM® XL capsules are contra-indicated in patients being hypersensitive to the active substance or to any of the excipients and in patients suffering from one of the following disorders:

- Obstruction or suspected obstruction of the bowel
- bladder outflow obstruction where urinary retention may be anticipated
- myasthenia gravis
- paralytic ileus
- ulcerative colitis

- toxic megacolon
- glaucoma
- renal impairment
- hepatic impairment
- tachydysrhythmias

Due to lack of data **DETRUNORM® XL** should not be used in children.

Pregnancy and lactation (see Pregnancy and Lactation)

WARNINGS AND SPECIAL PRECAUTIONS:

During long-term therapy hepatic enzymes should be monitored, because reversible changes of liver enzymes may occur. Monitoring of intraocular pressure is recommended in patients at risk of developing glaucoma.

Particular attention should be paid to the residual urine volume in cases of urinary tract infections.

DETRUNORM® XL should be used with caution in patients suffering from autonomic neuropathy.

Conditions that may be aggravated following administration of DETRUNORM® XL are:

Hyperthyroidism

Severe congestive heart failure

Hiatus hernia with reflux oesophagitis

Cardiac dysrhythmias

Tachycardia

Prostatic hypertrophy

Sedative medicines may enhance the drowsiness caused by DETRUNORM® XL.

DETRUNORM® XL contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactose deficiency or glucose-galactose malabsorption should not take DETRUNORM® XL

Effects on ability to drive and use machinery

DETRUNORM® XL may produce drowsiness and blurred vision. Patients should be cautioned regarding activities requiring mental alertness such as operating a motor vehicle or other machinery or performing hazardous work while taking DETRUNORM® XL.

INTERACTIONS

Increased side effects due to concomitant medication with tricyclic antidepressants (e.g. imipramine), tranquilisers (e.g. benzodiazepines), anticholinergics, amantadine, neuroleptics (e.g. phenothiazines) and β - sympathomimetics. Decreased activity due to concomitant medication with cholinergic medicines such as neostigmine. Reduced blood pressure in patients treated with isoniazid. The effect of prokinetics such as metoclopramide and cisapride may be decreased.

PREGNANCY AND LACTATION:

Contra-indicated in pregnancy and lactation.

DOSAGE AND DIRECTIONS FOR USE:

For oral use.

The recommended daily doses are as follows:

Adults:

One capsule (= 30 mg propiverine hydrochloride) once a day

Elderly:

There is no special dosage regimen for the elderly.

SIDE-EFFECTS

The following side-effects can be associated with the use of **DETRUNORM® XL**:

Nervous system disorders:

Frequent: headache

Less frequent: tremor, dizziness, dysgeusia

Gastrointestinal disorders:

Frequent*:* dryness of the mouth

Less frequent*:* constipation, abdominal pain, dyspepsia, nausea/vomiting

Eye disorders:

Frequent*:* abnormal accommodation, accommodation disturbances, abnormal vision

Vascular disorder:

Frequen : decreased blood pressure , drowsiness, heat sensation (flushing)

Renal and urinary system disorders:

Less frequen*:* increased residual urine

General disorders and administrative site conditions:

Less frequent*:* tiredness

Skin and subcutaneous tissue disorders:

Less frequent : rash due to idiosyncrasy (propiverine hydrochloride) or hypersensitivity (excipients, e.g. colourant)

Psychiatric disorders:

Less frequent*:* restlessness, confusion

Frequency unknown: hallucinations

Cardiac disorders:

Less frequent: palpitation.

All side-effects recede after a dose reduction or termination of the therapy after maximum 1 – 4 days.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

A maximal dosage of 1 mg / kg body weight / day should not be exceeded. Ingestion of **DETRUNORM® XL** greater than 120 mg single dose may result in:

Restlessness, dizziness, muscular weakness, disorders in speech and vision, dryness of mucosa, vertigo, cardiovascular disorders.

Therapy: Initiation of vomiting or gastric lavage followed by symptomatic treatment as in atropine overdose. Fever should be treated symptomatically with tepid sponging or ice-packs. In cases of pronounced restlessness or excitation, diazepam may be given by intravenous injection up to 10 mg. Tachycardia can be treated with propranolol and urinary retention can be treated by catheterisation. In the event of curare-like muscle paralysis, mechanical ventilation may be required.

IDENTIFICATION:

Non-transparent orange cap, non-transparent white body, contents of capsule shall be white or almost white pellets.

PRESENTATION:

Strips (Alu-PVC blister foil) in carton with 7 capsules per strip:

14, 21, 28, 35, 42 or 70 Capsules (2/3/4/5/6 or 10 strips per carton)

STORAGE INSTRUCTIONS:

Store at or below 30 °C.

Keep out of reach of children

REGISTRATION NUMBER:

A40/5.4/0439

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

Acino Pharma (Pty) Ltd

106 16th Road

Midrand

1685

South Africa

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