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1. NAME OF THE MEDICINAL PRODUCT:

Coldril Capsule

2. QUALITATIVE AND QUANTITAVE COMPOSITION

Each capsule contains: Pseudoephedrine 30mg, Paracetamol 500mg and

Chlorpheniramine Maleate 2mg.

3. PHARMACEUTICAL FORM

Capsule.

4.0 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Coldril is indicated in cold, flu, nasal congestion and associated fever, body ache and headache.

4.2 Posology and Method of Administration

For oral administration only

Not recommended for children under 12 years.

12 years and above - 2 capsules maximum 8 capsules in 24hours.

4.3 Contraindications

Coldril should not be given to patients who are being treated with monoamine oxidase inhibitor or within about two weeks of discontinuation of such treatment. Coldril is contraindicated in coronary thrombosis and thyrotoxicosis. It should be used with caution in patients with urinary retention and hypertension.

4.4 Special Warnings and Precautions for Use

If you are pregnant or under care of a doctor or receiving other prescribed medicines, consult your doctor before using this medicine. If symptoms persist consult a doctor. Coldril should be used with caution to patients with urinary retention and hypertension. It may cause drowsiness and dizziness in some persons and its use constitutes a danger to patients who drive vehicles or work with moving machineries .Avoid alcoholic drinks. Keep the medicine out of reach of children

4.5 Interaction with other medicinal products and other forms of interaction

Taking Pseudoephedrine with sympathomimetic amines, including amphetamines, methamphetamines and ephedrine may be harmful because of the combined effects of the drugs on the cardiovascular system.

Additionally consuming large amounts of caffeine can worsen the side effects of the pseudoephedrine.

4.6 Adverse Reactions

Common adverse effects are blurred vision, diplopia, fatigue, dizziness, sedation and dryness of the mouth, throat and nose. Occasionally abdominal pain with vomiting or diarrhoea, anxiety restlessness, nausea, muscular weakness, tremor and sweating may occur. purpura may occur. Renal damage may occur rarely after long time usage.

4.7 Overdose

Large doses of coldril may cause convulsions and precipitate fits in epileptics, hepatic damage may also occur. Less frequent complications include; cardiac damage, generalized bleeding, renal damage and hypoglycaemia.

Treatment

Gastric lavage should be carried out whenever the patient is seen within 4 hours. Charcoal or cholestyramine may be given but should be withheld until any necessary treatment with methionine or cysteamine has been initiated. In severe cases the treatment with methionine or cysteamine should be initiated as soon as possible within the first 10 hours to minimize damage to the liver by toxic metabolites.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacological Properties

Chlorpheniramine Maleate

Chlorpheniramine Maleate competes with histamine for histamine H1-receptor sites on smooth muscles of the bronchi, gastrointestinal tract, uterus and large blood vessels; it binds to cellular receptors, preventing access of histamine, thereby suppressing histamine-induced allergic symptoms. Chlorpheniramine does not directly alter histamine or its release.

Pseudoephedrine Hydrochloride

Pseudoephedrine is rapidly and completely absorbed after oral administration. After an oral dose of 180 mg to man, peak plasma concentrations of 500-900 ng/ml were obtained about 2 hours post dose. The plasma half-life was about 5.5 hours and was increased in subjects with alkaline urine and decreased in subjects with acid urine. The only metabolism was N-demethylation which occurred to a small extent. Excretion was mainly via the urine.

Paracetamol

Absorption: paracetamol is readily absorbed from the gastrointestinal tract.

Distribution: peak plasma concentrations occur about 10 to 60 minutes after oral doses. Paracetamol is distributed into most body tissues. It crosses the placenta and is present in breast

milk. Plasma-protein binding is negligible at usual therapeutic concentrations but increases with increasing concentrations.

Metabolism: It is metabolised in the liver. A minor hydroxylated metabolite which is usually produced in very small amounts by mixed-function oxidases in the liver and which is usually detoxified by conjugation with liver glutathione may accumulate following paracetamol overdosage and cause tissue damage.

Elimination: It is excreted in the urine, mainly as the glucuronide and sulphate conjugates. The elimination half-life varies from about 1 to 4 hours.

5.2 Pharmacokinetic Properties

Chlorpheniramine Maleate

Chlorpheniramine maleate is absorbed relatively slowly from the gastro – intestinal tract, peak plasma concentrations occurring about 2.5 to 6 hours after administration by mouth. Bioavailability is low, values of 25 to 50% having been reported. Chlorpheniramine appears to undergo considerable first – pass metabolism. About 70% of chlorpheniramine in the circulation is bound to plasma proteins. There is wide inter -individual variations in pharmacokinetics of chlorpheniramine. Values ranging from 2to 43 hours have been reported for the half life. Chlorpheniramine is widely distributed in the body including passage into CNS. Chlorpheniramine maleate is extensively metabolized. Unchanged drug and metabolites are excreted primarily in the urine .Only trace amounts have been found in the feaces. Ammonium chloride is absorbed from the gastro- intestinal tract. The ammonium ICN is converted into urea in the liver the anion thus liberated into the blood stream and extracellular fluid causes a metabolic acidosis and decreases the PH of the urine; this is followed by transient dieresis. Sodium citrate is metabolized, after absorption, to bicarbonate.

Pseudoephedrine

Pseudoephedrine is a sympathomimetic agent, structurally similar to ephedrine, used to relieve nasal and sinus congestion and reduce air-travel-related otalgia in adults. The salts

pseudoephedrine hydrochloride and pseudoephedrine sulfate are found in many over-the-counter preparations either as single-ingredient preparations, or more commonly in combination with antihistamines and/or paracetamol/ibuprofen. Unlike antihistamines, which modify the systemic histamine-mediated allergic response, pseudoephedrine only serves to relieve nasal congestion commonly associated with colds or allergies. The advantage of oral pseudoephedrine over topical nasal preparations, such as oxymetazoline, is that it does not cause rebound congestion (rhinitis medicamentosa).

Pseudoephedrine is a phenethylamine and a diastereomer of ephedrine with sympathomimetic property. Pseudoephedrine displaces norepinephrine from storage vesicles in presynaptic neurones, thereby releasing norepinephrine into the neuronal synapses where it stimulates primarily alpha-adrenergic receptors. It also has weak direct agonist activity at alpha- and beta-adrenergic receptors. Receptor stimulation results in vasoconstriction and decreases nasal and sinus congestion.

Paracetamol

Absorption: paracetamol is readily absorbed from the gastrointestinal tract.

Distribution: peak plasma concentrations occur about 10 to 60 minutes after oral doses. Paracetamol is distributed into most body tissues. It crosses the placenta and is present in breast milk. Plasma-protein binding is negligible at usual therapeutic concentrations but increases with increasing concentrations.

Metabolism: It is metabolised in the liver. A minor hydroxylated metabolite which is usually produced in very small amounts by mixed-function oxidases in the liver and which is usually detoxified by conjugation with liver glutathione may accumulate following paracetamol overdosage and cause tissue damage.

Elimination: It is excreted in the urine, mainly as the glucuronide and sulphate conjugates. The elimination half-life varies from about 1 to 4 hours.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber in addition to that included in other sections of the summary of product characteristics.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Purified Talc, Maize starch, Ethanol, Magnesium Stearate.

6.2 Incompatibilities

None known

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store in a cool dry place below 30^0C. Keep out of reach of children

6.5 Nature and contents of container

Coldril Capsule is blistered in 10's packed 2 blisters in a small box then 12 small boxes are packed in a bigger box.

Pack sizes: 2x10 blister packed Tablet

6.6 Special precautions for disposal and other handling

No special requirements.

7.0 Name & Address of Manufacturer

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8.0 Date of revision of the text

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