NAME OF THE MEDICINAL PRODUCT
Decongestant Tablets with Paracetamol or Otrivine Mu-Cron

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

<table>
<thead>
<tr>
<th>Active ingredient</th>
<th>mg/tab</th>
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<tbody>
<tr>
<td>Paracetamol Ph Eur</td>
<td>500.0</td>
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<tr>
<td>Pseudoephedrine hydrochloride BP</td>
<td>60.0</td>
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</tbody>
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3. PHARMACEUTICAL FORM
Tablets

4. CLINICAL PARTICULARS

4.1 Therapeutic indications
For the symptomatic relief of the symptoms of colds and influenza including feverishness, aches and pains, headache, nasal and sinus congestion (blocked nose and sinuses).

For oral administration.

4.2 Posology and method of administration

Adults and children over 12 years
One tablet to be taken three or four times a day, up to a maximum daily dose of 4 tablets (240mg pseudoephedrine and 2g paracetamol).

Children 6 to 12 years
Half a tablet to be taken four times a day, up to a maximum daily dose of 2 tablets (120mg pseudoephedrine and 1g paracetamol).

Children under 6 years
Not recommended.

Elderly
Although no specific studies have been carried out in this age group, there is no need for dosage reduction in the elderly.
Administration in those with hepatic disorders

Care should be taken in administering this product to patients with severe hepatic impairment.

Administration in those with renal disorders

Care should be taken in administering this product to patients with moderate to severe renal impairment, particularly if accompanied by cardiovascular disease.

4.3 Contraindications

Hypersensitivity to any of the ingredients. Severe liver disease, severe hypertension and severe coronary artery disease. This medicine is contraindicated in patients who are taking or who have taken monoamine oxidase inhibitors in the preceding two weeks. Concomitant use of pseudoephedrine and this product may cause a rise in blood pressure.

4.4 Special warnings and precautions for use

Should be taken with caution by patients with hepatic impairment or moderate to severe renal impairment (particularly if accompanied by cardiovascular disease).

This product should be used with caution in patients with cardiovascular disease, diabetes mellitus, closed angle glaucoma/elevated intraocular pressure, hyperthyroidism, phaeochromocytoma, prostatic enlargement and alcohol dependence.

Warning: Do not exceed the stated dose.

Not to be given to children under 6 years.

Do not take for longer than seven days, unless your doctor agrees.

If symptoms persist, consult your doctor.

Do not take with any other decongestant-containing products.

Do not take with any other paracetamol-containing products.

This medicine has little pressor effect in normotensive patients but should be used with caution in patients with mild to moderate hypertension.

Keep all medicines out of the reach of children.

Label
Immediate medical advice should be sought in the event of an overdose, even if you feel well.

Leaflet or combination label/leaflet

Immediate medical advice should be sought in the event of an overdose, even if you feel well, because of the risk of delayed, serious liver damage.

4.5 Interaction with other medicinal products and other forms of interaction

Should not be given to patients being treated with monoamine oxidase inhibitors or within 14 days of stopping such treatment. May enhance the effects of anticholinergic drugs such as tricyclic antidepressants. Concomitant use of this medicine with tricyclic antidepressants, monoamine oxidase inhibitors and sympathomimetics agents (such as decongestants, appetite suppressants and amphetamine-like stimulants) may cause a rise in blood pressure. May increase the possibility of arrhythmias in digitalised patients.

This medicine may partially reverse the hypotensive action of drugs which modify sympathetic activity including bretylium, bethanidine, guanethidine debrisoquine, methyldopa and the alpha- and beta-adrenergic blocking agents.

Drugs which induce hepatic microsomal enzymes, such as anticonvulsants and oral contraceptive steroids, may increase the rate at which paracetamol is metabolised, leading to a reduced plasma concentration of the drug.

Alcohol may reduce the capacity of the liver to metabolise paracetamol.

Chronic use of paracetamol enhances the effects of anticoagulants.

Concurrent use of paracetamol with NSAIDs may increase the risk of adverse renal effects. The prolonged combined use of these compounds may increase the risk of renal damage.

4.6 Pregnancy and lactation

The safety of this medicine during pregnancy and lactation has not been established but in view of a possible association of foetal abnormalities with first trimester exposure to pseudoephedrine, the use of the product during pregnancy should be avoided. The amounts of paracetamol and pseudoephedrine secreted into breast milk are considered to be too small to be harmful.

4.7 Effects on ability to drive and use machines
No adverse effects known.

4.8 Undesirable effects

Adverse effects may include restlessness, tremor, sleep disturbance, rarely hallucinations, tachycardia, cardiac arrhythmias, palpitations, skin rashes, hypertension, nausea, vomiting, headache and occasionally urinary retention in males.

There have rarely been reports of blood dyscrasias including thrombocytopenia and agranulocytosis, but these were not necessarily causally related to paracetamol.

4.9 Overdose

Immediate symptoms of overdosage in the first 24 hours include pallor, nausea, vomiting, anorexia, abdominal pain, irritability, restlessness, palpitations, hypertension, difficulty in micturition, thirst and convulsions.

Liver damage may become apparent 12 to 48 hours after ingestion. Though hepatic enzymes may become elevated and prothrombin time prolonged within 10-12 hours of paracetamol overdosage, clinical symptoms may not be apparent for 1 to 6 days following ingestion. Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, coma and death. Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported.

In paracetamol overdosage with hepatic damage, paracetamol half life is often prolonged from around 2 hours in normal adults to 4 hours or longer. Liver damage and nephrotoxic effects have been reported after the daily ingestion of excessive amounts of paracetamol.

Liver damage is likely in adults who have taken 10g or more of paracetamol. It is considered that excess quantities of a toxic metabolite (usually adequately detoxified by glutathione when normal doses of paracetamol are ingested), become irreversibly bound to liver tissue.

Immediate treatment is essential in the management of overdosage. Despite a lack of significant early symptoms, patients should be referred to hospital urgently for immediate medical attention and any patient who has ingested around 7.5g or more of paracetamol in the preceding 4 hours should undergo gastric lavage and activated charcoal administered to reduce paracetamol absorption. As peak plasma concentrations may be delayed by up to 4 hours following overdose, to accurately assess the risk of hepatotoxicity, plasma paracetamol levels should be measured at least 4 hours post-ingestion.
Generally treatment is required if the blood-paracetamol concentration is higher than a line drawn on semi-log/linear paper joining the points 200mg per litre (1.32 mmol/litre) at 4 hours and 30mg per litre (0.2mmol/litre) at 15 hours following ingestion. Administration of oral methionine or intravenous N-acetylcysteine, which may have a beneficial effect up to at least 48 hours after overdose, may be required. It has been proposed that the threshold for treatment with N-acetylcysteine should be reduced by 30-50% in patients taking drugs which induce hepatic enzymes, who abuse alcohol long-term or who are chronically malnourished. These patients may be more susceptible to toxic effects of paracetamol.

Symptomatic and supportive measures should be undertaken, particularly with regard to the cardiovascular and respiratory systems. Convulsions should be controlled with intravenous diazepam. Chlorpromazine may be used to control marked excitement and hallucinations. Severe hypertension may need to be treated with an alpha-adrenoreceptor blocking drug, such as phentolamine. A beta blocker may be required to control cardiac arrhythmias.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Paracetamol is a peripherally acting analgesic with antipyretic activity.

Pseudoephedrine is a sympathomimetic agent with direct and indirect effects on adrenergic receptors. It has alpha and beta adrenergic activity and some stimulant effect on the central nervous system. The sympathomimetic effect of pseudoephedrine produces vasoconstriction which in turn relieves nasal congestion.

5.2 Pharmacokinetic properties
Paracetamol is readily absorbed from the gastrointestinal tract with peak plasma concentrations occurring about 30 minutes to 2 hours after ingestion. Paracetamol is metabolised in the liver and excreted in the urine mainly as the glucuronide and sulphate conjugates, with about 10% as glutathione conjugates. Less than 5% is excreted as unchanged paracetamol. The elimination half-life varies from about 1-4 hours. Plasma protein binding is negligible at usual therapeutic concentrations, although this is dose-dependent.

The rate and extent of paracetamol absorption is normal in the elderly but plasma half life is longer and paracetamol clearance lower than in young adults.
In renal impairment though the mean plasma half-life of paracetamol is similar in normal and renally impaired subjects at 2-8 hours, from 8-24 hours paracetamol is eliminated less rapidly. An increase in the interval between doses of paracetamol has been recommended for adults with chronic renal failure.

With severe hepatic impairment the mean plasma half life of paracetamol is significantly prolonged (by approximately 75%). The clinical significance of this is however unclear, as no evidence exists of drug accumulation or hepatotoxicity in patients with liver disease.

Pseudoephedrine is readily and completely absorbed from the gastrointestinal tract. It is resistant to metabolism by monoamine oxidase and is largely excreted in the urine unchanged. It has an elimination half-life of 5 to 8 hours but its urinary elimination and hence half-life is pH dependent. Pseudoephedrine is rapidly distributed throughout the body, its volume of distribution being 2 to 3L/Kg bodyweight.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6. PHARMACEUTICAL PARTICULARS

5.1 List of excipients

Pregelatinised maize starch

Microcrystalline cellulose

Sodium lauryl sulphate

Magnesium stearate

Quinoline yellow (E104)

Croscarmellose sodium