NEMEL COLD AND CATARRH®
Ephedrine HCl 30mg + Dextromethophan HBr 10mg + Paracetamol 250mg

This information is intended for use by health professionals.

1. Name of the medicinal product.
   NEMEL COLD AND CATARRH® (Ephedrine HCl 30mg + Dextromethophan HBr 10mg + Paracetamol 250mg).

2. Qualitative and quantitative composition.
   Each uncoated tablet contains 30mg Ephedrine (as Ephedrine HCl); 10mg Dextromethophan (as Dextromethophan HBr); 250mg Paracetamol.

   For the full list of excipients, see section 6.1.

3. Pharmaceutical form

   Tablet

   The tablets are orange, biconcave tablet embossed with "N" on one side and plain on the other side.

4. Clinical particulars

4.1 Therapeutic indications

Nemel cold and catarrh is used for relieve of symptoms associated with common cold and catarrah. The drug product provides the analgesic effect against the pains resulting from the stress of catarrh and helps in nasal and bronchial decongestion. Also serves as a cough suppressant.

4.2 Posology and method of administration

Adults, Elderly and Children over 16 years:
Two tablets every eight hours as required.

Not recommended for children under 1 year.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Bronchial asthma.
- Chronic obstructive pulmonary disease (chronic bronchitis and emphysema).
- Pneumonia.
- Respiratory failure.
- Respiratory depression.

- Severe hepatic impairment.
- Hypertension.
- Thyrotoxicosis.
- Prostatic hypertrophy.
- This drug product contains ephedrine which has positive inotropic and chronotropic effects on the heart and its use should be avoided in patients with ischaemic heart disease.
- Patients with hyperthyroidism may be susceptible to a substance contained in this drug (ephedrine). Ephedrine may precipitate acute urinary retention in patients with prostatic hypertrophy.

4.4 Special warnings and precautions for use

Nemel Cold and Catarrh should be given with care to patients with hyperthyroidism, diabetes mellitus, angle-closure glaucoma and renal impairment.

Nemel Cold and Catarrh has potentially life threatening effects in its acute cardiovascular and central stimulant effects.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Care is advised in the administration of Nemel cold and catarrh to patients with severe renal or severe hepatic impairment because it contains paracetamol. The hazard of overdose is greater in those with non-cirrhotic alcoholic liver disease.

Do not exceed the recommended dose.

Do not take tablet with any other paracetamol-containing products.

If symptoms persist, consult your doctor.

Keep out of the reach of children.

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

Other adrenoceptor stimulants: Concurrent use of Nemel cold and catarrh tablet with theophylline may result in increased nausea, nervousness, and insomnia due to ephedrine content of the drug.

Anaesthetics: There may be an increased risk of arrhythmias when used with volatile liquid anaesthetics.

Antidepressants: Nemel cold and catarrh should not be given to patients who are being treated with monoamine oxidase inhibitors as they may cause hypertensive crisis with marked headache, severe hypertension and subarachnoid haemorrhage. Noradrenaline is displaced by ephedrine with the release of large amounts of catecholamine. The interaction may occur up to two weeks after stopping MAOI therapy. There may be an increased risk of arrhythmias when ephedrine is used with tricyclic antidepressants.

Antihypertensives: Loss of blood pressure control has been detected in hypertensive patients undergoing concurrent therapy with ephedrine and adrenergic neurone blocking drugs and may also occur with other antihypertensives.

Antimigraine drugs: Enhanced vasoconstriction and pressor effects with ergotamine or methysergide; concurrent use of ergotamine not recommended (risk of gangrene).

Cardiac glycosides: Increased risk of arrhythmias in patients receiving Nemel cold and catarrh and cardiac glycosides.

Corticosteroids: Nemel cold and catarrh due to the ephedrine content has been shown to increase the clearance and prolong the half-life of dexamethasone in asthmatic patients.

Oxytocin: Increased risk of vasoconstrictor or pressor effects in patients receiving oxytocin and ephedrine.

Urinary acidifiers/alkalinisers: Effects of Nemel cold and catarrh due to ephedrine may be reduced by acidification and increased by alkalinization of the urine.

Nemel cold and catarrh contains paracetamol and the speed of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by cholestyramine. The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular daily use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.

Concomitant use with other medicinal products having a sedative effect on the central nervous system can lead to mutual potentiation of effects.

Cytochrome P450-2D6 inhibitors: Concomitant use of drugs that inhibit the cytochrome P450-2D6 enzyme system in the liver and thus inhibit the metabolism of dextromethorphan (especially amiodarone, quinidine, fluoxetine, haloperidol, paroxetine, propafenone, thioridazine, cimetidine and ritonavir) can lead to an increased concentration of dextromethorphan. This information may also apply to medicinal products used shortly beforehand.

Secretolytics: The concomitant use of Dextromethorphan Hydrobromide containing drugs with secretolytics (expectorant cough medicines) can lead to dangerous accumulation of secretion due to the impaired cough reflex.

Alcohol: Additional alcohol ingestion should be avoided.

Hypotensive medicinal products: Some medicinal products (e.g. certain hypotensive medicinal products called ACE inhibitors) can induce cough. When using these products, the package leaflet indicates that a doctor should be consulted before using a cough suppressant.

4.6 Pregnancy and lactation

The use of Nemel cold and catarrh tablet in pregnancy should be avoided as some of its content (Ephedrine) crosses the placenta and this has been associated with an increase in foetal heart rate and beat to beat variability.

Nemel cold and catarrh tablet is excreted in breast milk and therefore its use during lactation should be avoided. Irritability and disturbed sleep patterns have been reported in breast fed infants.

4.7 Effects on ability to drive and use machines

Even when used as instructed, this medicinal product can occasionally lead to slight tiredness and thus alter reactions so much that the ability to drive vehicles or to use machines is impaired. This applies to a greater extent in combination with alcohol or drugs which themselves can impair reactions.

4.8 Undesirable effects

The most common side-effects are tachycardia, anxiety, nausea, restlessness and insomnia. Tremor, dry mouth, impaired circulation to the extremities, hypertension, headache, hypersensitivity reactions including anaphylactic shock, skin rash, dyspnea, oropharyngeal swelling and cardiac arrhythmias may occur. Tolerance with dependence has been reported with prolonged administration.

Myocardial infarction has occurred very rarely.

Nemel cold and catarrh tablet may act as stimulant in children with nocturnal enuresis and cause sleeplessness. It may have sedative effects in some children.

The elderly are more sensitive to the cardiovascular effects of ephedrine.

<u>Reporting of suspected adverse reactions</u>

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

4.9 Overdose

a) Symptoms

The symptoms of overdose are normally seen as nausea, vomiting, hypertension, fever, palpitations, tachycardia, restlessness, respiratory depression and convulsions. Paranoid psychosis, delusions and hallucinations. States of excitation, dizziness, hallucinations, impairment of consciousness, fall in blood pressure, increased muscle tone and ataxia and liver damage may also follow tablet overdosage.

b) Treatment

In severe overdosage, the stomach should be emptied by emesis and lavage. Treatment with activated charcoal should be considered if the overdose has been taken within 1 hour. Management is by supportive medical monitoring and symptomatic therapy.

5 Pharmacological properties

5.1 Pharmacodynamic properties

Nemel Cold and Catarrh contains the following active pharmaceutical ingredient: Ephedrine, Dextromethophan and Paracetamol.

Ephedrine is a sympathomimetic agent with direct and indirect effects on adrenergic receptors. When given by mouth in therapeutic doses, ephedrine constricts the peripheral vessels, thus increasing blood pressure. It also relaxes bronchioles.

Dextromethorphan hydrobromide is a 3-methoxy derivative of levorphanol. It has an antitussive effect but at therapeutic doses has no analgesic, respiratory depressant or psychomimetic activity and has only low potential for dependence. The completely synthetic D-isomer is free of the L-isomer with its opiate-like activity. Ciliary activity is not inhibited by dextromethorphan hydrobromide at therapeutic doses.

Paracetamol is an effective analgesic and antipyretic agent, but has only weak anti-inflammatory properties. Its mechanism of action is not fully understood. It has been suggested that it may act predominantly by inhibiting prostaglandin synthesis in the CNS and to a lesser extent through a peripheral action by blocking pain-impulse generation. The peripheral action may also be due to inhibition of prostaglandin synthesis or to inhibition of the synthesis or actions of other substances that sensitise pain receptors to mechanical or chemical stimulation. Paracetamol probably produces an antipyretic action by a central effect on the hypothalmic heat-regulating centre to produce peripheral vasodilatation resulting in increased blood flow through the skin, sweating and heat loss. The central action probably involves inhibition of prostaglandin synthesis in the hypothalamus. The drug has no effect on the cardiovascular and respiratory systems, and unlike salicylates it does not cause gastric irritation or bleeding.

5.2 Pharmacokinetic properties

Ephedrine is rapidly and completely absorbed after oral administration and extensively distributed throughout the body with accumulation in the liver, lungs, kidneys, spleen and brain. Peak plasma concentrations are attained during therapy of 65-120 ug/ml; effective

bronchodilator plasma levels are in the range 35-80 ug/ml. The plasma half-life is reported to be between 3-11 hours, with up to 95% being excreted in the urine.

Absorption: Dextromethorphan hydrobromide is rapidly absorbed after oral administration. Peak plasma levels are reached within two hours.

Biotranformation: Dextromethorphan is metabolised in the liver (first pass effect). Dextromethorphan is not metabolised to morphine, codeine or other opiates, nor is there any in vitro or in vivo racemisation to the laevorotatory levomethorphan with its opiate-like activity.

Elimination: The genetic polymorphism in oxidative metabolism (debrisoquine type) amounts to 5-10%. As a result, the fraction renally excreted within 48 hours after oral administration varies from 20% to 86% of the administered dose. Free or conjugated metabolites are recovered in the urine and only a small fraction of the active substance is excreted unchanged. Less than 1% is found in the faeces. The plasma elimination half life is 1.2 - 2.2 hours but can reach up to 45 hours in the case of abnormal metabolism (polymorphism).

The onset of action is 15-30 minutes after oral ingestion and the duration of action is about 3-6 hours

Paracetamol is readily absorbed from the gastrointestinal tract with peak plasma concentrations occurring about 30 minutes to 2 hours after ingestion. It is metabolised in the liver (90-95%) and excreted in the urine mainly as the glucuronide and sulphate conjugates. Less than 5% is excreted as unchanged paracetamol. The elimination half-life varies from about 1 to 4 hours. Plasma protein binding is negligible at usual therapeutic concentrations but increases with increasing concentrations.

A minor hydroxylated metabolite (N-acetyl-p-benzoquinoneimine) 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 liver damage. The time to peak plasma concentration of paracetamol is 0.5 to 2 hours, the time to peak effect 1 to 3 hours and the duration of action 3 to 4 hours.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber

6 Pharmaceutical particulars

6.1 List of excipients

Corn starch

Gelatin

Methyl paraben

Sunset yellow

Magnesium stearate

6.2 Incompatibilities

None known

6.3 Shelf life

36 months (3 Years)

6.4 Special precautions for storage

Do not store above 30°C.

Store in the original package in order to protect from light.

6.5 Nature and contents of container

Blister strips of 10 tablets.

6.6 Special precautions for disposal and other handling

Not applicable

7 Marketing authorisation holder

Nemel Pharmaceuticals limited

8 Marketing authorisation number(s)

A4-6022

9 Date of first authorisation/renewal of the authorisation

08/04/2011

10 Date of revision of the text

12/04/2019