For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

NIMUNICE P

WARNING

Nimesulide should be used only as a second line drug, only after exhausting first line options.

Nimesulide should not be used in pregnant, lactating and women planning for pregnancy.

Nimesulide should not be used in patients with renal and hepatic impairment and also should not be co-administered with other hepatotoxic and renal toxic drugs.

1. Generic Name

Nimesulide and Paracetamol Tablets

2. Qualitative and quantitative Composition:

Each uncoated tablet contains:

Nimesulide B.P. ……100 mg

Paracetamol I.P. …….325 mg

Excipients ……...q.s.

Colour: Sunset Yellow FCF

The List of Excipients used are Starch, Sunset Yellow Lake FCF, Polyvinylpyrrolidone, Methyl Paraben, Propyl Paraben, Magnesium Stearate, Talc, Sodium starch Glycolate, Colloidal silicon Dioxide.

3. Dosage form and strength

Dosage form: Uncoated tablets

Strength: Nimesulide & Paracetamol 100 mg / 325 mg

4. Clinical particulars

4.1. Therapeutic indication

It is indicated for the short term use in fever, acute painful and inflammatory conditions such as headache, toothache, backache, rheumatic and muscle pains, dysmenorrhoea, sore throat in adults.

4.2. Posology and method of administration

Posology

Nimesulide and Paracetamol tablets should be used for the shortest possible duration, as required by the clinical situation. Moreover, undesirable effects may be minimised by using the minimum effective dose for the shortest duration necessary to control symptoms.

Taking more than the daily dose of paracetamol may cause serious liver damage or allergic reaction (e.g. swelling of face, mouth and throat, difficulty in breathing, itching or rash).

Use of Nimesulide should ordinarily be restricted to 10 days. If longer clinical use is warranted liver function test should be assessed periodically.

Adults: Tablets or Granules: one 100 mg / 325 mg tablet twice a day after meals.

Elderly: In elderly patients there is no need to reduce the daily dosage.

Children (< 12 years): 100 mg / 325 mg tablet is contraindicated in these patients.

Acute pain:

An initial dose is 50-100 mg depending on the intensity of pain. Tablets should be used for the shortest possible duration, as required by the clinical situation. Moreover, undesirable effects may be minimised by using the minimum effective dose for the shortest duration necessary to control symptoms.

Children

Nimesulide tablets are not suitable for children below the age of 12 years.

Renal insufficiency/Dialysis and hepatic impairment

Impaired renal function: On the basis of pharmacokinetics, no dosage adjustment is necessary in patients with mild to moderate renal impairment (creatinine clearance of 30-80 ml/min).

Method of administration

For oral use.

4.3. Contraindications

- Hypersensitivity to nimesulide or to any of the excipients.
- History of hypersensitivity reactions (e.g. bronchospasm, rhinitis, urticaria, nasal polyps) in response to acetylsalicylic acid or other non-steroidal anti-inflammatory drugs.
- History of hepatotoxic reactions to Nimesulide.
- Concomitant exposure to other potentially hepatotoxic substances.
- Alcoholism, drug addiction
- History of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy
- Active, or history of recurrent peptic ulcer / haemorrhage (two or more distinct episodes of proven ulceration or bleeding)
- Cerebrovascular bleeding or other active bleeding or bleeding disorders
- Severe coagulation disorders
- Severe heart failure

4.4. Special warnings and precautions for use

Nimesulide should be used only as a second line drug, only after exhausting first line options.

Nimesulide should not be used in pregnant, lactating and women planning for pregnancy.

Nimesulide should not be used in patients with renal and hepatic impairment and also should not be co-administered with other hepatotoxic and renal toxic drugs.

Nimesulide and paracetamol is contraindicated in patients with a history of hypersensitivity (allergic) reaction to nimesulide and paracetamol, paracetamol, nimesulide, or other pain killers. Please inform your doctor before starting nimesulide and paracetamol if you have an active stomach ulcer, recent gastrointestinal bleeding, asthma, recent by-pass heart surgery or severe kidney/liver impairment. Nimesulide present in nimesulide and paracetamol is known to affect fertility, so if you are planning for pregnancy, contact the doctor.

Nimesulide and paracetamol should be avoided in both pregnant (especially last trimester of pregnancy) and breastfeeding women, as it may pass the milk affecting the baby. Patients with heart diseases and recent stroke (bleeding in the brain) should not take nimesulide and paracetamol as a substitute for aspirin. It should not be given to children (below 12 years) with symptoms of fever and chills or suffering from influenza (flu) or chickenpox.

4.5. Drugs interactions

Drug-Drug Interactions

Nimesulide and paracetamol is shown to interact with various drugs. Some of them include lithium, anticancer/antimetabolites (methotrexate), blood thinner or anticoagulant (warfarin, coumadin, aspirin), blood pressure or heart medicine, nausea medicine (metoclopramide, domperidone), diuretic/water pills (thiazides, furosemide), steroid medicine (prednisone), quinolones antibiotics (ciprofloxacin), respiratory medicines (theophyllines, ephedrine), immune system affecting medicine (cyclosporine), cholesterol-reducing medicine (cholestyramine) and antidepressants (duloxetine). These drugs may affect the working of Nimesulide + Paracetamol and may alter its efficacy.

Drug-Food Interactions

Excessive intake of alcoholic beverages, caffeine-containing food or drinks like coffee, tea, chocolate, and some fizzy drinks should be avoided while taking nimesulide and paracetamol. Taking together may lead to drowsiness, dizziness and sleepiness.

Drug-Disease Interactions

Nimesulide and paracetamol should not recommend for people having bleeding disorders, like haemophilia, von Willebrand disease, or low blood platelets. Besides this, it should not be given to children suffering from influenza (flu) or chickenpox. It should also be avoided in case of the presence of gastric or duodenal ulcers.

4.6. Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

Pregnancy

Use of nimesulide and paracetamol during pregnancy is not recommended as taking this medicine during the last 3 months of pregnancy may harm the unborn baby. Consult your doctor for further advice.

Lactation

Use of nimesulide and paracetamol during breastfeeding is not recommended as it may pass through the milk and harm the baby. Consult your doctor for further advice.

4.7. Effects on ability to drive and use machines

No studies on the effect of nimesulide containing medicinal products on the ability to drive or use machines have been performed. However, patients who experience dizziness, vertigo, or somnolence after receiving nimesulide should refrain from driving or operating machines.

4.8. Undesirable effects

The following is a list of possible side effects that may occur from all constituting ingredients of nimesulide and paracetamol tablet. This is not a comprehensive list. These side effects are possible, but do not always occur. Some of the side effects may be rare but serious. Consult your doctor if you observe any of the following side effects, especially if they do not go away.

- Feeling of sickness
- Skin redness
- Allergic reactions
- Shortness of breath
- Swollen facial features
- Liver damage

Reporting of adverse reactions

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. Report suspected adverse reactions via any point of contact available at www.torrentpharma.com.

4.9. Overdose

Symptoms following acute NSAID overdoses are usually limited to lethargy, drowsiness, nausea, vomiting and epigastric pain, which are generally reversible with supportive care. Gastrointestinal bleeding can occur.

Hypertension, acute renal failure, respiratory depression and coma may occur, but are rare. Anaphylactoid reactions have been reported with therapeutic ingestion of NSAIDs, and may occur following an overdose. Patients should be managed by symptomatic and supportive care following an NSAID overdose.

5. Pharmacological properties

5.1. Mechanism of Action

Nimesulide:

Nimesulide only weakly inhibits prostaglandin synthesis and appears to exert its effects through various mechanisms. It inhibits the release of oxidants from activated neutrophils and has a scavenging effect on hypochlorous acid without affecting neutrophil function.

Paracetamol:

Analgesic – the mechanism of analgesic action has not been fully determined. Paracetamol may act predominantly by inhibiting prostaglandin synthesis in the central nervous system (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 is an antipyretic analgesic. The mechanism of action is probably similar to that of aspirin and dependant on the inhibition of prostaglandin synthesis. This inhibition appears, however to be on a selective basis.

5.2. Pharmacodynamic properties

Nimesulide and paracetamol tablet improves the patient's condition by performing the following functions:

- Increasing the pain threshold and increases the blood flow across the skin, heat loss and sweating.
- Blocking the production of prostaglandins thereby relieving pain and inflammation.

5.3. Pharmacokinetic properties

Nimesulide:

Nimesulide is rapidly absorbed following oral administration. Food, gender and advanced age have negligible effects on Nimesulide pharmacokinetics. The protein binding of Nimesulide is > 97.5%. Nimesulide possess a shorter half-life (1.8-4.7) and is hepatically metabolized. 50% of the drug is renally eliminated.

Paracetamol:

Paracetamol is a widely used analgesic and antipyretic agent. Paracetamol is well absorbed in gastrointestinal tract. Oral bioavailability is dose dependent since the half-life of Paracetamol

is 1-3 hrs. Paracetamol is distributed throughout the body fluids in a homogeneous way. Paracetamol given at therapeutic doses binds to plasma proteins at less than 20% Metabolites are excreted through the kidneys in the urine.

6. Nonclinical properties

6.1. Animal Toxicology or Pharmacology

Nimesulide:

Preclinical data reveal no special hazards for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and carcinogenic potential.

In repeated dose toxicity studies, nimesulide showed gastrointestinal, renal and hepatic toxicity.

In reproductive toxicity studies, embryogenic and teratogenic effects (skeletal malformations, dilatation of cerebral ventricles) were observed in rabbits, but not in rats, at maternally non-toxic dose levels. In rats, increased mortality of offspring was observed in the early postnatal period and nimesulide showed adverse effects on fertility.

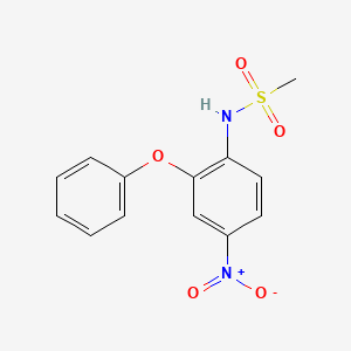
Paracetamol:

Conventional studies using the currently accepted standards for the evaluation of toxicity to reproduction and development are not available.

7. Description

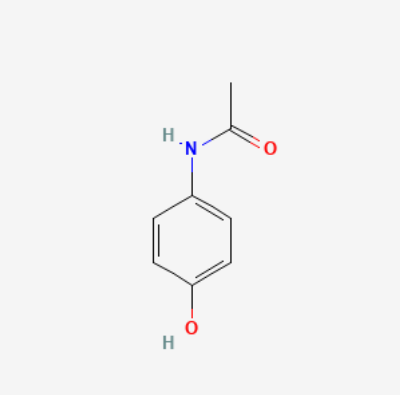
Nimesulide

Nimesulide is N-(4-nitro-2-phenoxyphenyl)methanesulfonamide with molecular weight of 308.31 g/mol and empirical formula is $C_{13}H_{12}N_2O_5S$. The chemical structure is:



Paracetamol

Paracetamol is N-(4-hydroxyphenyl)acetamide with molecular weight of 151.16 g/mol and empirical formula is $C_8H_9NO_2$. The chemical structure is:



Nimunice P

Nimunice P is orange coloured, elongated biconvex uncoated tablets, scored on one side. The list of excipients used are Starch, Sunset Yellow Lake FCF, Polyvinylpyrrolidone, Methyl Paraben, Propyl Paraben, Magnesium Stearate, Talc, Sodium starch Glycolate, Colloidal silicon Dioxide.

8. Pharmaceutical particulars

8.1. Incompatibilities

Not applicable

8.2. Shelf-life

Do not use later than date of expiry.

8.3. Packaging information

Nimunice P is available in pack of 10 Tablets.

8.4. Storage and handing instructions

Store protected from light & moisture at a temperature not exceeding 30^{o}C.

Keep the medicines out of reach of children.

Taking more than daily dose of paracetamol may cause serious liver damage or allergic reactions (e.g. swelling of the face, mouth and throat, difficulty in breathing, itching or rash).

Do not use in children below 12 years of age.

Use of Nimesulide should ordinarily be restricted to 10 days. If longer clinical use is warranted liver function test should be assessed periodically.

9. Patient Counselling Information

Ask the patients to inform the treating physicians in case of any of the below:

- Have any allergies
- Have kidney or liver problems
- Are pregnant or plan to become pregnant
- Are breastfeeding or plan to breastfeed
- Have any serious illness
- Are taking any medicines (prescription, over-the-counter, vitamins, or herbal products)

10. Details of manufacturer

Lucent Biotech Ltd. (Unit-II)

(An ISO 9001:2015 & WHO GMP Certified Co.)

K-165/3, Nalhera Anantpur, Roorkee,

Distt.- Haridwar (Uttarakhand)

11. Details of permission or licence number with date

Mfg. Licence No: 43/UA/2016 Issue date:18.09.2019

12. Date of revision

NA

MARKETED BY

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IN/Nimunice P 100 mg + 325 mg/FEB-2026/01/PI