APPROVED
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INSTRUCTION
for medical use

GRIPGO HOTMIX®

Composition:
active substances: paracetamol, phenylephrine hydrochloride, ascorbic acid;
each sachet contains paracetamol 750 mg, phenylephrine hydrochloride 10 mg, ascorbic acid coated, equivalent to ascorbic acid 60 mg;
excipients: sucrose, sodium saccharin, povidone, anhydrous citric acid, sodium citrate, pregelatinized starch, quinoline yellow (E 104), lemon flavor.

Pharmaceutical form. Granules for oral solution with lemon flavor.
Main physical and chemical properties: light yellow to yellow colored granular powder with the inclusion of white granules of various shapes.

Pharmacotherapeutic group. Analgesics and antipyretics. Paracetamol, combinations excl. psycholeptics. ATC Code N02B E51.

Pharmacological properties.
Pharmacodynamics.
Gripgo Hotmix® is a combined drug, the action of which is caused by the components that are included to its formulation.
Paracetamol has an analgesic and antipyretic effect. It has the ability to suppress the synthesis of prostaglandins due to the inhibition of arachidonic acid cyclooxygenase in the central nervous system (CNS). The consequence of this is a decrease in the sensitivity of the central nervous system to the action of kinins and serotonin, which leads to a decrease in sensitivity to pain. In addition, reducing the concentration of prostaglandins in the hypothalamus has an antipyretic effect. Paracetamol does not affect platelet aggregation.
Phenylephrine hydrochloride belongs to sympathomimetic amines, mainly directly affects adrenoceptors, generally acting on α-adrenoceptors, which leads to a decrease in hyperemia of the nasal mucosa.
Ascorbic acid (vitamin C) is a vital vitamin, the lack of which can occur at the beginning of acute viral infections.
The sedative effect of the drug's active substances has not been established.

Pharmacokinetics.
Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract and uniformly distributed throughout all body fluids. The rate of absorption decreases when paracetamol is used during meals. Protein binding is insignificant at therapeutic doses. The drug is metabolized in the liver and almost completely excreted in the urine, mainly in the form of glucuronides and sulphate conjugates.

Potentially hepatotoxic intermediate metabolite N-acetyl-p-benzoquinone imine (NAPQI), which is formed in small amounts (~5%), after conjugation with glutathione is excreted with cysteine or mercapturic acid. When using large doses of paracetamol, the glutathione stores in the liver are depleted, which leads to the accumulation of toxic metabolites in the liver. This can result in damage to hepatocytes, their death, and acute liver failure.
Less than 5% of the administered dose of paracetamol is excreted unchanged.
The average half-life of paracetamol is 1–4 hours.
Patients with impaired liver function. The half-life of paracetamol in patients with compensated hepatic insufficiency is the same as in healthy individuals. In case of severe hepatic failure, half-life of paracetamol may be increased. The clinical significance of increasing paracetamol half-life in patients with liver disease is unknown. At the same time, no accumulation, hepatotoxicity, or conjugation with glutathione was observed.
Patients with impaired renal function. More than 90% of the therapeutic dose of paracetamol is usually excreted in urine as metabolites within 24 hours. In patients with chronic renal insufficiency, the ability to excrete polar metabolites is limited, which may lead to their accumulation. In patients with chronic renal failure, it is recommended to increase the interval between paracetamol doses.
Ascorbic acid (vitamin C) is rapidly absorbed in the gastrointestinal tract and is delivered to all body tissues, 25% is bound to plasma proteins in the blood. Excess of ascorbic acid, which exceeds the needs of the body, is excreted in the urine in the form of metabolites.
Phenylephrine hydrochloride is easily and quickly absorbed in the gastrointestinal tract. The primary metabolism by monoamine oxidase occurs in the intestine and the liver, with bioavailability reaching 40%. The maximum concentration of the drug in blood plasma is reached in 1–2 hours. The half-life is 2–3 hours. It is excreted in the urine mainly in the form of sulphates.

Clinical characteristics.
Indications.
Short-term relief of symptoms of cold and flu, including headache, fever, nasal congestion, sinusitis and pain associated with it, sore throat, body ache.

Contraindications.
- Hypersensitivity to any components of the drug;
- severe liver impairment, congenital hyperbilirubinemia;
- blood disorders, including severe leukopenia, anemia, glucose-6-phosphate dehydrogenase deficiency, thrombosis, thrombophlebitis;
- severe heart failure, arterial hypertension, severe atherosclerosis, ischemic heart disease;
- severe renal impairments, hypertrophy of the prostate gland;
- increased irritability, sleep disorders, epilepsy;
- hyperthyreosis, severe diabetes mellitus, pheochromocytoma;
- acute pancreatitis;
- angle-closure glaucoma;
- alcoholism;
- concomitant use with:
  - monoamine oxidase inhibitors (MOI) and for 2 weeks after discontinuation of MOI inhibitors;
  - tricyclic antidepressants;
  - beta-blockers or antihypertension medicinal products;
  - sympathomimetics.

Interaction with other medicinal products and other forms of interactions.
The absorption rate of *paracetamol* may be increased during concomitant use with metoclopramide or domperidone; and may be reduced during concomitant use with cholestyramine. The anticoagulant effect of warfarin and other coumarins may be enhanced with increased risk of bleeding in case of simultaneous long-term regular daily use of paracetamol. With short-term use in accordance with the recommended regimen, these interactions are not of clinical significance. Caution should be taken when paracetamol is used concomitantly with flucloxacillin as concurrent intake has been associated with high anion gap metabolic acidosis due to pyroglutamic acidosis, especially in patients with risks factors (see "Special warnings and precautions for use" section). Barbiturates reduce the antipyretic effect of paracetamol. Anti-seizure drugs (including phenytoin, barbiturates, carbamazepine), that stimulate the activity of microsomal liver enzymes, may increase the toxic effect of paracetamol on the liver due to increasing in the degree of drug conversion to hepatotoxic metabolites. Simultaneous administration of high paracetamol doses with isoniazid increases the risk of hepatotoxic syndrome. Paracetamol reduces the effectiveness of diuretics. Do not use with alcohol.
The interaction of *phenylephrine* with MOI causes hypertensive effect; with tricyclic antidepressants (e.g. amitriptyline) it increases the risk of cardiovascular side effects; with digoxin and cardiac glycosides it leads to impaired heartbeat or myocardial infarction. Phenylephrine with other sympathomimetics increases the risk of the cardiovascular adverse reactions. Phenylephrine may reduce the efficacy of beta-blockers and other antihypertensive agents (including debrisoquine, guanethidine, reserpine, methyldopa) and increase the risk of hypertension and other cardiovascular side effects.
Simultaneous use of phenylephrine with ergot alkaloids (ergotamine and methysergide) increases the risk of ergotism.
When taken orally, *ascorbic acid* increases absorption of penicillin, iron, decreases the effectiveness of heparin and indirect anticoagulants, increases the risk of crystalluria in the treatment with salicylates. Antidepressants, antiparkinsonian drugs and antipsychotics, phenothiazine derivatives increase the risk of urine retention, dry mouth, constipation. Glucocorticosteroids increase the risk of glaucoma.
The absorption of vitamin C is decreased when applied simultaneously with oral contraceptives, fruit or vegetable juices, alkaline drinks. Ascorbic acid should be taken only 2 hours after deferoxamine injection, because their simultaneous use increases iron toxicity, especially in the myocardium. Long-term use of large doses of ascorbic acid inhibits the disulfiram-alcohol reaction in persons treated with disulfiram.

Special warnings and precautions for use.
Please consult your doctor before using this drug.
Gripgo Hotmix® contains paracetamol.
Cases of high anion gap metabolic acidosis due to pyroglutamic acidosis have been reported in patients with severe illness such as severe renal impairment and sepsis, or malnutrition and other sources of glutathione deficiency (e.g. chronic alcoholism) who were treated with paracetamol at therapeutic dose for a prolonged period or a combination of paracetamol and flucloxacillin. If high anion gap metabolic acidosis due to pyroglutamic acidosis is suspected, prompt discontinuation of paracetamol and close monitoring is recommended. The measurement of urinary 5-oxoproline may be useful to identify pyroglutamic acidosis as underlying cause of high anion gap metabolic acidosis in patients with multiple risk factors.
Avoid concomitant use with other drugs prescribed for symptomatic treatment of cold and flu, vasoconstrictor agents for treatment of rhinitis, drugs containing paracetamol. Concomitant use with other drugs containing paracetamol may lead to overdose. Overdose of paracetamol can cause hepatic failure, which may necessitate liver transplants or lead to death. The risk of overdose

increases in patients with non-cirrhotic alcoholic liver disease.
Cases of hepatic dysfunction/failure have been reported in patients with depleted glutathione levels, such as those who are severely malnourished, anorexic, have a low body mass index, are chronic heavy users of alcohol or have sepsis.
Before using the drug, it is recommended to consult a physician for patients taking warfarin; for patients with Raynaud's disease (which may be manifested by pain in the fingers and toes in response to cold or stress); for patients with arterial hypertension, cardiovascular diseases, impaired liver and kidney function.
The drug contains phenylephrine, which can cause angina attacks.
One sachet (1 dose) contains 2.9 g of sucrose. This should be taken into account by patients with diabetes.
This drug should not be used in patients taking other sympathomimetics (e.g., anti-inflammatory drugs, appetite suppressants, and amphetamine-type psychostimulants). Use with caution in patients taking digoxin, cardiac glycosides, or ergot alkaloids (e.g., ergotamine, methysergide).
Patients should seek medical attention if symptoms persist for more than 5 days, worsen, or if symptoms are accompanied by high fever, skin rash, or persistent headache.
In patients with severe infections such as sepsis, which are accompanied by a decrease in glutathione levels, the risk of metabolic acidosis increases when taking paracetamol. Signs of metabolic acidosis include deep, rapid, difficult breathing, nausea, vomiting, loss of appetite. Contact a doctor immediately if you get these symptoms.
Excipients.
The drug contains sucrose. If the patient has an intolerance to some sugars, a doctor should be consulted before taking this medicine.
The drug contains quinoline yellow (E 104), so it can cause allergic reactions.

Use in pregnancy and lactation.
Do not take this medicine during pregnancy and lactation.
Paracetamol and phenylephrine can be excreted in breast milk, so if you need to use the drug, you should stop breastfeeding.

Influence on velocity reactions in driving motor transport or operating other machines.
In the event of some side effects development, such as dizziness, the drug may affect velocity reactions in driving motor transport or operating other machines.

Administration and dosage.
The drug is intended for internal use. Empty contents of 1 sachet into a cup and pour hot water (but not boiling water). Stir until completely dissolved. If necessary, add cold water.
Adults and children aged 12 years and over: single dose is 1 sachet. The contents of 1 sachet should be taken every 4–6 hours as needed. The minimum interval between taking the drug is 4 hours. The maximum daily dose is 5 sachets. Do not use the drug for more than 5 days without consulting a doctor.
Do not exceed the recommended doses. The lowest effective dose should be taken for the shortest period of time.

Children.
It is not recommended to use the drug for children under 12 years.

Overdose.
Overdose is usually caused by paracetamol and is manifested by pale skin, anorexia, nausea, vomiting, abdominal pain, hepatonecrosis, increased activity of hepatic transaminases, and

increased prothrombin index.
In patients with such risk factors as long-term treatment with carbamazepine, phenobarbital, phenytoin, primidone, rifampicin, St. John's wort or other drugs that induce liver enzymes; regular alcohol abuse; with glutathione cachexia (digestive disorders, cystic fibrosis, HIV infection, malnutrition, cachexia), when taking 5 g or more of paracetamol, liver damage is possible.
Symptoms of liver damage are observed in 12–48 hours after overdose and may peak in 4–6 days. Disorders of glucose metabolism and metabolic acidosis may occur. In case of severe poisoning, hepatic impairment may progress and lead to the development of toxic encephalopathy with impaired consciousness, in some cases – to the need for liver transplantation or to lethal outcome. Liver damage is possible in adults who have taken 10 g or more of paracetamol, and in children who have taken paracetamol over 150 mg/kg of body weight.
Acute renal failure with acute tubular necrosis may be manifested by strong back pain, hematuria, proteinuria, and develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have also been observed.
Long-term treatment with high doses may lead to aplastic anemia, pancytopenia, agranulocytosis, neutropenia, leukopenia, thrombocytopenia.
Management of paracetamol overdose: in case of paracetamol overdose first medical aid is required, even if early symptoms of overdose have not been observed. Symptoms may be limited to nausea or vomiting and may not reflect the severity of overdose or the risk of organ damage. Gastric lavage is required, along with administration of activated charcoal (within 1 hour after the overdose) and symptomatic therapy. The use of paracetamol antidotes, N-acetylcysteine intravenously and methionine orally can give a positive effect within 24 hours after an overdose.
Phenylephrine overdose is likely to result in effects similar to those listed in the "Adverse reactions" section. Besides, irritability, restlessness, hypertension, and reflex bradycardia may occur. In severe cases, confusion, hallucinations, seizures and arrhythmia are possible. However, the amount of drug required to produce serious phenylephrine toxicity would be greater than required to cause paracetamol-related hepatic toxicity.
Treatment of phenylephrine overdose: in case of overdose, gastric lavage, administration of activated charcoal, symptomatic therapy, use of alpha-blockers such as phentolamine in severe hypertension are necessary.
High doses of ascorbic acid (>3000 mg) may cause transient osmotic diarrhea and gastrointestinal effects such as nausea and abdominal discomfort. Effects of ascorbic acid overdose can be classified as those caused by severe liver damage as a result of paracetamol overdose.

Adverse reactions.
Skin and subcutaneous tissue disorders: rashes on the skin and mucous membranes (usually erythematous, urticaria), itching, allergic dermatitis, exudative erythema multiforme, including Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome), purpura, hemorrhaging.
Immune system disorders: hypersensitivity reactions, allergic reactions (including angioneurotic edema), anaphylaxis, anaphylactic shock.
Mental disorders: psychomotor agitation and disturbance of orientation, anxiety, nervousness, feeling of fear, irritability, sleep disturbance, insomnia, confused consciousness, depression, hallucinations.
Central nervous system disorders: headache, tremor, paresthesia, uneasiness, sedation, anxiety, general weakness, dizziness, excitement; impaired concentration during the next day, especially with insufficient sleep duration after taking the drug.
Ear and labyrinth disorders: tinnitus, vertigo.
Eye disorders: mydriasis, increased intracranial pressure, angle-closure glaucoma (more often in patients with glaucoma), impaired vision and accommodation.

Gastrointestinal tract disorders: nausea, vomiting, discomfort and pain in the epigastrium, heartburn, decreased appetite, constipation, diarrhea, flatulence, dry mouth, ulcers of the oral mucosa, hypersalivation, hemorrhages.
Hepatobiliary system disorders: increased hepatic enzymes, usually without jaundice, hepatonecrosis (dose-dependent effect), impaired liver function, liver failure.
Endocrine system disorders: hypoglycemia, up to hypoglycemic coma.
Blood and lymphatic system disorders: anemia, sulfhemoglobinemia and methemoglobinemia (cyanosis, shortness of breath, cardiac pain), hemolytic anemia, thrombocytopenia, bruises or bleedings, leukopenia, agranulocytosis, pancytopenia.
Kidney and urinary system disorders: with high doses therapy – impaired urination, delayed urination (more likely in patients with prostatic hypertrophy), nephrotoxicity (renal colic, interstitial nephritis, papillary necrosis), oliguria, aseptic pyuria.
Cardiovascular system disorders: increased blood pressure, arterial hypertension, heart pain, palpitations, rapid heartbeat, tachycardia, sinus tachycardia, shortness of breath, edema, reflex bradycardia.
Respiratory, thoracic and mediastinal disorders: bronchospasm in patients sensitive to acetylsalicylic acid and other non-steroidal anti-inflammatory drugs.
Metabolism and nutrition disorders: high anion gap metabolic acidosis.
Other: general weakness, fever, glucosuria, impaired zinc and copper metabolism.
The drug may show a slight laxative effect.
Description of selected adverse reactions.
High anion gap metabolic acidosis. Cases of high anion gap metabolic acidosis due to pyroglutamic acidosis have been observed in patients with risk factors using paracetamol (see "Special warnings and precautions for use" section). Pyroglutamic acidosis may occur as a consequence of low glutathione levels in these patients.
Reporting of suspected adverse reactions.
Reporting adverse reactions after authorization of the medicinal product is very important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals and pharmaceutical workers, as well as patients or their legal representatives are asked to report any suspected adverse reactions and lack of efficacy of the medicinal product through the Automated Pharmacovigilance Information System: https://aisf.dec.gov.ua/.

Shelf-life.
3 years.

Storage conditions.
Store at a temperature not more than 25°C in the original package.
Keep out of reach of children.

Package.
5 g in a sachet. 5 or 10, or 20, or 50 sachets in a carton pack.

Conditions of supply.
Without prescription.

Manufacturer.
KUSUM HEALTHCARE PVT LTD.

Location of manufacturer and its address of business activity.
SP-289 (A), RIICO Industrial area, Chopanki, Bhiwadi, Dist. Alwar (Rajasthan), India.

Date of last revision.

11.04.2025