APPROVED
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Registration certificate
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INSTRUCTION
for medical use
GRIPGO®

Composition:
active substances: paracetamol, caffeine anhydrous, phenylephrine hydrochloride, chlorpheniramine maleate;
1 tablet contains paracetamol 500 mg, caffeine anhydrous 30 mg, phenylephrine hydrochloride 10 mg, chlorpheniramine maleate 2 mg;
excipients: microcrystalline cellulose, croscarmellose sodium, magnesium stearate.

Pharmaceutical form. Tablets.
Main physical and chemical properties: white biconvex capsule-shaped tablets.

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

Pharmacological properties.
Pharmacodynamics.
Gripgo® is a combined medicine, the action of which is caused by its components.
Paracetamol is an analgetic-antipyretic that has anti-inflammatory and analgesic properties; that is related to the effect of paracetamol on hypothalamus center of heat regulation and its possibility to inhibit the synthesis of prostaglandins.
Caffeine is an methylxanthine alkaloid, which has a stimulating effect on the central nervous system, mainly on the cerebral cortex, respiratory and vascular centers, increases mental and physical performance, reduces drowsiness, fatigue and weakens the action of drugs that depress the central nervous system. Increases the analgesic effect of paracetamol.
Phenylephrine hydrochloride is a sympathomimetic agent that reduces swelling of the nasal mucosa and paranasal sinuses, as well as the severity of exudative manifestations that promotes the improvement of nasal breathing. It stimulates mainly alpha-adrenoceptors, thereby narrowing and reducing the permeability of peripheral blood vessels, as well as decreasing the formation of mucous secretions.
Chlorpheniramine maleate is an antihistamine that has anti-allergic effects. It competitively blocks histamine H_1-receptors and prevents a development of histamine effects, eliminates the cold, nasal itch and eyes pruritus.
Pharmacokinetics.
Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract (GIT). The maximum concentration in blood plasma is reached in 30–60 minutes. The half-life is 1–4 hours. It is evenly distributed in all body fluids. Plasma protein binding is variable; 20 to 30% may be bound at concentrations formed during acute intoxication. It is excreted mainly by the kidneys in the form of conjugated metabolites.

Caffeine and its water-soluble salts are rapidly absorbed in the intestine (including the large intestine) and are rapidly distributed in all organs and tissues of the body. Binding to blood proteins (albumins) is 25–36%.
The plasma half-life is about 5–10 hours. The main part is demethylated and oxidized. About 10% is excreted unchanged by the kidneys. Caffeine and its metabolites are excreted by the kidneys (in adults 1–2% of caffeine is excreted unchanged).
Phenylephrine hydrochloride has low bioavailability due to uneven absorption and exposure to monoamine oxidase in GIT and liver during the first pass. It is excreted by the kidneys as metabolites. Acidification of urine accelerates excretion from the body.
Chlorpheniramine maleate is slowly absorbed from GIT; the maximum concentration in blood plasma is reached after 2.5–6 hours, 70% of it is bound to plasma proteins. Bioavailability is from 25% to 50% of the dose. Chlorpheniramine is metabolized during the first pass in the liver, and is largely metabolized in the liver with the formation of metabolites of desmethyl- and didesmethylchloropheniramine. Chlorpheniramine is distributed throughout the body and crosses the blood-brain barrier. Metabolites and the drug are excreted mainly in the urine unchanged for 4–6 hours. Excretion depends on the pH of the urine and the degree of excretion. In children, there is a faster and more extensive absorption, excretion and half-life.

Clinical characteristics.
Indications.
Treatment of symptoms of flu and acute respiratory viral diseases, such as fever, headache, nasal congestion, rhinitis, sinusitis, sore throat, muscles pain, and cough.

Contraindications.
• Hypersensitivity to any component of the drug, other xanthine derivatives (theophylline, theobromine), opioids, antihistamines, sympathomimetic amines, Stevens-Johnson syndrome;
• severe cardiovascular disease, including unstable angina, decompensated heart failure, disturbance of rhythm and conduction, congenital prolonged QT interval or long-term use of drugs that prolong the QT interval, arrhythmias, bradycardia, severe atherosclerosis, including coronary heart disease, predisposition to vasospasm, severe coronary heart disease; severe hypertension, acute myocardial infarction, organic diseases of the cardiovascular system, thrombosis, thrombophlebitis;
• severe hepatic impairment (including congenital hyperbilirubinemia; Gilbert's syndrome);
• severe renal impairment;
• prostate disease (prostate adenoma with difficulty urinating, acute urinary retention in prostate hypertrophy, prostatic hyperplasia, bladder neck obstruction);
• diseases of the gastrointestinal tract (gastric and duodenal ulcers in the acute stage, stenotic gastric and duodenal ulcers, pyloroduodenal obstruction; acute pancreatitis);
• epilepsy;
• blood diseases (including severe anemia; leukopenia; hematopoietic disorders);
• endocrine diseases (hyperthyroidism, diabetes, pheochromocytoma, thyrotoxicosis, phenylketonuria);
• diseases of the respiratory system (including bronchial asthma; chronic bronchitis; chronic obstructive pulmonary disease; emphysema; risk of respiratory failure);
• angle-closure glaucoma, increased intraocular pressure;
• glucose-6-phosphate dehydrogenase deficiency;
• Dubin-Johnson syndrome, Rotor syndrome;
• alcoholism;
• children under 12 years;
• old age (over 60 years);
• pregnancy or breastfeeding;

• increased excitability, sleep disorders, epilepsy;
• simultaneous use with:
- monoamine oxidase inhibitors (MAOIs), and for 2 weeks after discontinuation;
- tricyclic antidepressants;
- drugs that suppress or increase appetite and amphetamine-like psychostimulants;
- vasodilators;
- beta-blockers and other sympathomimetics.

Interaction with other medicinal products and other forms of interactions.

Concomitant use with other drugs containing paracetamol or other active substances that are included into the formulation of Gripgo® should be avoided.

Peculiarities of interaction are caused by the components that are included into its formulation.

Paracetamol.

The rate of absorption of paracetamol may increase under the action of metoclopramide and domperidone and decrease under the action of cholestyramine. The anticoagulant effect of warfarin and other coumarins may be enhanced by concomitant long-term regular daily use of paracetamol, with an increased risk of bleeding. Periodic use has no significant effect.

Barbiturates reduce the antipyretic effect of paracetamol.

Anticonvulsants (including phenytoin, barbiturates, carbamazepine), which stimulate the activity of liver microsomal enzymes, may increase the toxic effects of paracetamol on the liver by increasing the rate of conversion of the drug to hepatotoxic metabolites. Concomitant use of paracetamol with hepatotoxic drugs increases the toxic effects of drugs on the liver.

Concomitant use of high doses of paracetamol with isoniazid increases the risk of hepatotoxic syndrome.

Concomitant use of paracetamol with azidothymidine may lead to the development of neutropenia.

Paracetamol reduces the effectiveness of diuretics.

Do not use simultaneously with alcohol.

Caffeine.

Caffeine when used simultaneously enhances the effect of analgesics-antipyretics (improves bioavailability), xanthine derivatives, α- and β-adrenomimetics, psychostimulants, thyrotropic drugs, ergotamine (improves the absorption of ergotamine from the digestive tract).

Cimetidine, hormonal contraceptives, isoniazid increase the effect of caffeine.

Caffeine increases the likelihood of liver damage by hepatotoxic drugs.

Caffeine reduces the effect of opioid analgesics, anxiolytics, hypnotics and sedatives, is an antagonist of drugs for anesthesia and other drugs that depress the central nervous system, a competitive antagonist of drugs adenosine, adenosine triphosphate (ATP); reduces the concentration of lithium in the blood.

Ototoxic and photosensitizing drugs when used concomitantly may exacerbate side effects.

Caffeine reduces the hypotensive effect of guanethidine, which in turn increases the alpha-adrenostimulatory activity of phenylephrine. Caffeine enhances the action of indirect anticoagulants (coumarin derivatives). Metoclopramide increases, and cholestyramine reduces the rate of caffeine absorption. Antidepressants, antiparkinsonian and antipsychotic drugs, phenothiazine derivatives increase the risk of urinary retention, dry mouth, constipation. Glucocorticosteroids increase the risk of glaucoma.

Phenylephrine hydrochloride.

Phenylephrine hydrochloride should not be used with alpha-blockers, other antihypertensive agents, phenothiazine derivatives (e.g. promethazine), bronchodilator sympathomimetics, guanethidine, foxglove, rauwolfia alkaloids, indomethacin, indomethacin, methyldopa, glucocorticosteroids; drugs that affect appetite, amphetamine-like psychostimulants, labor

stimulants, anesthetics, ergot alkaloids, other drugs that stimulate the central nervous system, theophylline.
The use of phenylephrine hydrochloride with indomethacin and bromocriptine can cause severe hypertension. Concomitant use of phenylephrine hydrochloride with sympathomimetic amines, digoxin and cardiac glycosides increases the risk of arrhythmias and myocardial infarction.
There may be an increase in the vasoconstrictive effect of the drug when used concomitantly with labor stimulants and arrhythmias when used with anesthetics. There may be a significant increase in blood pressure with simultaneous intravenous administration of ergot alkaloids.
Atropine sulfate blocks phenylephrine-induced reflex bradycardia and increases the vasopressor response to phenylephrine. Concomitant use of phenylephrine with β-blockers may lead to hypertension and excessive bradycardia with possible heart block. It should be used with caution with thyroid hormones, drugs that affect cardiac conduction (cardiac glycosides, antiarrhythmic drugs). Concomitant use with drugs that increase potassium excretion, such as some furosemide-type diuretics, may increase hypokalaemia and reduce arterial sensitivity to vasopressor drugs such as phenylephrine.
It should not be used together with other vasoconstrictors (by any route of administration of the latter).
Concomitant use of phenylephrine and other sympathomimetics can lead to additional stimulation of the central nervous system to an extremely high level, accompanied by nervousness, irritability, insomnia. Seizures are also likely. In addition, concomitant use of other sympathomimetics with phenylephrine may increase the vasoconstrictive effect or cardiovascular effect of either of these two drugs.
Chlorpheniramine maleate.
Chlorpheniramine maleate enhances the anticholinergic effect (dry mouth, urinary retention, constipation) of atropine, antispasmodics, central nervous system depressants (tranquilizers, barbiturates), antiparkinsonian drugs.
The drug potentiates the effect of MAO inhibitors. Concomitant use of MAO inhibitors and furazolid with chlorpheniramine maleate may cause agitation, hypertensive crisis and hyperpyrexia.
Concomitant use with hypnotics, barbiturates, sedatives, neuroleptics and phenothiazine derivatives, tranquilizers, anesthetics, narcotic analgesics, alcohol enhances the effect of chlorpheniramine maleate.
Maprotiline (tetracyclic antidepressant) and other anticholinergic drugs: the anticholinergic effect of these drugs or antihistamines such as chlorpheniramine may be increased.
Do not use simultaneously with alcohol. Chlorpheniramine maleate and alcohol potentiate each other's action.

Special warnings and precautions for use.
Do not exceed the recommended doses.
Do not use concomitantly with other anti-cold drugs, sedatives, hypnotics and drugs containing paracetamol, as this may lead to overdose. Paracetamol overdose can cause liver failure, which may necessitate a liver transplant or lead to death.
If the symptoms of the disease do not disappear or the headache becomes constant, you should see a doctor.
The risk of overdose is increased in alcoholic liver disease. Alcohol consumption, which enhances the sedative effect of chlorpheniramine maleate and the hepatotoxicity of paracetamol, should be excluded during treatment. It should be borne in mind that patients with liver diseases have an increased risk of hepatotoxic effects of paracetamol. Patients taking daily analgesics for mild arthritis should consult a physician before using the drug.

In patients with severe infections, such as sepsis, which are accompanied by a decrease in glutathione levels, paracetamol increases the risk of metabolic acidosis. Symptoms of metabolic acidosis are deep, rapid or difficult breathing, nausea, vomiting, loss of appetite. You should see a doctor immediately if you experience these symptoms.
Serious skin reactions, such as acute generalized exanthematous pustulosis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported in rare cases in patients receiving paracetamol. Patients should be informed of the symptoms of severe skin reactions. The drug should be discontinued in the event of skin rashes or other signs of hypersensitivity.
Excessive coffee, strong tea, other tonics and caffeinated medicines should be avoided when using the drug. This can cause sleep problems, tremors, tension, irritability, and palpitations. Do not drink alcohol.
Use with caution in compensated heart failure, in patients at risk of seizures, in patients with chronic obstructive airways disease, persistent or chronic cough resulting from smoking or pulmonary emphysema, when cough is accompanied by excessive mucus secretion. Use with caution in persons prone to high blood pressure.
With prolonged use, it is necessary to monitor peripheral blood and functional status of the liver.
Do not use sedatives, hypnotics or other anti-cold drugs at the same time.
The drug may affect the results of laboratory tests for blood glucose and uric acid. The use of the drug may lead to a positive analytical result of doping control.
Before using the drug, it is necessary to consult a doctor if the patient is using warfarin or similar drugs that have an anticoagulant effect, or if the patient has impaired renal and liver function.
Phenylephrine may cause an increased heart rate, dizziness, or heart palpitations; patients should be warned, accordingly.
In case of accidental overdose, the patient should immediately consult a doctor, even if condition has not worsened.
Keep the medicine out of the sight of children and out of reach of children.

Use in pregnancy and lactation.
Gripgo® is contraindicated during pregnancy. Breastfeeding should be discontinued during treatment.

Influence on velocity reactions in driving motor transport or operating other machines.
Driving, operating machinery and other hazardous activities should be avoided during treatment.

Administration and dosage.
Adults and children over 12 years of age should be prescribed 1 tablet 3–4 times a day with intervals of at least 4 hours between doses. The maximum daily dose is 4 tablets. The maximum period of use without consulting a doctor is 3 days, further therapy should be on doctor's advice.

Children.
The drug is contraindicated in children under 12 years.

Overdose.
Symptoms.
Signs and symptoms of Gripgo® overdose are due to the action of its individual components.
Associated with paracetamol.
It is known that toxic effects in adults are possible after taking 10–15 g of paracetamol. The following symptoms may be observed: pale skin, anorexia, nausea, vomiting, diarrhea, discomfort in the epigastric region (0–24 hours); gastrointestinal bleeding; increased activity of hepatic transaminases, lactate dehydrogenase, bilirubin levels, as well as decreased prothrombin levels (24–48 hours); hepatotoxic effect, which is characterized by general (pain, weakness, adynamy, increased sweating) and specific (hepatomegaly, jaundice, increased activity of liver enzymes)

symptoms. Hepatotoxic effect can lead to the development of hepatonecrosis and be complicated by the development of hepatic encephalopathy (thinking disorder, suppression of higher nervous activity, agitation and stupor), disseminated intravascular coagulation syndrome (DIC syndrome), hypoglycemia, metabolic acidosis, arrhythmias, seizures, respiratory depression, coma, cerebral edema, hypocoagulation, collapse. Occasionally, liver dysfunction develops rapidly and may be complicated by renal failure. At high doses, there may be impaired orientation, agitation, dizziness, sleep and heart rhythm disorders, pancreatitis, bacterial infection, fungal infection, sepsis, coagulopathy, hypophosphatemia, lactic acidosis, cardiomyopathy, hypotension, respiratory failure. Glucose metabolism disorders may occur. With long-term use of high doses, aplastic anemia, pancytopenia, agranulocytosis, neutropenia, leukopenia, thrombocytopenia are possible.

Associated with phenylephrine hydrochloride and chlorpheniramine maleate.

Symptoms of overdose due to phenylephrine and chlorpheniramine maleate: headache, hyperhidrosis, drowsiness, insomnia, behavioral changes, anxiety, irritability, tremor, seizures, hyperreflexia, dizziness, nausea, vomiting, tachycardia, arrhythmias, extrasystoles.

Associated with chlorpheniramine maleate.

With an overdose of chlorpheniramine maleate, the condition can range from depressed to agitated (anxiety and seizures). Atropine-like symptoms may occur, including mydriasis, photophobia, dry skin and mucous membranes, increased body temperature, intestinal atony; depression of the central nervous system is accompanied by respiratory disorders and disorders of the cardiovascular system.

Associated with caffeine.

Caffeine overdose has the following symptoms: dehydration, hyperthermia, ringing in the ears, epigastric pain, increased diuresis, extrasystole, tachycardia, rapid breathing, arrhythmia, central nervous system effects (dizziness, insomnia, exaltation, irritability, psychomotor agitation, affective state, anxiety, tremor, vomiting, seizures, convulsions, agitation, anxiety, delirium, increased tactile or pain sensitivity).

Treatment of overdose.

In case of overdose, emergency medical care is required. The patient should be taken to a hospital immediately, even if there are no early symptoms of overdose. Symptoms may be limited to nausea and vomiting or may not reflect the severity of the overdose or the risk of organ damage. Activated charcoal treatment should be considered if an overdose of paracetamol has been taken within 1 hour. Plasma paracetamol concentrations should be measured 4 hours or later after intake (earlier concentrations are inaccurate). N-acetylcysteine treatment can be used within 24 hours after taking paracetamol, but the maximum protective effect occurs when using it within 8 hours after intake. The effectiveness of the antidote decreases sharply after this time. If necessary, the patient should be administered intravenous N-acetylcysteine in accordance with current guidelines. In the absence of vomiting, oral methionine can be used as a suitable alternative in remote areas outside the hospital.

Adverse reactions.

Immune system: hypersensitivity reactions, including anaphylaxis, itchy skin, hyperemia, rash on the skin and mucous membranes (usually generalized rash, erythematous, urticaria), anaphylactic shock, angioneurotic edema, exudative erythema multiforme (including Stevens-Johnson syndrome), toxic epidermal necrolysis, acute generalized exanthematous pustulosis.

Nervous system and mental disorders: psychomotor agitation and disorientation, anxiety, behavioral changes, fear, anxiety, irritability, sleep disturbances, insomnia, drowsiness, dizziness, mental confusion, hallucinations, depression, tremor, tingling sensation and heaviness in the limbs, tinnitus, headache, dizziness, coma, seizures, hyperexcitability, epileptic seizures, dyskinesia.

Respiratory system: bronchospasm in patients sensitive to aspirin and other NSAIDs, nasal congestion, throat irritation, hoarseness, pharyngitis.

Visual organs: impaired vision and accommodation, mydriasis, increased intraocular pressure, dry eyes.

Gastrointestinal tract: loss of appetite, nausea, vomiting, dry mouth, hypersalivation, heartburn, discomfort and pain in the epigastrium, exacerbation of peptic ulcer disease, flatulence, diarrhea, constipation.
Hepatobiliary system: liver dysfunction, increased activity of hepatic transaminases, usually without jaundice development, hepatonecrosis (at high doses), hepatotoxicity.
Endocrine system: hypoglycemia, up to hypoglycemic coma. With prolonged use in high doses, there is a possibility of damage to the insular apparatus of the pancreas (hyperglycemia, glucosuria) and impaired glycogen synthesis until the onset of diabetes mellitus.
Metabolic disorders: metabolic disorders of zinc, copper.
Blood and lymphatic system: anemia, including hemolytic anemia, bruising or bleeding; sulfhemoglobinemia and methemoglobinemia (cyanosis, shortness of breath, heart pain), thrombocytosis, hyperproteinemia, erythropenia, neutrophilic leukocytosis.
With prolonged use in high doses, aplastic anemia, pancytopenia, agranulocytosis, neutropenia, leukopenia, thrombocytopenia are possible.
Kidneys and urinary system: at high doses – nephrototoxicity (including papillary necrosis), urinary incontinence, urinary retention and difficulty urinating, dysuria, interstitial nephritis, increased creatinine clearance, increased excretion of sodium and calcium, aseptic pyuria, renal colic.
With prolonged use in high doses, there is a possibility of damage to the glomerular apparatus of the kidneys, crystalluria, the formation of urate, cystine and/or oxalate stones in the kidneys and urinary tract.
Cardiovascular system: hypertension, tachycardia or reflex bradycardia, arrhythmia, shortness of breath, heart pain, myocardial dystrophy (dose-dependent effect with prolonged use), heart palpitations.
Others: general weakness, increased sweating; possible false increase in uric acid in the blood, determined by the Bittner method; slight increase in the level of 5-hydroxyindoleacetic acid, vanillin mandelic acid and catecholamines in the urine.

Shelf-life. 4 years.

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

Package.
4 tablets in a blister; 1 blister in a cardboard package No. 4 (4×1).
4 tablets in a blister; 50 blisters in a cardboard package No. 200 (4×50).
10 tablets in a blister; 1 blister in a cardboard package No. 10 (10×1).
10 tablets in a blister; 1 blister in a cardboard package No. 10.
10 cardboard packages in a cardboard box No. 100 (10×1×10).
10 tablets in a blister; 10 blisters in a cardboard package No. 100 (10×10).

Conditions of supply.
Without prescription – No. 4 (4×1), No. 10 (10×1) in blisters.
By prescription – No. 200 (4×50), No. 100 (10×10), No. 100 (10×1×10) in blisters.

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.