PACKAGE LEAFLET: INFORMATION FOR THE USER

ANALGIN

500 mg tablet

METAMIZOLEE SODIUM

• This leaflet is a copy of the Summary of Product Characteristics and Patient Information Leaflet for a medicine, which outlines the conditions under which the medicine should be used and information on its known safety • The product information may be updated several times within its shelf life, and there could be differences between the version of information shown here and other information in the public domain or in the package insert • This leaflet may not contain all the information about the medicine or the information may not be the most up to date version for this product • If you have any questions or are not sure about anything, ask your doctor or pharmacist • Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

• Keep this leaflet • You may need to read it again • If you have any further questions, ask your doctor or pharmacist • This medicine has been prescribed for you only • Do not pass it on to others • It may harm them, even if their signs of illness are the same as yours • If you get any side effects, talk to your doctor or pharmacist • This includes any possible side effects not listed in this leaflet •

What is in this leaflet?

1. WHAT ANALGIN IS AND WHAT IT IS USED FOR

Analgin contains an active substance which is a derivative of metamizol pirazolone. Analgin works by soothing the pain and lowering raised body temperature. Analgin is indicated in case of:

- acute severe pain after injury or surgery,
- Spasmodic abdominal pain (colic)
- Cancer related pain,
- Other acute and chronic pain, unless other therapeutic measures are indicated,
- Raised body temperature (fever), which does not respond to other measures.

2. BEFORE YOU START TAKING ANALGIN

Do not take Analgin:

- if you are allergic (hypersensitive) to metamizol or to other pirazolone (e.g. phenazone, propyphenazone) and pirazolidins (for example, pheniylbutazone, oxyphenbutazone), or if after using these medicines you experience a strong decrease in the number of white blood cells (agranulocytosis);

• if you have been diagnosed intolerance to analgesics, followed by an asthma attack, or loss of breath (analgesic asthma syndrome) or intolerance to analgesics followed by hives and / or swelling of the face, tongue and throat (urticaria, angioedema), or if you react with spasmodic narrowing of the lower airway (bronhospazamom) or other forms of hypersensitivity, such as hives, runny nose and swelling of the face, tongue and throat (urticaria, rhinitis, angioedema) to pain medications, such as salicylates, acetaminophen, diclofenac, ibuprofen, indomethacin or naproxen ;
• if you have impaired function of the bone marrow, for example after treatment with cytostatics (cancer medicines);
• if you suffer from impaired formation of blood elements (hematopoietic system disorder);
• if you have an inborn deficiency of the enzyme glucose-6-phosphate dehydrogenase (an inherited metabolic disease which causes a risk of red blood cells decomposition);
• if you have a hereditary liver disease known as acute intermittent porphyria (hereditary disorder of blood pigment hemoglobin);
• if you are in the last trimester of pregnancy,
• if you are breast-feeding.

The use of this medicine in children under the age of ten is not recommended.

Be careful with Analgin:

Analgin Tablets contain metamizol, a derivative of pirazolone, which rarely can cause life-threatening dangerous shock (Sudden circulation failure) and agranulocytosis (severe disease that occurs due to a strong decrease in the number of white blood cells).
If you are hypersensitive to Analgin (anaphylactoid reactions), you are exposed to a particular risk of the appearance of the same reactions to other pain medicines.
If using Analgin causes an allergic or other (immune-mediated) defense reactions (e.g. agranulocytosis) you are exposed a particular risk of the appearance of the same reactions to other pyrazolones and pyrazolidinyl (chemically related substances).
When choosing a method of administration it is important to keep in mind that the parenteral administration is associated with a higher risk of occurrence of hypersensitivity reactions.
If you experience signs of agranulocytosis, pancytopenia and thrombocytopenia stop taking the medicine and consult a doctor (see section 4. "Possible side effects").

Severe hypersensitivity reactions (anaphylactic or anaphylactoid reactions)
If you suffer from any of the following diseases/intolerances, there is an increased risk of occurrence of severe hypersensitivity reactions to Analgin:

• Intolerance to pain / rheumatism medication (intolerance to analgesics) which manifests itself as hives or swelling of the face, tongue and throat, as well as emergence of asthma attacks and loss of breath (analgesic asthma syndrome) (see section 2. 'Do not take Analgin ");
•bronchial asthma, especially if at the same time you suffer from rhino sinusitis (inflammation of the nasal and sinus cavities) and the nasal polyps;
•chronic hives;
•hypersensitivity to color (for example, tartrazin), or preservatives (e.g. benzos);
• Alcohol intolerance. These patients respond to the slightest amount of alcohol with symptoms such as sneezing, watery eyes and redness of the face. Such intolerance to alcohol may indicate a previously unknown allergy to pain medication (see section 2. 'Do not take Analgin ").

In patients with an increased risk of hypersensitivity reactions, Analgin can be given only after careful assessment of the possible risks in relation to the expected benefits. If Analgin is however given in such cases, patients should be monitored closely and the doctor should be ready to react in case of emergency.
Anaphylactic shock mainly occurs in susceptible patients (see section 4. "Possible side effects"). Therefore, special care is required in patients with asthma or a predisposition for the occurrence of hypersensitivity reactions (atopy).

Severe skin reactions

During the use of metamisole, you may experience life-threatening skin reaction (Stevens-Johnson syndrome and toxic epidermal necrolysis). If you notice the severe redness on the skin (hives), often with blisters or mucosal damage, stop taking Analgin immediately (see section 4. "Possible side effects").

Drop in blood pressure (isolated hypotensive reaction)

Analgin may cause a drop in blood pressure (isolated hypotensive reactions) (see section 4. "Possible side effects").

The risk of such reactions is increased:

- If Analgin is rapidly injected into a vein,
- If you have low blood pressure (hypotension), if you are dehydrated, if you have circulatory problems or have initial circulatory failure (myocardial infarction or severe trauma)
- If you have a high fever.

A doctor will carefully monitor your condition and if necessary carry out preventive measures (e.g., stabilization of the circulatory system), to reduce the risk of lowering of blood pressure. If you should at all costs avoid a drop in blood pressure (eg. In case of severe coronary heart disease or significant narrowing of cerebral arteries), Analgin can be used only if the functions of a bloodstream are carefully monitored.

Patients with impaired liver or kidney function

If you have impaired liver or kidney function, Analgin should be used only after a rigorous assessment of the risk - benefit and with use of proper precautions (see section 3. "Impaired liver or kidney function").

Older patients

In older patients, the excretion of Analgin metabolites may be delayed.

Infants and children

Newborns and infants under the age of three months, or those that have less than 5 kg of body weight should not be given Analgin because there is no scientific knowledge on the use of the medicine in this age group.

Taking other medicines

Please tell your doctor or pharmacist about all medicines you are taking or have recently taken, including those that you bought without a prescription, as well as herbal remedies or natural products.

Analgin can cause a decrease in the concentration of cyclosporine (medicine for the Suppression of the immune system) in the blood. Concomitant use should be controlled levels of cyclosporine in the blood.

Concomitant use of Analgin with methotrexate (a medicine used to treat severe forms of rheumatoid arthritis, certain skin diseases and cancers) can increase the concentration of this medicine in the blood, which can lead to the occurrence of toxic side effects, especially in older patients. Therefore, this combination should be avoided.

Concomitant use of Analgin with Chlorpromazine (medicine used to treat schizophrenia) is associated with the risk of the appearance of serious hypothermia.

Group of medicines called pyrazolone (analgin belongs to this group) interacts with the following medicines:

- Medicines to thin the blood (oral anticoagulants)
- Captopril (used to treat high blood pressure and heart disease),
- Lithium (used for the treatment of certain mental disorders),
- Medicines for the removal of excess fluid (diuretics, eg, triamterene)
- Medicines used to treat high blood pressure (antihypertensives).

Taking Analgin with food and drinks

Do not consume alcohol while being treated with Analgin, because it can increase its effect.

Pregnancy and breastfeeding
Ask your doctor or pharmacist for advice before you start using any medicine.

Pregnancy
Since there are no adequate data, Analgin should not be used in the first trimester of pregnancy, while in the second trimester it can only be used after consultation with a doctor. In the last trimester of pregnancy Analgin should not be taken because it prevents the natural function of the squamous cells (thrombocytes aggregation), which can lead to excessive bleeding during childbirth. In addition, it can lead to closing of a blood vessel, which is important for a child (ie. Ductus Botalli, which normally closes after childbirth).

Breast feeding
Do not breast-feed at least 48 hours after taking the last dose of Analgin, because the metabolites pass into human breast milk.

Driving and using machines
If you are taking the recommended dose, Analgin has no effect on the ability of concentration and response. In the case of high doses, due to possible adverse impact, caution should be exercised when driving a car or machinery. This is especially true when you consume alcohol at the same time.

Analgin Tablets contain metamizol sodium.
Each tablet contains 1.42 mmol (32.7 mg) of sodium. This should be taken into consideration in patients with limited sodium intake.

3. HOW TO TAKE ANALGIN

Always take Analgin as recommended by a doctor. If you are not sure, consult with a doctor or pharmacist.

Dosage
Dosage depends on the intensity of the pain or raised body temperature, as well as of the individual reactions on the effects of the medicine. In general, you should consider the following recommendations:

- In general, the lowest dose that controls pain and fever should be selected;
- In case of raised body temperature, general dosing in children is 10 mg / kg of body weight;
- The effect of the medicine is achieved 30 to 60 minutes after oral administration;
- The recommended individual dose for children and adolescents from 10 to 14 years is 8 mg / kg to 16 mg / kg. In adults and adolescents who are older than 15 years (> 53 kg) individual dose may be up to 1,000 mg.

The following table shows the recommended individual and maximum daily dose.

Age (body weight)	Individual dose	Maximum daily dose
10 to 14 years (32 kg to 53 kg)	1 tablet of Analgin (corresponds to 500 mg of metamizole sodium monohydrate)	Up to 4 tablets of Analgin (corresponds to 2.000 mg of metamizole sodium monohydrate)
Adults and adolescents over 15 (> 53 kg)	1 to 2 tablets of Analgin (corresponds to 500 mg do 1.000 mg of metamizole sodium monohydrate)	Up to 8 tablets of Analgin (corresponds to 4.000 mg of metamizole sodium monohydrate)

Older patients
In older patients the dose should be reduced because the excretion of the metabolites of the medicine may be slower.

Patients with impaired general condition and reduced creatinine clearance
In patients with impaired general condition and reduced creatinine clearance, the dose should be reduced because the excretion of medicine metabolites can be slower.

Impaired liver or kidney function
Considering that in patients with impaired liver or kidney function the elimination of products of metabolism of the medicine are reduced, the repeated administration of high doses should be avoided. In short-term use a dose reduction is not required. There is no experience with prolonged use of this product.

Method of administration
The tablets should be swallowed whole with enough fluid (for example, with a full glass of water).

Duration of treatment
The duration of treatment depends on the type and severity of the disease, as determined by a doctor. It is not recommended to take Analgin for longer than three to five days without consultations with the physician or dentist.

If you take more medicine than you should
If you take more tablets than you should, tell your doctor so he/she can take adequate measures. Symptoms of overdose depend on the degree of overdosing. You may experience nausea, vomiting, pain in the abdomen, reddish coloration of urine, renal impairment, which can progress to renal insufficiency (interstitial nephritis), dizziness, drowsiness, fainting, spasm, lowering of blood pressure, which can progress to shock and rapid heart rate (tachycardia).

If you forget to take Analgin
Never take a double dose to replace the missed dose of the medicine. Analgin Tablets are taken as needed.

If you have any further questions on the use of Analgin, talk to your doctor or to the pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Analgin can cause side effects, although not everybody gets them.

If any of these symptoms occur, stop taking this medicine and inform your doctor or go to the nearest hospital, because some symptoms in certain circumstances can be life-threatening (e.g., severe hypersensitivity, severe skin reactions like Stevens-Johnson syndrome or toxic epidermal necrolysis, agranulocytosis, pancytopenia). Timely treatment interruption is crucial.
If you experience signs of agranulocytosis, pancytopenia and thrombocytopenia, treatment with metamizole should be discontinued immediately and blood counts should be monitored (including differential blood counts). Treatment should be stopped immediately, and you should not wait for the results of laboratory tests.

Analgin should not be taken anymore if you experience the following symptoms that indicate a possible agranulocytosis:
- unexpected deterioration of the general state (the increase in body temperature, chills, croup, difficulty swallowing),
- high body temperature which is not reduced or lowered,
- painful, inflammatory changes in the mucosa of the mouth, nose and throat, as well as inflammation of the anal and genital areas.

Other possible side effects are:
Uncommon side effects (occur in less than 1 in 100 users, but in more than one user in 1000):
- Purple to deep red skin rash, partly with blistering (fixed exanthema)

• Drop in blood pressure (isolated hypotensive reactions) directly caused by the application of dose without signs of anaphylactic or anaphylactic reactions. Such reactions can lead to a critical drop in blood pressure. The risk of a drop in blood pressure can be increased in case of extremely high temperature (hyperpyrexia). Typical signs of a serious drop in blood pressure are: tachycardia, paleness, tremor, dizziness, nausea and fainting.

Rare side effects (occur in less than one in 1000 users, but in more than one in 10000 users:

• Hypersensitivity reaction (anaphylactic or anaphylactoid reaction)

The typical signs of hypersensitivity to the drug include symptoms such as burning eyes, cough, runny nose, sneezing, feeling of tightness in the chest, redness of the skin (especially in the face and head), hives and swelling in the area of face, rarely nausea and stomach cramps. Particular care should be taken to the most common warning signs, such as burning, itching and feeling of heat on the tongue and under the tongue, especially on the hands and feet.

Such reactions can slowly turn into more severe symptoms with severe hives, severe angioedema (swelling in the area of the larynx and the Adam's apple), severe bronchospasm (narrowing of the lower respiratory tract), palpitations (sometimes with slower heart rate), cardiac dysrhythmia, drop in blood pressures (sometimes with transient increases in blood pressure), fainting and shock.

These reactions may occur in patients who have used Metamizole in the past without complications, and they can even be fatal.

In patients with analgesic asthma syndrome, hypersensitivity reactions are manifested in the form of asthma attacks (see section 2. 'Do not take Analgin ").

• Reduction in the number of white blood cells (leukopenia)

• Skin rash (maculopapular rash).

Very rare side effects (occur in less than one in 10000 users, but in more than one in 100,000 users):

• a reduction in the number of white blood cell count (agranulocytosis), which can be life-threatening, and reduction in the number of platelets (thrombocytopenia). These reactions are probably immune-mediated and may occur in patients who have used the metamizol earlier without complications. The risk of the occurrence of these reactions is increased if the Analgin is taken longer than seven days. Signs of agranulocytosis are: high fever, chills, croup, difficulty swallowing, painful, inflammatory changes in the mucosa of the mouth, nose and throat, as well as inflammation of the anal and genital areas.

In patients receiving antibiotic therapy, these signs may be reduced. Erythrocyte sedimentation rate is accelerated and swelling of the lymph nodes or spleen is mild or non-existent.

Typical signs of thrombocytopenia, for example, are tendency to bleed and petechiae (petechiae on the skin and mucous membranes).

• Asthma attack (shortness of breath due to narrowing of the smallest airways).

• Large blisters on the skin and peeling of the skin (Stevens-Johnson syndrome or toxic epidermal necrolysis).

• Acute renal impairment with decreased secretion of urine (oliguria), completely reduced secretion of urine (anuria) or increased excretion of protein in the urine (proteinuria), and acute kidney failure (acute renal failure) or acute inflammation of the kidneys (acute interstitial nephritis).

Frequency unknown (cannot be estimated from available data)

• Anaphylactic shock.

• Anemia with simultaneous disorder of the bone marrow (aplastic anemia), a visible decline in the number of white and red blood cells and platelets (pancytopenia), including cases with fatal outcome.

Signs of aplastic anemia and pancytopenia are: general weakness, infection, persistent high fever, bruising, bleeding, paleness, red coloration of urine, which is harmless.

If you notice any side effect, talk to your doctor or pharmacist!

5. HOW TO STORE ANALGIN

Keep out of reach and sight of children.

Analgin should not be used after the expiration date stated on the carton. Expiration date refers to the last day of that month.

The product should be stored at temperature below 25°C.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Analgin contains

- the active substance is metamizol sodium monohydrate. Each tablet contains 500 mg of metamizole sodium monohydrate.

The other substances are: calcium phosphate dibasic dihydrate; povidone; sodium laurylsulfate; magnesium stearate.

What Analgin looks like and contents of the pack

Analgin Tablets are white to light yellowish, round, flat, tablets with facet, with breaking line on one side and "ANALGIN" on the other side. The tablets are packaged in blister pack (aluminium foil/PVC foil). Each blister contains 10 tablets. Cardboard box contains 10 tablets (1 blister), along with the attached instructions. Cardboard box containing 500 tablets (50 blisters), along with the attached instructions.

Regime of dispensing

The medicine is issued on doctor's prescription.

Manufacturer

Alkaloid AD – Skopje BUL. Aleksandar Makedonski 12 1000 Skopje, Republic of Macedonia

Manufacturer of the medicinal product

Alkaloid AD – Skopje BUL. Aleksandar Makedonski 12 1000 Skopje, Republic of Macedonia