PACKAGE LEAFLET: Information for the patient

ANALGINE

Tablets – 500 mg

Solution for injection – 1000 mg / 2 ml

(Metamizole sodium)

Read this leaflet carefully before you start taking this medicine.

- 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 symptoms are the same as yours.
- If any of the side effects gets worse or if you notice any side effect not listed in this leaflet, please inform your doctor or pharmacist.

What is in this leaflet:

1. WHAT ANALGINE IS AND WHAT IT IS USED FOR

Analgine contains the active substance metamizole sodium, which has a significant analgesic and antipyretic effect, but its anti-inflammatory effect is weak. It has also a spasmolytic effect on the smooth muscles of the uterus, gallbladder and urinary tract. It inhibits the synthesis of prostaglandins through inhibition of cyclooxygenasis. The central analgesic action is due to the inhibition of the activation of adenylatecyclase.

It is indicated in severe or resistant conditions with pain or temperature.

Metamizole sodium is rapidly and completely absorbed after oral administration. The maximal plasmatic concentration is obtained after one hour. It is partially bound to plasmatic proteins. The drug is metabolised in the liver.

2. BEFORE YOU TAKE ANALGINE

Do not take Analgine if:

- you are allergic to the active substance metamizole sodium or to the other pirazolone or pirazolidine derivatives;
- you are allergic to any of the excipients mentioned at the end of this leaflet;
- you have agranulocytosis precedents accompanied with pirazolone use;
- you have compromised function of the spinal cord (e.g after the therapy with cytostatics) or haematopoietic system pathology, as granulocytopenia;
- you have been caused bronchospasm or other anaphylactoid reactions (e.g. urticaria, rhinitis, angioedema) from non - opioid analgesics (e.g. salicylates, paracetamol, diclofenac, ibuprofen, indomethacin, naproxen);
- you suffer from any metabolic disease (glucose-6-phosphate dehydrogenase deficiency, hepatic porphyria);
- if you are in the last three months of pregnancy;
- the patient is a child less than 3 years old.

It should not be administered as injection in patients with hypotension or who have circulatory instability.

It should not be used with chlorpromazine because it causes hypothermia and renal failure.

If you think you have any of the above-mentioned conditions, do not take the drug. Consult first your doctor and follow the given advices.

Take special care with Analgine

Because of the risks for serious side effects, drug administration may be justified only in cases when there does not exist any other safe alternative.

Inform your doctor if you are allergic to other drugs, especially if they are in the same drug class with Analgine.

The existence of hypersensitivity to Analgine (metamizole sodium) should be tested before treatment with it.
Drug administration increases the risk for agranulocytosis and shock. It is necessary to discontinue the treatment and consult immediately the doctor if any of the following symptoms develops that may be associated with neutropenia: fever, chills, sore throat, mouth ulcerations.

Pancytopenia
In case of pancytopenia, the treatment should be discontinued immediately and the complete blood count should be monitored until it is normalized.
Contact your doctor immediately if during treatment with Analgine you develop signs and symptoms that indicate blood dyscrasia (e.g. not a good general condition, infections, persistent fever, ecchymosis, bleeding, pallor).
Metamizole sodium may cause worsening of dyspnoea and cyanosis. It should be used with caution in asthmatic or atopic patients. Treatment should be immediately discontinued if any sign or symptom of anaphylaxis appears (urticaria, angioedema, rash, dyspnoea, general pallor or hyperemia, not a good general condition, hypotension, shock, oedema of the larynx), if signs of agranulocytosis or trombocytopenia appear.
The use of this medicine is not recommended in women who want to start a pregnancy.

Special warnings
It should be kept in mind that parenteral route (injection) is associated with a greater risk for anaphylactic / anaphylactoid reactions, which may cause death, because of patient hypersensitivity. For this reason, this route of administration remains only for those cases considered as absolutely necessary by the doctor. The doctor itself, through a very careful anamnese, should preliminarily exclude the patient hypersensitivity, which constitutes an absolute contraindication.

Patients who have high risk for severe anaphylactoid reactions are especially those with:
- asthma caused by analgesics or intolerance of urticaria-angioedema type from analgesics;
- bronchial asthma, especially if they also have polypose rhinosinusitis;
- chronic urticaria;

- intolerance to alcohol;
- intolerance to colorants or preservatives.

Before the administration of Analgine, specific questions should be made to the patients. If the doctor considers it necessary to administer Analgine, emergency treatment should be available.

Severe skin reactions

After the administration of metamizole, Stevens - Johnson syndrome and toxic epidermal necrolysis are reported, which are skin reactions that may endanger patient's life. If their signs or symptoms appear (progressive cutaneous eruption, often with blisters or mucous membrane damage), treatment with metamizole should be discontinued immediately and it should not start over again.

Hypotensive sporadic reactions

Metamizole may cause hypotensive reactions in sporadic cases. These reactions may be dose - dependent and it is more possible to happen after the administration as an injection. The risk for severe hypotensive reactions increases if:

- the injection is not administered slowly;
- the patient has an existing hypotension, dehydration or decreased volume, instability of the circulation or its insufficiency;
- the patient has high fever.

The administration of high doses of metamizole in patients with renal or liver failure should be avoided, because in these patients, the rate of elimination of the drug is decreased.

Taking other medicines

Inform your doctor or pharmacist if you are taking or have recently taken other medicines, including those obtained without a prescription. Inform your doctor if you are taking any of the following drugs:

- cyclosporin, because a reduction of the plasmatic levels of cyclosporin may occur;
- methotrexate, because by concomitant use with Analgine, blood toxicity caused by methotrexate may increase, especially in the elderly, thus this combination should be avoided;

- chlorpromazine, because it causes hypothermia and renal failure;
- neuroleptic and anxiolytic drugs because they potentiate metamizole sodium action against pain;
- some antidepressants, oral contraceptives and allopurinol slow down the metabolism of the drug and thus increase its toxicity.
- acetylsalicylic acid (aspirin), metamizole may reduce the effect of acetylsalicylic acid on platelet aggregation, when taken concomitantly. Therefore, this combination should be used with caution in patients taking low dose aspirin for cardioprotection;
- bupropione, metamizol may reduce its blood concentration.

In patients receiving metamizol, interference with laboratory tests has been reported who use the Tinder method, or a method similar to Tinder, for example tests to measure levels of creatinine, triglycerides, HDL cholesterol and uric acid in the blood.
During treatment with Analgine, alcohol consume should be avoided.

Taking Analgine with food and drinks
It is advised to take the tablets after food and with a lot of liquid.
During treatment with Analgine, alcohol consume should be avoided.

Pregnancy
Available data on the use of metamizole during the first three months of pregnancy is limited but do not indicate harmful effects to the embryo. In selected cases when no other treatment options exist, single doses of metamizole during the first and second trimester might be acceptable after consultation with your doctor or pharmacist and after the benefits and risks of metamizole use have been carefully weighed up. However, in general, the use of metamizole during the first and second trimester is not recommended.
During the last three months of pregnancy you must not take Analgine because of an increased risk of complications for the mother and child (haemorrhaging, premature closure of an important vessel, the so-called Ductus Botalli, of the unborn, which naturally closes only after birth).

Breastfeeding

The breakdown products of metamizole pass into breast milk in considerable amounts and a risk to the breastfed infant cannot be excluded. Especially the repeated use of metamizole during breastfeeding must therefore be avoided. In case of a single administration of metamizole, mothers are advised to collect and discard the breastmilk for 48 hours after the dose.

Driving and using machines

In patients taking Analgine the ability to concentrate and react may be altered, thus constituting a risk in situations in which these abilities are particularly important (e.g. driving vehicles or using machines), especially if you have taken it with alcohol.

Important information about some of the excipients of Analgine

Analgine - Solution for injection contains:

- about 43 mg / 2 ml benzyl alcohol. Benzyl alcohol may cause toxic reactions and allergic reactions, mainly in babies and children up to 3 years old, so this drug should not be used in these ages. Talk to your doctor or pharmacist if you have liver or renal problems, or if you are pregnant or breast - feeding, because high volumes may lead to toxicity.
- about 2.88 mmol sodium / 2 ml. It should be taken into consideration from patients who are on a sodium restriction diet.

3. HOW TO TAKE ANALGINE

Always take Analgine exactly as your doctor has told you. If you feel that its effects are too strong or too weak, talk to your doctor or pharmacist.

It is advised to take the tablets after food and with a lot of fluids.

Dosage for the tablets is as follows:

The dose is dependent on the intensity of the pain or fever and the individual’s sensitivity of response to Analgine

The lowest dose needed to control pain and fever should always be selected. Your doctor will tell you how to take Analgine.

Adults and adolescents of 15 years of age or older (weighting more than 53 kg) can take up to 1,000 mg metamizole as a single dose (2 tablets) which can be taken up to 4 times daily at intervals of 6-8 hours. 4,000 mg (corresponding to 8 tablets) is the maximum daily dose.
A clear effect can be expected 30 to 60 minutes after oral administration.
Analgine should not be used for children younger than 15 years of age.

The solution for injection Analgine should be used only if it is not possible to use the oral dosage form.

Dosage for the solution for injection is as follows:

The dose is dependent on the intensity of the pain or fever and the individual's sensitivity of response to Analgine. Analgine will be given to you as injection into your vein or into muscle. If the effect of a single dose is insufficient or later, when the analgesic effect subsides, your doctor may administer another dose up to a daily maximum dose as detailed below.

Adults and adolescents of 15 years of age or older

Adults and adolescents of 15 years of age or older (weighting more than 53 kg) can be given 1 - 2 mL intravenously or intramuscularly. The maximum daily dose is 8 mL.

The solution for injection Analgine should not be used in children less than 3 years old because of benzyl alcohol content.

Infants and children

The following dosage scheme for single doses intravenous or intramuscular should be used as a guide:

Children age range (body weight)	Single dose	Maximum daily dose
4 – 6 years (ca. 16 – 23 kg)	0.3 – 0.8 mL	1.2 – 3.2 mL
7 – 9 years (ca. 24 – 30 kg)	0.4 – 1.0 mL	1.6 – 4.0 mL
10 – 12 years (ca. 31 – 45 kg)	0.5 – 1.4 mL	2.0 – 5.6 mL
13 – 14 years (ca. 46 - 53 kg)	0.8 – 1.8 mL	3.2 – 7.2 mL

The injection should be administered slowly, with the patient lied down and controlling the heart and blood circulation.

Elderly and patients in poor general health/with renal impairment
The dose should be reduced in elderly people, in debilitated patients and in those with reduced renal function, as excretion of the breakdown products of metamizole may be delayed.

Patients with impaired kidney or liver function
As the rate of elimination is reduced in patients with impaired kidney or liver function, repeated high doses should be avoided. No dose reduction is required with short-term use only. There is no experience available with long-term use.

If you take more Analgine than you should
An overdosage of Analgine might cause: nausea, vomits, abdominal pain, renal problems (acute renal failure).
More rarely: symptoms including Central Nervous System, such as dizziness, drowsiness, coma, convulsions, hypotension (sometimes shock) and tachycardia.
After administration of very high doses, a red coloration of the urine may appear.

If you take more Analgine than you should, or if the children have taken this medicine incorrectly, please contact your doctor or call the hospital or emergency to get an opinion for the risk and an advice for the actions to be taken.

If you forget to take Analgine
If you forget a dose (or more doses), take the following dose when it is time to take it usually.
Do not take a double dose (or higher) to make up for a forgotten dose.
If you have further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

All medicines can cause side effects, although not everybody manifests them.

Tell your doctor if you notice any of the following side effects:

- allergic reactions (Analgine use is dangerous mainly in porphyric patients), these reactions may be severe and life-threatening and sometimes fatal; in some patients cross-sensitivity appeared by the simultaneous use of metamizole with aspirin; it causes and worsens dispnoea (difficulty on breathing), may cause cyanosis, apnea and also asthmatic paroxisms in patients who suffer from asthma;
- effects on the blood (risk for agranulocytosis, leukopenia, thrombocytopenia and shock);
- gastrointestinal bleeding;
- effects on the skin (toxic epidermal necrolysis, Stevens-Johnson syndrome, which may risk patient's life, urticarial rash with itching of the skin, mucous membranes and conjunctiva).

In people who suffer from kidney disease, temporary impairment of their function may appear, associated with olyguria, polyuria, proteinuria and interstitial nephritis; these effects may appear after the use of high doses.

In some cases, after its administration, sporadic transitory hypotensive reactions may appear.

If you notice side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

5. HOW TO STORE ANALGINE

Keep out of the reach and sight of children.

Do not use Analgine after the expiry date which is stated on the package.

Store below 25°C.

Keep in the original packaging to protect it from light and humidity!

6. OTHER INFORMATION

What Analgine tablets contain

The active substance is metamizole sodium.

Each tablet contains 500 mg metamizole sodium.

The excipients are*:* croscarmellose sodium, sodium laurylsulfate, sodium starch glycolate, magnesium stearate, purified talc, pregelatinized starch, hypromellose.

What Analgine solution for injection contains

The active substance is metamizole sodium.

Each ampoule 2 ml contains 1000 mg metamizole sodium.

The excipients are*:* sodium thiosulfate, sodium-EDTA, benzyl alcohol, hydrochloric acid, water for injection.

Contents of the pack:

Tablets: carton box with 30 tablets.

Solution for injection: carton box with 10 ampoules.

Marketing Authorisation Holder (MAH) and Manufacturer:

PROFARMA Sh.a.,

St. "Skënder Vila“,

Tirana, Albania.

Tel.: +355 4 23 89 602

This leaflet was last revised in August 2023.