

PACKAGE LEAFLET: INFORMATION FOR THE USER

TOPIRIN

250 + 250 + 50 mg Tablet

ACETYLSALICYLIC ACID + PARACETAMOL + CAFFEINE

• 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?

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1. WHAT TOPIRIN IS AND WHAT IT IS USED FOR

TOPIRIN tablets contain a combination of an analgesic, antipyretic and anti-inflammatory medicine (NSAID painkiller).

TOPIRIN is used:

- For adults and children older than 12 years for treatment of acute mild to moderate headaches
- during migraine attacks with or without aura and
- for the treatment of headaches caused by tension.

2. BEFORE YOU TAKE TOPIRIN

Do not take TOPIRIN

- If you are hypersensitive (allergic) to acetylsalicylic acid, salicylates or other NSAIDs (medicines for pain, fever and inflammation), paracetamol or any other ingredients contained in TOPIRIN tablets
- if you have a stomach or duodenal ulcer
- if you have severe liver damage
- if you have severe kidney damage

- if you have severe heart failure
- if you have increased tendency to bleed
- if you are receiving methotrexate at a dose of 15 mg / week or more
- if you are under 12 years of age
- if you are in the last trimester of pregnancy

Take special care with TOPIRIN, so you must tell the doctor if you

- Suffer from allergies or asthma, hay fever, nasal polyps, chronic respiratory diseases;
- are also taking anticoagulants
- If you have hypersensitivity reactions (eg, skin reactions) to other anti-inflammatory medicines (ie. Intolerance to analgesics / analgesic asthma) or other allergens
- If you have an acute, chronic or repeated problems with the stomach or intestines
- If you have stomach ulcers, gastrointestinal bleeding or perforation
- if you have renal impairment or existing kidney disease
- if you have liver damage (eg. From chronic alcoholism or hepatitis)
- If you have a deficiency of glucose-6-phosphate dehydrogenase
- if you suffer from Gilbert's syndrome (Gilbert's disease)
- before surgery
- If you have an overactive thyroid gland (hyperthyroidism).

Acetylsalicylic acid in low doses reduces the excretion of uric acid. In predisposed patients it sometimes can cause gout attack. Regular use of analgesics can permanently damage the kidneys, and carries the risk of renal failure (analgesic nephropathy).

Regular use should also be avoided in diabetes (diabetes mellitus), alcoholism, rheumatism, dehydration (severe dehydration for example, diarrhea, high temperature, excessive exercise with sweating), chronic low blood pressure and severe injuries.

With prolonged high doses, incorrect use of painkillers can cause headache that cannot be treated with increased doses of medicine. In these cases do not increase the dose without consulting a doctor.

Disruption of treatment with high doses, incorrect use of painkillers can lead to headaches and fatigue, muscle pain, anxiety, and vegetative symptoms. These symptoms wear thin within a few days. Until then, you cannot reuse painkillers without a doctor's recommendation.

TOPIRIN tablets may mask signs of infection. If, during the administration, there is development or worsening of signs of infection (such as redness, swelling, heat, pain, fever), you should contact your doctor.

As they contain acetylsalicylic acid, TOPIRIN tablets can be given to children in febrile conditions, such as chicken pox, but only after doctor's advice and they can be used only when other measures are not effective. Persistent vomiting, headache or loss of consciousness can be a sign of Reye's syndrome, a very rare disease, which can be fatal and requires urgent medical treatment.

Taking other medicines

Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Acetylsalicylic acid can increase the effects and side effects of the following medicines:

- anticoagulants (for example, derivatives of coumarin and heparin), certain antidepressants (selective serotonin reuptake inhibitors): increased risk of bleeding
- platelet aggregation inhibitors (medicines which prevent platelet aggregation) as ticlopidine
- certain pain medications (NSAIDs), corticosteroids, or concomitant use of alcohol: increased risk of gastrointestinal problems (for example, gastrointestinal bleeding)
- medicines for lowering blood glucose levels
- valproic acid, methotrexate, digoxin, lithium.

Acetylsalicylic acid can reduce the effects of the following medicines:

- medicines for increased urination (diuretics)
- medicines for increased ejection of uric acid in the urine (due to gout)
- medicines for blood pressure lowering (antihypertensive)

Concomitant administration with medicines which accelerate degradation of the paracetamol in the liver, such as barbiturates, sleeping medicines, anticonvulsants and rifampicin, can cause liver damage, even in harmless doses of acetaminophen; same applies to alcohol abuse.

The concomitant use of substances that lead to slowing of gastric emptying, such as propantheline, may delay the absorption and onset of action of paracetamol.

The concomitant use of substances that accelerate gastric emptying, such as metoclopramide may accelerate absorption and onset of paracetamol's effect.

Concomitant administration of paracetamol and chloramphenicol, inhibits elimination of chloramphenicol, and thus can increase the risk of side effects.

Concomitant administration of paracetamol and zidovudine increases the tendency of neutropenia. Therefore, this medicine should be used simultaneously with zidovudine only under medical supervision.

Other known effects:

- probenecid, salicylamide: reduced secretion of acetaminophen, an increased risk of side effects
- oral anticoagulants: increased risk of bleeding when used at the same time seven days or acetaminophen is taken in high doses
- cholestyramine: reduced absorption of paracetamol

Taking paracetamol may affect the results of tests to determine the levels of uric acid and blood sugar.

Caffeine has antagonistic effect on the sedative effect of many medicines, such as barbiturates, antihistamines, etc. Caffeine increases heart rate, accelerates the effects of sympathomimetic agents eg. thyroxine, etc.

For medicines with a wide spectrum of action, detailed interactions are different and unpredictable (e.g., benzodiazepines).

Oral contraceptives, cimetidine and disulfiram reduce the degradation of caffeine in the liver, and barbiturates and smoking accelerate it. The excretion of theophylline is reduced with caffeine.

Caffeine increases the potential for addiction to ephedrine.

Parallel use of gyrase inhibitors, type quinoline carboxylic acid may delay the elimination of caffeine and its degradation of products of Paraxanthine.

Therefore, TOPIRIN tablets should not be used in combination with any substance mentioned here, without strict doctor's instructions.

Taking food and drink with TOPIRIN tablets

While using TOPIRIN tablets do not drink alcohol.

Pregnancy and breast-feeding

Ask your doctor or pharmacist for advice before taking any medicine.

Pregnancy

TOPIRIN tablets should not be taken during pregnancy because they can affect the pregnancy and / or the development of the unborn child.

During the first and second quarter, TOPIRIN tablets can be used only after consulting a doctor or a dentist, and only in the lowest effective doses and for the shortest time possible, because there is evidence of an increased risk of miscarriage and malformation of the child.

The same applies for women who want children.

In the last three months of pregnancy and during labor, TOPRIN tablets cannot be used because there is an increased risk of complications for both mother and child.

Note:

During treatment in pregnancy, be sure to inform your doctor.

Breastfeeding

TOPIRIN is excreted into breast milk.

Caffeine that a child takes through breast milk, may affect the condition and behavior of the child. During a short-term use of the recommended dose interruption of breastfeeding is generally not be required.

During a prolonged use or taking the higher doses, breastfeeding should be discontinued.

Driving and using machines

TOPIRIN should not affect your ability to drive and use machines.

Other warnings

Important information about some ingredients of TOPIRIN tablets:

This product contains lactose. Please consult your doctor before using TOPIRIN tablet if you know that you have intolerance to some sugars.

3. HOW TO TAKE TOPIRIN

Take TOPIRIN tablets exactly as directed in this leaflet. Please check with your doctor or pharmacist if you are not sure.

Unless otherwise prescribed, the usual doses are:

Age	Individual daily dose	Maximum daily dose (24 hours)
adults and children over 12 years of age	1-2 tablets(Corresponding to 250 - 500 mg of acetylsalicylic acid, 250 - 500 mg of paracetamol, 50-100 mg of caffeine)	6 tablets(Corresponding to 1500 mg of acetylsalicylic acid, 1500 mg of paracetamol,300 mg of caffeine)

The maximum daily dose (24 hours) should not be exceeded, and the time interval for the next administration should be 4-8 hours.

The tablets can be dissolved in a drink or taken whole with a fluid.

Taking after meal may delay onset of action.

To prevent the risk of overdose, you should ensure that you do not apply medicines containing paracetamol at the same time.

Do not take them longer than 3-4 days without recommendation of a doctor or dentist.

Please talk to your doctor or pharmacist if you think the effect of TOPIRIN tablets is too strong or too weak.

If you take more TOPIRIN than you should

As the initial signs of overdose, you will feel (Day 1) nausea, vomiting, sweating, lethargy and general weakness, as well as dizziness and ringing in the ears, especially in children and elderly patients. Despite the improvement of the general condition on the second day, you will experience progressive liver damage that can lead to hepatic coma on the third day.

Overdose or prolonged, chronic use can cause serious liver damage, central nervous system disorders (such as headache, dizziness, vomiting, ringing in the ears, visual impairment or hearing loss), anemia due to iron deficiency, a disorder of acid-base balance and kidney damage.

Typically, the early symptoms of acute caffeine poisoning are tremors and restlessness.

Symptoms of caffeine poisoning (nausea, vomiting, decreased levels of potassium in the blood, lower blood sugar levels, symptoms of central nervous system, symptoms in cardiovascular system, infarction injury) also may occur when caffeine is entered in large quantities within a short time.

Other possible symptoms of acute poisoning may appear as hypoglycemia (low blood sugar levels), rash, gastrointestinal bleeding, hyperventilation and confusion.

Serious intoxication may cause delirium, tremors, convulsions, dyspnea, sweating, dehydration, increased body temperature and to whom.

There is increased risk of poisoning, with fatal outcome, in elderly, children, patients with liver disease, in chronic alcohol consumption or chronic malnutrition and in patients simultaneously taking other medicines that can lead to liver damage.

If you suspect an overdose, immediately contact your doctor, even if the symptoms are temporarily mitigated and do not take any other medication.

If you forget to take TOPIRIN

Do not take a double dose to make up for a forgotten individual dose.

Talk to your doctor or pharmacist if you have any additional questions.

4. POSSIBLE SIDE EFFECTS

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

Side effects are listed according to the following categories of frequency:

Very common: more than 1 treated person of 10

Common: 1 to 10 treated persons of 100

Uncommon: 1 to 10 treated persons of 1000

Rare: 1 to 10 treated persons of 10000

Very rare: less than 1 treated person of 10000

Not known: frequency cannot be estimated from the available data

Gastrointestinal disturbances are likely to occur more frequently when higher doses are administered.

Gastrointestinal system

Common: indigestion (heartburn, nausea, vomiting, abdominal pain) and micro bleeding

Uncommon: diarrhea, flatulence

Rare: gastrointestinal bleeding, which rarely may lead to anemia (in the case of black stools or bloody vomiting you should immediately inform your doctor), gastrointestinal ulcers, esophagitis.

Frequency unknown: gastritis

Endocrine system

Very rare: decrease of blood sugar levels

Liver

Rare: elevated levels of liver enzymes

Very rare: liver damage

Kidneys

Very rare: impaired kidney function

Blood and lymphatic system

Frequency unknown: bleeding, such as bleeding from the nose, bleeding of the gums or bleeding in the skin with possible prolongation of bleeding time. This effect can stop 4-8 days after discontinuation of treatment.

Very rare: blood disorders (eg. reduction in the number of blood cells)

Heart

Uncommon and rare: palpitations

Immune System

Uncommon: Hypersensitivity reactions (skin reactions)

Rare: hypersensitivity reactions such as acute difficulty breathing, severe skin reactions (eg, erythema multiforme), possibly with hypotension, anaphylactic shock, swelling of the face, tongue and throat (angioneurotic edema), especially in asthmatics.

Very rare: bronchospasm in patients who are allergic to certain pain medications (NSAIDs). At the first signs of hypersensitivity reactions to TOPIRIN tablets discontinue the use and contact a doctor.

Skin

Rare: increased sweating

Nervous system

Common: dizziness

Rare: concussion

Frequency unknown: headache, drowsiness and mental confusion may be signs of an overdose.

Psyche

Common: nervousness

Rare: Agitation

Eyes

Frequency unknown: blurred vision

Ears

Frequency unknown: hearing disorders, tinnitus

General

Rare: fatigue

In certain cases, temporarily related to the use of certain anti-inflammatory drugs (NSAIDs, including TOPIRIN tablets), there was worsening of inflammation caused by infections (such as development of necrotizing fasciitis).

The content of caffeine can lead to insomnia, anxiety, tremors, and stomach problems.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE TOPIRIN

Keep out of the reach and sight of children.

Do not store above 30 °C.

Do not use TOPIRIN after the expiry date which is stated on the label.

6. FURTHER INFORMATION

What TOPIRIN contains

The active ingredients: acetylsalicylic acid, acetaminophen and caffeine

1 tablet contains 250 mg of acetylsalicylic acid, 250 mg of acetaminophen and 50 mg of caffeine.

The other ingredients are lactose monohydrate, pregelatinized starch, croscarmellose sodium, povidone, colloidal silicon dioxide, stearic acid

What TOPIRIN looks like and contents of the pack

Cardboard box with 10 tablets from 250 + 250 + 50 mg in a blister pack (1 blister x 10 tablets)

Cardboard box with 20 tablets from 250 + 250 + 50 mg in a blister pack (2 blisters x 10 tablets)

Regime of dispensing

The medicine is issued without a doctor's prescription.

Manufacturer

ZADA Pharmaceuticals d.o.o.

Donji Bistarac bb

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