

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.

TOPIRIN tablete 250+250+50 mg
Acetylsalicylic acid + Paracetamol + Caffeine

What is in this leaflet:

1. What **TOPIRIN** is and what it is used for
2. What you need to know before you take **TOPIRIN**
3. How to take **TOPIRIN**
4. Possible side effects
5. How to store **TOPIRIN**
6. Contents of the pack and other information

1. What TOPIRIN is and what it is used for

Each tablet of **TOPIRIN** contains three active substances: acetylsalicylic acid, paracetamol and caffeine. Acetylsalicylic acid and paracetamol reduce pain and fever, and acetylsalicylic acid also reduces inflammation. Caffeine is a mild stimulant and increases the effect of acetylsalicylic acid and paracetamol.

TOPIRIN is used for the acute treatment of headache and migraine attacks (symptoms such as headache, nausea, and sensitivity to light and sound) with or without aura accompanied with pain of at least moderate intensity.

TOPIRIN is for adults and children older than 12 years.

2. What you need to know before you take TOPIRIN

Do not take TOPIRIN if you:

- are allergic (hypersensitive) to acetylsalicylic acid, paracetamol, caffeine or any of the other ingredients of **TOPIRIN** listed in section 6. Symptoms of an allergic reaction may include: asthma, wheezing or shortness of breath; skin rash or hives; swelling of the face or tongue; runny nose. If you are not sure, ask your doctor or pharmacist.
 - ever had an allergic reaction to other medicines used to treat pain, inflammation or fever, such as diclofenac or ibuprofen.
 - have a stomach or intestinal ulcer, or if you have a history of peptic ulceration.
 - have noticed blood in your stools or black stools (symptoms of gastrointestinal bleeding or perforation).
 - are a haemophiliac or suffering from other blood disorders.
 - have severe heart, liver and kidney problems
 - take more than 15 mg methotrexate per week (see Other medicines and **TOPIRIN**)
 - are in the last 3 months of pregnancy (see Pregnancy, breast-feeding and fertility)
 - if you are child younger than 12 years
 - if you are a child or adolescent suffering from measles or flu-like illness due to the risk of Rey syndrome.
- In rare cases of recent intolerance to some of the excipients, Topirin should not be used.
- Caffeine intake (eg coffee, tea, food, other medications, certain canned drinks) should be avoided while taking this medicine.

Warnings and precautions:

The following are reasons why **TOPIRIN** may not be suitable for you.

Talk to your doctor before you take this medicine if you:

- suffer from a hereditary condition called glucose 6-phosphate dehydrogenase deficiency that
- affects the red blood cells and could cause anaemia, jaundice or enlargement of the spleen when exposed to certain foods, medicinal products such as certain anti-inflammatory drugs (eg., acetylsalicylic acid), or to other diseases.
- have ever had gastrointestinal problems such as stomach ulcer, bleeding or black stools. If you have had stomach discomfort or heartburn after taking pain relievers or anti-inflammatory medicines in the past.
- suffer from bleeding disorders or abnormal vaginal bleeding other than your menstrual period (eg., unusually heavy and prolonged menstrual period).
- have recently undergone a surgical operation (including minor ones such dental surgery) or will undergo one within the next 7 days.
- have bronchial asthma, hay fever, nasal polyps, a chronic respiratory disease or develop allergic symptoms (eg., skin reaction, itching, urticaria).
- have gout, diabetes, hyperthyroidism, arrhythmia, uncontrolled hypertension, impaired kidney or liver function.
- have alcohol problems.
- are already taking other medicinal products containing acetylsalicylic acid or paracetamol, or other medicines, since certain may interfere with **TOPIRIN** and cause side effects (Other medicines and **TOPIRIN**).
- are at risk of being dehydrated (eg. by vomiting, diarrhoea, or before or after major surgery).
- are less than 12 years of age . There is a possible association between acetylsalicylic acid and Reye's syndrome when given to children and adolescents. Reye's syndrome is a rare disease, which affects the brain and liver, and can be fatal.

Other precautions

As with any type of painkiller for headaches, taking **TOPIRIN** too often (meaning on more than 10 days per month for this product) with concurrent chronic headaches (15 days or more per month), for more than 3 months, could worsen your headache or migraine. If you think that

this may be the case, please contact your doctor for advice. You may need to stop taking **TOPIRIN** to resolve the problem.

TOPIRIN may reduce the symptoms of an infection (e.g. headache, high temperature) and may therefore make it more difficult to detect. If you feel unwell and need to see a doctor, remember to tell him or her that you are taking **TOPIRIN**.

TOPIRIN may affect the results of laboratory tests. If you have been asked to have blood, urine or other laboratory testing, remember to tell that you are taking **TOPIRIN**.

Other medicines and TOPIRIN

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

In particular, tell your doctor if you are taking any of the following:

- any other medicinal product that contains paracetamol, acetylsalicylic acid or any other pain reliever/fever reducer.
- medicines used to prevent blood-clotting ("blood thinners") such as oral anticoagulants (eg., warfarin), heparin, thrombolytics (eg., streptokinase), or other antiplatelets (ticlopidine, clopidogrel, cilostazol).
- corticosteroids (used to provide relief of inflammation).
- barbiturates and benzodiazepines (to treat anxiety and insomnia).
- lithium, selective serotonin reuptake inhibitors or fluvoxamine (to treat depression).
- sulphonylureas and insulin (to treat diabetes).
- methotrexate (to treat some kinds of cancer, arthritis or psoriasis).
- some medicines used to treat infection (eg., rifampicin, isoniazide, chloramphenicol, ciprofloxacin or pipemidic acid).
- levothyroxine (to treat hypothyroidism).
- metoclopramide (to treat nausea and vomiting).
- epilepsy medication.
- high blood pressure and heart failure medication.
- diuretics (to increase urine production and reduce excess fluid).
- medicines to treat gout.
- oral contraceptives.
- zidovudine (to treat HIV).
- medicines to treat slow gastric emptying such as propantheline.
- clozapine (to treat schizophrenia).
- sympathomimetics (to raise low blood pressure or to treat nasal congestion).
- antiallergics (to prevent or relieve allergies).
- theophylline (to treat asthma).
- terbinafine (to treat fungal infections).
- cimetidine (to treat heartburn and peptic ulcers).
- disulfiram (to treat alcohol dependence).
- nicotine (used for smoking cessation)
- cholestyramin (to treat high cholesterol levels)

Taking TOPIRIN with food and drinks

Alcohol:

If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take this medicine or other pain relievers/fever reducers. Paracetamol and acetylsalicylic acid may cause liver damage and stomach bleeding.

Caffeine:

The recommended dose of this medicine contains about as much caffeine as a cup of coffee. Limit your intake of caffeine-containing medications, foods, or beverages while taking this medicine because too much caffeine may cause nervousness, irritability, sleeplessness, and occasionally, rapid heart beat.

Pregnancy, breast-feeding and fertility

If you are pregnant or think you might be pregnant or are planning to have a baby, tell your doctor and do not take **TOPIRIN**. It is especially important not to take **TOPIRIN** during the last 3 months of pregnancy, as it could harm your unborn child or cause problems at delivery. Do not take **TOPIRIN** if you are breast-feeding as it might be harmful for your infant. Ask your doctor or pharmacist for advice before taking any medicine. **TOPIRIN** belongs to a group of medicines (NSAIDs) which may impair the fertility in women. This effect is reversible on stopping the medicine.

Driving and using machines

Taking **TOPIRIN** is not known to affect your ability to drive and use machines.

This medicine contains lactose. If your doctor said that you have intolerance to some sugars, you should inform him/her before taking this medicine.

3. How to take TOPIRIN

Always take **TOPIRIN** exactly as stated in this package leaflet or as your doctor or pharmacist has told you. You should check with your doctor or pharmacist if you are not sure.

Adults (18 years of age and older):

- For headache treatment:
Take 1 tablet for mild pain and 2 tablets for moderate to severe pain with

a full glass of water when headache pain appears. If needed, you can take another 1-2 tablets 4 to 6 hours later.

Do not use **TOPIRIN** for more than 4 days for headache without consulting your doctor.

For migraine treatment:

Take 2 tablets with a full glass of water when migraine symptoms or migraine aura appear. If needed you can take an additional 2 tablets, with 4 to 6 hours between doses.

If you get no migraine relief within 2 hours from the first 2-tablet dose of **TOPIRIN**, you should seek the advice of a doctor.

Do not use **TOPIRIN** for more than 3 days for migraine without consulting your doctor.

For both headache and migraine treatment, do not exceed 6 tablets over a period of 24 hours. This corresponds to a dose of 1500 mg acetylsalicylic acid, 1500 mg paracetamol and 300 mg caffeine.

Prolonged use except under medical supervision may be harmful.

Children and adolescents:

TOPIRIN should not be given to children and adolescents under the age of 18 (see warnings and precautions).

Older people (over 65 years of age):

There are no special dosage recommendations. If you have low body weight you should seek the advice of a doctor or pharmacist.

Patients with kidney or liver problems

You should tell your doctor if you have kidney or liver problems. Your doctor may need to adjust the dose interval or treatment duration. Do not take **TOPIRIN** if you suffer from severe liver or kidney problems.

If you take more TOPIRIN than you should

These tablets contain acetylsalicylic acid, paracetamol and caffeine. Do not take more than the recommended dose and do not take any other medicines which may contain either of these ingredients or any other medicines used to treat pain, inflammation or fever (non-steroidal anti-inflammatory drugs) while using **TOPIRIN**.

Contact your doctor, pharmacist or go to the nearest hospital as soon as you think you might have taken an overdose. Immediate medical attention is critical, because of the potential risk of irreversible liver damage due to paracetamol. Do not wait for symptoms to appear as the overdose might not, at first, produce any noticeable symptoms.

If symptoms of overdose appear they could be:

For acetylsalicylic acid: dizziness, ringing in the ears, deafness, sweating, hyperventilation, fever, nausea, vomiting, headache, confusion or restlessness, circulatory collapse or respiratory failure.

For paracetamol: the first symptoms that may appear are nausea, vomiting, lack of appetite, pallor, sleepiness, sweating, and later abdominal pain.

For caffeine: anxiety, nervousness, restlessness, insomnia, excitement, muscle twitching, confusion, convulsions, hyperglycemia, tachycardia or cardiac arrhythmia.

Even if these symptoms do not appear or if they vanish, it is essential to seek medical help immediately.

If you forget to take TOPIRIN

Take the dose as soon as you remember but do not take a double dose to make up for a forgotten dose. Do not take more than 6 tablets over a period of 24 hours.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, **TOPIRIN** can cause side effects, although not everybody gets them. Stop taking **TOPIRIN** and tell your doctor immediately if you have any of these serious side effects:

·allergic reaction with swelling of the face, lips, mouth, tongue or throat.

This may cause difficulty in swallowing, wheezing, difficulty in breathing and feelings of tightness in the chest (signs of asthma). You may also have a rash or itching and experience fainting.

·skin reddening, blistering of lips, eyes or mouth, skin peeling.

·bleeding in the stomach or intestine, ulcer in stomach or intestine, which may be accompanied by severe stomach pain, bloody or black stools, or vomiting blood. As with all pain relievers and fever reducers, this can happen at any time during the treatment, without prior history, and may be fatal. This side effect is particularly serious in elderly people.

·yellowing of the skin or eyes (signs of liver failure).

·light-headedness or dizziness (signs of low blood pressure).

·irregular heart beat.

Below side effects were reported in the 16 clinical trials conducted with **TOPIRIN** over 4800 treated

subjects. Tell your doctor if you notice any of these other side effects:

Common (may affect up to 1 in 10 people):

·nervousness, dizziness

·nausea, abdominal discomfort

Uncommon (may affect up to 1 in 100 people):

·insomnia, trembling, numbness, headache

·ringing in the ears

·dry mouth, diarrhoea, vomiting

·fatigue, feeling jittery

·heart rate increased

Rare (may affect up to 1 in 1,000 people):

·sore throat, difficulty in swallowing, numbness or tingling around the mouth, too much saliva

·decreased appetite, altered taste

·anxiety, euphoric mood, tension

·disturbance in attention, memory loss, altered coordination

·feeling of pain in the cheeks and forehead

·eye pain, vision disorder

·hot flushes, peripheral blood vessels problems (eg., in arms or legs)

·nose bleeds, slow and shallow breathing, runny nose

·eructation, flatulence

·excessive sweating, itching, itchy rash, increased skin sensitivity

·stiffness in muscles, bones or joints; neck pain, back pain, muscles spasms

·weakness, chest discomfort

Below side effects have also been reported since marketing **TOPIRIN**. In general, frequency in postmarketing surveillance cannot be determined precisely, thus it is indicated as "not known":

·restlessness, generally feeling unwell or not normal

·somnolence, migraine

·skin reddening, rash

·palpitations, breathlessness, sudden difficulty breathing and feeling of tightness in chest with wheezing or

·coughing (asthma)

·abdominal pain, stomach discomfort after meals

Reporting of side effects

"If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly (see details below).

5. How to store TOPIRIN

Do not store above 25°C. Store in the original package. Keep out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton. The expiry date refers to the last day of that month.

6. Further information

What TOPIRIN contains

The active substances are: acetylsalicylic acid, paracetamol, caffeine. Each film-coated tablet contains 250 mg acetylsalicylic acid, 250 mg paracetamol and 50 mg caffeine.

The other ingredients are: lactose monohydrate, pregelatinized starch, croscarmellose sodium, copovidone, colloidal silica, stearic acid.

What TOPIRIN looks like and content of the pack

Box of 10 tablets of (250+250+50) mg in PVC/PVDC-Al blister pack (1 blister x 10 tablets)

Box of 20 tablets of (250+250+50) mg in PVC/PVDC-Al blister pack (2 blisters x 10 tablets)

Manufacturer and Marketing authorisation holder:

ZADA Pharmaceuticals Ltd.

Donji Bistarac without number

75300 Lukavac

Bosnia and Herzegovina

Date and number of the renewal of authorization:

Topirin, tablets 10x(250mg+250mg+50mg):

Number: 04-07.3-2-1719/18

Date: 01.11.2018.

Topirin, tablets 20x(250mg+250mg+50mg):

Number: 04-07.3-2-1718/18

Date: 01.11.2018.