Package leaflet: Information for patient

ZADA PHARMACEUTICALS

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.

METOCOR tablets 50 mg
METOCOR tablets 100 mg
metoprolol

What is in this leaflet

1. What METOCOR is and what it is used for

The active ingredient, metoprolol tartrate, belongs to a group of drugs called beta blockers.
Metoprolol tartrate has an effect on how the heart works and reduces blood pressure. Metoprolol tartrate can be used to treat a number of conditions.

It can be prescribed to patients:
- to reduce high blood pressure
- with chest pain due to angina
- with fast or irregular heart rhythm
- who have had a heart attack, as protection against a possible further heart attack to prevent migraines

2. What you need to know before you take METOCOR

Do not take METOCOR:
- if you are allergic (hypersensitive) to metoprolol or any other beta-blocer or any the other ingridients of this medicine (listed i section 6)
- if the heart muscle is failure (decompressed or manifested heart failure)
- in case of cardiogenic shock if the conduct of electrical impulses from arthritis to the ventricle is disturbed (a second or third degree block)
- in sinus syndrome
- if sudden pain in the chest occurs as a symptom of a heart attack
- when impulse transmission between the sinus nodes and atria is disturbed
- if you have a very slow heart rate less than 50 beats per minute (bradycardia)
- if you have extremely low blood pressure (hypotension; systolic blood pressure less than 90mmHg)
- if you are suffering from increased acidity of the blood (metabolic acidosis)
- if you are prone to bronchial spasm (bronchial hyperactivity eg. bronchial asthma)
- when the circulation in the arms or legs is very disturbed (peripheral circulation disorder)
- if you are suffering from untreated the tumor squeezes the inflamed glands that produces hormones (ferohormocytoma)
- in severe lung asthma or if you have had previous problems with spasm of bronchi
- if you use a certain type of antidepressant at the same time (MAO inhibitors, except MAO-B inhibitors)

You should not use metocor after a heart attack if:
- your pulse is below 45-50 beats per minute
- if you have noticed certain changes to EKG (PR interval >0,24s)
- if your systolic pressure is below 100mmHg
- if your heart muscle is severely weakened (heart failure)

During therapy you must not apply verapamil or diltiazem – type of calcium antagonists or another Intravenous medications used to treat heart rhythm disorders (anti-arrhythmics such as dizopyramide), intensive care is an exeption

Take special care with METOCOR tablets
You should warn your doctor or pharmacist before you start using **METOCOR**.

You should warn your doctor if:
- you have a small disorder of conducting electrical impulses from atrium to ventricles (first-degree AV block)
- have been on a strict post for a long time or have been exposed to severe physical effort for a long time (possible low blood sugar levels)
- in patients with diagnosed or suspected tumors of the adrenal gland in patients diagnosed with or suspected of the tumor of the adrenal gland (phaeochromocytoma; requiring previous therapy with alpha receptor blockers)
- in patients with impaired hepatic function (see section 3 "how to take **METOCOR**")
- in patients with diabetes mellitus, in whom the levels of sugar vary significantly (possible conditions of meaningly lowered blood sugar)
- in diabetics, especially when using insulin or other medicines to lower blood sugar. **METOCOR** can mask the symptoms of reduced blood sugar (hypoglycaemia), fast heartbeat and trembling (tremor).
- in patients with certain disorders of the blood vessels (Raynand's phenomenon or certain forms of peripheral occlusive disease-intermittent claudication).
- in patients with bronchial spasm
- in patients with a specific form of angina pectoris (Prinzmetal angina)
- in patients with an increased risk of severe hypersensitivity reactions (anaphylactic reactions).
- in patients with a history of severe hypersensitivity reactions and in patients on therapy for the reduction or elimination of allergic reactions (desensitization therapy)

Note: strong hypersensitivity reactions caused by other drugs may be particularly severe during **METOCOR** and resistant to usual doses of epinephrine in patients with diagnosed or suspected hyperactivity of the thyroid gland in patients with personal or family history of psoriasis. Beta-blockers (such as **METOCOR**) can cause psoriasis, exacerbate the symptoms of the disorder, or cause skin-like psoriasis (see section 4 "Possible side effects").

If your pulse drops below 50-55 beats per minute during therapy, the doctor should gradually reduce the dose of **METOCOR**. If you notice irregular heartbeats, contact your doctor.

Therapy with **METOCOR** should not be interrupted suddenly, especially in patients with ischemic heart disease. In order to avoid angina pectoris deterioration, the doctor should gradually reduce the dose during 1-3 weeks. If it is necessary, at the same time it is possible to start an alternative therapy.

You should contact your doctor immediately if you notice spontaneous bleeding and bruising (hematoma) during therapy with **METOCOR** (see section 4 "Possible side effects") . If you notice skin and eye yellowness, loss of appetite and urine, immediately inform doctor.

You should contact your doctor immediately if you experience hallucinations during **METOCOR** therapy (see section 4 "Possible side effects").

Tell your doctor if you experience dry eye symptoms, alone or in combination with a skin rash. In that case it should be considerer interruption of therapy.
If you carry lenses there is a possibility of reduced eye reduction during therapy with **METOCOR**.
In severe renal dysfunction, **METOCOR** should be used only with adequate renal function monitoring.
You should tell your doctor immediately if you have been diagnosed with a severe disorder of the kidney function (see section 4 "Possible side effects").

If you receive continuous therapy with beta-blockers and you need to undergo surgery, an experienced cardiologist should check if it is needed to stop therapy with beta-blockers before surgery. An increased incidence of general anesthesia or surgery is possible. For each individual case, the benefits of continuing therapy with **METOCOR** should be assessed in relation to interruption of therapy. Anesthesiologist should be notified before general anesthesia, on **METOCOR** therapy.
If it is considered necessary to discontinue the **METOCOR** before surgery, it should be done gradually and approximately 48 hours prior to general anesthesia.

The impact on the doping test and when the drug is abused for doping purposes.
The use of **METOCOR** gives positive results on the doping test.

Other medicines and METOCOR
Tell your doctor or pharmacist if you are taking or have recently taken or if you can take some other medicines, including those that you have obtained without a prescription.

The effect of **METOCOR** and other drugs for lowering blood pressure can be increased when taken simultaneously. Careful monitoring of patients receiving concurrent beta-blockers (including eye drops), monoamino oxidase inhibitors (MAO) (see section 2 "Do not take **METOCOR**"), drugs that inhibit the sympathetic nervous system or drugs that lower catecholamine levels.

Following drugs can enhance the effect of **METOCOR**:
Calcium antagonists such as verapamil or diltiazem:
The effect on depression of blood pressure and heart is increased.
Therefore careful monitoring is required when used simultaneously.

Note: During **METOCOR** therapy, you should not receive intravenous verapamil and diltiazem-type of calcium antagonists or other medicines for heart rhythm disorders (anti-arrhythmias such as dispropamide) (the exception is intensive medicine).

Nifedipine-type of calcium antagonists:
As with other beta-blockers, concomitant therapy with dihydropyridines (such as nifedipine and amlodipine), may increase the risk of hypotension, and cardiac failure may occur in patients with latent cardiac insufficiency

Medicines for the treatment of heart rhythm disorders (amiodarone, propafenone and other anti-arrhythmics of class I, such as quinidine and disporamide):
Increased depression effect of **METOCOR** on heartbeats and impulse conduction through the heart (atrioventricular conduction).

Certain medicines for the treatment of depression *(tricyclic antidepressants), tranquilizers (barbiturates, phenothiazines), glycerol trinitrate, medicines for intensified urination (diuretics), medicines for spreading blood vessels (vasodilators):*
Enhanced blood pressure lowering effect.

Anestetisc:
The effect of lowering blood pressure and weakening the effect of the output volume is strengthened.
Note: in case of need for surgery, an anesthetist must be informed of **METOCOR** therapy. Active substance of **METOCOR** (metoprolol tartrate) is decomposed in the body by specific liver enzymes (cytochrome P450 2D6). Therefore, caution should be exercised if the medicinal products that inhibit this enzyme are taken at the same time as **METOCOR** 100, as the effect of **METOCOR**.

Such drugs include the following:
- medicines for the treatment of depression, such as fluoxetine, paroxetine and bupropion
- medicines for the treatment of psychiatric disorders such as thioridazine
- medicines for the treatment of heart rhythm disorders, such as quinidine and propafenone
- medicines for the treatment of viral infections, such as ritonavir
- medicines for the treatment of allergies (antihistasmini), such as diphenhydramine
- medications for the treatment of malaria, such as hydroxychloroquine or quinine
- medicines for the treatment of fungal diseases such as terbinafine
- medicines for the treatment of gastric ulcer such as cimetidine

The following drugs can reduce the effect of **METOCOR**:
Certain pain medications *(nesteroid antiinflammatory drugs such as indomethacin):*
Reduced blood pressure lowering effect.

Enzyme inducer *(cytochrome P450 2D6) such as rifampicin and dexamethasone:*
Blood concentrations are likely to be reduced, and therefore the **METOCOR** effect is reduced.

The impact of **METOCOR** on other drugs
Prazosin:
If you already receive **METOCOR** after a first dose of prazosine, there may be a sudden decrease in blood pressure when changing the position (eg. from the stool in the standing position). Special caution is needed if **METOCOR** and prazosin are used for the first time at the same time.

Digitalis, resin, alpha methyl dopa, guanfacine or clonidine:
Increased heart rate drop, or delayed impulse conduction through the heart. In order to avoid a strong increase in blood pressure, therapy with clonidine should be discontinued only after a few days earlier before **METOCOR** therapy has been completed.

Medicines used in general muscle relaxation anesthesia (peripheral muscle relaxants such as suxamethonium, tubocuranine):
METOCOR can increase the effect of these drugs.

Substances that activate the sympathetic nervous system (norepinephrine, epinephrine or other substances of similar action, eg for medications for treating cough, nose and eye drops):

Possible significant increase in blood pressure.
Note: During treatment with **METOCOR** the effect of epinephrine can be reduced in the treatment of allergic reactions.

Monoamine oxidase inhibitors
Possible high blood pressure increase. MAO inhibitors should therefore not be used together with **METOCOR** (see section 2 "Do not take **METOCOR**").

Insulin and sulfonylurea:
In diabetics receiving insulin **METOCOR** can lead to increased or prolonged lowering of blood sugar levels (hypoglycaemia), concealing or alleviating warning symptoms of low blood sugar , such as particularly heartbeat and trembling.

Ergot Alkaloid: Concomitant administration with beta-blockers may enhance the vasoconstrictive action of ergot alkaloids.

Dipyridamole: In general, administration of a beta-blocker should be withheld before dipyridamole testing, with careful monitoring of heart rate following the dipyridamole injection.

If you are not sure if any of the above apply to you, talk to your doctor or pharmacist before taking METOCOR.

Taking METOCOR with food and drink
You should minimise your alcohol intake when taking this medicine as it may increase the effect of metoprolol.

Pregnancy and breast-feeding and fertility
If you are pregnant or breast-feeding, think that you may be pregnant or plan a pregnancy, ask your doctor or pharmacist for advice before taking this medicine.

Pregnancy
METOCOR should be used in pregnancy (especially during the first trimester of pregnancy) only in strictly indicated cases and after a rigorous assessment of the benefit / risk.
There is evidence that the active substance **METOCOR** (metoprolol) decreases the placental blood flow that can lead to fetal developmental disorders. After the use of other beta-blockers, abortions, premature births, and intrauterine deaths have been reported.

Due to the possibility of reporting reduced pulse (bradycardia), low blood pressure (hypotension) or blood sugar levels (hypoglycaemia) in the newborn, treatment with metoprolol should be interrupted by 48-72 hours before the estimated birth date. If this is not possible, newborns should carefully monitor 48-72 hours after delivery.

Breast - feeding
Active supstance of **METOCOR** (metoprolol) is excreted in breast milk. Breast-feeding should generally be discontinued during treatment with metoprolol although your doctor may decide to use metoprolol in a nursing mother with close supervision of the infant.
Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines
Metoprolol may influence your ability to drive and use machines becauseit may cause dizziness and fatigue. This applies to a greater extent at the beginning of treatment. Do not drive or use any tools or machines if side effects such as fatigue or dizziness occur .

Important information about some of the ingredients of METOCOR tablets
This medicine contains:
• Lactose (a type of sugar): If you have been told by your doctor that you cannot tolerate or digest some sugars (have an intolerance to some sugars), talk to your doctor before taking this medicine

3. How to take METOCOR
Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.
Metoprolol tartrate should be taken without food and on an empty stomach.

High blood pressure(hypertension):
100 or 200 mg, preferably once a day, as a single dose in the morning, or in divided doses (morning and evening). Your doctor may ask you to start with a lower dose.

Chest pain (angina):
depending on the symptoms 100 to 200 mg per day,in divided doses (morning and evening).
Your doctor may ask you to start with a lower dose.

Abnormalna heart rhythm:
100 to 150 mg per day, in divided doses (in the morning and in the evening).
If necessary, your doctor can increase your dosage further.

Protection against a further heart attack
100 mg twice a day (in the morning and in the evening).

Migraine prevention:
100 to 200 mg per day, in divided doses, in the morning and evening.

Severe liver problems
The dose may be reduced in patients with severe liver problems.

Severe renal problems
Dose adjustment is not necessary.

Elderly:
Dose adjustment is not necessary.

Children and adolescents
METOCOR should not be given to children and adolescents.

This medicine is generally taken for long-term. Never change the dosage yourself.

If you take more METOCOR than you should
Symptoms of overdose include a low blood pressure, slow heart beat, shortness of breath, dizziness, fatigue,cough,wheezingand, in severe cases, cardiac arrest,contact your doctor immediately.
Take with you the empty packs of themedicines you consumed. Sometimes, hospitalisation may be necessary.

If you forget to take METOCOR
If you forget to take a dose, take it as soon as you remember, unless it is nearly time for your next dose. Do not take a double dose to make up for a forgotten dose.

If you stop taking METOCOR
Discontinuing metoprolol treatment should always be undertaken in consultation with your doctor who will direct you how to gradually reduce the dose until the treatment is stopped altogether.
If you suffer problems during the tapering-off period, consult your doctor.

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

4. Possible side effects
Like all medicines, **METOCOR** tablets can cause side effects, although not everybody gets them.

Stop treatment and contact a doctor at once if you have the following symptoms of:
• an allergic reaction such as itching, difficulty breathing or swelling of the face, lips, throat or tongue.
• very slow heart and blood pressure (you may feel very dizzy or weak) or in case of breathing difficulties.
The following terms are used to describe how often side effects have been reported.

Very common: affects 1 or more than 1 user in 10
Common: affects 1 to 10 users in 100
Uncommon: affects 1 to 10 users in 1,000
Rare affects: 1 to 10 users in 10,000
Very rare: affects less than 1 user in 10,000

Very common:
• fatigue

Common:
• dizziness
• headache
• slow heart rate
• low blood pressure which might make you faint or dizzy particularly when standing up quickly from a sitting or lying position
• irregular heart beat
• poor blood circulation which makes the toes and fingers numb and pale
• shortness of breath on exertion
• feeling sick
• abdominal pain
• diarrohea
• constipation

Uncommon:
• an increase in weight
• depression
• reduced alertness
• drowsiness
• difficulty in sleeping
• nightmares
• abnormal skin sensations (tingling, tickling, itching or burning)
• muscle weakness and cramps
• an aggravation of heart failure
• water retention
• chest pain
• wheezing
• vomiting
• skin rash
• increased sweating

Rare:
• nervousness
• anxiety
• difficulty or loss of interest in sex
• eye problems (blurred vision, dry and/or irritated eyes, inflammation)
• runny nose
• dry mouth
• abnormal blood test results of liver function
• reversible hair loss

Very rare:
• severe reduction in number of white blood cells which makes infections more likely
• reduction in blood platelets, which increases risk of bleeding or bruising
• change in levels of blood fats.
• low blood sugar in diabetics taking insulin
• memory impairment
• confusion
• hallucination
• personality changes
• ringing in the ears
• reversible hearing loss
• gangrene
• taste disorders
• inflammation of liver (hepatitis)
• hypersensitivity to light
• deterioration in psoriasis
• joint pain
• abnormal curvature of the penis
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 pharmacis.

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.

5. How to store METOCOR
Do not store above 25°C. Store in the original pack.
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.

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. Contents of the pack and other information
What METOCOR contains?
METOCOR 50 mg: Each **METOCOR 50 mg** tablet contains 50 mg of the active substance, metoprolol tartarate.
METOCOR 100 mg: Each **METOCOR 100 mg** tablet contains 100 mg of the active substance, metoprolol tartarate.

The other ingredients are lactose monohydrate, microcrystaline cellulose, povidone, sodium starch glycolate, magnesium stearate, colloidal starch glycolate.

What METOCOR looks like and contents of the pack
METOCOR 50 mg are round,white tablets.
They are supplied as PVC / PVDC Aluminium blister packs in a carton box in pack sizes of 30 (3 x 10) tablets.
METOCOR 100 mg are round,white tablets.
They are supplied as PVC / PVDC Aluminium blister packs in a carton box in pack sizes of 30 (3 x 10) tablets.

Marketing Authorisation Holder and Manufacturer:
ZADA Pharmaceuticals d.o.o.
Donji Bistarac without number
75300 Lukavac, Bosnia and Herzegovina.

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Data of first authorisation / renewal of the authorisation in BIH:
METOCOR film tablets, 30 x 50 mg
Date: 07.11.2016. **Number:** 04-07.3-2-5194/15
METOCOR film tablets, 30 x 100 mg
Date: 07.11.2016. **Number:** 04-07.3-2-5195/15