Package leaflet

Concor® 10 plus

MERCK

Bisoprolol fumarate (2:1) and hydrochlorothiazide

Composition
Medicinally active substances
One film-coated tablet contains 10 mg bisoprolol fumarate (2:1) and 25 mg hydrochlorothiazide
Other ingredients:
Colloidal silicon dioxide, magnesium stearate, microcrystalline cellulose, corn starch, calcium hydrogen phosphate, dimethicone 100, macrogol 400, methylhydroxypropyl cellulose, colourings E 171, E 172.

Presentation and contents
Film-coated tablets, heart-shaped, with dividing score
Packs of 30 tablets

Substance group
Cardioselective beta-blocker and diuretic

Marketing authorization holder and manufacturer
Merck KGaA, Frankfurter Strasse 250,
64293 Darmstadt, Germany

Indications
High blood pressure (hypertension)
The combination preparation Concor 10 plus is recommended only if therapy with one of the individual active substances, bisoprolol or hydrochlorothiazide - with which management of high blood pressure should first be attempted - was inadequately effective and the dosage of the individual active substances as present in the Concor 10 plus combination has proven to be appropriate.

Contraindications
When must you not take Concor 10 plus?
Concor 10 plus must not be used in myocardial insufficiency (congestive heart failure), shock, disturbances of atrioventricular conduction (2nd and 3rd degree AV block), sick sinus syndrome, disturbance of sinoatrial conduction (sinoatrial block), markedly slowed heart rate (pulse less than 50 beats/min) before the start of treatment, accumulation of acid in the blood (acidosis), tendency to bronchospasm (e.g. in bronchial asthma), late stages of peripheral circulatory disturbances, concomitant administration of MAO inhibitors (exception: MAO-B inhibitors), severe disturbances of kidney function (renal insufficiency with severely impaired or absent urine production; creatinine clearance less than 30 ml/min and/or serum creatinine values over 1.8 mg/100 ml), acute inflammation of the kidney (glomerulonephritis), liver failure involving disturbed consciousness (coma and hepatic precoma), potassium deficiency states (hypokalaemia) not responding to treatment, severe sodium deficiency states (severe hyponatraemia), increased calcium concentrations in the blood (hypercalcaemia), gout, hypersensitivity to hydrochlorothiazide and other thiazides, sulphonamides or beta-blockers, children (no therapeutic experience).
The intravenous administration of calcium antagonists of the verapamil and diltiazem type or other antiarrhythmics (such as disopyramide) in patients undergoing treatment with Concor 10 plus is contraindicated (exception: intensive care medicine).
Concor 10 plus must not be used during pregnancy and the nursing period.
When may you take Concor 10 plus only after consulting your doctor?
The following section describes when you may take Concor 10 plus only under certain conditions and only with special caution. Please ask your doctor about this. This also applies if you have been affected by any of the following in the past:
Mild disturbances of atrioventricular conduction (1st degree AV block), in existing or latent diabetes mellitus, as severe hypoglycaemic conditions are possible (regular monitoring of blood glucose), prolonged periods of strict fasting and heavy physical strain (possibility of severely reduced blood glucose levels), patients with hormone-producing tumour of the adrenal medulla (phaeochromocytoma; patients should first be treated with alpha-blockers), decreased volume of circulating blood (hypovolaemia), severe cerebral sclerosis, severe coronary sclerosis, chestpain at rest (Prinzmetal's angina), impaired kidney function of mild degree and co-existing impairment of liver function. In patients with a personal or family history of psoriasis, drugs that contain beta-receptor blockers (e.g. Concor 10 plus) should only be used if the benefit-to-risk ratio has been carefully weighed.
In renal insufficiency (glomerular filtrate less than 30 ml/min and/or serum creatinine more than 1.8 mg/100 ml) HCT is ineffective and, since the glomerular filtration rate is further reduced, even harmful.
Beta-blockers can increase the sensitivity to allergens and the severity of anaphylactic reactions, i.e. acute general allergic reactions. Therefore, this drug should only be prescribed if considered essential in patients with a history of severe hypersensitivity reactions and in patients undergoing desensitisation therapy (beware of the possibility of excessive anaphylactic reactions).
What must pregnant women and nursing mothers pay attention to?
Concor 10 plus must not be used during pregnancy due to suspected thrombocytopenia in newborns.
Use of Concor 10 plus during the nursing period is contraindicated since the active substance hydrochlorothiazide can inhibit milk production. If use during this period is essential, breast-feeding should be avoided.
What must be especially observed in children and elderly people?
Concor 10 plus should not be used in children, since no adequate therapeutic experience in human beings has been gained to date in this respect. No special notes apply to the treatment of elderly people.

Precautions for use and warnings
What precautions must be observed?
Drugs that contain beta-blockers can increase the sensitivity to allergens and the severity of anaphylactic reactions, i.e. acute general allergic reactions. In patients with a history of severe hypersensitivity reactions and in patients undergoing therapy to reduce or eliminate the tendency towards allergic reactions (desensitisation therapy) this may result in excessive anaphylactic reactions; beware of this when administering this drug.
In severely impaired hepatic and renal function, elimination of the HCT proportion contained in Concor 10 plus is reduced due to which dose reduction may become necessary (see dosage instructions).
The warning signs of reduced blood glucose (hypoglycaemia) may be masked making regular monitoring of blood glucose necessary.
During long-term therapy with Concor 10 plus the serum electrolytes (especially potassium, sodium, calcium), creatinine and urea, serum lipids (cholesterol and triglycerides), and uric acid should be monitored regularly. The possibility of reduced lacrimation is to be borne in mind if contact lenses are worn.
During treatment with Concor 10 plus patients should ensure an adequate supply of fluid and food rich in potassium (e.g. bananas, vegetables, nuts) to compensate for the increased loss of potassium.
The potassium losses may be reduced or prevented by concomitant therapy with potassium-sparing diuretics.
What must you pay attention to if you are driving a vehicle, operating machinery, or working without a firm hold?
The treatment of hypertension with this drug requires regular monitoring by the physician. The occurrence of reactions varying from one individual to another may impair the ability to drive a vehicle, to operate machinery, or to work without a firm hold. This is particularly the case at the start of treatment, when the dosage is increased or the medication changed, as well as in conjunction with alcohol.
What else must you pay attention to?
In individual cases, drugs that contain beta-blockers (e.g. Concor 10 plus) may trigger psoriasis, exacerbate the symptoms of this disease, or lead to psoriasiform rashes.

Special warnings
THIS IS A MEDICAMENT
- Medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are experts in medicine, its benefits and risks.
- Do not by yourself interrupt the period of the treatment prescribed.
- Do not repeat the same prescription without consulting your doctor.

Keep medicament out of reach of children.
Council of Arab Health Ministers
Union of Arab Pharmacists

Drug interactions
What other drugs have interactions with Concor 10 plus?
During treatment with Concor 10 plus and with concomitant administration of ACE inhibitors (e.g. captopril, enalapril) there is the risk of an excessive decrease in blood pressure at the start of therapy.
The concomitant administration of Concor 10 plus and insulin or oral antidiabetics may potentiate or prolong or else attenuate their effect. Warning signs of reduced blood glucose (hypoglycaemia), especially accelerated pulse (tachycardia) and tremor, can be masked or attenuated. Therefore, regular monitoring of blood glucose is necessary.
Salicylates and other non-steroidal anti-inflammatory drugs (e.g. indomethacin) may attenuate the antihypertensive and diuretic effects of Concor 10 plus. In high-dose salicylate administration the toxic effect of salicylates on the central nervous system may be potentiated. In patients with decreasing volume of circulating blood (hypovolaemia) under Concor 10 plus therapy the concomitant administration of non-steroidal anti-inflammatory drugs can trigger acute renal failure.
The antihypertensive effect of Concor 10 plus may be potentiated by other antihypertensive drugs, barbiturates, phenothiazines, tricyclic antidepressants, vasodilators, or alcohol.
The concomitant administration of Concor 10 plus and calcium antagonists of the nifedipine type may lead to a pronounced drop in blood pressure and, in individual cases, to the development of heart failure.
An addition of the cardiodepressant effects of Concor 10 plus and antiarrhythmics is possible.
In concurrent use of Concor 10 plus and calcium antagonists of the verapamil or diltiazem type or other antiarrhythmics (such as disopyramide) patients should be closely monitored since hypotension, bradycardia or other cardiac arrhythmias may occur.
The concomitant administration of Concor 10 plus, reserpine, alpha-methyldopa, guanfacine or clonidine may lead to an excessive decrease in heart rate or to delayed cardiac conduction.
The abrupt withdrawal of clonidine in concomitant administration of Concor 10 plus may lead to an excessive rise in blood pressure. Therefore, clonidine must not be withdrawn unless the use of Concor 10 plus was stopped some days previously. This may be then followed by the step-wise withdrawal of clonidine.
The concurrent use of Concor 10 plus and noradrenaline, adrenaline or other sympathomimetic compounds (e.g. contained in cough preparations, nose and eye drops) may lead to a rise in blood pressure.
Monoaminooxidase (MAO) inhibitors should not be taken simultaneously with Concor 10 plus due to the possibility of excessive hypertension.
The effect of uric-acid-lowering agents may be attenuated in concomitant administration of Concor 10 plus.
In concurrent therapy with cardiac glycosides it should be borne in mind that in potassium deficiency (hypokalaemia) and/or magnesium deficiency (hypomagnesaemia) developing during treatment with Concor 10 plus the heart muscle shows increased sensitivity to cardiac glycosides, thus leading to a potentiation of their effects and adverse reactions.
The concurrent administration of ergotamine derivatives (e.g. ergotamine-containing drugs against migraine) and Concor 10 plus may exacerbate peripheral circulatory disturbances.
The concurrent use of Concor 10 plus and glucocorticoids, ACTH, carbenoxolone, amphotericin B, frusemide or laxatives may result in elevated potassium losses.
The concomitant administration of Concor 10 plus and lithium potentiates the damaging effects of lithium on heart and nerves (cardiotoxic and neurotoxic effects) through a reduction of lithium excretion.
The concurrent administration of Concor 10 plus and anaesthetics may lead to a pronounced drop in blood pressure. These two agents may have additive cardiodepressant (negative inotropic) effects.
The effect of curare-type muscle relaxants may be potentiated or prolonged by Concor 10 plus.
Should it not be possible to withdraw Concor 10 plus prior to surgery under general anaesthesia or prior to use of curare-type muscle relaxants, the anaesthetist should be informed that the patient is being treated with Concor 10 plus.
In concomitant administration of cytostatics (e.g. cyclophosphamide, fluorouracil, methotrexate) increased bone marrow toxicity is to be expected.
Rifampicin may reduce the antihypertensive effect of Concor 10 plus.
The antihypertensive effect of Concor 10 plus may be potentiated by cimetidine.
Concor 10 plus may reduce the excretion of lidocaine.
The concomitant administration of colestyramine or colestipol reduces the absorption of the hydrochlorothiazide component of Concor 10 plus.
In concurrent use of methyldopa haemolysis due to the formation of antibodies to hydrochlorothiazide has been described in isolated cases.
The intravenous administration of calcium antagonists of the verapamil and diltiazem type or other antiarrhythmics (such as disopyramide) in patients undergoing treatment with Concor 10 plus is contraindicated (exception: intensive care medicine).

Dosage instructions, mode and duration of administration
The following dosage instructions apply for Concor 10 plus, unless your doctor has prescribed otherwise. Please follow these directions carefully, otherwise Concor 10 plus cannot have the proper effect.
How many Concor 10 plus tablets should you take and how often should you take them?
The treatment of high blood pressure should principally be started with low doses of a single active substance and then increased gradually. The fixed combination of Concor 10 plus consisting of bisoprolol and hydrochlorothiazide should be administered only if the blood pressure could not be normalised by the individual active substances or else excessive adverse reactions had occurred at high doses, and the dosage of the individual active substances as present in the Concor 10 plus combination has proven to be appropriate. The dosage must not be altered without the doctor's direction.
If not prescribed otherwise, take ½ film-coated tablet of Concor 10 plus (5 mg bisoprolol fumarate (2:1) and 12.5 mg hydrochlorothiazide) once daily.
If the blood pressure is only inadequately reduced the dose may be increased to 1 film-coated tablet of Concor 10 plus (equivalent to 10 mg bisoprolol fumarate (2:1) and 25 mg hydrochlorothiazide) once daily.
In co-existing impairment of kidney and/or liver function, the dose of 5 mg bisoprolol fumarate (2:1) + 12.5 mg hydrochlorothiazide should not be exceeded.
How and when should you take Concor 10 plus?
The film-coated tablets are to be swallowed whole with the breakfast with some liquid.
How long should you take Concor 10 plus?
The doctor decides on the duration of treatment. It depends upon the nature and severity of the disease. The dose of Concor 10 plus must not be altered or therapy discontinued without the doctor's direction. After long-term therapy – particularly in the presence of ischaemic heart disease - Concor 10 plus should be discontinued gradually (i.e. over 7 -10 days), since abrupt withdrawal may lead to an acute deterioration of the patient's condition.

Incorrect intake
What must you do if you have taken too many Concor 10 plus tablets?
Please inform your doctor.
In the event of overdosage or a precarious drop in heart rate (pulse) and/or blood pressure the therapy with Concor 10 plus must be discontinued immediately. In overdosage the cardiodepressant effect predominates with slowing of the pulse. Shortness of breath may be caused by bronchospasms. As a result of fluid losses, thirst, weakness, dizziness, muscle pain, increased heart rate, circulatory collapse, acute renal failure, cardiac arrhythmias and constipation to the point of ileus may occur.
If necessary, the following antidotes should be administered alone or consecutively: - Intravenous atropine 0.5-2.0 mg as bolus injection
- Intravenous glucagon initially 1-10 mg, thereafter 2-2.5 mg per hour as continuous infusion.
- Orciprenaline by slow intravenous injection until the onset of effect.
- In the event of convulsions intravenous diazepam should be administered slowly.
- Fluid and potassium substitution may be necessary.
- Should bronchospasms occur, bronchodilators may be administered, e.g. fenoterol or salbumatol as aerosol.

What must you pay attention to if you have taken too little Concor 10 plus or have forgotten to take it?
Take the normal dose again the next morning.
What must you pay attention to if you interrupt treatment or stop it prematurely?
Treatment with Concor 10 plus must not be stopped abruptly but must always be discontinued gradually. This is to be borne in mind particularly in patients with diseases of the coronary vessels. The dosage of this drug must never be changed without the doctor's direction.

Adverse effects
What adverse reactions may occur when you are taking Concor 10 plus?
Nervous system
Central nervous disturbances, such as tiredness, depression, dizziness, confusion, headache, perspiration, nightmares or vivid dreams, sleep disturbances and hallucinations, can occur occasionally.
Eyes
Rare: Visual disturbances, reduced lacrimation (to be borne in mind if contact lenses are worn), conjunctivitis.
Cardiovascular system
Therapy with Concor 10 plus may occasionally lead to extremely reduced heart rate (bradycardia), disturbances of atrioventricular impulse conduction, exacerbation of myocardial insufficiency (heart failure) with peripheral oedemas and/or exertional dyspnoea, pronounced drop in blood pressure, also upon changing from the supine to the upright posture (orthostatic hypotension), as well as temporary, attack-like suspension of consciousness (syncope) and palpitation. In patients with angina pectoris an exacerbation of attacks cannot to be excluded in isolated cases.
Paraesthesia and cold sensation in the extremities, muscle weakness and cramps (e.g. in the calves) may occasionally occur. Also an aggravation of complaints in patients with peripheral circulatory disturbances (including patients with Raynaud's disease) has been observed.
Respiratory system
Due to the possible increase in airway resistance, respiratory distress may occur in patients predisposed to bronchospastic reactions (especially with obstructive airway diseases).
Gastrointestinal tract
Lack of appetite and gastrointestinal complaints e.g. nausea, vomiting, diarrhoea, constipation, abdominal pain and cramp have been observed occasionally. Rare: Dryness of the mouth.
Muscles and skeleton
Under therapy with beta-blockers (bisoprolol as active substance in Concor 10 plus) arthropathy with affection of one or more joints (mono- and polyarthritis) has been observed in individual cases.
Skin
Skin reactions (e.g. reddening, itching, rash upon exposure to light (photoallergic exanthema), pinpoint red spots due to intradermal or submucous bleeding (petechiae), severely itching wheals (urticaria) may occur occasionally.
Genito-urinary organs
In individual cases: Disturbed libido and potency.
Metabolism
In individual cases: Increases of liver enzymes (GOT, GPT) in serum, inflammation of the liver (hepatitis). Latent diabetes mellitus may appear and already existing diabetes mellitus may deteriorate. After prolonged periods of strict fasting or heavy physical strain concomitant therapy with Concor 10 plus may lead to hypoglycaemic conditions. Warning signs of reduced blood glucose (hypoglycaemia), especially accelerated pulse (tachycardia) and tremor, can be masked.
Excess of uric acid in the blood (hyperuricaemia) frequently occurs which may lead to attacks of gout in predisposed patients. A temporary increase in serum of substances excreted with the urine (creatinine, urea) may be observed occasionally.
In rare cases, therapy with Concor 10 plus leads to a rise in serum lipids (cholesterol, triglycerides).
Blood
In individual cases: Thrombocytopenia, anaemia or leucopenia.
Fluid and electrolyte balance:
Due to the hydrochlorothiazide component the long-term, regular intake of Concor 10 plus leads frequently to disturbances of the fluid and electrolyte balance, especially to hypokalaemia and hyponatraemia, further to hypomagnesaemia and hypochloraemia, as well as hypercalcaemia.
Hypokalaemia can cause abnormal sensations in the limbs (paraesthesia), paresis, apathy, excessive gas accumulation in the gastrointestinal tract (meteorism) or cardiac arrhythmia. Extreme potassium losses may lead to inhibition of bowel motility (paralytic ileus) or to disturbances of consciousness to the point of coma.
As a result of electrolyte and fluid losses, metabolic alkalosis may develop or already existing metabolic alkalosis may deteriorate.
Other
Rare adverse reactions to the diuretic component (hydrochlorothiazide) of Concor 10 plus may include drug fever, acute interstitial nephritis, vasculitis, e.g. as picture of purpura, jaundice, pancreatitis and - especially in pre-existing cholelithiasis - acute cholecystitis. Existing myopia may deteriorate.
Sudden occurrence of pulmonary oedema with symptoms of shock has been described in individual cases, presumably due to an allergic reaction to hydrochlorothiazide. Further, hair loss, impaired hearing or tinnitus, gain in weight, mood swings, short-term memory loss, allergic rhinitis or penile induration (Peyronie's disease) have been observed in individual cases.
Special note:
In individual cases, drugs that contain beta-blockers (e.g. Concor 10 plus) may trigger psoriasis, exacerbate the symptoms of this disease, or lead to psoriasiform rashes.
Drugs that contain beta-blockers can increase the sensitivity to allergens and the severity of anaphylactic reactions, i.e. acute general allergic reactions. Therefore, in patients with a history of severe hypersensitivity reactions and in patients undergoing desensitisation therapy this may result in excessive anaphylactic reactions.
The therapy should be discontinued in:
- refractory disturbances of the electrolyte balance
- orthostatic dysregulation, e.g. blackout, dizziness or tinnitus
- hypersensitivity reactions
- pronounced gastrointestinal complaints
- central nervous disorders
- pancreatitis
- changes in blood count (anaemia, leucopenia, thrombocytopenia)
- acute cholecystitis
- occurrence of vasculitis
- deterioration of existing myopia

- serum creatinine concentration more than 1.8 mg/100 ml and/or creatinine clearance ≤ 30 ml/min.

If you should experience any adverse reactions not referred to in this package leaflet, you should report these also to your doctor or pharmacist.
What countermeasures are to be taken in the case of adverse reactions?
Your doctor will decide about any possibly required countermeasures.

Stability
The expiry date of this pack is printed on the folding box and on the brim of each blister strip. This pack must not be used after the expiry date!

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Packed by Pharmaline - Lebanon
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