

Bilocor 5

Bilocor 10

SCHEDULING STATUS:

S3

PROPRIETARY NAME AND DOSAGE FORM:

BILOCOR 5 TABLETS

BILOCOR 10 TABLETS

COMPOSITION:

Each **BILOCOR 5** tablet contains 5 mg bisoprolol fumarate

Each **BILOCOR 10** tablet contains 10 mg bisoprolol fumarate.

PHARMACOLOGICAL CLASSIFICATION:

A 5.2 Adrenolytics (sympatholytics).

PHARMACOLOGICAL ACTION:

Bisoprolol is a selective β_1 -adrenoceptor antagonist devoid of intrinsic sympathomimetic and membrane-stabilising activity.

Pharmacokinetics:

Bisoprolol is well absorbed following oral administration with a resultant bioavailability of about 90%. Bisoprolol undergoes minimal hepatic first-pass metabolism. About 50% of a dose is metabolised in the liver and the remainder is excreted unchanged via the kidneys. The plasma elimination half-life is approximately 10 to 12 hours and the duration of action is about 24 hours.

INDICATIONS:

BILOCOR is indicated for the management of mild to moderate hypertension and angina pectoris.

CONTRA-INDICATIONS:

- Hypersensitivity to bisoprolol or to any of the ingredients

- Uncontrolled asthma
- Second and third-degree heart block and bradycardia (less than 50 beats per minute)
- Pregnancy and lactation
- Uncontrolled cardiac failure
- Metabolic acidosis
- Sinus bradycardia (less than 50 beats per minute)
- Pheochromocytoma
- Hyperthyroidism, as clinical manifestations may be masked.

Particular caution should be exercised with patients suffering from the following: asthma, bronchitis, chronic respiratory diseases, peripheral vascular diseases and Raynaud's phenomenon.

The normal dose should be reduced in elderly patients, or in patients suffering from renal dysfunction. In the perioperative period it is generally unwise to reduce the dosage to which the patient is accustomed, as there may be danger of aggravation of angina pectoris or hypertension. A patient's normal tachycardiac response to hypovolaemia or blood loss may be obscured during or after surgery. Particular caution should be taken in this regard and in diabetes mellitus, as symptoms and signs of hypoglycaemia may be masked, and as responses to hypoglycaemia is diminished.

WARNINGS:

Safety and efficacy in children have not been established.

If the decision is made to withdraw **BILOCOR** before anaesthesia, at least 48 hours should be allowed to elapse between the last dose and surgery. If the medicine is to be continued, care should be taken when using anaesthetics such as ether, cyclopropane and trichloroethylene. Atropine (1-2 mg I.V.) may be used to correct vagal dominance. The patient must be maintained on their usual dosage perioperatively to avoid aggravation of angina pectoris or hypertension.

Tachycardia responses may be obscured. Particular caution should be taken in this regard.

The dosage of **BILOCOR** should be adjusted in severe renal impairment. (See **DOSAGE AND DIRECTIONS FOR USE**).

Care should be taken in prescribing **BILOCOR** together with Class 1 antidysrhythmic agents such as disopyramide, myocardial depressants and inhibitors of AV conduction such as calcium antagonists.

Caution should be exercised when transferring a patient from clonidine, as the withdrawal of clonidine may result in the release of large amounts of catecholamines that may give rise to a hypertensive crisis. If **BILOCOR** is administered in these circumstances, the unopposed alpha-receptor stimulation may potentiate this effect. If **BILOCOR** and clonidine are given concurrently, the clonidine should not be discontinued until several days after the withdrawal of **BILOCOR** as severe rebound hypertension may occur.

BILOCOR should be used with caution in combination with verapamil in patients with impaired ventricular function. This combination should not be given to patients with conduction abnormalities. Neither drug should be administered intravenously within 48 hours of discontinuing the other. The intravenous administration of calcium antagonists and antiarrhythmic agents is not recommended during therapy with **BILOCOR**.

BILOCOR modifies the tachycardia associated with hypoglycaemia.

Patients with phaeochromocytoma usually require treatment with an alpha-adrenergic blocker.

INTERACTIONS:

- Concomitant use of **BILOCOR** with hypoglycaemic agents, phenothiazines and various antiarrhythmic agents can have life-threatening consequences, e.g.
 - profound hypoglycaemia with oral hypoglycaemic agents and insulin;
 - myocardial depression with antiarrhythmic agents.
- Beta-adrenoceptor stimulating agents (e.g. isoprenaline) may antagonise the effects of **BILOCOR**.

- Alpha-adrenoceptor stimulants as well as adrenergic neurone blocking agents such as guanethidine and reserpine may lead to life-threatening vasoconstriction in combination with **BILOCOR**.
- **BILOCOR** and digoxin may be used concomitantly for patients with congestive heart failure provided that the pulse rate and patient response is monitored.

PREGNANCY AND LACTATION:

Administration of **BILOCOR** to pregnant mothers shortly before birth or during labour may result in hypotonia, collapse or hypoglycaemia in the newborn. (See **CONTRA-INDICATIONS**).

DOSAGE AND DIRECTIONS FOR USE:

Adults: 5 to 10 mg once a day in the morning with or without food. The dose must be individualised according to response and tolerance. The maximum recommended daily dose is 20 mg daily.

Severe renal impairment (creatinine clearance <20 ml/min) or severe hepatic impairment:

Do not exceed the daily dose of 10 mg.

Elderly:

The normal dose should be reduced in these patients.

SIDE EFFECTS AND SPECIAL PRECAUTIONS:

Side-effects:

Haematological:

Blood disorders such as leukopenia and thrombocytopenia.

Cardiovascular system:

Bradycardia and congestive cardiac failure, heart block, fluid retention, exacerbation of peripheral vascular disease or the development of Raynaud's phenomenon, peripheral gangrene may be precipitated. Congestive cardiac failure and marked bradycardia may occur.

Central nervous system:

Lassitude, dizziness, mild headache, sleep disorders, restlessness, cold extremities, hypotension, paradoxical hypertension, depression, paraesthesia, hallucinations, psychosis.

Endocrine/Metabolic:

Metabolic disturbances, hypoglycaemia, increase in uric acid levels, hypercholesterolaemia.

Gastrointestinal:

Nausea, vomiting, diarrhoea, constipation, mass gain, stomatitis.

Liver:

Raised liver enzymes.

Musculoskeletal:

Muscle cramps, myopathy, skeletal muscle weakness.

Ocular:

Disturbances of vision.

Skin:

Perspiration, skin rash, alopecia.

Other:

Transient hearing loss, hypersensitivity reactions, sexual impotence.

Respiratory system disorders:

Bronchoconstriction may occur in patients suffering from asthma, bronchitis and other chronic pulmonary diseases.

Adverse reactions are more common in patients with renal decompensation.

Special Precautions:

Abrupt discontinuation of therapy may cause exacerbation of angina pectoris in patients suffering from ischaemic heart disease. Discontinuation of therapy should be gradual, and

patients should be advised to limit the extent of their physical activity during the period that the medicine is being discontinued.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

(See **SIDE-EFFECTS AND SPECIAL PRECAUTIONS**)

Overdosage may produce bradycardia and severe hypotension. Bronchospasm and heart failure may be produced in certain individuals.

Cases of overdose should be observed for at least 4 hours, as apnoea and cardiovascular collapse may appear suddenly.

Repeated activated charcoal may be necessary in overdose.

Atropine may be used to treat severe bradycardia. If the response is inadequate, glucagon may be given intravenously. Alternatively, dobutamine may be required to reverse beta-blockade. Cardiac pacing may be required for severe bradycardia. Bronchospasm should be treated with IV aminophylline or inhaled or IV beta-agonist e.g. salbutamol.

IDENTIFICATION:

BILOCOR 5: Pale yellow, mottled, round normal convex tablet embossed with BI over break-line and 5 on one side and plain on the reverse.

BILOCOR 10: Mottled dark beige, round normal convex tablet embossed with BI over break-line and 10 on one side and plain on the reverse.

PRESENTATION:

Opaque or clear Al/PVC/PVdC blister packs containing 30 tablets.

STORAGE INSTRUCTIONS:

Store below 25 °C in well-closed containers. Protect from light.

Keep blister packs in carton until required for use.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBERS:

BILOCOR 5: 38/5.2/0053

BILOCOR 10: 38/5.2/0051

**NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF
REGISTRATION:**

Pharma Dynamics (Pty) Ltd

F02 Grapevine House

Steenberg Office Park

Westlake

7945

DATE OF PUBLICATION OF THE PACKAGE INSERT:

12 August 2004

Bilocor 5

Bilocor 10

SKEDULERINGSSTATUS:

S3

EIENDOMSNAAM EN DOSEERVORM:

BILOCOR 5 TABLETTE

BILOCOR 10 TABLETTE

SAMESTELLING:

Elke **BILOCOR 5** tablet bevat 5 mg bisoprololfumaraat.

Elke **BILOCOR 10** tablet bevat 10 mg bisoprololfumaraat.

FARMAKOLOGIESE KLASSIFIKASIE:

A 5.2 Adrenolitika (simpatolitika)

FARMAKOLOGIESE WERKING:

Bisoprolol is 'n selektiewe β -1-adrenoseptorantagonis sonder intrinsieke simpatomimetiese en membraanstabilerende aktiwiteit.

Farmakokinetika:

Bisoprolol word na orale toediening goed geabsorbeer met 'n biobeskikbaarheid van ongeveer 90%. Bisoprolol ondergaan minimale eerstedeurgangsmetabolisme in die lewer. Ongeveer 50% van 'n dosis word in die lewer gemetaboliseer en die res word onveranderd deur die niere uitgeskei. Die eliminasihalfleeftyd vanuit die plasma is ongeveer 10 tot 12 uur en die duur van werking is ongeveer 24 uur.

INDIKASIES:

BILOCOR is aangedui vir die beheer van ligte tot matige hipertensie en angina pectoris.

KONTRA-INDIKASIES:

- Hipersensitiwiteit teenoor bisoprolol of teenoor enige van die bestanddele

- Ongekontroleerde asma
- Tweede- en derdegraadse hartblok en bradikardie (minder as 50 slae per minuut)
- Swangerskap en laktasie
- Onbeheerde hartversaking
- Metaboliese asidose
- Sinusbradikardie (minder as 50 slae per minuut)
- Feochromositoom
- Hipertiroïedisme omdat kliniese tekens maskeer kan word

Wees besonder versigtig met pasiënte wat aan die volgende ly: asma, brongitis, chroniese respiratoriese siekte, perifere vaskulêre siekte en Raynaud se verskynsel.

Die normale dosis moet verminder word vir bejaarde pasiënte of pasiënte wat aan nierdisfunksie ly. In die peri-operatiewe periode is dit oor die algemeen onwys om die dosis waaraan die pasiënt gewoon is te verminder omdat die gevaar bestaan dat angina pectoris of hipertensie kan vererger. Die pasiënt se normale tagikardiale respons op hipovolemie of bloedverlies tydens of na die operasie kan verberg word. Wees besonder versigtig hiervoor asook met diabetes mellitus omdat simptome en tekens van hipoglisemie maskeer kan word omdat die respons teenoor hipoglisemie minder is.

WAARSKUWINGS:

Die veiligheid en effektiwiteit in kinders is nie bepaal nie.

As besluit word om **BILOCOR** voor narkose te onttrek, moet ten minste 48 uur tussen die laaste dosis en die operasie verloop. As die medisyne voortgesit moet word, moet anestetika soos eter, siklopropan of trichlooretileen versigtig gebruik word. Atropien (1-2 mg IV) kan gebruik word om vagale dominansie reg te stel. Die pasiënt moet tydens die operasie op die gewone dosis gehou word om verergering van angina pectoris of hipertensie te voorkom.

Tagikardiale respons kan verberg word. Wees besonder versigtig hiervoor.

Die dosis van **BILOCOR** moet aangepas word vir pasiënte met ernstige swak nierfunksie (kyk **DOSIS EN GEBRUIKSAANWYSINGS**).

Wees versigtig as **BILOCOR** saam met Klas 1 antidisritmiese middels, soos disopiramied, miokardiale onderdrukkers, en remmers van AV-geleiding, soos kalsiumantagoniste, voorgeskryf word.

Wees versigtig wanneer 'n pasiënt van klonidien af oorgeskakel word omdat die onttrekking van klonidien tot die vrystelling van groot hoeveelhede katesjolamiene kan lei wat 'n hipertensiewe krisis kan veroorsaak. As **BILOCOR** onder hierdie omstandighede toegedien word, kan die ongeopponeerde stimulasie van alfa-reseptore hierdie effek versterk. As **BILOCOR** en klonidien saam gegee word, moet die klonidien nie gestaak word tot etlike dae na onttrekking van **BILOCOR** nie omdat erge terugslaghipertensie kan voorkom.

BILOCOR in kombinasie met verapamiel moet versigtig gebruik word vir pasiënte met swak ventrikulêre funksie. Hierdie kombinasie moet nie aan pasiënte met abnormaliteite in geleiding gegee word nie. Nie een van die middels moet binne 48 uur na staking van die ander een intraveneus toegedien word nie. Die intraveneuse toediening van kalsiumantagoniste en anti-aritmiese middels tydens behandeling met **BILOCOR** word nie aanbeveel nie.

BILOCOR modifiseer die tagikardie wat met hipoglisemie gepaardgaan.

Pasiënte met feochromositoom het gewoonlik behandeling met 'n alfa-adrenergiese blokkeerder nodig.

INTERAKSIES:

- Gelyktydige gebruik vir **BILOCOR** en hipoglisemiese middels, fenotiasiene en verskeie anti-aritmiese middels kan lewensbedreigende gevolge hê, soos
 - Uitgesproke hipoglisemie met orale hipoglisemiese middels en insulien
 - Miokardiale onderdrukking deur anti-aritmiese middels.
- Beta-adrenoseptor stimulerende middels (bv. isoprenalien) kan die effekte van **BILOCOR** antagoniseer.
- Alfa-adrenoseptorstimulante asook adrenergiese neuronblokkeerders soos guanetidien en reserpien saam met **BILOCOR** kan tot lewensbedreigende vasokonstriksie lei.

- **BILOCOR** en digoksien kan gelyktydig gebruik word vir pasiënte met kongestiewe hartversaking op voorwaarde dat die polsslag en die respons van die pasiënt gemonitor word.

SWANGERSKAP EN LAKTASIE:

Toediening van **BILOCOR** aan swanger moeders kort voor of tydens die bevalling kan tot hipotonie, ineenstorting of hipoglisemie in die pasgeborene lei (kyk **KONTRA-INDIKASIES**).

DOSIS EN GEBRUIKSAANWYSINGS:

Volwassenes: 5 tot 10 mg een keer per dag in die oggend met of sonder voedsel. Die dosis moet volgens die respons en verdraagbaarheid vir elke individu aangepas word. Die maksimum aanbevole daaglikse dosis is 20 mg per dag.

Ernstige swak nierfunksie (kreatinienopruiming < 20 ml/min) of ernstige swak lewerfunksie:

Die daaglikse dosis van 10 mg moet nie oorskry word nie.

Bejaardes:

Die normale dosis moet vir hierdie pasiënte verminder word.

NEWE-EFFEKTE EN SPESIALE VOORSORGMAATREËLS:

Neuwe-effekte:

Hematologies:

Bloedversteurings soos leukopenie en trombositopenie.

Kardiovaskulêre stelsel:

Bradikardie en kongestiewe hartversaking, hartblok, vloeistofretensie, verergering van perifere vasculêre siekte of die ontwikkeling van Raynaud se verskynsel en perifere gangreen kan aangebring word. Kongestiewe hartversaking en uitgesproke bradikardie kan voorkom.

Sentrale sensustelsel:

Lusteloosheid, duiseligheid, ligte hoofpyn, slaapversteurings, rusteloosheid, koue ekstremitate, hipotensie, paradoksale hipertensie, depressie, parestesie, hallusinasies, psigose.

Endokrien/Metabolies:

Metaboliese versteurings, hipoglisemie, toename in vlakke van uriensuur, hipercholesterolemie.

Gastro-intestinaal:

Naarheid, braking, diarree, hardlywigheid, gewigstoename, stomatitis.

Lewer:

Toename in lewerensieme.

Muskuloskeetaal:

Spierkrampe, miopatie, swakheid van skeletspiere.

Okulêr:

Steurings in visie.

Vel:

Sweet, veluitslag, alopesie.

Ander:

Tydlike gehoorverlies, hipersensitiwiteitsreaksies, seksuele impotensie.

Versteurings van asemhalingstelsel:

Brongokonstriksie kan voorkom in pasiënte wat aan asma, brongitis en ander chroniese longsiektes ly.

Nadelige reaksies is meer algemeen in pasiënte met swak nierfunksie.

Spesiale voorsorgmaatreëls:

Skielike staking van behandeling kan 'n verergering van angina pectoris veroorsaak in pasiënte wat aan isgemiese hartsiekte ly. Staking van behandeling moet geleidelik wees en pasiënte moet aangeraai word om die mate van hulle fisiese aktiwiteit te beperk in die periode waartydens die medisyne gestaak word.

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VIR DIE BEHANDELING DAARVAN

(kyk **NEWE-EFFEKTE EN SPESIALE VOORSORGMAATREËLS**):

Oordosering kan bradikardie en erge hipotensie veroorsaak. Brongospasma en hartversaking kan in sekere individue voorkom.

Gevalle van oordosering moet vir ten minste 4 uur dopgehou word omdat apnee en kardio-vaskulêre ineenstorting skielik kan voorkom.

Dit kan nodig wees om geaktiveerde koolstof herhaaldelik tydens oordosering toe te dien.

Atropien kan gebruik word om erge bradikardie te behandel. As die respons nie voldoende is nie, kan glukagon intraveneus toegedien word. As alternatief kan dopamien gebruik word om beta-blokkade om te keer. Tydens erge bradikardie kan dit nodig wees om vir die hart pas aan te gee. Brongospasma moet met intraveneuse aminofillien of ingeasemde of intraveneuse beta-antagoniste, bv. salbutamol, behandel word.

IDENTIFIKASIE:

BILOCOR 5: Liggeel, gespikkelde, ronde, normale konvekse tablet met BI bo 'n breeklyn en 5 op die een kant gedruk en die ander kant skoon.

BILOCOR 10: Gespikkelde, donker beige, ronde, normale konvekse tablet met BI bo 'n breeklyn en 10 op die een kant gedruk en die ander kant skoon.

AANBIEDING:

Ondeursigtige of helder Al/PVC/PVdC-stulppakke met 30 tablette.

BEWARINGSINSTRUKSIES:

Bewaar onder 25°C in diggeslote houers. Beskerm teen lig.

Hou die stulppakke in die karton totdat hulle benodig word.

HOU BUIE BEREIK VAN KINDERS.

REGISTRASIENOMMERS:

BILOCOR 5: 38/5.2/0053

BILOCOR 10: 38/5.2/0051

NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE REGISTRASIESERTIFIKAAT:

Pharma Dynamics (Edms) Bpk

F02 Grapevine House

Steenberg Office Park

Westlake

7945

DATUM VAN PUBLIKASIE VAN HIERDIE VOUBILJET:

12 Augustus 2004