M110078-2/18

台田藥品股份有限公司　函

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傳　　真：(02) 2651-5769
聯 絡 人：蘇怡亭; E-mail : agnessu@tanabe.com.tw

受文者：各醫療院所
發文日期：中華民國 110 年 02 月 18 日
發文字號：台田顧服函字第 110001 號
附件：變更前後對照表；原廠公文

主　旨：函知 本公司代理銷售之『康肯 1.25 毫克 ；Concor 1.25mg/Tab』、『康肯 5 毫克 ；Concor 5mg/Tab 』外紙箱尺寸、包裝型態、中文品名、製造廠名、仿單變更乙案，請 查照惠鑑。

說　明：

一、 感謝 貴院長期採用本公司所代理銷售之各項藥品，殊深銘感。

二、 經原廠「台灣默克股份有限公司」通知，Concor 1.25mg、5mg，外紙箱尺寸、包裝型態有變更，
※Concor 1.25mg 改為一箱 144 盒、8 盒/束
※Concor 5mg 改為一箱 90 盒、3 盒/束
詳細請參閱附檔變更前後對照。

三、 另外商品外盒、鋁箔片、仿單，有以下變更，
(1)中文品名→公絲改毫克
(2)製造廠名→Merck KGaA 改 Merck Healthcare KGaA
(3)仿單因應安全性變更。
其變更內容詳如附檔變更前後對照表。

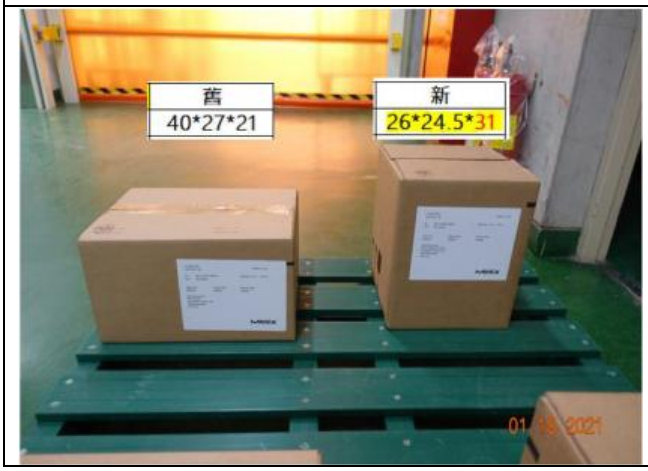
四、 預計四月中起，自以下批號陸續變更。

	Concor 1.25mg	Concor 5mg
批號	G00UE6	G00UKL
	G00UAP	G00UKM
	G00UE8	

五、 本公司保證除上述說明之變更外，其外觀、品質、療效、健保碼完全不變，造成不便之處，尚祈見諒。

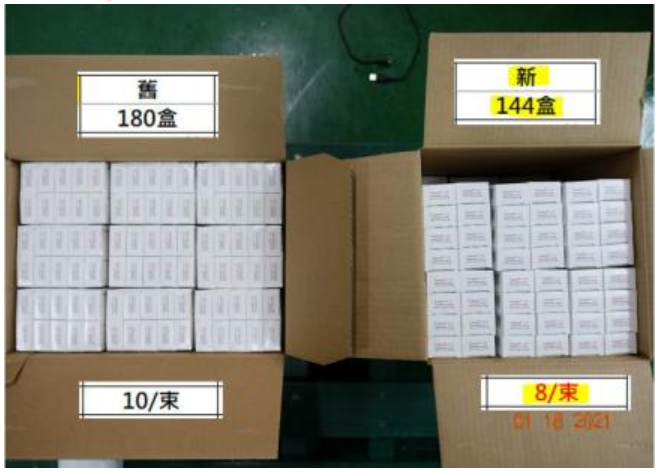
台田藥品股份有限公司
董事長　李明珍

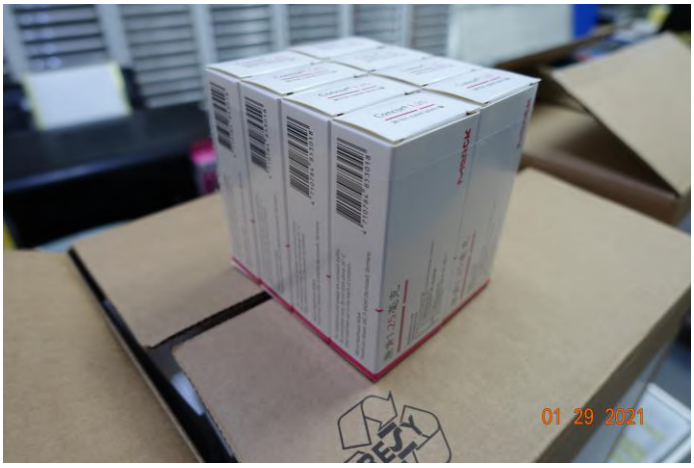
Concor 1.25mg & 5mg 外紙箱尺寸、包裝型態前後變更對照

1.25mg -外紙箱尺寸	5mg -外紙箱尺寸
	

1.25mg -包裝型態

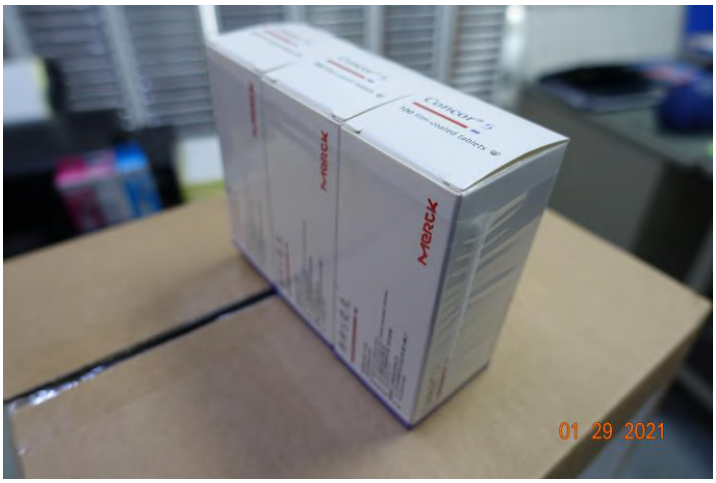
1.25mg 改為一箱 144 盒、8 盒/束





5mg -包裝型態

5mg 改為一箱 90 盒、3 盒/束

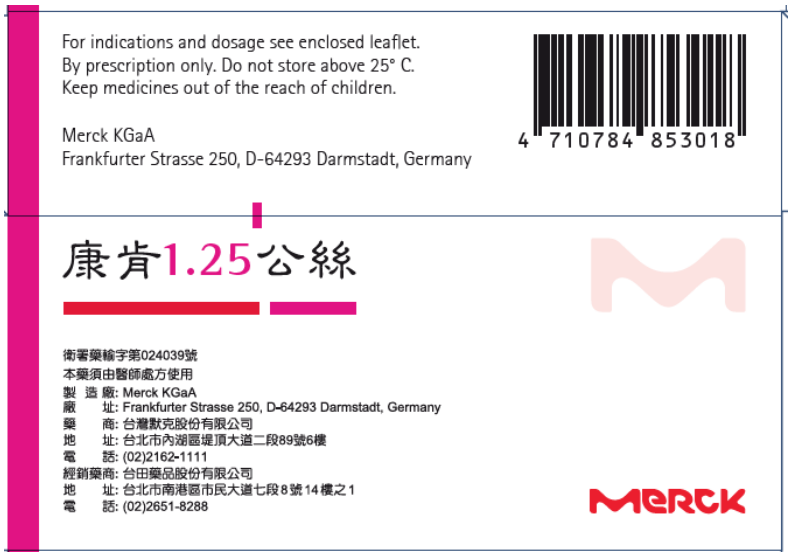


Concor 1.25mg -中文品名變更前後對照	
變更前	變更後
康肯 1.25 公絲	康肯 1.25 毫克

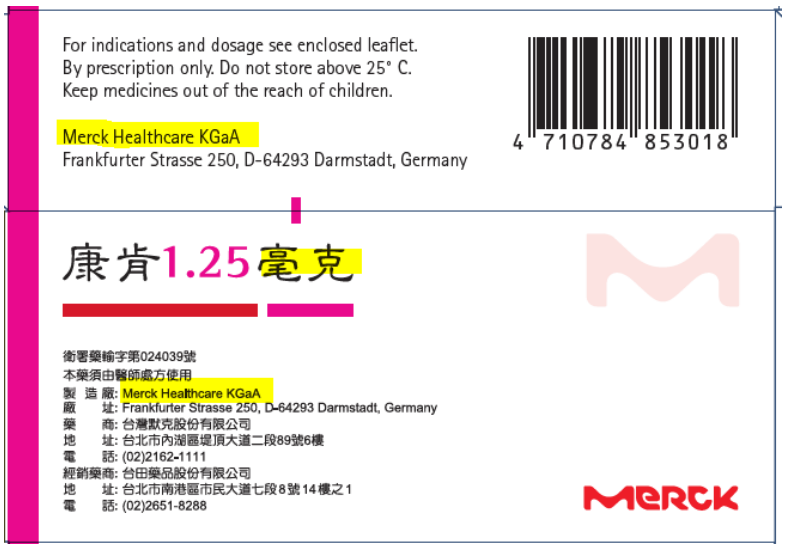
Concor 1.25mg -製造廠名變更前後對照	
變更前舊廠名	變更後新廠名
Merck KGaA	Merck Healthcare KGaA

Concor 1.25mg -新舊外盒比較圖

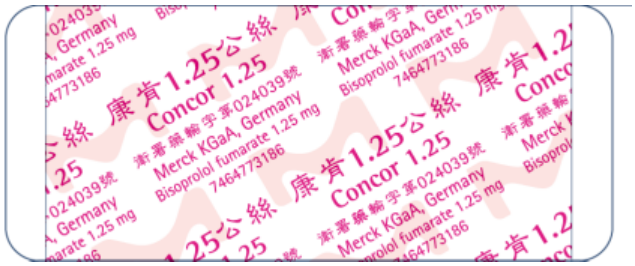
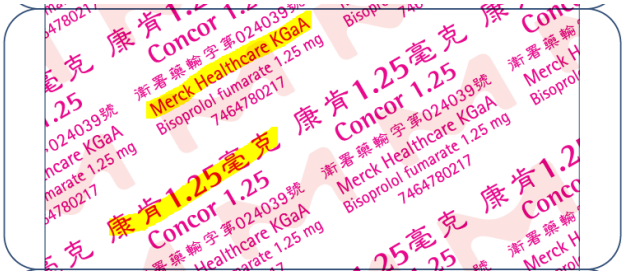
舊外盒



新外盒



Concor 1.25mg -內部新舊鋁箔比較圖(品名、製造廠名處有變更)

舊鋁箔	新鋁箔
	

Concor 1.25mg -中文仿單變更

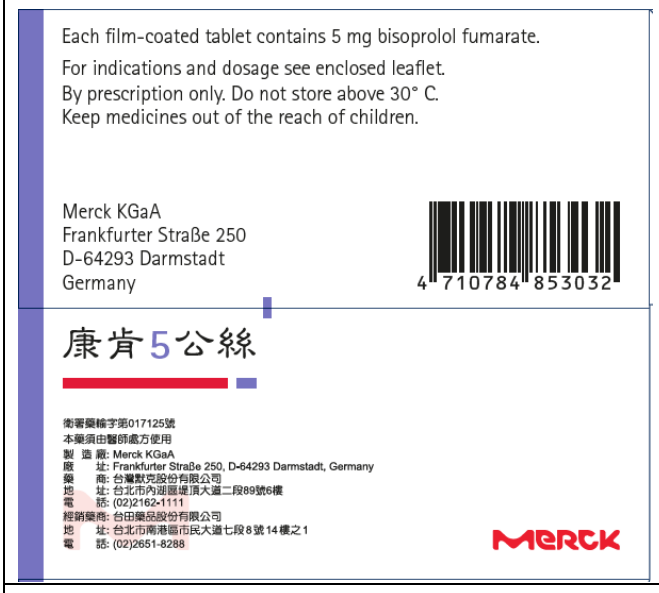
	變更前	變更後
品名	公絲	毫克
仿單內文	Bisoprolol	Bisoprolol fumarate
	病患、患者	病人
不良反應	皮膚及皮下組織異常 罕 見：過敏反應，包括搔癢、潮紅、皮疹 極 罕 見：禿髮。β-阻斷劑可能會誘發牛皮癬或使其惡化，或引起類似牛皮癬的皮疹。	皮膚及皮下組織異常 罕 見：過敏反應，包括搔癢、潮紅、皮疹及血管性水腫 極 罕 見：禿髮。β-阻斷劑可能會誘發牛皮癬 或使其惡化，或引起類似牛皮癬的皮疹。
資料日期	2019 年 10 月	2020 年 8 月
製造廠資訊	製 造 廠：Merck KGaA 廠 址：Frankfurter Strasse 250, D-64293 Darmstadt, Germany	製 造 廠：Merck Healthcare KGaA 廠 址：Frankfurter Strasse 250, D-64293 Darmstadt, Germany

Concor 5mg -中文品名變更前後對照	
變更前	變更後
康肯 5 公絲	康肯 5 毫克

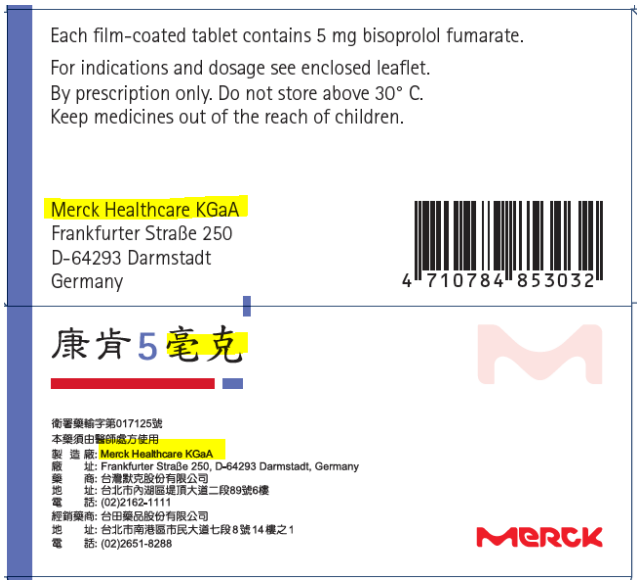
Concor 5mg -製造廠名變更前後對照	
變更前舊廠名	變更後新廠名
Merck KGaA	Merck Healthcare KGaA

Concor 5mg -新舊外盒比較圖

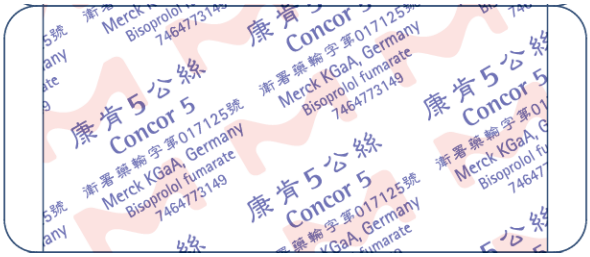
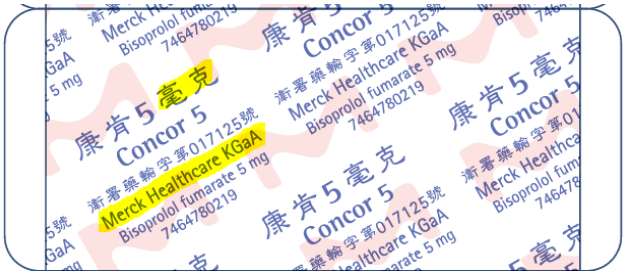
舊外盒



新外盒



Concor 5mg -內部新舊鋁箔比較圖(品名、製造廠名處有變更)

舊鋁箔	新鋁箔
	

Concor 5mg -中文仿單變更

	變更前	變更後
品名	公絲	毫克
仿單內文	Bisoprolol	Bisoprolol fumarate
	病患、患者	病人
不良反應	皮膚及皮下組織異常 罕　見：過敏反應，包括搔癢、潮紅、皮疹 極　罕　見：禿髮。β-阻斷劑可能會誘發牛皮癬或使其惡化，或引起類似牛皮癬的皮疹。	皮膚及皮下組織異常 罕　見：過敏反應，包括搔癢、潮紅、皮疹及血管性水腫 極　罕　見：禿髮。β-阻斷劑可能會誘發牛皮癬或使其惡化，或引起類似牛皮癬的皮疹。
資料日期	2019 年 10 月	2020 年 8 月
製造廠資訊	製　造　廠：Merck KGaA 廠　　址：Frankfurter Strasse 250, D-64293 Darmstadt, Germany	製　造　廠：Merck Healthcare KGaA 廠　　址：Frankfurter Strasse 250, D-64293 Darmstadt, Germany

台灣默克股份有限公司　函

地　　址：11493 台北市內湖區堤頂大道二段 89 號 6 樓
聯 絡 人：余忠佑
電　　話：(02) 2162-1111 ext.1526
傳　　真：(02) 8751-0507

受文者： 台田藥品股份有限公司

發文日期：中華民國 110 年 1 月 27 日
發文字號：台灣默克藥字第 110009 號

康肯 1.25 毫克(衛署藥輸字第 024039 號) 與康肯 5 公絲（衛署藥輸字第 017125 號）外箱包裝更改說明

簡述 (以下由 Concor 1.25 mg/5mg 代稱)

與包裝產線更換連動，本公司德國 Darmstadt 原廠於近期更改外箱包裝方式如下，將收縮膜束口方式改為束帶、並增加每個棧板可盛裝數量。從 2021 年一月開始到貨批次，如 Concor 1.25mg G00UAP, G00UE8, G00UE6 與 Concor 5mg G00UKM, G00UKL 皆已採用此變更。煩請協調各單位知悉。

更改前：

Before		packs / carton	cartons/ pallet	packs / pallet	wrapped	packs / wrap
Concor 1.25mg	3014481261	180	24	4320	shrink film	10
Concor 5mg	3028031262	120	20	2400	shrink film	10

更改後：

As-is		packs / carton	cartons/ pallet	packs / pallet	wrapped	packs / wrap
Concor 1.25mg	3014481261	144	36	5184	strap	8
Concor 5mg	3028031262	90	36	3240	strap	3

藥 商：台灣默克股份有限公司
負責人：李俊隆

Merck Ltd. Taiwan
6F, No.89, Sec.2, Tiding Blvd.,
Taipei(11493), Taiwan.
Phone 886-2-2162-1111
Fax 886-2-8751-0507
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台灣默克股份有限公司　函

地　　址：11493 台北市內湖區堤頂大道二段 89 號 6 樓
聯 絡 人：張詔翔
電　　話：(02) 2162-1111 ext.1529
傳　　真：(02) 8751-0507

115 台北市南港區市民大道七段八號 14 樓之一

受文者：台田藥品股份有限公司

發文日期：中華民國 110 年 1 月 12 日
發文字號：台灣默克藥字第 110004 號
附件：光碟

主旨：通知 貴公司關於本公司產品「康肯1.25毫克(衛署藥輸字第024039號)」及「康肯5毫克(衛署藥輸字第017125號)」，因應原廠通知進行製造廠名稱變更及仿單安全性更新乙事，請查照。

說明：

一、本公司接獲原廠通知進行上述產品之製造廠名稱變更及仿單安全性更新，業經食品藥物管理署核准在案，請詳見核准公文如光碟附件一。

二、有關新版外盒、標籤及仿單資訊，請參考光碟附件二，另新包裝貨品將於近日交付至貴公司，相關產品批號如下所示。

	Concor 1.25 mg	Concor 5 mg
LOT	G00UAP	G00UKL
	G00UE6	G00UKM
	G00UE8	

此致

正本：台田藥品股份有限公司

藥　商：台灣默克股份有限公司
負責人：謝志宏

台灣默克股份有限公司
11493 臺北市內湖區堤頂大道二段
89 號 6 樓
Tel: +886 (02) 2162-1111
Fax: +886 (02) 8751-6262

MERCK

Concor® 1.25

Active ingredient: bisoprolol fumarate

Composition

Concor® 1.25

Each film-coated tablet contains 1.25 mg bisoprolol fumarate as active ingredient.

Excipients:

Tablet core: Silica, colloidal anhydrous, magnesium stearate, crospovidone, microcrystalline cellulose, pregelatinized maize starch, maize starch, calcium hydrogen phosphate, anhydrous.

Film coating: Dimethicone, talcum, macrogol 400, titanium dioxide, hypromellose.

Properties

Pharmacodynamics

Bisoprolol fumarate, the active ingredient of Concor®, is a beta1-selective-adrenoceptor blocking agent, lacking intrinsic stimulating and relevant membrane stabilising activity. It only shows very low affinity to the beta2-receptor of the smooth muscles of bronchi and vessels as well as to the beta2-receptors concerned with metabolic regulation. Therefore, bisoprolol fumarate is generally not to be expected to influence the airway resistance and beta2-mediated metabolic effects. Its beta1-selectivity extends beyond the therapeutic dose range.

Pharmacokinetics

Absorption. Bisoprolol fumarate is almost completely (>90%) absorbed from the gastrointestinal tract and, because of its small first pass metabolism of approximately 10%, has an bioavailability of approximately 90% after oral administration. The bioavailability is not affected by food intake. Bisoprolol fumarate shows linear kinetics and the plasma concentrations are proportional to the administered dose over the dose range 5 to 20 mg. Peak plasma concentrations occur within 2-3 hours.

Distribution. Bisoprolol fumarate is extensively distributed. The volume of distribution is 3.5 l/kg. Binding to plasma proteins is approximately 30%.

Metabolism. Bisoprolol fumarate is metabolised via oxidative pathways with no subsequent conjugation. All metabolites, being very polar, are renally eliminated. The major metabolites in human plasma and urine were found to be without pharmacological activity. *In vitro* data from studies in human liver microsomes show that bisoprolol fumarate is primarily metabolised via CYP3A4 (~95%) with CYP2D6 having only a minor role.

Elimination. The clearance of bisoprolol fumarate is 'balanced' between renal elimination of the unchanged molecule (~50%) and hepatic metabolism (~50%) to metabolites which are also renally excreted. The total clearance of bisoprolol fumarate is approximately 15 l/h. Bisoprolol fumarate has an elimination half-life of 10-12 hours.

Indication

- Treatment of stable chronic moderate to severe heart failure with reduced systolic ventricular function (ejection fraction ≤ 35%, based on echocardiography) in addition to ACE inhibitors, and diuretics, and optionally cardiac glycosides.

Dosage and Administration

Treatment of stable chronic moderate to severe heart failure (CHF)

The initiation of treatment of stable chronic heart failure with Concor® necessitates a special titration phase and requires regular monitoring by the doctor.

Preconditions for treatment with bisoprolol fumarate are:

- stable chronic heart failure without acute failure during the past six weeks,
- mainly unchanged basic therapy during the past two weeks,
- treatment at optimal dose with an ACE inhibitor (or other vasodilator in case of intolerance to ACE inhibitors) and a diuretic, and optionally cardiac glycosides

It is recommended that the treating physician be experienced in the management of chronic heart failure.

The treatment of stable chronic heart failure with bisoprolol fumarate is initiated according to the following titration scheme, individual adaptation may be necessary depending on how well the patient tolerates each dose, i.e. the dose is to be increased only, if the previous dose is well tolerated.

1st week: 1.25 mg bisoprolol fumarate once daily

2nd week: 2.5 mg bisoprolol fumarate once daily

3rd week: 3.75 mg bisoprolol fumarate once daily

4th – 7th week: 5 mg bisoprolol fumarate once daily

8th –11th week: 7.5 mg bisoprolol fumarate once daily

12th week and beyond: 10 mg bisoprolol fumarate once daily as maintenance treatment

The treatment of stable chronic heart failure must be stated with a lower dose.

The maximum recommended dose is 10 mg bisoprolol fumarate once daily. Patients should be titrated to and maintained at this dose unless prevented by adverse effects.

After initiation of treatment with 1.25 mg bisoprolol fumarate, the patient should be observed over a period of approximately 4 hours (especially as regards blood pressure, heart rate, conduction disturbances, signs of worsening of heart failure).

During the titration phase or thereafter, transient worsening of heart failure with acute pulmonary edema, severe hypotension, cardiogenic shock, symptomatic bradycardia and AV block may occur. In this case it is recommended first to reduce the dose of bisoprolol fumarate. Bisoprolol fumarate should be discontinued only if clearly necessary, but its reintroduction and/or uptitration should always be considered when the patient becomes stable again.

Treatment with Concor® is generally a long-term therapy.

The treatment may be interrupted if necessary and reintroduced as appropriate.

Do not stop treatment abruptly or change the recommended dose without talking to your doctor first since this might lead to a transitory worsening of heart condition. If discontinuation is necessary, the daily dose is gradually decreased and should be tapered half dose per week.

Special populations

Renal or hepatic impairment:

- There is no information regarding pharmacokinetics of bisoprolol fumarate in patients with chronic heart failure and concomitant hepatic or renal impairment. Titration of the dose in these populations must therefore be made with particular caution.

Elderly:

- No dosage adjustment is required.

Children:

- There is insufficient experience with bisoprolol fumarate in children, therefore the use of Concor® cannot be recommended for children.

Administration

Concor® tablets are taken in the morning with or without food. They are swallowed with some liquid and not to be chewed.

Contraindications

Concor® must not be used in patients with:

- acute heart failure or during episodes of heart failure decompensation requiring intravenous therapy with substances increasing the contractility of the heart,
- shock induced by disorders of cardiac function (cardiogenic shock),
- severe disturbances of atrioventricular conduction (second or third degree AV block) without a pacemaker,
- sick sinus syndrome,
- sinoatrial block,
- symptomatic bradycardia
- symptomatic hypotension
- severe bronchial asthma
- severe forms of peripheral arterial occlusive disease or Raynaud's syndrome,
- untreated tumours of the adrenal gland (phaeochromocytoma),
- metabolic acidosis,
- hypersensitivity to bisoprolol fumarate or to any of the excipients (see Composition).

Special warnings and precautions

The following section describes when Concor® must be used with special caution:

- diabetes mellitus with extremely fluctuating blood glucose levels: symptoms of markedly reduced blood glucose (hypoglycaemia) such as tachycardia, palpitations or sweating can be masked,
- strict fasting,
- ongoing desensitisation therapy,
- mild disturbances of atrioventricular conduction (first degree AV block),
- Prinzmetal's angina; Cases of coronary vasospasm have been observed. Despite its high beta1-selectivity, angina attacks cannot be completely excluded when bisoprolol fumarate is administered to patients with Prinzmetal's angina. Utmost caution must be exercised.
- peripheral arterial occlusive disease (aggravation of symptoms may occur especially when starting therapy),
- patients with psoriasis or with a personal history of psoriasis

Respiratory system: Although cardioselective (beta1) beta-blockers may have less effect on lung function than non-selective beta-blockers, as with all beta-blockers these should be avoid in patients with obstructive airways diseases, unless there are compelling clinical reasons for their use. Where such reasons exist, Concor® may be used with caution. In bronchial asthma or other symptomatic chronic obstructive pulmonary diseases, which may cause symptoms, concomitant bronchodilating therapy is recommended. Occasionally an increase of the airway resistance may occur in patients with asthma, therefore the dose of beta2-stimulants may have to be increased.

Allergic reactions: Beta-blockers, including Concor®, may increase the sensitivity to allergens and the severity of anaphylactic reactions because the adrenergic counterregulation under beta-blockade may be alleviated. Treatment with adrenaline may not always yield the expected therapeutic effect.

General anaesthesia: In patients undergoing general anaesthesia the anaesthetist must be aware of beta-blockade. If it is thought necessary to withdraw Concor® before surgery, this should be done gradually and completed about 48 hours prior to anaesthesia.

Phaeochromocytoma: In patients with a tumour of the adrenal gland (phaeochromocytoma) Concor® may only be administered after previous alpha-receptor blockade.

Thyrotoxicosis: Under treatment with Concor® the symptoms of a thyroid hyperfunction (thyrotoxicosis) may be masked.

Special populations

So far no sufficient therapeutic experience is available for Concor® in patients with heart failure and concomitant insulin dependent type I diabetes mellitus, severely impaired kidney function, severely impaired hepatic function, restrictive cardiomyopathy, congenital heart diseases or haemodynamically relevant organic valvular heart disease. No sufficient therapeutic experience is available in patients with heart failure and myocardial infarction within the last 3 months.

There is insufficient experience with bisoprolol fumarate in children, therefore the use of Concor® cannot be recommended for children.

Effects on the ability to drive and use machines

In a study with patients suffering from coronary heart disease bisoprolol fumarate did not affect the driving performance of the patients. However, depending on the individual patients response to treatment an effect on the ability to drive a vehicle or to use machines may be impaired. This needs to be considered particularly at the start of treatment, upon change of medication, or in conjunction with alcohol.

Pregnancy and lactation

During pregnancy Concor® is only recommended following careful assessment of benefit-to-risk ratio by the doctor. In general, beta-blockers reduce placental blood flow and may affect the development of the unborn child. Placental and uterine blood flow as well as the growth of the unborn child must be monitored and, in case of harmful effects on pregnancy or the foetus, alternative therapeutic measures considered.

The newborn infant must be monitored closely after delivery. Symptoms of reduced blood glucose and slowed pulse rate generally may occur within the first 3 days of life.

There are no data on the excretion of bisoprolol fumarate in human breast milk or the safety of bisoprolol fumarate exposure in infants. Therefore administration of Concor® is not recommended during breastfeeding.

Adverse effects

The adverse effects described below are sorted according to system organ classes. Frequencies are classified as follows:

Very common (affects more than 1 person in 10)

Common (affects less than 1 person in 10)

Uncommon (affects less than 1 person in 100)

Rare (affects less than 1 person in 1,000)

Very rare (affects less than 1 person in 10,000)

Frequency not known (cannot be estimated from available data)

- Investigations

Rare: increased triglycerides, increased liver enzymes (ALAT, ASAT)

- *Cardiac disorders*

Very common: bradycardia

Common: worsening of pre-existing heart failure

Uncommon: AV-conduction disturbances;

- *Nervous system disorders*

Common: dizziness*, headache*

- *Eye disorders*

Rare: reduced tear flow (to be considered if the patient uses contact lenses)

Very rare: conjunctivitis

- *Ear and labyrinth disorders*

Rare: hearing disorders

- *Respiratory, thoracic and mediastinal disorders*

Uncommon: bronchospasm in patients with bronchial asthma or a history of obstructive airways disease

Rare: allergic rhinitis

- *Gastrointestinal disorders*

Common: gastrointestinal complaints such as nausea, vomiting, diarrhoea, constipation

- *Skin and subcutaneous tissue disorders*

Rare: hypersensitivity reactions such as pruritus, flush, rash and angioedema

Very rare: alopecia. Beta-blockers may provoke or worsen psoriasis or induce psoriasis-like rash.

- *Musculoskeletal and connective tissue disorders*

Uncommon: muscle weakness, muscle cramps

- *Vascular disorders*

Common: feeling of coldness or numbness in the extremities, hypotension especially in patients with heart failure

Frequency not known: syncope

- *General disorders*

Common: asthenia, fatigue*

- *Hepatobilary disorders*

Rare: hepatitis

- *Reproductive system and breast disorders*

Rare: erectile dysfunction

- *Psychiatric disorders*

Uncommon: depression, sleep disorder

Rare: nightmare, hallucination

*These symptoms especially occur at the beginning of the therapy. They are generally mild and usually disappear within 1-2 weeks.

Tell your doctor if you notice any of the side effects listed above or any other unwanted or unexpected effects. To prevent serious reactions, speak to a doctor immediately if a side effect is severe, occurred suddenly or gets worse rapidly.

Interactions

The effect and tolerability of medicines can be influenced by simultaneous intake of other medication. Such interactions can also occur if a short time has elapsed since the use of the other medication. Tell your doctor if you are taking any other medicine – even those not prescribed to you by a doctor.

Combinations not recommended

Class-I antiarrhythmic medicines (e.g. quinidine, disopyramide, lidocaine, phenytoin; flecainide, propafenone) may increase the depressant effect of Concor® on atrio-ventricular impulse conduction and the contractility of the heart.

Calcium antagonists of the verapamil type and to a lesser extent of the diltiazem type may lead to reduced contractility of the heart muscle and delayed atrio-ventricular impulse conduction when used concomitantly with Concor®. Especially intravenous administration of verapamil in patients on ß-blocker treatment may lead to profound hypotension and atrioventricular block.

Centrally acting blood pressure-lowering medicines (such as clonidine, methyldopa, moxonodine, rilmenidine) may lead to a reduction of heart rate and cardiac output, as well as to vasodilation due to a decrease in the central sympathetic tonus. Abrupt withdrawal, particularly if prior to beta-blocker discontinuation, may increase risk of "rebound hypertension".

Combinations to be used with caution

Calcium antagonists of the dihydropyridine type (e.g. nifedipine, felodipine, amlodipine) may increase the risk of hypotension when used concomitantly with Concor®. An increased risk of a further deterioration of the ventricular pump function in patients with heart failure cannot be excluded.

Class-III antiarrhythmic medicines (e.g. amiodarone) may increase the inhibitory effect of Concor® on atrio-ventricular impulse conduction.

Topical ß-blockers (e.g. eye drops for glaucoma treatment) may add to the systemic effects of Concor®.

Parasympathomimetic medicines may increase the inhibitory effect on atrio-ventricular impulse conduction and the risk of bradycardia when used concomitantly with Concor®.

The blood sugar lowering effect of insulin or oral antidiabetic medicines may be increased. Warning signs of reduced blood glucose (hypoglycaemia) – especially accelerated heart rate (tachycardia)- may be masked or suppressed. Such interactions are considered to be more likely with nonselective ß-blockers.

Anaesthetic agents may increase the risk of cardiodepressive actions of Concor®, leading to hypotension (for further information on general anaesthesia see also section special warnings and precautions)

Cardiac glycosides (digitalis) may lead to an increase in impulse conduction time and thus reduction in heart rate when used concomitantly with Concor®.

Non-steroidal anti-inflammatory medicines (NSAIDs) may reduce the blood pressure-lowering effect of Concor®.

ß-Sympathomimetics (e.g. isoprenaline, dobutamine) used in combination with Concor® may lead to a reduced effect of both agents.

A combination of Concor® with sympathomimetics that activate both ß- and α-adrenoceptors (e.g. noradrenaline, adrenaline) may intensify the α-adrenoceptor-mediated vasoconstrictor effects of these agents leading to blood pressure increase. Such interactions are considered to be more likely with nonselective ß-blockers.

Antihypertensive agents as well as other medicines with blood pressure lowering potential (e.g. tricyclic antidepressants, barbiturates, phenothiazines) may increase the blood pressure lowering effect of Concor®.

Combinations to be considered

Mefloquine may increase the risk of decelerating the heart rate (bradycardia), if used in combination with Concor®.

Monoamine oxidase inhibitors (except MAO-B inhibitors) may enhance the hypotensive effect of the beta-blockers. Concomitant use may also be a risk for hypertensive crisis.

Overdose

The most frequent signs of Concor® overdose include slow heart rate (bradycardia), marked drop in blood pressure, acute heart failure, hypoglycaemia and bronchospasm.

In the case of suspected Concor® overdose please inform your doctor immediately. The effect of overdose may vary from one person to the next and patients with heart failure are probably very sensitive. Depending on the degree of overdose your doctor can then decide which measures to take.

In general, if overdose occurs, bisoprolol fumarate treatment is stopped and supportive and symptomatic treatment is provided. Limited data suggest that bisoprolol fumarate is hardly dialysable.

Storage and Stability

Do not store above 25°C.

Do not use after the expiry date.

Keep medicines out of the reach of children.

Presentations

Concor® 1.25: blister with box pack

Date of Information

Aug, 2020

Merck Healthcare KGaA
Frankfurter Strasse 250, D-64293 Darmstadt , Germany

MERCK

康肯® 1.25毫克 Concor® 1.25

衛署藥輸字第024039號

有效成分：Bisoprolol fumarate

本藥須由醫師處方使用

成分

每顆膜衣錠中含有的有效成分為1.25毫克Bisoprolol fumarate。

賦形劑：錠劑核心：無水膠質狀的二氧化矽、硬脂酸鎂、聚乙烯聚吡咯烷酮、微晶性纖維素、預先膠狀的玉米澱粉、玉米澱粉、無水磷酸氫鈣。

膜衣成分：聚二甲矽烷、滑石、聚乙二醇400、二氧化鈦、羥丙基甲基纖維素。

特性

藥物藥效學

Bisoprolol fumarate為康肯®的有效成分，它是一種β_1-選擇性腎上腺受體阻斷劑，它不具有內在刺激性，以及對細胞膜的相關安定作用。它與支氣管及血管平滑肌上之β_2受體，及與代謝調節有關之β_2受體的親合力都相當低。因此，一般認為Bisoprolol fumarate不會影響呼吸道的阻力，也不會影響受β_2-調節的代謝作用。它的β_1-選擇性涵蓋範圍超過其治療劑量範圍。

藥物動力學

*吸收：*Bisoprolol fumarate幾乎全部（> 90%）經由胃腸道吸收，因為其首渡代謝效應只佔了一小部分（約10%），所以它在口服之後的生體可用率約為90%。其生體可用率不受食物所影響。Bisoprolol fumarate具線性藥動學，藥物劑量在5-20毫克範圍內，其血漿濃度會與藥物劑量呈正比。最高血漿濃度在服藥後2-3小時內出現。

*分佈：*Bisoprolol fumarate的分布相當廣泛，其分佈體積為3.5公升/公斤，與血漿蛋白結合的比例約為30%。

*代謝：*Bisoprolol fumarate是經由氧化作用代謝，之後不會進行結合反應（conjuction）。所有的代謝物都具有高度極性並經由腎臟排除。在人體血漿及尿液中的主要代謝物都不具有藥理活性。根據在人體肝臟原漿微粒（microsome）中所進行的體外試驗數據顯示，Bisoprolol fumarate主要是經由CYP3A4所代謝（~95%），經由CYP2D6代謝只佔了一小部分。

*排除：*Bisoprolol fumarate一部分是以原型經由腎臟排除（~50%），另一部分則為肝臟代謝後形成代謝物再經由腎臟排除（~50%），這兩者之間維持著‘均衡’的關係。Bisoprolol fumarate的總廓清率約為15公升/小時。Bisoprolol fumarate的排除半衰期為10-12小時。

適應症

- 穩定型慢性中度至重度心衰竭

【說明】：合併心室收縮功能不良（LVEF ≤ 35%）且已合併使用ACE inhibitors、利尿劑或強心配醣體者。

用法用量

治療穩定型慢性中度至重度心衰竭（CHF）

剛開始以康肯®治療穩定型慢性心衰竭時，需要一段特殊的劑量調整期，所以必須接受醫師的定期監測。

適合接受Bisoprolol fumarate治療的條件如下：

- 在過去6週內不曾發生過急性心衰竭之穩定型慢性心衰竭病人
- 在過去2週內其基礎治療沒有改變者
- 接受適當劑量的ACE抑制劑（或對ACE抑制劑耐受性不佳而使用其他的血管擴張劑）及利尿劑治療，或亦有合併接受強心配醣體之治療者

建議治療的醫師應具有治療慢性心衰竭的經驗。

剛開始以Bisoprolol fumarate治療穩定型慢性心衰竭時，可根據以下的方式逐漸增加劑量，病人的劑量必須視個人的耐受程度來加以調整，例如，必須在前一劑量耐受性良好的情況下，方可以增加劑量。

第1週：	1.25毫克Bisoprolol fumarate每日一次
第2週：	2.5 毫克Bisoprolol fumarate每日一次
第3週：	3.75毫克Bisoprolol fumarate每日一次
第4~7週：	5 毫克Bisoprolol fumarate每日一次
第8~11週：	7.5 毫克Bisoprolol fumarate每日一次
第12週及之後：	10 毫克Bisoprolol fumarate每日一次，並作為維持劑量剛開始治療穩定型慢性心衰竭時，可先給予較低的治療劑量。

Bisoprolol fumarate的最大建議劑量為10毫克，每日一次。除非有不良反應，否則病人應逐漸增加至此劑量，並維持服用該劑量。

病人開始Bisoprolol fumarate 1.25毫克的治療後，應該接受大約4小時的觀察期（尤其應該注意血壓、心跳速率、傳導障礙、心臟衰竭的惡化徵兆）。

於劑量調整期間或之後，有可能出現心衰竭惡化合併急性肺水腫、嚴重低血壓、心因性休克、心搏徐緩症候群、房室傳導阻斷。若有這種情況發生，建議先降低Bisoprolol fumarate的劑量。只有在絕對必要時，Bisoprolol fumarate才必須停藥，但是在病人狀況穩定後，仍應考慮重新給藥及/或慢慢增加其劑量。

接受康肯®的治療通常為一種長期性的治療。

必要時，治療可能須中斷，之後於適當時間可再重新給藥。

在未與醫師討論前，請勿突然停藥或變更建議劑量，因為這有可能導致心臟功能暫時性惡化。如果需要中斷，原則上要逐漸遞減用量，分別每星期減少一半用量。

特殊族群

腎或肝功能不全的病人：

目前尚無慢性心衰竭同時併有肝或腎功能不全的病人使用Bisoprolol fumarate的藥物動力學資料。這群病人在調整劑量時應特別小心。

老年人：

不需要調整劑量。

兒童：

目前在兒童尚無足夠的使用經驗，因此不建議兒童使用本藥物。

給藥方式

康肯®於早上餐前或餐後給藥皆可。請伴隨液體吞服，不要嚼碎。

禁忌

康肯®不應給予有下列情況之病人：

- 急性心衰竭，或正處於心衰竭喪失代償能力期間而必需要給予靜脈注射藥物以增加心臟收縮能力時
- 心臟功能障礙引發之休克（心因性休克）
- 沒有裝上心臟節律器的嚴重房室傳導障礙（第二級或第三級的房室阻斷）
- 病態性竇症候群
- 竇房結阻斷
- 症狀性心搏過緩
- 症狀性低血壓
- 嚴重的支氣管氣喘
- 嚴重的週邊動脈血管閉塞疾病或Raynaud氏症候群
- 腎上腺有尚未接受治療的腫瘤（嗜鉻細胞瘤）
- 代謝性酸中毒
- 對Bisoprolol fumarate或賦形劑中的任何成分過敏者（參閱“成分”欄）

警語及注意事項

康肯®使用於下列情況時應特別小心：

- 血糖值變化波動很大的糖尿病病人：須注意血糖明顯下降（低血糖）的症狀例如，心搏過速、心悸或出汗等可能會被遮蔽
- 在嚴格的禁食狀態下
- 正在接受減敏（desensitisation）療法
- 有輕微的房室傳導障礙（第一級房室傳導阻斷）
- Prinzmetal氏心絞痛；已觀察到冠狀血管痙攣的病例。儘管是高度β_1選擇性，但當病人有Prinzmetal氏心絞痛並給予Bisoprolol fumarate治療時，心絞痛發作無法完全被排除掉。必須非常謹慎
- 週邊動脈血管閉塞疾病（開始使用本藥治療時，症狀可能會變明顯）
- 病人有或曾有牛皮癬之病史

*呼吸系統：*雖然心臟選擇性β-阻斷劑（β_1）比非選擇性β-阻斷劑對於肺臟功能有較少的作用，但就像所有的β-阻斷劑避免使用在患有阻塞性呼吸道疾病的病人一樣，除非臨床上有強力證據顯示，投與本藥物時仍要小心。支氣管氣喘或其他慢性阻塞性肺病病人如症狀發作時可以併用支氣管擴張劑治療。氣喘病人的呼吸道阻力有時候可能會增加，此時會需要較高劑量的β_2-交感神經興奮劑。

*過敏反應：*包括康肯®在內的β-阻斷劑可能會加重過敏原的敏感性及過敏反應的嚴重程度，因為β-阻斷劑會減弱腎上腺素的反向調節作用。給予腎上腺素治療不一定能獲得預期的療效。

*全身麻醉：*病人如欲接受全身麻醉，必須告知麻醉醫師其正在使用β-阻斷劑。若經過考量認為有必要在手術前停用康肯®，則應該逐漸降低劑量並於麻醉前48小時完全停藥。

*嗜鉻細胞瘤：*對於腎上腺腫瘤（嗜鉻細胞瘤）病人，康肯®只能用於已服用過α受體阻斷劑。

*甲狀腺毒症：*在康肯®的治療下，甲狀腺機能亢進的症狀（甲狀腺毒症）有可能會被隱蔽。

特殊族群

到目前為止，以康肯®治療心衰竭同時患有胰島素依賴性第一型糖尿病、嚴重腎功能不全、嚴重肝功能不全、限制型心肌症、先天性心臟疾病或與血流動力相關的心臟瓣膜疾病病人尚無足夠的治療經驗。對於最近3個月內發生心衰竭及心肌梗塞之病人，亦無足夠的治療經驗。

Bisoprolol fumarate使用於兒童尚無足夠的經驗，因此康肯®不建議兒童使用。

對開車及操作機械的影響

根據單一研究顯示，Bisoprolol fumarate對於冠狀動脈心臟疾病病人的開車能力並不會有影響。然而，因為個人體質的差異，有些人的開車及機械操作能力可能會受到影響。這種情況在治療初期、調整劑量後及併用酒精時必須特別注意。

懷孕與授乳

懷孕期間，康肯®必須經過醫師小心評估其利益與風險後才能使用。一般說來，β-阻斷劑會降低胎盤的血流量，因此有可能會影響胎兒的發育。在這種情況下，應監測胎盤及子宮的血流量與胎兒的生長發育狀況，若對懷孕及胎兒造成不良影響，則應考慮改用其他的替代性治療。

新生嬰兒在出生後應予以嚴密監測。通常血糖降低及脈搏減緩的症狀有可能在出生後的3天內出現。

目前尚無有關Bisoprolol fumarate分泌於母乳及嬰兒攝取Bisoprolol fumarate的安全性數據。因此，康肯®不建議於授乳期間服用。

不良反應

以下的不良反應乃依照系統器官來加以分類。發生頻率的標準如下：

非常常見：（≥ 1/10）
常　　見：（≥ 1/100 to < 1/10）
不 常 見：（≥ 1/1,000 to < 1/100）
罕　　見：（≥ 1/10,000 to < 1/1,000）
極 罕 見：（< 1/10,000）
頻率未明（無法從現行數據中評估）

- 檢驗數據異常
  - 罕　　見：三酸甘油脂增加，肝臟酵素增加（麩丙氨轉移酶、麩草氨轉移酶）
- 心臟方面異常
  - 非常常見：心搏徐緩
  - 常　　見：心衰竭更加惡化
  - 不 常 見：房室傳導障礙
- 神經系統失調
  - 常　　見：頭暈*、頭痛*
- 眼睛異常
  - 罕　　見：淚液減少（若病人有配戴隱形眼鏡應加以注意）
  - 極 罕 見：結膜炎
- 耳朵及迷路異常
  - 罕　　見：聽力異常
- 呼吸、胸腔及縱隔腔異常
  - 不 常 見：有氣喘或呼吸道阻塞疾病病史者，可能會出現支氣管痙攣
  - 罕　　見：過敏性鼻炎
- 胃腸道異常
  - 常　　見：胃腸道的不適包括，噁心、嘔吐、腹瀉及便祕
- 皮膚及皮下組織異常
  - 罕　　見：過敏反應，包括搔癢、潮紅、皮疹及血管性水腫
  - 極 罕 見：禿髮。β-阻斷劑可能會誘發牛皮癬或使其惡化，或引起類似牛皮癬的皮疹。
- 肌肉骨骼及結締組織異常
  - 不 常 見：肌肉衰弱及痙攣
- 血管方面異常
  - 常　　見：四肢冰冷或麻木；低血壓，特別是心衰竭病人
  - 頻率未明：昏厥
- 全身性不適
  - 常　　見：無力、疲勞*
- 肝膽異常
  - 罕　　見：肝炎
- 生殖系統及乳房異常
  - 罕　　見：勃起功能障礙
- 精神方面失調
  - 不 常 見：憂鬱、睡眠障礙
  - 罕　　見：做惡夢、幻覺

* 這些症狀大多出現於治療初期。它們一般皆屬輕微，且常會在1-2週內消失。

若您出現上述的任何不良反應或其他任何不舒服或未預期的反應，請告訴您的醫師。為了避免出現嚴重的情況，當不良反應為嚴重、突然發生或快速惡化時，應立刻就醫。

交互作用

藥物的反應和耐受性有可能受其他同時服用之藥物所影響。若在服用本藥之前不久曾經服用其他藥物，也有可能出現這類交互作用。如果您有服用其他的任何藥物，請告訴您的醫師－非處方藥也包括在內。

不建議併用

第I類（Class-I）抗心律不整藥物（例如，quinidine、disopyramide、lidocaine、phenytoin、flecainide、propafenone）可能會加強康肯®對房室傳導及心臟收縮能力的抑制作用。

當verapamil類的鈣離子拮抗劑（diltiazem類藥物亦然，但情況或許較為輕微）與康肯®併用時，可能會導致心肌的收縮力下降，並且延遲房室的傳導。特別是正在接受β-阻斷劑治療的病人，若給予verapamil靜脈注射，可能會使其低血壓及房室傳導阻斷的情況顯著加重。

中樞性降血壓藥（例如，clonidine、methyldopa、moxonodine、rilmenidine）可能會降低心跳速率及心輸出量，並且由於中樞交感神經活性降低而導致血管擴張。如果在停用β-阻斷劑之前突然停用，則可能會增加“反彈性高血壓（rebound hypertension）”的風險。

併用時應小心

Dihydropyridine類的鈣離子拮抗劑（例如，nifedipine、felodipine、amlodipine）與康肯®併用時，可能會增加低血壓的風險。另外，心衰竭病人之心室輸出功能進一步惡化的風險無法被排除。

第III類（Class-III）抗心律不整藥物（例如，amiodarone）可能會加強康肯®在房室傳導的抑制作用。

局部β-阻斷劑（例如，治療青光眼的眼藥水）可能對康肯®的全身性作用有加成反應。

副交感神經興奮劑與康肯®併用時，可能會加強其房室傳導的抑制作用及增加心搏徐緩的風險。

胰島素或口服抗糖尿病藥物的降血糖作用有可能會被加強。血糖降低（低血糖）的警訊－特別是心跳速率加快（心搏過速）－有可能被隱蔽或壓抑。非選擇性的β-阻斷劑較容易出現這類的交互作用。

麻醉劑可能會使康肯®對心臟抑制作用的風險提高而導致低血壓（全身麻醉的進一步資訊可參閱“警語及注意事項”）

強心配醣體（毛地黃）與康肯®併用時，心搏傳導的時間會增長，因此會降低心跳速率。

非類固醇抗發炎藥物（NSAIDs）可能會降低康肯®的降血壓效果。

β-交感神經興奮劑（例如，isoprenaline、dobutamine）與康肯®併用時，兩種藥物的作用可能都會減弱。

康肯®與同時活化β-及α腎上腺受體的交感神經興奮劑（例如，noradrenaline、adrenaline）併用時，可能會強化該類藥物活化α腎上腺受體所致的血管收縮作用，造成血壓上升。這類交互作用較常見於非選擇性的β-阻斷劑。

降血壓藥及其他可能引起血壓下降的藥物（例如，三環抗憂鬱劑、barbiturates、phenothiazines）可能會加強康肯®的降血壓效果。

併用時須加以考量

Mefloquine與康肯®併用時，可能會使心跳速率降低（心搏徐緩）的風險增加。

單胺氧化酶抑制劑（MAO-B抑制劑除外）可能會強化β-阻斷劑的降血壓效果。與康肯®併用可能會有引發高血壓危象的風險。

過量

康肯®藥物過量最常見的症狀包括心跳速率變慢（心搏徐緩），血壓明顯下降、急性心衰竭、低血糖及支氣管痙攣。

當懷疑有康肯®過量時，請立刻通知您的醫師。藥物過量的作用因人而異，且心衰竭的病人多半非常敏感，您的醫師會視藥物過量的情況來加以處理。

一般說來，當有過量的情況發生時，Bisoprolol fumarate會予以停藥並給予支持性及症狀性治療。根據有限的資料顯示，Bisoprolol fumarate不容易被透析清除。

儲存及安定性

請儲存於25℃以下。

請勿使用超過有效期限之藥物。

請將藥物置於兒童無法觸及處。

包裝

康肯® 1.25毫克：鋁箔盒裝

資料日期

2020年8月

製 造 廠：Merck Healthcare KGaA
廠　　址：Frankfurter Strasse 250, D-64293 Darmstadt , Germany
藥　　商：台灣默克股份有限公司
地　　址：台北市內湖區堤頂大道二段89號6樓
電　　話：(02) 2162-1111
經銷藥商：台田藥品股份有限公司
地　　址：台北市南港區市民大道七段8號14樓之1
電　　話：(02) 2651-8288

7871448008

MERCK

Concor® 5
Concor® 10

Active ingredient: bisoprolol fumarate

Composition

Each film-coated tablet contains 5 mg or 10 mg bisoprolol fumarate as active ingredient.

Excipients:

Tablet core: Silica, colloidal anhydrous; magnesium stearate, crospovidone, microcrystalline cellulose, maize starch, calcium hydrogen phosphate, anhydrous.

Film coating: Iron oxide yellow, dimethicone, macrogol 400, titanium dioxide, hypromellose.

Concor 10: All the above excipients include additional Iron oxide red.

Properties

Pharmacodynamics

Bisoprolol fumarate, the active ingredient of Concor, is a beta1-selective-adrenoceptor blocking agent, lacking intrinsic stimulating and relevant membrane stabilising activity. It only shows very low affinity to the beta2-receptor of the smooth muscles of bronchi and vessels as well as to the beta2-receptors concerned with metabolic regulation. Therefore, bisoprolol fumarate is generally not to be expected to influence the airway resistance and beta2-mediated metabolic effects. Its beta1-selectivity extends beyond the therapeutic dose range.

Pharmacokinetics

Absorption. Bisoprolol fumarate is almost completely (>90%) absorbed from the gastrointestinal tract and, because of its small first pass metabolism of approximately 10%, has an bioavailability of approximately 90% after oral administration. The bioavailability is not affected by food intake. Bisoprolol fumarate shows linear kinetics and the plasma concentrations are proportional to the administered dose over the dose range 5 to 20 mg. Peak plasma concentrations occur within 2-3 hours.

Distribution. Bisoprolol fumarate is extensively distributed. The volume of distribution is 3.5 l/kg. Binding to plasma proteins is approximately 30%.

Metabolism. Bisoprolol fumarate is metabolised via oxidative pathways with no subsequent conjugation. All metabolites, being very polar, are renally eliminated. The major metabolites in human plasma and urine were found to be without pharmacological activity. *In vitro* data from studies in human liver microsomes show that bisoprolol fumarate is primarily metabolised via CYP3A4 (~95%) with CYP2D6 having only a minor role.

Elimination. The clearance of bisoprolol fumarate is 'balanced' between renal elimination of the unchanged molecule (~50%) and hepatic metabolism (~50%) to metabolites which are also renally excreted. The total clearance of bisoprolol fumarate is approximately 15 l/h. Bisoprolol fumarate has an elimination half-life of 10-12 hours.

Indication

- Treatment of high blood pressure (hypertension)
- Treatment of coronary heart disease (angina pectoris)
- Treatment of stable chronic moderate to severe heart failure with reduced systolic ventricular function (ejection fraction ≤ 35%, based on echocardiography) in addition to ACE inhibitors, and diuretics, and optionally cardiac glycosides.

Dosage and Administration

Treatment of hypertension or angina pectoris

In all cases the dose regimen is adjusted individually by your doctor, in particular according to the pulse rate and therapeutic success.

The usual initial dose is 5 mg bisoprolol fumarate once daily. If necessary, the dose may be increased to 10 mg bisoprolol fumarate once daily.

The maximum recommended dose is 20 mg bisoprolol fumarate once daily.

Concor must be used with caution in patients with hypertension or angina pectoris and accompanying heart failure.

Treatment of stable chronic moderate to severe heart failure

The initiation of treatment of stable chronic heart failure with Concor necessitates a special titration phase and requires regular monitoring by the doctor.

Preconditions for treatment with bisoprolol fumarate are:

- stable chronic heart failure without acute failure during the past six weeks,
- mainly unchanged basic therapy during the past two weeks,
- treatment at optimal dose with an ACE inhibitor (or other vasodilator in case of intolerance to ACE inhibitors) and a diuretic, and optionally cardiac glycosides.

It is recommended that the treating physician be experienced in the management of chronic heart failure.

The treatment of stable chronic heart failure with bisoprolol fumarate is initiated according to the following titration scheme, individual adaptation may be necessary depending on how well the patient tolerates each dose, i.e. the dose is to be increased only, if the previous dose is well tolerated.

1st week: 1.25 mg bisoprolol fumarate once daily
2nd week: 2.5 mg bisoprolol fumarate once daily
3rd week: 3.75 mg bisoprolol fumarate once daily
4th – 7th week: 5 mg bisoprolol fumarate once daily
8th –11th week: 7.5 mg bisoprolol fumarate once daily
12th week and beyond: 10 mg bisoprolol fumarate once daily as maintenance treatment

The treatment of stable chronic heart failure must be stated with a lower dose.

The maximum recommended dose is 10 mg bisoprolol fumarate once daily. Patients should be titrated to and maintained at this dose unless prevented by adverse effects.

After initiation of treatment with 1.25 mg bisoprolol fumarate, the patient should be observed over a period of approximately 4 hours (especially as regards blood pressure, heart rate, conduction disturbances, signs of worsening of heart failure).

During the titration phase or thereafter, transient worsening of heart failure, fluid retention, hypotension or bradycardia may occur. In this case it is recommended first to reduce the dose of bisoprolol fumarate. Bisoprolol fumarate should be discontinued only if clearly necessary, but its reintroduction and/or uptitration should always be considered when the patient becomes stable again.

Duration of treatment for all indications

Treatment with Concor is generally a long-term therapy.

Do not stop treatment abruptly or change the recommended dose without talking to your doctor first since this might lead to a transitory worsening of heart condition. Especially in patients with ischaemic heart disease, treatment must not be discontinued suddenly. If discontinuation is necessary, the daily dose is gradually decreased.

Special populations

Renal or hepatic impairment:

- *Treatment of hypertension or angina pectoris:* In patients with liver or kidney function disorders of mild to moderate severity no dosage adjustment is normally required. In patients with severe renal impairment (creatinine clearance < 20 ml/min) and in patients with severe hepatic impairment a daily dose of 10 mg bisoprolol fumarate must not be exceeded.
- *Treatment of stable chronic heart failure:* There is no information regarding pharmacokinetics of bisoprolol fumarate in patients with chronic heart failure and concomitant hepatic or renal impairment. Titration of the dose in these populations must therefore be made with particular caution.

Elderly:

No dosage adjustment is required.

Administration

Concor tablets are taken in the morning with or without food. They are swallowed with some liquid and not to be chewed.

Contraindications

Concor must not be used in patients with:

- acute heart failure or during episodes of heart failure decompensation requiring intravenous therapy with substances increasing the contractility of the heart,
- shock induced by disorders of cardiac function (cardiogenic shock),
- severe disturbances of atrioventricular conduction (second or third degree AV block) without a pacemaker,
- sick sinus syndrome,
- sinoatrial block,
- symptomatic bradycardia
- symptomatic hypotension
- severe bronchial asthma,
- severe forms of peripheral arterial occlusive disease or Raynaud's syndrome,
- untreated tumours of the adrenal gland (phaeochromocytoma),
- metabolic acidosis,
- hypersensitivity to bisoprolol fumarate or to any of the excipients (see Composition).

Special warnings and precautions

The following section describes when Concor must be used with special caution:

- diabetes mellitus with extremely fluctuating blood glucose levels: symptoms of markedly reduced blood glucose (hypoglycaemia) such as tachycardia, palpitations or sweating can be masked,
- strict fasting,
- ongoing desensitisation therapy,
- mild disturbances of atrioventricular conduction (first degree AV block),
- Prinzmetal's angina; Cases of coronary vasospasm have been observed. Despite its high beta1-selectivity, angina attacks cannot be completely excluded when bisoprolol fumarate is administered to patients with Prinzmetal's angina. Utmost caution must be exercised.
- peripheral arterial occlusive disease (aggravation of symptoms may occur especially when starting therapy),
- patients with psoriasis or with a personal history of psoriasis

Respiratory system: Although cardioselective (beta1) beta-blockers may have less effect on lung function than non-selective beta-blockers, as with all beta-blockers these should be avoid in patients with obstructive airways diseases, unless there are compelling clinical reasons for their use. Where such reasons exist, Concor may be used with caution. In bronchial asthma or other symptomatic chronic obstructive pulmonary diseases, which may cause symptoms, concomitant bronchodilating therapy is recommended. Occasionally an increase of the airway resistance may occur in patients with asthma, therefore the dose of beta2-stimulants may have to be increased.

Allergic reactions: Beta-blockers, including Concor, may increase the sensitivity to allergens and the severity of anaphylactic reactions because the adrenergic counterregulation under beta-blockade may be alleviated. Treatment with adrenaline may not always yield the expected therapeutic effect.

General anaesthesia: In patients undergoing general anaesthesia the anaesthetist must be aware of beta-blockade. If it is thought necessary to withdraw Concor before surgery, this should be done gradually and completed about 48 hours prior to anaesthesia.

Phaeochromocytoma: In patients with a tumour of the adrenal gland (phaeochromocytoma) Concor may only be administered after previous alpha-receptor blockade.

Thyrotoxicosis: Under treatment with Concor the symptoms of a thyroid hyperfunction (thyrotoxicosis) may be masked.

Special populations

So far no sufficient therapeutic experience is available for Concor in patients with heart failure and concomitant insulin dependent type I diabetes mellitus, severely impaired kidney function, severely impaired hepatic function, restrictive cardiomyopathy, congenital heart diseases or haemodynamically relevant organic valvular heart disease. No sufficient therapeutic experience is available in patients with heart failure and myocardial infarction within the last 3 months.

There is insufficient experience with bisoprolol fumarate in children, therefore the use of Concor cannot be recommended for children.

Effects on the ability to drive and use machines

In a study with patients suffering from coronary heart disease bisoprolol fumarate did not affect the driving performance of the patients. However, depending on the individual patients response to treatment an effect on the ability to drive a vehicle or to use machines may be impaired. This needs to be considered particularly at the start of treatment, upon change of medication, or in conjunction with alcohol.

Pregnancy and lactation

During pregnancy Concor is only recommended following careful assessment of benefit-to-risk ratio by the doctor. In general, beta-blockers reduce placental blood flow and may affect the development of the unborn child. Placental and uterine blood flow as well as the growth of the unborn child must be monitored and, in case of harmful effects on pregnancy or the foetus, alternative therapeutic measures considered.

The newborn infant must be monitored closely after delivery. Symptoms of reduced blood glucose and slowed pulse rate generally may occur within the first 3 days of life.

There are no data on the excretion of bisoprolol fumarate in human breast milk or the safety of bisoprolol fumarate exposure in infants. Therefore administration of Concor is not recommended during breastfeeding.

Adverse effects

The adverse effects described below are sorted according to system organ classes. Frequencies are classified as follows:

Very common (affects more than 1 person in 10)
Common (affects less than 1 person in 10)
Uncommon (affects less than 1 person in 100)
Rare (affects less than 1 person in 1,000)
Very rare (affects less than 1 person in 10,000)
Frequency not known (cannot be estimated from available data)

- *Investigations*

Rare: increased triglycerides, increased liver enzymes (ALAT, ASAT)

- *Cardiac disorders*

Very common: bradycardia (in patients with chronic heart failure)
Common: worsening of pre-existing heart failure (in patients with chronic heart failure)
Uncommon: AV-conduction disturbances; bradycardia (in patients with hypertension or angina pectoris); worsening of pre-existing heart failure (in patients with hypertension or angina pectoris)

- *Nervous system disorders*

Common: dizziness*, headache*

- *Eye disorders*

Rare: reduced tear flow (to be considered if the patient uses contact lenses)
Very rare: conjunctivitis

- *Ear and labyrinth disorders*

Rare: hearing disorders

- *Respiratory, thoracic and mediastinal disorders*

Uncommon: bronchospasm in patients with bronchial asthma or a history of obstructive airways disease
Rare: allergic rhinitis

- *Gastrointestinal disorders*

Common: gastrointestinal complaints such as nausea, vomiting, diarrhoea, constipation

- *Skin and subcutaneous tissue disorders*

Rare: hypersensitivity reactions such as pruritus, flush, rash and angioedema
Very rare: alopecia. Beta-blockers may provoke or worsen psoriasis or induce psoriasis-like rash.

- *Musculoskeletal and connective tissue disorders*

Uncommon: muscle weakness, muscle cramps

- *Vascular disorders*

Common: feeling of coldness or numbness in the extremities, hypotension especially in patients with heart failure
Frequency not known: syncope

- *General disorders*

Common: asthenia (in patients with chronic heart failure), fatigue*
Uncommon: asthenia (in patients with hypertension or angina pectoris)

- *Hepatobilary disorders*

Rare: hepatitis

- *Reproductive system and breast disorders*

Rare: erectile dysfunction

- *Psychiatric disorders*

Uncommon: depression, sleep disorder
Rare: nightmare, hallucination

*These symptoms especially occur at the beginning of the therapy. They are generally mild and usually disappear within 1-2 weeks.

Tell your doctor if you notice any of the side effects listed above or any other unwanted or unexpected effects. To prevent serious reactions, speak to a doctor immediately if a side effect is severe, occurred suddenly or gets worse rapidly.

Interactions

The effect and tolerability of medicines can be influenced by simultaneous intake of other medication. Such interactions can also occur if a short time has elapsed since the use of the other medication. Tell your doctor if you are taking any other medicine – even those not prescribed to you by a doctor.

Combinations not recommended

Treatment of stable chronic heart failure

Class-I antiarrhythmic medicines (e.g. quinidine, disopyramide, lidocaine, phenytoin; flecainide, propafenone) may increase the depressant effect of Concor on atrio-ventricular impulse conduction and the contractility of the heart.

All indications

Calcium antagonists of the verapamil type and to a lesser extent of the diltiazem type may lead to reduced contractility of the heart muscle and delayed atrio-ventricular impulse conduction when used concomitantly with Concor. Especially intravenous administration of verapamil in patients on ß-blocker treatment may lead to profound hypotension and atrioventricular block.

Centrally acting blood pressure-lowering medicines (such as clonidine, methyldopa, moxonodine, rilmenidine) may lead to a reduction of heart rate and cardiac output, as well as to vasodilation due to a decrease in the central sympathetic tonus. Abrupt withdrawal, particularly if prior to beta-blocker discontinuation, may increase risk of "rebound hypertension".

Combinations to be used with caution

Treatment of hypertension or coronary heart disease (angina pectoris)

Class-I antiarrhythmic medicines (e.g. quinidine, disopyramide, lidocaine, phenytoin; flecainide, propafenone) may increase the depressant effect of Concor on atrio-ventricular impulse conduction and the contractility of the heart.

All indications

Calcium antagonists of the dihydropyridine type (e.g. nifedipine, felodipine, amlodipine) may increase the risk of hypotension when used concomitantly with Concor. An increased risk of a further deterioration of the ventricular pump function in patients with heart failure cannot be excluded.

Class-III antiarrhythmic medicines (e.g. amiodarone) may increase the inhibitory effect of Concor on atrio-ventricular impulse conduction.

Topical ß-blockers (e.g. eye drops for glaucoma treatment) may add to the systemic effects of Concor.

Parasympathomimetic medicines may increase the inhibitory effect on atrio-ventricular impulse conduction and the risk of bradycardia when used concomitantly with Concor.

The blood sugar lowering effect of insulin or oral antidiabetic medicines may be increased. Warning signs of reduced blood glucose (hypoglycaemia) – especially accelerated heart rate (tachycardia)- may be masked or suppressed. Such interactions are considered to be more likely with nonselective ß-blockers.

Anaesthetic agents may increase the risk of cardiodepressive actions of Concor, leading to hypotension (for further information on general anaesthesia see also section special warnings and precautions).

Cardiac glycosides (digitalis) may lead to an increase in impulse conduction time and thus reduction in heart rate when used concomitantly with Concor.

Non-steroidal anti-inflammatory medicines (NSAIDs) may reduce the blood pressure-lowering effect of Concor.

ß-Sympathomimetics (e.g. isoprenaline, dobutamine) used in combination with Concor may lead to a reduced effect of both agents.

A combination of Concor with sympathomimetics that activate both ß- and α-adrenoceptors (e.g. noradrenaline, adrenaline) may intensify the α-adrenoceptor-mediated vasoconstrictor effects of these agents leading to blood pressure increase. Such interactions are considered to be more likely with nonselective ß-blockers.

Antihypertensive agents as well as other medicines with blood pressure lowering potential (e.g. tricyclic antidepressants, barbiturates, phenothiazines) may increase the blood pressure lowering effect of Concor.

Combinations to be considered

Mefloquine may increase the risk of decelerating the heart rate (bradycardia), if used in combination with Concor.

Monoamine oxidase inhibitors (except MAO-B inhibitors) may enhance the hypotensive effect of the beta-blockers. Concomitant use may also be a risk for hypertensive crisis.

Overdose

The most frequent signs of Concor overdose include slow heart rate (bradycardia), marked drop in blood pressure, acute heart failure, hypoglycaemia and bronchospasm.

In the case of suspected Concor overdose please inform your doctor immediately. The effect of overdose may vary from one person to the next and patients with heart failure are probably very sensitive.

Depending on the degree of overdose your doctor can then decide which measures to take.

In general, if overdose occurs, bisoprolol fumarate treatment is stopped and supportive and symptomatic treatment is provided. Limited data suggest that bisoprolol fumarate is hardly dialysable.

Storage and Stability

Do not store above 30°C.

Do not use after the expiry date.

Keep medicines out of the reach of children.

Presentations

Concor 5: blister with box pack
Concor 10: blister with box pack

Date of Information

Aug, 2020

Merck Healthcare KGaA

Frankfurter Strasse 250, D-64293 Darmstadt, Germany

康肯®5毫克 Concor® 5（衛署藥輸字第017125號）
康肯®10毫克 Concor® 10（衛署藥輸字第017090號）

有效成分：Bisoprolol fumarate

本藥須由醫師處方使用

成分

每顆膜衣錠中含有的有效成分為5毫克或10毫克的Bisoprolol fumarate。

賦形劑：錠劑核心：無水膠質狀的二氧化矽、硬脂酸鎂、聚乙烯聚吡咯烷酮、微晶性纖維素、玉米澱粉、無水磷酸氫鈣。

膜衣成分：黃色氧化鐵、聚二甲矽烷、聚乙二醇400、二氧化鈦、羥丙基甲基纖維素。

康肯®10毫克膜衣成分除上述外加含紅色氧化鐵。

特性

藥物藥效學

Bisoprolol fumarate為康肯®的有效成分，它是一種β_1-選擇性腎上腺受體阻斷劑，它不具有內在刺激性，以及對細胞膜的相關安定作用。它與支氣管及血管平滑肌上之β_2受體，及與代謝調節有關之β_2受體的親合力都相當低。因此，一般認為Bisoprolol fumarate不會影響呼吸道的阻力，也不會影響受β_2-調節的代謝作用。它的β_1-選擇性涵蓋範圍超過其治療劑量範圍。

藥物動力學

吸收：Bisoprolol fumarate幾乎全部（＞90%）經由胃腸道吸收，因為其首渡代謝效應只佔了一小部分（約10%），所以它在口服之後的生體可用率約為90%。其生體可用率不受食物所影響。Bisoprolol fumarate具線性藥動學，藥物劑量在5-20毫克範圍內，其血漿濃度會與藥物劑量呈正比。最高血漿濃度在服藥後2-3小時內出現。

分佈：Bisoprolol fumarate的分布相當廣泛，其分佈體積為3.5公升/公斤，與血漿蛋白結合的比例約為30%。

代謝：Bisoprolol fumarate是經由氧化作用代謝，之後不會進行結合反應（conjuction）。所有的代謝物都具有高度極性並經由腎臟排除。在人體血漿及尿液中的主要代謝物都不具有藥理活性。根據在人體肝臟原漿微粒（microsome）中所進行的體外試驗數據顯示，Bisoprolol fumarate主要是經由CYP3A4所代謝（~95%），經由CYP2D6代謝只佔了一小部分。

排除：Bisoprolol fumarate一部分是以原型經由腎臟排除（~50%），另一部分則為肝臟代謝後形成代謝物再經由腎臟排除（~50%），這兩者之間維持著“均衡”的關係。Bisoprolol fumarate的總廓清率約為15公升/小時。Bisoprolol fumarate的排除半衰期為10-12小時。

適應症

- 高血壓
- 狹心症
- 穩定型慢性中度至重度（NYHA class III、IV）心衰竭【見下方說明欄】

【說明】：須為合併心室收縮功能不良（LVEF ≦ 35%），且已使用ACE inhibitors及利尿劑及/或強心配醣體來治療者。

用法用量

治療高血壓或狹心症

所有病人的劑量都必須經由醫師依個人的脈搏速率及療效狀況加以調整。

Bisoprolol fumarate一般的起始劑量為5毫克，每日一次。必要時，Bisoprolol fumarate的劑量可以增加至10毫克，每日一次。

Bisoprolol fumarate的最大建議劑量為20毫克，每日一次。

高血壓或伴隨有心衰竭的狹心症病人需小心使用康肯®。

治療穩定型慢性中度至重度心衰竭

剛開始以康肯®治療穩定型慢性心衰竭時，需要一段特殊的劑量調整期，所以必須接受醫師的定期監測。

適合接受Bisoprolol fumarate治療的條件如下：

- 在過去6週內不曾發生過急性心衰竭之穩定型慢性心衰竭病人
- 在過去2週內其基礎治療沒有改變者
- 接受適當劑量的ACE抑制劑（或對ACE抑制劑耐受性不佳而使用其他的血管擴張劑）及利尿劑治療，或亦有合併接受強心配醣體之治療者

建議治療的醫師應具有治療慢性心衰竭劑量調整方面的經驗。

剛開始以Bisoprolol fumarate治療穩定型慢性心衰竭時，可根據以下的方式逐漸增加劑量，病人的劑量必須視個人的耐受程度來加以調整，例如，必須在前一劑量耐受性良好的情況下，方可以增加劑量。

第1週：	1.25毫克Bisoprolol fumarate每日一次
第2週：	2.5 毫克Bisoprolol fumarate每日一次
第3週：	3.75毫克Bisoprolol fumarate每日一次
第4~7週：	5 毫克Bisoprolol fumarate每日一次
第8~11週：	7.5 毫克Bisoprolol fumarate每日一次
第12週及之後：	10 毫克Bisoprolol fumarate每日一次，並作為維持劑量剛開始治療穩定性慢性心衰竭時，可先給予較低的治療劑量。

Bisoprolol fumarate的最大建議劑量為10毫克，每日一次。除非有不良反應，否則病人應逐漸增加至此劑量，並維持服用該劑量。

病人開始Bisoprolol fumarate 1.25毫克的治療後，應該接受大約4小時的觀察期（尤其應該注意血壓、心跳、傳導障礙、心臟衰竭的惡化徵兆）。

於劑量調整期間或之後，有可能出現心臟衰竭的暫時性惡化、體液滯留、低血壓或心搏徐緩。若有這種情況發生，建議先降低Bisoprolol fumarate的劑量。只有在絕對必要時，Bisoprolol fumarate才必須停藥，但是在病人狀況穩定後，仍應考慮重新給藥及/或慢慢增加其劑量。

所有適應症的治療期間

接受康肯®的治療通常為一種長期性的治療。

在未與醫師討論前，請勿突然停藥或變更建議劑量，因為這有可能導致心臟功能暫時性惡化。特別是缺血性心臟病的病人，治療不可以突然中斷。若必須停藥，劑量應逐漸降低。

特殊族群

腎或肝功能不全的病人：

- *治療高血壓或狹心症*：輕度至中度肝或腎功能不全的病人通常不需要調整劑量。嚴重腎功能不全（肌酸酐廓清率＜20毫升/分鐘）及嚴重肝功能不全的病人，Bisoprolol fumarate的每日劑量不可超過10毫克。
- *治療穩定型慢性心衰竭*：目前尚無慢性心衰竭同時併有肝或腎功能不全的病人使用Bisoprolol fumarate的藥物動力學資料。這群病人在調整劑量時應特別小心。

老年人：

不需要調整劑量。

給藥方式

康肯®於早上餐前或餐後給藥皆可。請伴隨液體吞服，不要嚼碎。

禁忌

康肯®不應給予有下列情況之病人：

- 急性心衰竭，或正處於心衰竭喪失代償能力期間而必需要給予靜脈注射藥物以增加心臟收縮能力時
- 心臟功能障礙引發之休克（心因性休克）
- 沒有裝上心臟節律器的嚴重房室傳導障礙（第二級或第三級的房室阻斷）
- 病態性竇症候群
- 竇房結阻斷
- 症狀性心搏過緩
- 症狀性低血壓
- 嚴重的支氣管氣喘
- 嚴重的週邊動脈血管閉塞疾病或Raynaud氏症候群
- 腎上腺有尚未接受治療的腫瘤（嗜鉻細胞瘤）
- 代謝性酸中毒
- 對Bisoprolol fumarate或賦形劑中的任何成分過敏者（參閱“成分”欄）

警語及注意事項

康肯®使用於下列情況時應特別小心：

- 血糖值變化波動很大的糖尿病病人：須注意血糖明顯下降（低血糖）的症狀例如，心搏過速、心悸或出汗等可能會被遮蔽
- 在嚴格的禁食狀態下
- 正在接受減敏（desensitisation）療法
- 有輕微的房室傳導障礙（第一級房室傳導阻斷）
- Prinzmetal氏心絞痛；已觀察到冠狀血管痙攣的病例。儘管是高度β_1選擇性，但當病人有Prinzmetal氏心絞痛並給予Bisoprolol fumarate治療時，心絞痛發作無法完全被排除掉。必須非常謹慎
- 週邊動脈血管閉塞疾病（開始使用本藥治療時，症狀可能會變明顯）
- 病人有或曾有牛皮癬之病史

呼吸系統：雖然心臟選擇性β-阻斷劑（β_1）比非選擇性β-阻斷劑對於肺臟功能有較少的作用，但就像所有的β-阻斷劑避免使用在患有阻塞性呼吸道疾病的病人一樣，除非臨床上有強力證據顯示，投與本藥物時仍要小心使用。支氣管氣喘或其他慢性阻塞性肺病病人如症狀發作時可以併用支氣管擴張劑治療。氣喘病人的呼吸道阻力有時候可能會增加，此時會需要較高劑量的β_2-交感神經興奮劑。

過敏反應：包括康肯®在內的β-阻斷劑可能會加重過敏原的敏感性及過敏反應的嚴重程度，因為β-阻斷劑會弱化腎上腺素的反向調節作用。給予腎上腺素治療不一定能獲得預期的療效。

全身麻醉：病人如欲接受全身麻醉，必須告知麻醉醫師其正在使用β-阻斷劑。若經過考量認為有必要在手術前停用康肯®，則應該逐漸降低劑量並於麻醉前48小時完全停藥。

嗜鉻細胞瘤：對於腎上腺腫瘤（嗜鉻細胞瘤）病人，康肯®只能用於已服用過α受體阻斷劑。

甲狀腺毒症：在康肯®的治療下，甲狀腺機能亢進的症狀（甲狀腺毒症）有可能會被隱蔽。

特殊族群

到目前為止，以康肯®治療心衰竭同時患有胰島素依賴性第一型糖尿病、腎功能不全、肝功能不全、限制型心肌症、先天性心臟疾病或與血流動力相關的心臟瓣膜疾病病人尚無足夠的治療經驗。對於最近3個月內發生心衰竭及心肌梗塞之病人，亦無足夠的治療經驗。

Bisoprolol fumarate使用於兒童尚無足夠的經驗，因此康肯®不建議兒童使用。

對開車及操作機械的影響

根據單一研究顯示，Bisoprolol fumarate對於冠狀動脈心臟疾病病人的開車能力並不會有影響。然而，因為個人體質的差異，有些人的開車及機械操作能力可能會受到影響。這種情況在治療初期、調整劑量後及併用酒精時必須特別注意。

懷孕與授乳

懷孕期間，康肯®必須經過醫師小心評估其利益與風險後才能使用。一般說來，β-阻斷劑會降低胎盤的血流量，因此有可能會影響胎兒的發育。在這種情況下，應監測胎盤及子宮的血流量與胎兒的生長發育狀況，若對懷孕及胎兒造成不良影響，則應考慮改用其他的替代性治療。

新生嬰兒在出生後應予以嚴密監測。通常血糖降低及脈搏減緩的症狀有可能在出生後的3天內出現。

目前尚無有關Bisoprolol fumarate分泌於母乳及嬰兒攝取Bisoprolol fumarate的安全性數據。因此，康肯®不建議於授乳期間服用。

不良反應

以下的不良反應乃依照系統器官來加以分類。發生頻率的標準如下：

非常常見：（≥ 1/10）
常　　見：（≥ 1/100 to < 1/10）
不 常 見：（≥ 1/1,000 to < 1/100）
罕　　見：（≥ 1/10,000 to < 1/1,000）
極 罕 見：（< 1/10,000）
頻率未明：（無法從現行數據中評估）

- ***檢驗數據異常***
  罕　　見：三酸甘油脂增加，肝臟酵素增加（麩丙氨轉移酶、麩草氨轉移酶）
- ***心臟方面異常***
  非常常見：心搏徐緩（慢性心衰竭病人）
  常　　見：心衰竭更加惡化（慢性心衰竭病人）
  不 常 見：心搏徐緩及原有的心衰竭情況更加惡化（高血壓或狹心症病人）；房室傳導障礙
- ***神經系統失調***
  常　　見：頭暈*、頭痛*
- ***眼睛異常***
  罕　　見：淚液減少（若病人有配戴隱形眼鏡應加以注意）
  極 罕 見：結膜炎
- ***耳朵及迷路異常***
  罕　　見：聽力異常
- ***呼吸、胸腔及縱隔腔異常***
  不 常 見：有氣喘或呼吸道阻塞疾病病史者，可能會出現支氣管痙攣
  罕　　見：過敏性鼻炎
- ***胃腸道異常***
  常　　見：胃腸道的不適包括，噁心、嘔吐、腹瀉及便祕
- ***皮膚及皮下組織異常***
  罕　　見：過敏反應，包括搔癢、潮紅、皮疹及血管性水腫
  極 罕 見：禿髮。β-阻斷劑可能會誘發牛皮癬或使其惡化，或引起類似牛皮癬的皮疹。
- ***肌肉骨骼及結締組織異常***
  不 常 見：肌肉衰弱及痙攣
- ***血管方面異常***
  常　　見：四肢冰冷或麻木；低血壓，特別是心衰竭病人
  頻率未明：昏厥
- ***全身性不適***
  常　　見：無力（慢性心衰竭病人）、疲勞*
  不 常 見：無力（高血壓或狹心症病人）
- ***肝膽異常***
  罕　　見：肝炎
- ***生殖系統及乳房異常***
  罕　　見：勃起功能障礙
- ***精神方面失調***
  不 常 見：憂鬱、睡眠障礙
  罕　　見：做惡夢、幻覺

*這些症狀大多出現於治療初期。它們一般皆屬輕微，且常會在1-2週內消失。

若您出現上述的任何不良反應或其他任何不舒服或未預期的反應，請告訴您的醫師。為了避免出現嚴重的情況，當不良反應為嚴重、突然發生或快速惡化時，應立刻就醫。

交互作用

藥物的反應和耐受性有可能受其他同時服用之藥物所影響。若在服用本藥之前不久曾經服用其他藥物，也有可能出現這類交互作用。如果您有服用其他的任何藥物，請告訴您的醫師－非處方藥也包括在內。

不建議併用

治療穩定型慢性心衰竭

第I類（Class-I）抗心律不整藥物（例如，quinidine、disopyramide、lidocaine、phenytoin、flecainide、propafenone）可能會加強康肯®對房室傳導及心臟收縮能力的抑制作用。

所有適應症

當verapamil類的鈣離子拮抗劑（diltiazem類藥物亦然，但情況或許較為輕微）與康肯®併用時，可能會導致心肌的收縮力下降，並且延遲心房室的傳導。特別是正在接受β-阻斷劑治療的病人，若給予verapamil靜脈注射，可能會使其低血壓及房室傳導阻斷的情況顯著加重。

中樞性降血壓藥（例如，clonidine、methyldopa、moxonodine、rilmenidine）可能會降低心跳速率及心輸出量，並且由於中樞交感神經活性降低而導致血管擴張。如果在停用β-阻斷劑之前突然停用，則可能會增加“反彈性高血壓（rebound hypertension）”的風險。

併用時應小心

治療高血壓或心臟冠狀動脈疾病（狹心症）

第I類（Class-I）抗心律不整藥物（例如，quinidine、disopyramide、lidocaine、phenytoin、flecainide、propafenone）可能會加強康肯®對房室傳導及心臟收縮能力的抑制作用。

所有適應症

Dihydropyridine類的鈣離子拮抗劑（例如，nifedipine、felodipine、amlodipine）與康肯®併用時，可能會增加低血壓的風險。另外，心衰竭病人之心室輸出功能進一步惡化的風險無法被排除。

第III類（Class-III）抗心律不整藥物（例如，amiodarone）可能會加強康肯®在房室傳導的抑制作用。

局部β-阻斷劑（例如，治療青光眼的眼藥水）可能對康肯®的全身性作用有加成反應。

副交感神經興奮劑與康肯®併用時，可能會加強其房室傳導的抑制作用及增加心搏徐緩的風險。

胰島素或口服抗糖尿病藥物的降血糖作用有可能會被加強。血糖降低（低血糖）的警訊－特別是心跳速率加快（心搏過速）－有可能被隱蔽或壓抑。非選擇性的β-阻斷劑較容易出現這類的交互作用。

麻醉劑可能會使康肯®對心臟抑制作用的風險提高而導致低血壓（全身麻醉的進一步資訊可參閱“警語及注意事項”）

強心配醣體（毛地黃）與康肯®併用時，心搏傳導的時間會增長，因此會降低心跳速率。

非類固醇抗發炎藥物（NSAIDs）可能會降低康肯®的降血壓效果。

β-交感神經興奮劑（例如，isoprenaline、dobutamine）與康肯®併用時，兩種藥物的作用可能都會減弱。

康肯®與同時活化β-及α腎上腺受體的交感神經興奮劑（例如，noradrenaline、adrenaline）併用時，可能會強化該類藥物活化α腎上腺受體所致的血管收縮作用，造成血壓上升。這類交互作用較常見於非選擇性的β-阻斷劑。

降血壓藥及其他可能引起血壓下降的藥物（例如，三環抗憂鬱劑、barbiturates、phenothiazines）可能會加強康肯®的降血壓效果。

併用時須加以考量

Mefloquine與康肯®併用時，可能會使心跳速率降低（心搏徐緩）的風險增加。

單胺氧化酶抑制劑（MAO-B抑制劑除外）可能會強化β-阻斷劑的降血壓效果。與康肯®併用可能會有引發高血壓危象的風險。

過量

康肯®藥物過量最常見的症狀包括心跳速率變慢（心搏徐緩），血壓明顯下降、急性心衰竭、低血糖及支氣管痙攣。

當懷疑有康肯®過量時，請立刻通知您的醫師。藥物過量的作用因人而異，且心衰竭的病人多半非常敏感，您的醫師會視藥物過量的情況來加以處理。

一般說來，當有過量的情況發生時，Bisoprolol fumarate會予以停藥並給予支持性及症狀性治療。根據有限的資料顯示，Bisoprolol fumarate不容易被透析清除。

儲存及安定性

請儲存於30°C以下。

請勿使用超過有效期限之藥物。

請將藥物置於兒童無法觸及處。

包裝

康肯®5毫克：鋁箔盒裝

康肯®10毫克：鋁箔盒裝

資料日期

2020年8月

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