Calcium antagonist
HERBESSER® CD 100
HERBESSER® CD 200

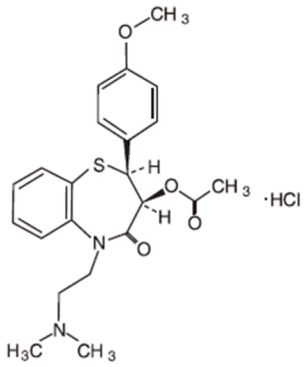
Diltiazem hydrochloride

Sustained Released Capsules

COMPOSITION AND DESCRIPTION

Physicochemical properties of active ingredient

- International non-proprietary name : Diltiazem hydrochloride
- Chemical name : (2S,3S)-5-[2-(Dimethylamino) ethyl]-2-(4-methoxyphenyl)-4-oxo-2,3,4,5-tetahydro-1,5benzothiazepin-3-yl-acetate monohydrochloride



$C_{22}H_{26}N_2O_4S \cdot HCl$:450.98

Description:

- Diltiazem hydrochloride occurs as white crystals or crystalline powder. It is odorless.
- It is very soluble in formic acid, feely soluble in water, in methanol and in chloroform, sparingly soluble in acetonitrile, slightly soluble in acetic anhydride and in ethanol (99.5), and practically insoluble in diethyl ether.
- Optical rotation $[\alpha]_D^{20}$: + 115 - + 120° (after drying, 0.20 g, water, 20 mL, 100 mm).
- Melting point: 210 - 215°C (with decomposition

Product's name	Content of Diltiazem hydrochloride	Description of the product	Excipients
HERBESSER® CD 100	100 mg	Hard capsule No.4 with white cap and white body, containing white to pale yellowish white beads.	Povidone K-30, Talc, Gelatine capsules, Fumaric acid, Ammonioalkyl Methacrylate Copolymer Type A, Ammonioalkyl Methacrylate Copolymer Type B, and Sucrose and Starch Spheres combination.
HERBESSER® CD 200	200 mg	Hard capsule No.2 with red cap and white body, containing white to pale yellowish white beads.	

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ACTIONS

Pharmacological studies :

Diltiazem hydrochloride dilates blood vessels. improves myocardial ischemia, and exerts antihypertensive effect by inhibiting calcium channel influx to cells in vascular smooth muscles such as coronary vessels, peripheral vessels, etc.

1. Action on myocardial ischemia

1) Improvement of myocardial oxygen demand and supply balance

(1) It dilates large coronary vessels and collateral channels, and increases blood flow to myocardial ischaemic lesion (dogs).6-9)

(2) It inhibits coronary artery spasm (monkeys and humans).10,11)

(3) It decreases myocardial oxygen consumption by afterload reduction due to peripheral vasodilation and decreased heart rate without decreasing cardiac output (dogs).12)

2) Myocardial protective action

It maintains cardiac function and myocardial energy metabolism, and reduces the extension of infarct lesions by inhibiting calcium channel influx to cells at the time of myocardial ischaemia (rats).13)

2. Action on blood pressure

1) It has almost no effect on normal blood pressure, while decreases high blood pressure gradually (rats and humans)[14-16], and inhibits exercise-induced blood pressure elevation (humans).[17)]

2) It does not decrease cerebral and renal blood flow, while decreases blood pressure (dogs and humans).[18-21)]

3) It inhibits myocardial and vascular hypertrophies along with decreased blood pressure (rats).[22)]

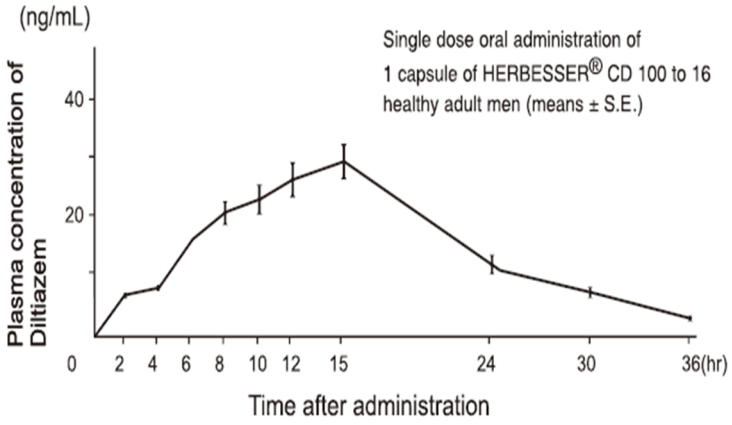
3. Effects on cardiac stimulation and cardiac conduction

It slightly prolongs sinus node spontaneous cycle length and slows atrioventricular nodal conduction (AH interval), while it does not effect His -Purkinje system conduction (HV interval) (dogs and humans).[12,23,24)]

Pharmacokinetics :

1. Plasma concentration

Plasma concentration of this product after oral administration of one capsule of HERBESSER® CD Capsules 100 mg to healthy male adults reached maximum at about 14 hours after the administration, and the elimination half-life was about 7 hours.[1)]



2. Metabolism

When this product was administered orally to healthy male adults, the main metabolic pathways were oxidative deaminization, oxidative demethylation, deacetylation, and conjugation.[25]

CLINICAL STUDIES

Clinical efficacy

The usefulness of this product was proven for essential hypertension, angina pectoris and variant angina in clinical studies including a double-blind comparative study using diltiazem hydrochloride (HERBESSER tablets 30) as a control.[3-5)]

Diseases	Efficacy rate	No. of patients	No. of patients evaluated as effective
Essential hypertension	73.9%	222	164 (“decreased” or better)
Angina pectoris	84.7%	124	105 ("moderate" improvement or better)
Variant angina	90.2%	51	46 (“moderate” improvement or better)

INDICATIONS

- Essential hypertension (mild to moderate)
- Angina pectoris, variant angina pectoris

CONTRAINDICATIONS

(HERBESSER® CD is contraindicated in the following patients.)

(1) Patients with severe congestive cardiac failure [Symptoms of cardiac failure may be aggravated].
(2) Patients with second or third degree atrioventricular block or sick sinus syndrome (persistent sinus bradycardia) (less than 50 beats/ minute), sinus arrest, sinoatrial block, etc.) [Depression of cardiac stimulation and cardiac conduction may occur excessively].
(3) Patients with a history of hypersensitivity to any of the ingredients of this product.
(4) Pregnant women and women who may possibly be pregnant [See "Use during Pregnancy, Delivery or Lactation" section].

DOSAGE AND ADMINITRATION

- Essential hypertension (mild to moderate)
  Usually, for adults, 100 mg to 200 mg of Diltiazem hydrochloride is orally administered once daily. The dosage may be adjusted according to the patient's age and symptoms.
- Angina pectoris, variant angina
  Usually, for adults, 100 mg to 200 mg of Diltiazem hydrochloride is orally administered once daily. If the effect is insufficient, the dosage may be increased to 200 mg once daily.

PRECAUTIONS

1. Important Precautions

1) It has been reported that abrupt cessation of calcium antagonists may aggravate the patient's symptoms. In case where **cessation** of this product is required, the dosage should be **reduced gradually** under careful observation of the patient. Patients should be instructed not to discontinue taking this product without consulting physicians.
2) Since dizziness, etc. may occur due to antihypertensive action of this product, patients should be cautioned against engaging in potentially hazardous activities, such as working at altitude or driving motor vehicles.
3) Prolonged QT and ventricular arrhythmia have been reported in coadministration of terfenadine with other antiarrhythmic agents (disopyramide phosphate).

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2. Careful Administration (HERBESSER should be administered with care in the following patients.)

1) Patients with congestive cardiac failure. [Symptoms of cardiac failure may be aggravated.]
2) Patients with severe bradycardia (less than 50 beats/min) or first grade atrioventricular block. [Depression of cardiac stimulation and cardiac conduction may occur excessively.]
3) Patients with excessively low blood pressure [Blood pressure may be further decreased.]
4) Patients with severe hepatic or renal impairment. [The metabolism and excretion of this product may be prolonged, and effects may be intensified.]

3. Drug interaction

This product is metabolized mainly by cytochrome P450 3A4 (CYP3A4) metabolizing enzyme.

Precautions for co-administration (HERBESSER CD should be administered with care when coadministered with the following drugs.)

Drugs	Signs, Symptoms, and Treatment	Mechanism and Risk Factors
Drugs with antihypertensive effects (antihypertensive drugs, nitric acid preparation, etc.)	Antihypertensive effects may be intensified. Blood pressure should be measured periodically to adjust the dosage	Antihypertensive effects may be intensified additively.
Beta blockers (bisoprolol) fumarate, propranolol hydrochloride, atenolol, etc.) Rauwolfia preparations (reserpine, etc.)	Bradycardia, atrioventricular block, sinoatrial block, etc. may occur. Pulse rate should be measured periodically, and electrocardiogram should be performed as needed. If any abnormalities are observed, the dosage should be reduced or administration should be discontinued.	Depression of cardiac stimulation and cardiac conduction, negative inotropic effects, and antihypertensive effects may be intensified additively. Particular attention should be given to triple therapy using this product with digitalis preparation and beta blocker or rauwolfia preparation.
Digitalis preparations (digoxin, methyldigoxin)	Bradycardia, atrioventricular block, etc. may occur. In addition, toxic symptoms (nausea, vomiting, headache, dizziness, abnormal vision, etc.) including above arrhythmic symptoms may occur due to an increased blood concentration of digitalis preparation. Presence or absence of digitalis toxicity should be observed periodically, and electrocardiogram should	Depression of cardiac stimulation and cardiac conduction may be intensified additively. Particular attention should be given to triple therapy using this product with digitalis preparation and beta blocker. This product may be increase blood concentrations of digitalis preparations.

	be performed. In addition, blood concentration of digitalis preparation should be measured as needed. If any abnormalities are observed, the dosage should be reduced or administration should be discontinued.	
Antiarrhythmic agents (amiodarone hydrochloride, mexiletine hydrochloride, etc.)	Bradycardia, atrioventricular block, sinus arrest, etc. may occur. Pulse rate should be measured periodically, and electrocardiogram should be performed as needed. If any abnormalities are observed, the dosage should be reduced or administration should be discontinued.	Depression of cardiac stimulation and cardiac conduction may be intensified additively.
Aprindine hydrochloride [antiarrythmic agents]	Symptoms (bradycardia, atrioventricular block, sinus arrest, tremor, dizziness, light-headedness, etc.) may occur due to increased blood concentrations of both drugs. Clinical symptoms should be observed periodically, and electrocardiogram should be performed as needed. If any abnormalities are observed, the dosage should be reduced or administration should be discontinued.	Each drug may affect a common metabolizing enzyme (cytochrome P450), and increase blood concentration of each drug.
Dihydropyridine calcium antagonists (nifedipine, amlodipine besilate, etc.)	Symptoms (intensified antihypertensive effects, etc.) may occur due to increased blood concentration of dihydropyridine calcium antagonist. Clinical symptoms should be observed periodically. If any abnormalities are observed the dosage should be reduced or administration should be discontinued.	This product may inhibit the metabolizing enzyme (cytochrome P450) of these drugs, and increase their blood concentrations.
Triazolam [hypnotic agent]	Symptoms (prolonged sleeping time, etc.) may occur due to increased blood concentration of	

	triazolam. Clinical symptoms should be observed periodically. If any abnormalities are observed, the dosage should be reduced or administration should be discontinued.	
Midazolam [hypnotic sedative agent]	Symptoms (intensified sedative and hypnotic effect, etc.) may occur due to increased blood concentration of midazolam. Clinical symptoms should be observed periodically. If any abnormalities are observed, the dosage should be reduced or administration should be discontinued.	
Carbamazepine [psychotropic antiepileptic agent, antimanic agent]	Symptoms (sleepiness, nausea, vomiting, dizziness, etc.) may occur due to increased blood concentration of carbamazepine, Clinical symptoms should be observed periodically. If any abnormalities are observed, the dosage should be reduced or administration should be discontinued.	Effects of muscle relaxants may be intensified. Caution should be exercised to muscle relaxants action. If any abnormalities are observed, the dosage should be reduced or administration should be discontinued.
Selegiline hydrochloride [antiparkinson agent]	Effects and toxicity of selegiline hydrochloride may be intensified. Clinical symptoms should be observed periodically. If any abnormalities are observed, the dosage should be reduced or administration should be discontinued.	
Theophylline [bronchodilator]	Symptoms (nausea, vomiting, headache, insomnia, etc.) may occur due to increased blood concentration of theophylline. Clinical symptoms should be observed periodically. If any abnormalities are observed, the dosage should be reduced or administration should be discontinued.	

Cilostazol [antiplatelet agent]	Effects of cilostazol may be intensified. Clinical symptoms should be observed periodically. If any abnormalities are observed, the dosage should be reduced or administration should be discontinued.	
Vinorelbine tartrate [anticancer drug]	Effects of vinorelbine tartrate may be intensified. Clinical symptoms should be observed periodically. If any abnormalities are observed, the dosage should be reduced or administration should be discontinued.	
Cyclosporin [immunosuppressant]	Symptoms (renal disorder, etc.) may occur due to increased blood concentration of cyclosporin. Clinical symptoms should be observed periodically, and blood concentration of cyclosporin should be measured. If any abnormalities are observed, the dosage should be reduced or administration should be discontinued.	
Tacrolimus hydrate [immunosuppressant]	Symptoms (renal disorder, etc.) may occur due to increased blood concentration of tacrolimus. Clinical symptoms should be observed periodically, and blood concentration of tacrolimus should be measured. If any abnormalities are observed, the dosage should be reduced or administration should be discontinued.	
Phenytoin [antiepileptic drug]	Symptoms (ataxia, dizziness, nystagmus, etc.) may occur due to increased blood concentration of phenytoin. Clinical symptoms should be observed periodically. If any abnormalities are observed, the dosage should be reduced or administration	This product may inhibit the metabolizing enzyme (cytochrome P450) of phenytoin. and increase blood concentrations of phenytoin. In addition: phenytoin may stimulate metabolism of this product, and decrease

	should be discontinued. Effect of this product may be attenuated.	blood concentration of this product
Cimetidine [H2 receptor antagonist] HIV protease inhibitors (ritonavir, saquinavir mesylate, etc.)	Symptoms (intensified antihypertensive effect, bradycardia, etc.) may occur due to increased blood concentration of this product. Clinical symptoms should be observed periodically, and electrocardiogram should be performed as needed. If any abnormalities are observed, the dosage should be reduced or administration should be discontinued.	These drugs may inhibit the metabolizing enzyme (cytochrome P450) of this product, and increase blood concentration of this product.
Rifampicin [antituberculous drug]	Effects of this product may be attenuated. Clinical symptoms should be observed periodically, and if possible, blood concentration of this product should be measured. If any abnormalities are observed, appropriate therapeutic measures such as changing to other drugs or increasing the dosage of this product should be taken.	Rifampicin may induce the metabolizing enzyme (cytochrome P450) of this product, and decrease blood concentrations of this product.
Anesthetics drugs (isoflurane, enflurane, halothane, etc.)	Bradycardia, atrioventricular block, sinus arrest, etc. may occur. Electrocardiogram should be monitored. If any abnormalities are observed, the dosage should be reduced or administration should be discontinued.	Rifampicin may induce the metabolizing enzyme (cytochrome P450) of this product, and decrease blood concentrations of this product.
Muscle relaxants (pancuronium bromide, vecuronium bromide, etc.)	Effects of muscle relaxants may be intensified. Caution should be exercised to muscle relaxants action. If any abnormalities are observed, the dosage should be reduced or administration should be discontinued.	Rifampicin may induce the metabolizing enzyme (cytochrome P450) of this product, and decrease blood concentrations of this product.

4. Adverse Reactions

Adverse reactions were reported in 74 (2.1%) of 3,577 patients. The major adverse reactions were cardiovascular symptoms in 0.7% (bradycardia in 0.2%, atrioventricular block in 0.1%, facial flushing in 0.1 %, etc.), gastrointestinal symptoms in 0.6% (constipation in 0.2%, nausea in 0.2%, stomach discomfort in 0.1%, etc.), headache and headache dull in 0.4%, hypersensitivity in 0.3%, etc. (at the time of completion of re-examination).

(1) Clinically significant adverse reactions

(rarely: <0.1%, no adverb: incidence unknown because of spontaneous reports)

1) **Complete atrioventricular block, severe bradycardia**
(early symptom: bradycardia, dizziness, light-headedness, etc.) may occur rarely. If any abnormalities are observed, administration should be discontinued, and atropine sulfate hydrate, isoprenaline, etc. should be administered or appropriate therapeutic measures such as cardiac pacing should be taken as needed.
2) **Congestive cardiac failure** may occur. If any abnormalities are observed, administration should be discontinued, and appropriate therapeutic measures such as administration of cardiotonic drug, etc. should be taken.
3) **Oculomucocutaneous syndrome (Steven-Johnson syndrome), toxic epidermal necrolysis (Lyell syndrome), erythroderma (exfoliative dermatitis), acute generalized exanthematous pustulosis** may occur. If erythema, blister, pustule, pruritis, fever, enanthema, etc. occur, administration should be discontinued, and appropriate therapeutic measures should be taken.
4) **Hepatic function disorder or jaundice** with increased AST (GOT), ALT (GPT) or γ-GTP may occur. The patient's conditions should be observed carefully. If any abnormalities are observed, administration should be discontinued, and appropriate therapeutic measures should be taken.

(2) **Other adverse reactions**

If any adverse reactions are observed, appropriate therapeutic measures such as discontinuation of treatment should be taken.

Incidence / Type	5% > ≥ 0.1%	< 0.1%	Incidence unknown
Cardiovascular	Bradycardia, atrioventricular block, facial flushing, dizziness	Sinus arrest, decreased blood pressure, palpitation, chest pain, oedema	Sinoatrial block
Psychoneurotic	Malaise, headache, headache dull	Cramps in the calves, feelings of weakness, sleepiness, insomnia	Parkinsonian-like symptom
Hepatic	Increased AST (GOT), increased ALT(GPT)	Jaundice	Increased Al-P, increased LDH, increased γ-GTP, hepatic hypertrophy
Hypersensitivity	Rash	Pruritis, multiforme erythematous, rash, urticaria	Photosensitivity, pustule
Gastrointestinal	Stomach discomfort, constipation, abdominal pain,	Soft stool, diarrhea, thirst.	----------

	heartburn, anorexia, nausea		
Hematologic	----------	----------	Decreased platelets count, decreased white blood cell count
Other	----------	----------	Gingival hypertrophy, gynaecomastia: numbness

Reporting of suspected side effects

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to:
Pusat Farmakovigilans/ MESO Nasional
Direktorat Pengawasan Keamanan, Mutu, dan Ekspor Impor Obat, Narkotika, Psikotropika, Prekursor dan Zat Adiktif
Badan Pengawas Obat dan Makanan
Jl. Percetakan Negara No.23, Jakarta Pusat, 10560
Email: pv-center@pom.go.id.
Website: https://e-meso.pom.go.id/ADR

5. Use during Pregnancy, Delivery or Lactation

1) HERBESSER contraindicated to pregnant women or women who may possibly be pregnant. [Animal studies have shown teratogenicity (mice: skeletal abnormality, appearance abnormality) and embryotoxicity (mice, rats: fatality).]
2) Use of this product in lactating women is not recommended. If treatment with this product is judged to be essential, breast feeding must be discontinued during treatment. [It has been reported that diltiazem is excreted in human breast milk.]

6. Pediatric Use

The safety of HERBESSER in children has not been established.

7. Use in the Elderly

Excessive decrease in blood pressure is generally considered undesirable in elderly patients. Therefore, HERBESSER should he administered with care such as starting from a lower dosage while, carefully monitoring the patient's condition.

8. Overdosage

Symptoms: Bradycardia, complete atrioventricular block, cardiac failure, hypotension, etc. may occur after overdosage of HERBESSER. These symptoms have been also reported as adverse reactions.
Treatment: In case of overdosage, administration should be discontinued, and gastric lavage should be performed to remove the product as needed, and the following appropriate therapeutic measures should be taken.

1) Bradycardia, complete atrioventricular block Atropine sulfate hydrate, isoprenaline, etc. should be administered or cardiac pacing should be taken.
2) Cardiac failure, hypotension Cardiotonic drug, vasopressor, infusion, etc. should be administered or assisted circulation should be performed.

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9. Precautions concerning Use

(1) Precautions regarding dispensing: For drugs that are dispensed in a press-through package (PTP), instruct the patients to remove the drug from the PTP sheet prior to use. [It was reported that, if the PTP sheet is swallowed, the sharp comers of the sheet may puncture the esophageal mucosa, resulting in severe complications such as mediastinitis.]

(2) Precautions during oral administration: This product should be taken without opening and chewing the capsule.

HANDLING

Caution :

- Dispense by physician's prescription or direction.
- Keep out of reach of children.
- Swallow the capsules without chewing or opening

ON DOCTOR'S PRESCRIPTION ONLY
HARUS DENGAN RESEP DOKTER

Storage : Store in a tight and light resistant container at below 30°C.

Expiration date : 3 years

PRESENTATION

HERBESSER® CD 100		HERBESSER® CD 200	
Boxes of 30 capsules (3 blisters x 10 capsules)	Reg. No. DKL1025202503A1	Boxes of 30 capsules (3 blisters x 10 capsules)	Reg. No. DKL1025202503B1
Boxes of I00 capsules (10 blisters x 10 capsules)	Reg. No. DKL1025202503A1	Boxes of I00 capsules (10 blisters x 10 capsules)	Reg. No. DKL1025202503B1

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Ota, Japan

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Bandung, Indonesia

Under License from
Mitsubishi Tanabe Pharma Corporation
Osaka, Japan

Leaflet: Informasi Produk Untuk Pasien

HERBESSER® CD 100
HERBESSER® CD 200

Diltiazem Hydrochloride
Kapsul

Mohon leaflet ini dibaca baik-baik sebelum Anda mulai mengonsumsi obat ini karena mengandung informasi penting untuk Anda.

- Simpanlah leaflet ini. Anda mungkin perlu membacanya lagi.
- Jika Anda memiliki pertanyaan lebih lanjut, tanyakan pada dokter atau tenaga kesehatan lainnya.
- Jika Anda mengalami efek samping, konsultasikan kepada dokter atau tenaga kesehatan lainnya. Termasuk kemungkinan efek samping yang tidak tercantum di leaflet ini. Lihat bagian 4.

Apa yang ada dalam leaflet ini

1. Apa itu HERBESSER® CD dan apa kegunaannya

HERBESSER® CD mengandung zat aktif *diltiazem hydrochloride* yang digunakan untuk pengobatan tekanan darah tinggi (hipertensi) ringan hingga sedang dan nyeri dada yang disebabkan oleh kurangnya pasokan oksigen dan darah ke jantung (angina pektoris, angina varian).

HERBESSER® CD bekerja dengan melebarkan pembuluh darah, memperbaiki iskemia miokardial, dan memberikan efek antihipertensi melalui penghambatan masuknya ion kalsium ke sel otot polos pembuluh darah.

2. Apa yang perlu Anda tahu sebelum menggunakan HERBESSER® CD

Jangan menggunakan HERBESSER® CD:

- Jika Anda pasien dengan gagal jantung kongestif parah, yaitu ketidakmampuan jantung memompa cukup darah ke seluruh tubuh
- Jika Anda pasien dengan blok antrioventrikular (gangguan konduksi listrik jantung) derajat kedua atau ketiga atau sindrom sinus sakit (gangguan irama jantung yang memengaruhi alat pacu jantung alami / nodus sinus, yang mengendalikan detak jantung).
- Jika Anda pasien dengan riwayat alergi atau hipersensitif terhadap diltiazem atau bahan lain pada obat ini (tercantum di bagian 6).

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- Jika Anda pasien wanita yang sedang hamil, ada kemungkinan hamil atau sedang menyusui (tercantum di bagian ”Kehamilan dan Menyusui”).

HERBESSER® CD diberikan harus secara hati-hati:

- Jika Anda pasien dengan gangguan irama jantung, penyakit jantung atau gagal jantung kongestif (ketidakmampuan jantung memompa cukup darah ke seluruh tubuh).
- Jika Anda pasien dengan bradikardia parah (jantung berdetak lebih lambat mencapai <50 kali per menit) atau jika Anda pasien dengan derajat satu blok atrioventrikular.
- Jika Anda pasien dengan tekanan darah yang telalu rendah.
- Jika Anda pasien dengan kerusakan hati atau ginjal parah.

Jika hal-hal di atas berlaku untuk Anda, jangan gunakan HERBESSER® CD dan beri tahu dokter atau tenaga kesehatan lainnya. Jika Anda tidak yakin, konsultasikanlah kepada dokter atau tenaga kesehatan lain sebelum menggunakan HERBESSER® CD.

Obat lain dan HERBESSER® CD

Beritahukan kepada dokter Anda jika Anda baru saja atau mungkin akan mengonsumsi obat-obatan berikut ini. Termasuk obat-obatan yang Anda beli tanpa resep dokter dan obat-obatan herbal. Dikarenakan HERBESSER® CD dapat mempengaruhi cara kerja beberapa obat dan beberapa obat dapat berpengaruh pada HERBESSER® CD.

- Jika menggunakan obat antihipertensi, kemungkinan akan meningkatkan efek antihipertensi akibat interaksi obat dengan HERBESSER® CD. Tekanan darah pasien harus diukur untuk menyesuaikan dosis.
- Jika menggunakan obat golongan beta bloker (*bisprolol fumarate*, *propanolol hydrochloride*, *atenolol*, dan lain-lain) dan preparat Rauwolfia (*reserpine*, dan lain-lain), kemungkinan akan terjadi jantung berdebar lebih lambat (bradikardia) atau tidak beraturan (blok atrioventrikular). Elektrokardigram (EKG) pasien harus dimonitor.
- Jika menggunakan preparat digitalis (digoksin, metildigoksin), kemungkinan akan terjadi jantung berdebar lebih lambat (bradikardia), tidak beraturan (blok atrioventrikular), mual, muntah, sakit kepala, pusing, penglihatan abnormal dan lain-lain. Elektrokardigram (EKG) pasien harus dimonitor.
- Jika menggunakan obat yang dapat memperlambat denyut jantung (antiaritmia) seperti amiodaron hidroklorida, meksiletine hidroklorida, dan lain-lain, kemungkinan akan terjadi jantung berdebar lebih lambat (bradikardia) atau tidak beraturan (blok atrioventrikular). Elektrokardigram (EKG) pasien harus dimonitor.
- Jika menggunakan menggunakan obat Aprindin hidroklorida kemungkinan terjadi jantung berdebar lebih lambat (bradikardia), tidak beraturan (blok atrioventrikular), tremor, pusing, dan lain-lain. Elektrokardigram (EKG) pasien harus dimonitor.
- Jika menggunakan agonis dihidropiridin kalsium (nifedipin, amlodipin besilat, dan lain-lain), kemungkinan akan meningkatkan konsentrasi darah dari agonis dihidropiridin kalsium. Gejala klinis harus diamati secara berkala.
- Jika menggunakan triazolam (agen hipnotik /penenang), kemungkinan akan memperpanjang waktu tidur pasien. Gejala klinis harus diamati secara berkala.
- Jika menggunakan midazolam (agen hipnotik sedatif / obat yang menekan aktivitas sistem saraf pusat) kemungkinan akan meningkatkan efek sedatif (penenang) dan hipnotik (menyebabkan tidur). Gejala klinis harus diamati secara berkala.
- Jika menggunakan karbamazepin (agen antiepilepsi psikotropik / obat kejang yang berpotensi memengaruhi suasana hati dan perilaku, agen antimania / obat pengatur suasana hati),

kemungkinan akan terjadi kantuk, mual, muntah, pusing, dan lain-lain. Gejala klinis harus diamati secara berkala.

- Jika menggunakan selegilin hidroklorida (agen antiparkinson), kemungkinan akan meningkatkan efek dan toksisitas / tingkat bahaya dari obat selegilin hidroklorida. Gejala klinis harus diamati secara berkala.
- Jika menggunakan teofilin (bronkodilator / obat yang dapat membantu pernafasan lebih mudah) kemungkinan akan terjadi mual, muntah, sakit kepala, susah tidur (insomnia). Gejala klinis harus diamati secara berkala.
- Jika menggunakan silostazol (agen antiplatelet / obat pencegah terjadinya penggumpalan darah) dan vinorelbin tartat (agen antikanker), kemungkinan akan meningkatkan efek kedua obat ini. Gejala klinis harus diamati secara berkala.
- Jika menggunakan siklosporin dan takrolimus hidrat (imunosupresan / obat yang melemahkan sistem kekebalan tubuh) kemungkinan akan terjadi gangguan ginjal. Gejala klinis harus diamati secara berkala dan konsentrasi darah harus diukur.
- Jika menggunakan fenitoin (obat antiepilepsi / obat antikejang), kemungkinan akan terjadi pusing, gangguan gerak dan keseimbangan tubuh (ataksia), bola mata bergerak cepat dan berulang tanpa disengaja (nistagmus), dan lain-lain. Gejala klinis harus diamati secara berkala.
- Jika menggunakan simetidin (antagonis reseptor H_2) dan inhibitor protease HIV (ritonavir, saquinavir mesilat, dan lain-lain) kemungkinan akan meningkatkan efek antihipertensi, jantung berdebar lebih lambat (bradikardia), dan lain-lain. Tekanan darah harus diukur dan Elektrokardigram (EKG) pasien harus dimonitor.
- Jika menggunakan rifampisin (obat antituberkulosis), kemungkinan akan melemahkan efek obat . Gejala klinis harus diamati secara berkala dan konsentrasi darah harus diukur.
- Jika menggunakan obat bius (isoflurane, enflurane, halothane, dan lain-lain), kemungkinan akan terjadi jantung berdebar lebih lambat (bradikardia) atau tidak beraturan (blok atrioventrikular), elektrokardigram (EKG) pasien harus dimonitor.
- Jika menggunakan relaksan otot (pankuronium bromida, vekuronium bromida, dan lain-lain) kemungkinan akan meningkatkan efek obat. Penggunaan relaksan otot oleh pasien harus berhati-hati.

Kehamilan dan Menyusui
Jika Anda sedang hamil atau menyusui, berpikir mungkin sedang hamil atau berencana untuk memiliki anak, mintalah saran dokter Anda sebelum Anda menggunakan obat ini,

HERBESSER® CD tidak diperbolehkan untuk diberikan kepada ibu hamil dan ada kemungkinan hamil. [Penelitian pada hewan tikus menunjukkan bahwa obat memiliki efek yang menyebabkan kecacatan bagi janin di dalam kandungan (teratogenik) dan efek yang berbahaya bagi janin dalam kandungan (embriotoksik).]

HERBESSER® CD tidak dianjurkan untuk diberikan kepada ibu menyusui. Jika penggunaan obat dianggap penting, pemberian ASI harus dihentikan selama pengobatan [Dilaporkan bahwa *diltiazem hydrochloride* dikeluarkan dalam ASI.]

Penggunaan pada anak-anak
Keamanan penggunaan HERBESSER® CD pada anak-anak belum diketahui.

Penggunaan pada usia lanjut
Penggunaan pada usia lanjut harus dimulai dengan dosis yang telah dikurangi dan didampingi dengan pemantauan terhadap kondisi pasien untuk mencegah penurunan tekanan darah berlebihan yang tidak diinginkan.

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3. Bagaimana cara penggunaan HERBESSER® CD

Anda akan diresepkan HERBESSER® CD oleh dokter. Dokter akan menginformasikan kepada Anda seberapa banyak penggunaan HERBESSER® CD dan kapan Anda harus mengonsumsinya. Gunakan HERBESSER® CD sesuai yang diinformasikan oleh dokter Anda dan jangan menghentikan penggunaan HERBESSER® CD tanpa terlebih dahulu mengonsultasikannya kepada dokter.

Hipertensi (ringan hingga sedang): Secara umum, pada orang dewasa, gunakan 100 mg hingga 200 mg HERBESSER® CD, satu kali sehari. Dosis dapat disesuaikan dengan usia dan gejala yang Anda alami.

Angina pektoris, angina varian: Secara umum, pada orang dewasa, gunakan 100 mg HERBESSER® CD, satu kali sehari. Jika efek yang diharapkan belum tercapai, dosis dapat ditingkatkan menjadi 200 mg HERBESSER® CD, satu kali sehari.

Telan obat ini tanpa mengunyah atau membuka kapsulnya.

Jika Anda menggunakan HERBESSER® CD terlalu banyak
Jika Anda telah menggunakan HERBESSER® CD melebihi dosis yang dianjurkan oleh dokter, segera hubungi dokter Anda. Tanda-tanda dari pemberian HERBESSER® CD yang terlalu banyak biasanya adalah sebagai berikut:

- Jantung berdebar lebih lambat (bradikardia)
- Jantung berdebar tidak beraturan (blok atrioventrikular)
- Kegagalan jantung
- Tekanan darah rendah (hipotensi)
- dan lain-lain.

Mengemudi dan menggunakan mesin
HERBESSER® CD dapat menyebabkan pusing karena efek penurunan tekanan darah. Hindari melakukan aktivitas seperti mengendarai mobil, menggunakan mesin yang mungkin dapat membahayakan Anda, atau bekerja pada ketinggian.

4. Kemungkinan efek samping

Seperti semua obat-obatan, obat ini dapat menyebabkan efek samping, meskipun tidak semua orang mengalaminya.

Efek samping berikut dapat terjadi. Jika terjadi, informasikanlah kepada dokter Anda sehingga Anda akan diberi perawatan yang tepat.

Jika Anda mengalami salah satu efek samping, atau jika anda melihat efek samping yang tidak tercantum dalam leaflet ini, silakan beri tahu dokter atau tenaga kesehatan lainnya.

Jika salah satu dari gejala-gejala ini terjadi, hentikan penggunaan obat dan segera temui dokter Anda.
Efek samping yang paling sering dilaporkan yaitu:
- Jantung berdebar lebih lambat (bradikardia) atau tidak beraturan (blok atrioventrikular)
- Wajah memerah
- Pusing
- Rasa tidak enak badan (malaise)
- Pemeriksaan laboratorium abnormal

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- Ruam
- Kesulitan buang air besar (sembelit)
- Mual
- Ketidaknyamanan pada perut atau sakit perut
- Sakit kepala
- Nyeri ulu hati
- Gangguan makan (anoreksia)
- Reaksi alergi yang parah (hipersensitivitas)

Efek samping yang jarang terjadi:
- Sinus arrest (kondisi saat nodus sinoatrial jantung berhenti memicu aktivitas listrik secara tiba-tiba, menyebabkan jeda panjang dalam detak jantung)
- Penurunan tekanan darah
- Jantung berdetak cepat (palpitasi)
- Nyeri dada
- Pembengkakan karena adanya penumpukan cairan (edema)
- Keram pada betis
- Merasa lemah
- Mengantuk
- Sulit tidur
- Penyakit kuning
- Gatal pada kulit
- Biduran
- Feses lunak
- Diare
- Haus

Efek samping lainnya:
- Blok sinoatrial, yaitu gangguan pada konduksi listrik normal dari nodus sinoatrial (alat pacu alami jantung).
- Gejala seperti parkinson, yaitu tremor, gerakan melambat, dan kekakuan
- Peningkatan enzim hepatik
- Pembesaran payudara pada pria (ginekomastia)Jumlah sel darah abnormal
- Sensitif terhadap cahaya
- Jerawat pustula
- Pembengkakan pada gusi
- Mati rasa

Pelaporan efek samping
Jika anda mengalami efek samping, bicarakan dengan dokter, apoteker, atau perawat Anda. Ini termasuk kemungkinan efek samping yang tidak tercantum dalam leaflet ini.
Anda juga dapat melaporkan efek samping langsung melalui situs web kami https://mt-pharma-id.com/id/contact dan pilih subjek *Pharmacovigilance.*
Dengan melaporkan efek samping, Anda dapat membantu memberikan informasi lebih lanjut tentang keamanan obat ini.

5. Bagaimana penyimpanan HERBESSER®

- Simpan dalam wadah tertutup rapat dan tahan cahaya.

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- Jangan simpan obat ini pada suhu diatas 30°C.
- Jauhkan dari jangkauan anak-anak.
- Jangan gunakan obat ini setelah tanggal kedaluwarsa yang tercantum pada kemasan.

6. Kemasan dan informasi lainnya

Apa kandungan HERBESSER® CD
HERBESSER® CD 100 mengandung zat aktif diltiazem hydrochloride 100 mg.
HERBESSER® CD 200 mengandung zat aktif diltiazem hydrochloride 200 mg.

Bahan lainnya adalah ammonialkyl methacrylate copolymer, talc, starch, sucrose, fumaric acid, povidone, dan kapsul gelatin.

Seperti apa HERBESSER® CD dan isi kemasannya
HERBESSER® CD 100 adalah kapsul keras berwarna putih pada bagian badan dan tutup kapsul, berisi beads putih hingga putih kekuningan pucat.
HERBESSER® CD 200 adalah kapsul keras berwarna putih bagian badan dan merah bagian tutup kapsul, berisi beads putih hingga putih kekuningan pucat.
Kapsul dikemas dalam blister PVC disegel dengan aluminum foil. Dus berisi 3 blister @ 10 kapsul dan 10 blister @ 10 kapsul.

7. Nomor izin edar

HERBESSER® CD 100	Reg. No.: DKL1025202503A1
HERBESSER® CD 200	Reg. No.: DKL1025202503B1

8. Peringatan khusus

HARUS DENGAN RESEP DOKTER

Di bawah lisensi oleh:
Mitsubishi Tanabe Pharma Corporation
Osaka, Jepang

Beads diiproduksi oleh:
Alfresa Pharma Corporation
Ota, Japan

Beads diimpor, dienkapsulasi, dan dikemas soleh:
PT Mitsubishi Tanabe Pharma Indonesia
Bandung, Indonesia

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