

CELIPROLOL HYDROCHLORIDE 200MG TABLETS

PL 13931/0031

UKPAR

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CELIPROLOL HYDROCHLORIDE 200MG TABLETS

PL 13931/0031

LAY SUMMARY

The MHRA granted Chanelle Medical a Marketing Authorisation (licence) for the medicinal product Celiprolol Hydrochloride 200mg Tablets (PL 13931/0031). This medicine is available by prescription only and used to treat high blood pressure (Hypertension).

Celiprolol Hydrochloride is one of a group of medicines called beta-blockers. These medicines work by reducing blood pressure in patients with hypertension.

No new or unexpected safety concerns arose from this application and it was therefore judged that the benefits of taking Celiprolol Hydrochloride 200mg Tablets outweigh the risks, hence Marketing Authorisation has been granted.

CELIPROLOL HYDROCHLORIDE 200MG TABLETS

PL 13931/0031

SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy the UK granted marketing authorisation for the medicinal product Celiprolol Hydrochloride 200mg Tablets (PL 13931/0031) to Chanelle Medical on 3rd May 2007. This is a prescription-only medicine (POM) used to treat high blood pressure.

This is a national application for Celiprolol Hydrochloride 200mg Tablets submitted under Article 10.1 of Directive 2001/83, claiming to be a generic medicinal product of Celectol 200mg Tablets, currently PL 15638/0008, held by Concord Pharmaceuticals Ltd., but originally PL 00012/0231, granted to May & Baker Ltd. on 08/07/1991. A bioequivalence study has been performed comparing the applicant's product with Celectol 200mg tablets from the French market.

Celiprolol is a relatively cardioselective β_1 -adrenoceptor blocking agent, that is stated to possess intrinsic sympathomimetic activity, acting as a partial agonist on β_2 -receptors; it also has a direct vasodilator effect. It is indicated for the treatment of mild to moderate hypertension.

PHARMACEUTICAL ASSESSMENT

DRUG SUBSTANCE

Nomenclature

INN: Celiprolol hydrochloride

Chemical name: (RS)-N'-[3-acetyl-4-[3-(1,1-dimethylethyl)amino]-2-hydroxypropoxy]phenyl]-N,N-diethylurea monohydrochloride

CAS number: 57470-78-7

Molecular formula: C₂₀H₃₃N₃O₄.HCl

Molecular Weight: 415.96

A white to off-white crystalline powder. Freely soluble in water and methanol, sparingly soluble in ethanol and slightly soluble in chloroform. It is a racemic mixture. The drug substance exhibits polymorphism; form I is that which is intended for use in the drug product.

This is subject to DMF. A letter of access has been provided

Synthesis of the drug substance from the designated starting material has been adequately described and appropriate in-process controls and intermediate specifications are applied. Satisfactory specifications are in place for all starting materials and reagents and these are supported by relevant certificates of analysis.

An appropriate specification based on the European Pharmacopoeia has been provided.

Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications.

Active celiprolol hydrochloride is stored in appropriate packaging. The specifications and typical analytical test reports are provided and are satisfactory.

Batch analysis data have been provided and comply with the proposed specification.

Acceptable justification of the proposed specifications are provided.

Satisfactory certificates of analysis have been provided for working standards used by the active substance manufacturer and finished product manufacturer during validation studies.

Appropriate stability data has been provided.

DRUG PRODUCT

Other ingredients

Other ingredients consist of pharmaceutical excipients, namely lactose monohydrate, cellulose, microcrystalline, croscarmellose sodium, colloidal anhydrous silica, magnesium

stearate, OPADRY II White, and water purified. All excipients used comply with their respective European Pharmacopoeia monograph with the exception of OPADRY II White which complies with in house specification. Satisfactory certificates of analysis have been provided for all excipients.

The only excipients used that contain material of animal or human origin are lactose monohydrate and magnesium stearate. The applicant has provided a declaration that the milk used in the production of lactose monohydrate is sourced from healthy animals under the same conditions as that for human consumption. Confirmation has been given that the magnesium stearate used in the tablets is of vegetable origin.

There were no novel excipients used and no overages.

Pharmaceutical development

The objective of the pharmaceutical development programme was to produce a product containing Celiprolol 200mg Tablets that are tolerable and which could be considered as generic product to the originator product Celectol 200mg Tablets.

The rationale for the type of pharmaceutical form developed and formulation variables evaluated during development have been stated and are satisfactory.

Dissolution and impurity profiles

Dissolution and impurity profiles for the drug product were found to be similar to that for the reference product.

Manufacture

A description and flow-chart of the manufacturing method has been provided.

In-process controls are appropriate considering the nature of the product and the method of manufacture. Process validation has been carried out on batches. The results are satisfactory.

Satisfactory batch formulae have been provided for the manufacture of the product along with an appropriate account of the manufacturing process. The manufacturing process has been validated and appropriate in-process controls are applied.

Finished product specification

The finished product specification is satisfactory. Acceptance limits have been justified with respect to conventional pharmaceutical requirements and, where appropriate, safety. Test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of analysis have been provided for any working standards used.

Container Closure System

Product is packaged in to PVC/Aluminium blisters. Specifications and Certificates of Analysis for all packaging types used have been provided. These are satisfactory. All primary product packaging complies with EU legislation regarding contact with food.

Stability

Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a shelf-life of 3 years with storage conditions “Store in the original package” and “Keep container in the outer carton” have been set. These are acceptable.

Bioequivalence/bioavailability

Satisfactory certificates of analysis have been provided for the test and reference batches used in the bioequivalence study. Bio-analytical methods used have been satisfactorily validated. Satisfactory bioequivalence is seen between the test and reference product.

SPC, PIL, Labels

The SPC, PIL and Labels are pharmaceutically acceptable.

The PIL is in compliance with current guidelines. The marketing authorisation holder has provided a commitment to update the marketing authorisation with a package leaflet in compliance with Article 59 of Council Directive 2001/83/EC and that the leaflet shall reflect the results of consultation with target patient groups, no later than 1st July 2008.

Conclusion

The proposed product has been shown to be a generic product of the reference product and has met the requirements with respect to qualitative and quantitative content of the active substance. Similar dissolution profiles have been demonstrated for the proposed and reference products. It is recommended that Marketing Authorisation should be granted for this application.

PRECLINICAL ASSESSMENT

No new preclinical data have been supplied with this application and none are required for an application of this type.

CLINICAL ASSESSMENT

1. INTRODUCTION

This national abridged application claims to be a generic medicinal product of Celectol (PL 15638/0008) Concorde Pharmaceuticals.

2. INDICATIONS

Satisfactory. Consistent with originator.

3. DOSE & DOSE SCHEDULE

Satisfactory. Consistent with originator.

4 TOXICOLOGY

No new data.

5. CLINICAL PHARMACOLOGY

The applicant has conducted a single dose comparative bioavailability study. The study compared single doses 200 mg test product with 200 mg originator.

Table 1

Bioavailability parameters for celiprolol (n=40) after administration of
1 tablet of Celiprolol Biogaran 200 mg
and of 1 tablet of Celectol® 200 mg
(arithmetic average)

Parameter	CELIPROLOL BIOGARAN	CELECTOL®	P	CI 90%
T _{max} (h) Median	3.00 (2.0 - 6.0)	3.50 (2.0 - 6.0)	NS	-0.25 - 0.25
C _{max} (ng/ml)	754 ± 343 (236 - 1615)	767 ± 333 (301 - 1564)	NS	87.1 - 108.0 (97.0)
AUC _p (ng.h/ml)	3597 ± 1050 (1449 - 6297)	3540 ± 948 (1492 - 5459)	NS	94.0 - 108.0 (101)
AUC _{inf} (ng.h/ml)	3795 ± 1093 (1593 - 6704)	3742 ± 974 (1653 - 5813)	NS	94.0 - 108.0 (101)
T _{1/2} (h)	5.38 ± 0.54	5.39 ± 0.54	NS	

The 90% CI ratios of C_{max} and AUC both fell within the guideline range 80 - 125%.

No serious adverse events were encountered.

6. EFFICACY

No new data.

7. SAFETY

No new data.

8. EXPERT REPORTS

The clinical expert report has been written by an appropriately qualified pharmaceutical physician. It is an adequate summary of the clinical data provided in the dossier.

9. PATIENT INFORMATION LEAFLET (PIL)

Satisfactory.

10. LABELLING

Satisfactory.

11. SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

Satisfactory. Fully consistent with originator.

12. DISCUSSION

Satisfactory demonstration of comparable bioavailability has been carried out.

13. MEDICAL CONCLUSION

Marketing authorisation is recommended.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

The important quality characteristics of Celiprolol Hydrochloride 200mg Tablets are well defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

PRECLINICAL

No new preclinical data were submitted and none are required for applications of this type.

EFFICACY

Based on the submitted bioequivalence study Celiprolol Hydrochloride 200mg Tablets are considered bioequivalent with Celectol 200mg Tablets.

No new or unexpected safety concerns arise from this application.

The SPC, PIL and Labelling are satisfactory.

RISK BENEFIT ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The bioequivalence study supports the claim that the applicant's product and the innovator product are interchangeable. Extensive clinical experience with Celiprolol Hydrochloride 200mg Tablets is considered to have demonstrated the therapeutic value of the compound. The risk benefit is, therefore, considered to be positive.

CELIPROLOL HYDROCHLORIDE 200MG TABLETS**PL 13931/0031****STEPS TAKEN FOR ASSESMENT**

1	The MHRA received the marketing authorisation applications on 26 th June 2003
2	Following standard checks and communication with the applicant the MHRA considered the applications valid on 3 rd September 2003
3	Following assessment of the applications the MHRA requested further information relating to the quality dossier on 23 rd December 2003, 22 nd November 2004, and 24 th January 2006
4	The applicant responded to the MHRA's requests, providing further information to the quality section on 4 th August 2004, 14 th October 2004, 11 th November 2004, 11 th January 2006, and 17 th August 2006
5	The application was determined on 3 rd May 2007

CELIPROLOL HYDROCHLORIDE 200MG TABLETS

PL 13931/0031

STEPS TAKEN AFTER AUTHORISATION - SUMMARY

Date submitted	Application type	Scope	Outcome

SUMMARY OF PRODUCT CHARACTERISTICS**1 NAME OF THE MEDICINAL PRODUCT**

Celiprolol Hydrochloride 200mg Tablets.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Celiprolol Hydrochloride 200mg.

For excipients see section 6.1.

3 PHARMACEUTICAL FORM

Film coated tablet

White, biconvex, film coated tablets with a score on one side.

4 CLINICAL PARTICULARS**4.1 THERAPEUTIC INDICATIONS**

The management of mild to moderate hypertension.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

Route of Administration: Oral

Adults:

The initial dose is 200mg orally taken once daily with a glass of water. Celiprolol 200 Tablets should be taken on rising, half an hour before food. If response is inadequate, the dose may be increased to 400 mg once daily.

Elderly patients:

Dosage as for adults.

Children:

Not recommended.

4.3 CONTRAINDICATIONS

As with other beta-adrenoceptor antagonists, celiprolol should not be used in cases of cardiogenic shock, uncontrolled heart failure, sick-sinus syndrome, second or third degree heart block, severe bradycardia, severe renal impairment with creatinine clearance less than 15ml per minute, acute episodes of asthma, untreated phaeochromocytoma, metabolic acidosis, hypotension, hypersensitivity to the substance, or severe peripheral arterial circulatory disturbances.

Although cardio selective beta blockers may have less effect on lung function than non selective beta blockers, as with all beta blockers these should be avoided in patients with chronic obstructive airways disease, and in patients with a history of bronchospasm or bronchial asthma, unless there are compelling clinical reasons for their use. Where such reasons exist, celiprolol may be used but with the utmost caution. The label will carry the following warning: *If you have a history of asthma or wheezing, please ask your doctor before taking this medicine.*

Celiprolol 200 tablets should not be prescribed for patients being treated with theophylline.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

The pharmacokinetics are not significantly different in the elderly, however these patients should be regularly monitored and due regard made for decreased renal and liver function in this age group.

Celiprolol 200 tablets may be used in patients with mild to moderate degrees of reduced renal function as celiprolol is cleared by both renal and non-renal excretory pathways. A reduction in dosage by half may be appropriate in patients with creatinine clearances in the range of 15 to 40ml per minute. However, careful surveillance of such patients is recommended until steady state blood levels are achieved which typically would be within one week. Celiprolol 200 tablets are not recommended for patients with creatinine clearance less than 15ml per minute. Patients with hepatic impairment should also be carefully monitored after commencing therapy and a reduced dosage should be considered.

Sudden withdrawal of beta-adrenoceptor blocking agents in patients with ischemic heart disease may result in the appearance of anginal attacks of increased frequency or severity or deterioration in cardiac state. Although no adverse effects due to abrupt cessation of Celiprolol 200 tablets have been seen in clinical trials, therapy should be gradually reduced over 1-2 weeks, at the same time, if necessary, initiating replacement therapy to prevent exacerbation of angina pectoris.

Celiprolol 200 tablet therapy must be reported to the anaesthetist prior to general anaesthesia. If it is decided to withdraw the drug before surgery, 48 hours should be allowed to elapse between the last dose and anaesthesia. Continuation of beta blockade reduces the risk of arrhythmias during induction and intubation, although reflex tachycardia may be attenuated and the risk of hypotension may be increased (see "Interactions"). In the event of continuation of Celiprolol 200 tablet treatment special care should be exercised when using anaesthetic agents such as ether, cyclopropane or trichloroethylene. The patient may be protected against vagal reactions by the intravenous administration of atropine.

Celiprolol 200 tablets should only be used with caution in patients with controlled congestive cardiac failure. Evidence of decompensation should be regarded as a signal to discontinue therapy.

In patients with peripheral circulatory disorders (Raynaud's disease or syndrome, intermittent claudication), beta blockers should be used with great caution as aggravation of these disorders may occur.

Celiprolol may induce bradycardia. If the pulse rate decreases to less than 50-55 beats per minute at rest and the patient experiences symptoms related to the bradycardia, the dosage should be reduced.

Due to its negative effect on conduction time, celiprolol should only be given with caution to patients with first degree heart block.

Beta blockers may increase the number and the duration of anginal attacks in patients with Prinzmetal's angina, due to unopposed alpha-receptor mediated coronary artery vasoconstriction. The use of beta-i selective adrenoceptor blocking drugs such as celiprolol may be considered in these patients, but the utmost care should be exercised.

Beta blockers have been reported to exacerbate psoriasis, and patients with a history of psoriasis should take celiprolol only after careful consideration.

In patients with a history of anaphylactic reactions, beta blockers may increase the sensitivity to allergens and the seriousness of the reactions.

Beta blockers may mask the symptoms of thyrotoxicosis or hypoglycaemia (in particular, tachycardia).

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

Not recommended association

It has been shown that the bioavailability of celiprolol is impaired when it is given with food. Co-administration of chlortalidone and hydrochlorothiazide also reduces the bioavailability of celiprolol.

Calcium channel antagonists such as verapamil (and to a lesser extent diltiazem) and beta blockers both slow A-V conduction and depress myocardial contractility through different mechanisms. When changing from verapamil to celiprolol and vice versa, a period between stopping one and starting the other is recommended. Concomitant administration of both drugs is not recommended and should only be initiated with ECG monitoring. Patients with pre existing conduction abnormalities should not be given the two drugs together.

Digitalis glycosides, in association with beta-adrenoceptor blocking drugs, may increase A-V conduction time.

Beta blockers may exacerbate the rebound hypertension, which can follow the withdrawal of clonidine. If the two drugs are co-administered, the beta-adrenoceptor blocking drug should be withdrawn several days before discontinuing clonidine. There is a theoretical risk that concurrent administration of monoamine oxidase inhibitors and high doses of beta-adrenoceptor blockers, even if they are cardio selective, can produce hypertension.

Precautions for use

Care should be taken in prescribing beta-adrenoceptor blockers with Class I antiarrhythmic agents (e.g. disopyramide, quinidine) and amiodarone, since these agents may potentiate the negative effects on A-V conduction and myocardial contractility.

Beta blockers may intensify the blood sugar lowering effects of insulin and oral antidiabetic drugs, and the dosage of antidiabetics may therefore require adjustment. In addition, beta-adrenoceptor blockers may mask the symptoms of thyrotoxicosis or hypoglycaemia (in particular, tachycardia).

Therapy with beta-adrenoceptor blockers must be reported to the anaesthetist prior to general anaesthesia (see "Special warnings and special precautions for use"). Continuation of beta blockade reduces the risk of arrhythmias during induction and intubation, but reflex tachycardia may be attenuated and the risk of hypotension may be increased. Anaesthetic agents causing myocardial depression (e.g. ether, cyclopropane, trichloroethylene) are best avoided.

Take into account

Concomitant therapy with dihydropyridine calcium channel antagonists, such as nifedipine, may increase the risk of hypotension, and cardiac failure may occur in patients with latent cardiac insufficiency.

Drugs inhibiting prostaglandin synthetase, such as ibuprofen or indomethacin, may decrease the hypotensive effects of beta-adrenoceptor blocking drugs.

Sympathomimetic agents, such as adrenaline, may counteract the effects of beta blockers.

Concomitant use of other antihypertensive agents, or of tricyclic antidepressants, barbiturates or phenothiazines, may potentiate the hypotensive effects of beta blockers.

4.6 PREGNANCY AND LACTATION

The safety of this medicinal product for use in human pregnancy have not been established. An evaluation of experimental animal studies does not indicate direct or indirect harmful effects with respect to reproduction, development of the embryo or foetus, the course of gestation and peri- and post-natal development.

However, beta-adrenoceptor blocking drugs in general have been associated with reduced placental perfusion, which may result in intrauterine foetal death, immature and premature deliveries. In addition, adverse effects (especially hypoglycaemia and bradycardia) may occur in foetus and neonate, together with an increased risk of cardiac and pulmonary complications in the neonate in the post natal period. Most beta blockers will pass into breast milk, although to variable extents. The use of Celiprolol 200 tablets is not recommended in breast-feeding mothers.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

It has been shown that driving ability is unlikely to be impaired in patients taking Celiprolol 200 tablets. However, it should be taken into account that occasional dizziness or fatigue may occur.

4.8 UNDESIRABLE EFFECTS

Beta-adrenoceptor blockers may mask the symptoms of thyrotoxicosis or hypoglycaemia (in particular, tachycardia).

Occasional side effects, which are usually mild and transient have occurred. These include headache, dizziness, fatigue, nausea, somnolence and insomnia (sleep disturbances). Additional side effects associated with beta-2 agonist activity, tremor and palpitations, have been reported. These effects usually do not require withdrawal of therapy. Depression and hypersensitivity pneumonitis have been reported rarely.

Bronchospasm, skin rashes and/or visual disturbances have been reported in association with the use of beta blockers. Celiprolol 200 tablets should be discontinued if these effects occur.

In addition, the following undesirable effects, listed by body system, are generally attributable to the pharmacological activity of beta-adrenergic blockers:

Cardiovascular: bradycardia, slowed A-V conduction, hypotension, heart failure, cold and cyanotic extremities. In susceptible patients: precipitation of existing A-V block, exacerbation of intermittent claudication, Raynaud's disease or syndrome.

CNS: confusion, hallucinations, psychoses, nightmares.

Neurological: paraesthesia.

Respiratory: bronchospasm may occur in patients with bronchial asthma or with a history of bronchial complaints.

Gastro-intestinal: vomiting, diarrhoea.

Integumentary: skin disorders (especially rash), dry eyes.

Others: disturbances of libido and potency. An increase in ANA (antinuclear antibodies) has been reported, although its clinical relevance is not clear.

4.9 OVERDOSE

No data are available regarding celiprolol overdose in humans.

The most common symptoms to be expected following overdosage with a beta-adrenoceptor blocking drug are bradycardia, hypotension, bronchospasm and acute cardiac insufficiency.

General treatment should include close supervision, with the use of gastric lavage, activated charcoal and a laxative to prevent absorption of any drug still present in the gastro-intestinal tract. Haemodialysis or haemoperfusion may be considered.

Bradycardia or extensive vagal reactions should be treated with intravenous atropine, 1-2mg. Cardiac pacing should be considered in refractory bradycardia and heart block. Hypotension should be treated with plasma or plasma substitutes and, if necessary, intravenous catecholamines including dopamine and dobutamine.

The effects of excessive beta blockade can be counteracted by the slow intravenous infusion of a beta-adrenoceptor stimulant such as isoprenaline, starting with a dose of approximately 5 micrograms per minute with close cardiac monitoring, or dobutamine, starting with a dose of 2.5 micrograms per kilogram per minute, until the required effect has been obtained. In severe overdose, intravenous glucagon may be considered: an initial bolus dose of 10mg may be repeated within one hour, if required, or followed by intravenous infusion of glucagon at a rate of 1-10mg per hour, depending on response.

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Beta blocking agents, selective

ATC Code: C07A B08

Celiprolol is a vasoactive beta-1 selective adrenoceptor antagonist with partial beta-2 agonist activity indicated in mild to moderate hypertension. The beta-2 agonist activity is thought to account for its mild vasodilating properties. It lowers blood pressure in hypertensive patients at rest and on exercise. The effects on heart rate and cardiac output are dependant on the pre-existing background level of sympathetic tone.

Under conditions of stress such as exercise celiprolol attenuates chronotropic and inotropic responses to sympathetic stimulation. However, at rest minimal impairment of cardiac function is seen.

Celiprolol 200 tablet therapy has not been shown to adversely affect plasma lipid profiles.

5.2 PHARMACOKINETIC PROPERTIES

Celiprolol is a hydrophilic compound that is incompletely absorbed from the gastrointestinal tract. Plasma half-life is approximately 5-6 hours and pharmacodynamic effects are present for at least 24 hours. After once daily administration celiprolol is only slightly metabolised before excretion in the bile and urine in almost equal quantities.

It has been shown that the bioavailability of celiprolol is impaired when it is given with food. Co-administration of chlortalidone, hydrochlorothiazide and theophylline also reduces the bioavailability of celiprolol.

5.3 PRECLINICAL SAFETY DATA

There are no preclinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

microcrystalline cellulose

Lactose Monohydrate

Croscarmellose Sodium

Silica Colloidal anhydrous

Magnesium stearate

Film coating Opadry II White oY-L-28900 contains;

Hypromellose

Lactose monohydrate

Titanium Dioxide

Macrogol 4000

6.2 INCOMPATIBILITIES

None stated.

6.3 SHELF LIFE

3 Years.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store in the original package. Keep blister in the outer carton.

6.5 NATURE AND CONTENTS OF CONTAINER

Blister strips composed of transparent PVC and aluminium foil.

Pack sizes: 28 and 30 tablets

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

No special instructions.

- 7 MARKETING AUTHORISATION HOLDER**
Chanelle Medical

Dublin Road

Loughrea

Co. Galway

Ireland
- 8 MARKETING AUTHORISATION NUMBER(S)**
PL 13931/0031
- 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**
03/05/2007
- 10 DATE OF REVISION OF THE TEXT**
03/05/2007

PATIENT INFORMATION LEAFLET



PACKAGE LEAFLET: INFORMATION FOR THE USER

CELIPROLOL HYDROCHLORIDE 200 MG TABLETS

Please read this leaflet carefully BEFORE you start to take the Celiprolol Hydrochloride 200 mg Tablets. This leaflet is a summary of the important information about your medicine. Keep it in a safe place as you may want to refer to it again. If you have any questions or are not sure about anything to do with your treatment, ask your doctor or pharmacist for more information.

In this leaflet:

- 1 What Celiprolol Hydrochloride 200mg Tablet is and what it is used for
- 2 Before you take Celiprolol Hydrochloride 200mg Tablet
- 3 How to take Celiprolol Hydrochloride 200mg Tablet
- 4 Possible side effects
- 5 How to store Celiprolol Hydrochloride 200mg Tablet
- 6 Further information

1 What Celiprolol Hydrochloride 200mg Tablets is and what it is used for?

Celiprolol Hydrochloride 200mg Tablets are used to treat high blood pressure (hypertension). If you need any further information on your condition, please ask your doctor.

2 Before you take Celiprolol Hydrochloride 200 mg Tablets?

Tell your doctor or pharmacist if any of the following apply:

- If you are sensitive or allergic to celiprolol hydrochloride 200mg tablets or any other beta-blockers
- If you are sensitive or allergic to any of the inactive ingredients
- If you suffer from a slow heart beat (bradycardia)
- If your heart is not pumping blood as well as it should (heart failure)
- If you have low blood pressure (hypotension)
- If you suffer from a type of chest pain called Prinzmetal's angina
- If you suffer from very poor circulation in the hands and feet (Raynaud's disease)
- If you suffer from any other problems with your heart or blood circulation
- If you have any liver problems
- If you have any kidney problems, in particular kidney failure
- If you have phaeochromocytoma (high blood pressure caused by a tumour, usually near the kidney) which is not being treated
- If you have metabolic acidosis (abnormal levels of acid in your blood)
- If you have a history of wheezing, asthma, bronchitis, emphysema or other breathing problems
- If you have ever suffered from psoriasis
- If you have previously suffered from allergic reactions (e.g. to insect stings)
- If you have diabetes, or an overactive thyroid gland
- If you are pregnant or think you might be pregnant
- If you are breast feeding
- If the patient is under 12 years of age
- If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product
- If you are taking any other medicines

Some medicines may change the way Celiprolol Hydrochloride 200mg Tablet works, or should not be taken with it. If you are taking any of the following, tell your doctor:

- Amiodarone
- Digitalis glycosides
- Diltiazem
- Disopyramide
- Verapamil (may be used to treat irregular heart beat)
- Theophylline (may be used to treat asthma)
- Chlorthalidone or hydrochlorothiazide, sometimes called "water" tablets (may be used to lower blood pressure)
- Clonidine
- Quinidine
- Insulin and oral antidiabetic drugs
- Ether, cyclopropane and trichloroethylene
- Nifedipine
- Ibuprofen or indomethacin
- Adrenaline
- Antihypertensive agents, tricyclic antidepressants, barbiturates or phenothiazines

If you have to go to a doctor, dentist or hospital for any reason, tell them that you are taking Celiprolol Hydrochloride 200mg Tablets. This is very important if you are likely to be given an anaesthetic.

3 How To Take Celiprolol Hydrochloride 200mg Tablets?

The usual adult dosage is 200 mg to 400 mg first thing in the morning, half an hour before food. The tablets should be swallowed with water. It is important to take your tablets at the right time. If your doctor decides to stop or change your treatment, you may be asked to reduce the number of tablets you are taking. Always take the number of tablets your doctor has told you. The pharmacist's label will tell you how many to take and how often. If it does not, or you are not sure, ask your doctor or pharmacist.

What if you forget to take your medicine?

Do not worry, just take your tablets as soon as you remember, then go on as before. **Do not** take double the dose on the same day.

What if you or a child takes too much?

If you accidentally take too many tablets or a child swallows any tablets, contact your nearest hospital casualty department or tell your doctor immediately.

Driving and operating machinery

Celiprolol Hydrochloride is unlikely to affect your ability to drive or to operate machinery. However, some people may occasionally feel dizzy or drowsy when taking a beta-blocker. If this happens to you, ask your doctor for advice.

Important information about some of the ingredients of Celiprolol Hydrochloride 200mg Tablets

This product contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

4 Possible Side Effects

As well as benefits, all medicines may occasionally have unwanted effects in some patients. These are called side effects.

Side effects of Celiprolol Hydrochloride 200mg Tablets that are well known are headache, dizziness, light-headedness, slow heart beat (bradycardia) or other heart effects, tiredness or fatigue, nausea or feeling sick, vomiting, diarrhoea, sleepiness, insomnia (sleep disturbances).

Patients with an overactive thyroid gland or diabetes should be aware that the symptoms of thyrotoxicosis or hypoglycaemia may be hidden by Celiprolol Hydrochloride 200mg Tablets. Rarer effects are nightmares, hallucinations, confusion and loss of sex drive. You do not need to worry about them unless they become troublesome – in which case, you should contact your doctor.

Some side effects may be more serious and you should tell your doctor immediately if you have any of the following:

- Skin rashes
- Any changes in your eyesight
- Breathlessness
- Wheezing or coughing
- Depression
- Shakiness
- Palpitations (fast heart rate)
- Coldness
- Numbness or tingling of hands and feet

Do not be alarmed by this list of possible events. Most people take Celiprolol Hydrochloride 200mg Tablets without any problems.

All medicines may have unwanted side effects which are not mentioned in the product leaflet. If you notice any other changes in your health whilst taking this medicine, **tell your doctor immediately.**

5 How to store Celiprolol Hydrochloride 200mg Tablets?

Your tablets should be stored in the pack in which you are given them.

Keep your tablets in a safe place, out of the sight and reach of children.

Do not keep the tablets if your doctor decides to stop treatment. Return them to your pharmacist who will arrange for their safe destruction.

REMEMBER: These tablets are for you. Only a doctor may prescribe them for you. Never give your tablets to other people. They may harm other people even if their symptoms appear to be the same as yours.

Expiry Date

You must not take these tablets after the expiry date. This can be found on the carton and blister.

It is given as 'EXP' followed by the month and year. The tablets should not be used after the end of the month. If you are not sure when this is, check with your doctor or pharmacist.

6 Further information

What Celiprolol Hydrochloride 200 mg Tablets contain

The active substance is Celiprolol Hydrochloride. The other core ingredients are Microcrystalline Cellulose, Lactose Monohydrate, Croscarmellose Sodium, Silica Colloidal Anhydrous and Magnesium Stearate. The film coating ingredients are Opadry II White OY L 28900 which contains; Hypromellose, Lactose monohydrate, Titanium Dioxide, and Macrogol 4000.

What Celiprolol Hydrochloride 200 mg Tablets look like and contents of the pack

Celiprolol 200 mg Tablets are white, biconvex, film coated tablets with a scoreline on one side. They are available in blister packs containing 28 or 30 tablets.

The marketing authorisation holder and manufacturer is:

Chanelle Medical, Loughrea, Co. Galway, Ireland.

The distributor is:

Chanelle Medical U.K. Ltd, The Lodge, Stanford Bridge Farm, Station Road, Pluckley, Ashford, Kent TN27 0RU, United Kingdom.

This leaflet was last approved in



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