IRISH MEDICINES BOARD ACTS 1995 AND 2006

MEDICINAL PRODUCTS(CONTROL OF PLACING ON THE MARKET)REGULATIONS,2007

(S.I. No.540 of 2007)

PA0013/001/002
Case No: 2059261

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

Novartis Pharmaceuticals UK Ltd

Frimley Business Park, **Frimley**, **Camberley**, **Surrey, GU16 7SR**, **United Kingdom**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

VISKEN 5 mg Tablets

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **18/02/2009** until **30/09/2009**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

VISKEN 5mg Tablets.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 5.0mg of pindolol.

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Tablet.

White, circular, flat, bevelled edge, anglescored and scored as well as coded “LB” on one side, “SANDOZ” on the other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the control of essential hypertension and in the prophylactic treatment of angina pectoris.

4.2 Posology and method of administration

Adults

Hypertension

Initially, one 15mg tablet daily with breakfast, or 5mg two or three times daily. Most patients respond to a once-daily dose of between 15mg and 30mg.

If necessary, dosage may be increased at weekly intervals up to a maximum of 45mg daily in single or divided doses. Patients not responding after three to four weeks at this dosage level rarely benefit from further elevation in dosage. Addition of VISKEN to existing diuretic therapy increases the hypotensive effect and combination with other antihypertensives enables reduction in dosage of these agents.

Angina Pectoris

Usually half to one 5mg tablet up to three times a day according to response.

Use in the elderly

No evidence exists that elderly patients require different dosages or show difference side effects from younger patients.

Method of administration

Oral.

4.3 Contraindications

Untreated cardiac failure (see also precautions). Cardiogenic shock, sick sinus syndrome, first degree A-V block, second and third degree heart block, Prinzmetal's angina, untreated phaeochromocytoma, pronounced bradycardia, cor pulmonale, metabolic acidosis, prolonged fasting, severe renal failure, hypotension, obstructive lung disease, hypersensitivity to pindolol or to any of the excipients.

VISKEN should not be taken in conjunction with agents, which inhibit calcium transport, e.g. verapamil.

4.4 Special warnings and precautions for use

Patients with poor cardiac reserve should be established before treatment with VISKEN to prevent impairment of myocardial contractility. In treatment of severe hypertension care should be taken to avoid sudden reduction in the diastolic pressure below 110mm Hg.

As for other beta-blockers, and especially in patients with ischaemic heart disease, treatment should not be discontinued suddenly. The dosage should gradually be reduced, i.e. over 1-2 weeks, if necessary at the same time initiating replacement therapy, to prevent exacerbation of angina pectoris.

As with all beta-blockers, VISKEN should be used with caution in patients with a history of obstructive lung disease, recent myocardial infarction or thyrotoxicosis. VISKEN can be administered with caution to patients with obstructive respiratory disorders provided that adequate supervision is maintained. If increased airways resistance develops consideration must be given to discontinuation of the ß-blocker, depending on the degree of airways resistance and benefit derived from ß-blockade. Caution must be exercised when β-blocking agents are administered to patients with spontaneous hypoglycaemia or diabetes under treatment with insulin or oral hypoglycaemic agents, since hypoglycaemia may occur during prolonged fasting and some of its symptoms (tachycardia, tremor) may be masked.

During treatment with VISKEN, patients should not undergo anaesthesia with agents causing myocardial depression (e.g. halothane, cyclopropane, trichlorethylene, ether, chloroform). VISKEN should be gradually withdrawn before elective surgery. In emergency surgery or cases where withdrawal of VISKEN might cause deterioration in cardiac condition, atropine sulphate 1 to 2mg intravenously might need to be given to prevent severe bradycardia and expert advice should be sought.

The beta-blocker should only be used with caution in patients with controlled congestive cardiac failure or with a family history of asthma. Evidence of recrudescence of either condition should be regarded as a signal to discontinue therapy.

If a beta-blocker is indicated in a patient with phaeochromocytoma it must always be given in conjunction with an alpha-blocker. Pre-existing peripheral vascular disorders may be aggravated by beta-blockers.

In severe renal failure a further impairment of renal function following beta blockade has been reported in a few cases. In such patients it may be necessary to increase the intervals between doses or to reduce the dosage of drug.

There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenoceptor blocking drugs. The reported incidence is small and in most cases the symptoms have cleared when treatment was withdrawn. Discontinuance of the drug should be considered if any such reaction is not otherwise explicable.

Patients with known psoriasis should take beta-blockers only after careful consideration.

Beta blockers may increase both the sensitivity towards allergens and the seriousness of anaphylactic reactions.

Visken is contraindicated in patients with untreated congestive heart failure (this condition should first be stabilized).

Caution should be exercised with pre-existing peripheral vascular diseases resulting in cold extremities and paresthaesia and in patients treated with antidiabetic therapy.

There may be an increased risk of encephalopathy in patients with portal hypertension.

4.5 Interaction with other medicinal products and other forms of interaction

Calcium-channel blocking agents: Visken should not be used with calcium-channel blockers with negative ionotropic effects e.g. verapamil and to a lesser extent diltiazem. The concomitant use of oral beta-blockers and calcium antagonists of the dihydropyridine type can be useful in hypertension or angina pectoris. However, because of their potential effect on the cardiac conduction system and contractility, the iv route must be avoided. The concomitant use with dihydropyridines e.g. nifedipine may increase the risk of hypotension. In patients with cardiac insufficiency, treatment with beta-blocking agents may lead to cardiac failure.

Use of digitalis glycosides, in association with beta-adrenoceptor blocking drugs, may increase atrio-ventricular conduction time.

Clonidine: when therapy is discontinued in patients receiving a beta-blocker and clonidine concurrently, the beta-blockers should be gradually discontinued several days before clonidine is discontinued, in order to reduce the potential risk of a clonidine withdrawal hypertensive crisis.

MAO inhibitors: concurrent use with beta-blockers is not recommended. Possibly significant hypertension may theoretically occur up to 14 days following discontinuation of the MAO inhibitor.

Caution should be exercised in the concurrent use of beta-blocking agents with class 1 antiarrhythmics (e.g. disopyramide, quinidine, lignocaine, procainamide), other anti-hypertensive agents, ergotamine, phenobarbital, fluoxetin, rifamycine, phenothiazin and amiodarone.

Concomitant use of beta-blocking agents may intensify blood sugar lowering effect of insulin and other antidiabetic drugs.

Cimetidine, hydralazine and alcohol may induce increased plasma levels of hepatically metabolised ß-blockers.

Prostaglandin synthetase inhibiting drugs e.g. indomethacin and ibuprofen and other non-steroidal anti-inflammatory drugs (NSAIDs) may decrease the hypotensive effects of beta-blockers.

Sympathomimetics with beta-adrenergic stimulant activity, α-adrenoceptor stimulants (e.g. noradrenaline) and xanthines: concurrent use with beta-blockers may result in mutual inhibition of therapeutic effects. In addition, beta-blockers may decrease theophylline clearance.

Concomitant use of beta-blockers with tricyclic antidepressants, barbiturates and phenothiazines as well as other anti-hypertensive agents such as neurone blocking agents (e.g. guanethidine or bethanidine and reserpine) and diuretics may increase the blood pressure lowering effect.

Reserpine: concurrent use may result in an additive and possibly excessive beta-adrenergic blockade.

4.6 Pregnancy and lactation

VISKEN is contra-indicated in pregnancy and passes in small quantities into breast milk. Breastfeeding is therefore not recommended following administration.

4.7 Effects on ability to drive and use machines

Because dizziness or fatigue may occur during the initial phase of treatment with anti-hypertensive drugs, patients driving vehicles or operating machinery should exercise caution until their individual response treatment has been determined.

4.8 Undesirable effects

Bradycardia, a slowed AV-conduction or increase of an existing AV-block, hypotension, heart failure, cold and cyanotic extremities, Raynaud's phenomenon, increase of an existing intermittent claudication, fatigue, headaches, impaired vision, hallucinations, psychoses, confusion, impotence, dizziness, sleep disturbances, depression, nightmares, gastro-intestinal problems, nausea, vomiting, diarrhoea, nervousness, somnolence, paresthesia, edema, transaminases increase, muscular weakness, myalgia, arthralgia, palpitations, syncope, bleeding disturbances, dyspnea, erythema, hypo/hyperglycemia in non-diabetics, bronchospasm in patients with bronchial asthma or a history of asthmatic complaints, disorder of the skin, especially rash, dry eyes, worsening of psoriasis, thrombocytopenia, agranulocytosis, blood alkaline phosphatase increase and blood lactate dehydrogenase. Beta-blockers may mask the symptoms of thyrotoxicosis or hypoglycaemia. An increase in ANA (anti nuclear antibodies) has been seen; its clinical relevance is not clear.

4.9 Overdose

Potential symptoms include hypotension, atrioventricular block, bradycardia leading to cardiac arrest, cardiac failure, cardiogenic shock, tachycardia, hypertension, CNS symptoms, respiratory depression (especially with children and adolescents), bronchospasms, vomiting, impairment of consciousness and eventually generalized cramps can also occur.
Treat by elimination of any unabsorbed drug and general supportive measures. Marked bradycardia as a result of overdosage or idiosyncracy should be treated with atropine sulphate, 1 to 2mg intravenously. If necessary, isoprenaline hydrochloride can be administered by a slow intravenous injection and under constant supervision beginning with 25 micrograms (5mcg/min) until the desired effect is achieved. A cardiac pacemaker may be required; iv glucagon (5 to 10mg) has been reported to overcome some of the features of serious overdosage and may be useful.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

VISKEN is a specific ß-adrenoceptor blocking agent with low cardiodepressant activity at therapeutic doses. Its ß-blocking activity prevents excessive sympathetic drive to the heart, resulting in a fall in heart rate and a decrease in cardiac work and myocardial oxygen consumption. VISKEN possesses some intrinsic sympathomimetic activity even at low dosage, which may prevent reduction of resting sympathetic tone to an undesirably low level and minimise myocardial depression.

5.2 Pharmacokinetic properties

The rapid nearly complete absorption (>95%) and the negligible hepatic first pass effect (13%) of VISKEN result in a high bioavailability (87%). Maximum plasma concentration is reached within one hour after oral administration. VISKEN has a plasma protein binding of 40%, a volume of distribution of 2-3l/kg and a total clearance of 500ml/min. The elimination half-life of VISKEN is 3-4 hours; 30-40% is excreted unchanged in the urine, while 60-70% is excreted via kidney and liver as inactive metabolites. VISKEN crosses the placental barrier and passes in small quantities into breast milk.

5.3 Preclinical safety data

None.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cellulose, microcrystalline
Maize starch
Magnesium stearate
Silica, colloidal anhydrous

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

5 years.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Clear PVC/PVDC blister packs containing 50, 56 or 100 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Novartis Pharmaceuticals UK Limited.
Frimley Business Park,
Frimley,
Camberley,
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United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA 0013/001/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 17th January 1975

Date of last renewal: 30th September 2004

10 DATE OF REVISION OF THE TEXT

February 2009