SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Veramil
Verapamil Tablets 40 mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Verapamil Hydrochloride BP 40 mg

3 PHARMACEUTICAL FORM

Film-coated tablet

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

1. The prophylaxis and treatment of angina pectoris.

2. Prophylaxis and treatment of supraventricular paroxysmal tachycardia; atrial fibrillation and premature supraventricular contractions; atrial fibrillation and flutter and supraventricular paroxysmal tachycardia of the reciprocating type, associated with the Wolff-Parkinson-White Syndrome.

3. Treatment either alone or in conjunction with other anti-hypertensive therapy of mild to moderate hypertension (including renal hypertension).

4.2 Posology and method of administration

Angina:

Adults: 120 mg t.d.s. is recommended. 80 mg t.d.s. can be completely satisfactory in some patients with angina of effort. Less than 120 mg t.d.s. is not likely to be effective in angina at rest and variant angina.

Children: Not applicable.

Elderly: As for adults, unless liver or renal function is impaired.

Supraventricular paroxysmal tachycardia:

Adults: 40-120 t.d.s. according to the severity of the condition.

Children: Up to 2 years: 20 mg 2-3 t.d.s.

2 years and above: 40-120 mg 2-3 t.d.s. according to age and effect.

Elderly: It is recommended to commence with lowest dose and adjust as required.

Hypertension:

Adults: The usual dose range is 80-160 mg t.d.s. The dose should be increased from 80 mg t.d.s. at weekly intervals according to response, either alone or in conjunction with other antihypertensive therapy. A further reduction in blood pressure may be obtained by combining VERAMIL with other antihypertensive agents, e.g. thiazide diuretics.

Children: Up to 10 mg per kilo bodyweight per day in divided doses, according to severity of disease.

Elderly: It is recommended to commence with the lowest dose and adjust as required.

Route of administration: Oral

4.3 Contraindications

Sick sinus syndrome, second or third degree atrioventricular block, cardiogenic shock, acute myocardial infarction complicated by bradycardia, marked hypotension or left ventricular failure, sino-atrial block, history of heart failure, bradycardia of less than 50 beats/minute or hypotension of less than 90mmHg systolic.

Atrial flutter or fibrillation complicating Wolff-Parkinson-White syndrome.

Porphyria.

Concomitant ingestion of grapefruit juice.

4.4 Special warnings and precautions for use

Care should be exercised when beta-blockers are administered either concurrently or closely together because the effects of beta-blockers and VERAMIL may be additive with respect to both contraction and conduction. This is particularly important when either drug is administered intravenously.

VERAMIL should be used with caution in patients with first-degree atrioventricular block because impulse conduction may be affected.

Left ventricular contractility may be affected by VERAMIL because of its mode of action; cardiac failure may therefore be precipitated or, if it already exists, may be aggravated by VERAMIL.

It is therefore important that VERAMIL should only be administered after appropriate

therapy for cardiac failure has been instituted, e.g. digoxin etc. Patients with impaired liver function exhibit reduced drug metabolism and therefore careful attention should be paid to dosage in these patients.

The disposition of verapamil in patients with renal impairment has not been fully

established and therefore careful patient monitoring is recommended. Verapamil is not

removed during dialysis.

VERAMIL should not be used in children with arrhythmias without specialist advice; some supraventricular arrhythmias in childhood can be accelerated by verapamil with dangerous consequences.

Patients starting therapy with simvastatin should be advised of the risk of myopathy and told to report promptly unexplained muscle pain, tenderness or weakness. A CPK level above 10x ULN in a patient with unexplained muscle symptoms indicates myopathy. Simvastatin therapy should be discontinued if myopathy is diagnosed or suspected. Periodic CPK determinations may be considered (see section 4.5 'Interactions with other Medicaments and forms of Interaction').

Patients with rare hereditary problems of galactose intolerance, Lapp lactase deficiency

or glucose/galactose malabsorbtion should not take Veramil.

4.5 Interaction with other medicinal products and other forms of interaction

VERAMIL increases the serum concentration of digoxin with increased risk AV block and bradycardia; the awareness of the possibility of digitalis toxicity should also be borne in mind.

Verapamil also increases the plasma concentration of imipramine and possibly other tricyclics, ciclosporin, theophylline and drugs under CYP-450 system (e.g. buspirone, dutasteride, eplerenone, atazanavir, ritonavir, sirolimus simvastatin).

There is an increased risk of myopathy when verapamil is given with simvastatin (see section 4.4 'Special Warnings and Precautions for Use').

Verapamil inhibits the metabolism of midazolam; increased plasma-midazolam increases sedation.

The effects of carbamazepine and suxamethonium are enhanced by verapamil.

Verapamil enhances the effect of non-depolarising muscle relaxants (e.g. atracurium, pancuronium) possibly causing hypotension, myocardial depression and hyperkalaemia.

Concomitant use of verapamil and intravenous dantrolene may cause hypotension, myocardial depression and hyperkalaemia.

Grapefruit juice - an increase in verapamil serum level has been reported.

The effects of verapamil may be additive to other drugs which can produce a hypotensive effect. Examples of these are alcohol, aldesleukin, alprostadil, and anaesthetics with risk of AV delay, antihypertensives, diuretics, antipsychotics, anxiolytics & hypnotics, baclofen, isoflurane, levodopa, MAOIs, nitrates, nitroprusside and tizanidine.

Hypotensive effect of calcium-channel blockers e.g. verapamil is antagonised with concomitant use of NSAIDs, corticosteroids or oestrogens.

Concomitant use of beta-blockers and verapamil may cause severe hypotension and even heart failure and should only be given together if myocardial function is well preserved.

Enhanced hypotensive effect has been reported when calcium channel blockers are given with alpha-blockers. There is also an increased risk of first-dose hypotension with postsynaptic alpha-blockers such as prazosin.

Cimetidine may inhibit metabolism of verapamil causing increased verapamil-plasma concentrations.

Amiodarone-induced risk of bradycardia, AV block and myocardial depression is increased by verapamil.

There is possibly increased risk of bradycardia when calcium-channel blockers are given with mefloquine.

Concomitant use of verapamil with disopyramide and flecainide increases risk of myocardial depression and asystole.

Verapamil may raise the plasma concentration of quinidine resulting in extreme hypotension.

Rifampicin increases the metabolism of verapamil thereby significantly reducing its plasma concentration.

The effect of verapamil is also reduced by phenobarbitol, primidone and phenytoin.

Neurotoxicity may occur without increased plasma-lithium concentrations in patients given verapamil.

4.6 Pregnancy and lactation

Verapamil is not recommended for use during pregnancy unless the benefits of the drug outweigh the possible hazards to the foetus.

4.7 Effects on ability to drive and use machines

Depending on individual susceptibility, the patient's ability to drive a vehicle or operate machinery may be impaired, particularly in the initial stages of treatment, or when changing over from another drug. Verapamil has been shown to increase the blood levels of alcohol and slow its elimination. Therefore, the effects of alcohol may be exaggerated.

4.8 Undesirable effects

Administration of Verapamil is commonly associated with constipation. Occasionally the following side- effects may be experienced: Nausea and vomiting, flushing, headache, dizziness, fatigue ankle oedema, myalgia, arthralgia, paraesthesia, and erythromelalgia; increased prolactin concentration. On rare occasions gynaecomastia and gingival hyperplasia may occur after long-term treatment, after intravenous administration of high doses, hypotension, heart failure, bradycardia, heart block, and asystole.

Sensitivity or allergy to Verapamil is rare. Symptoms of allergy are erythema, pruritis, urticaria, angioedema and Stevens-Johnson syndrome.

4.9 Overdose

The classical measures for cardiovascular side effects should be instituted immediately. Cardiac arrest should be treated by heart massage, mechanical respiration and the necessary intensive are appropriate to the condition should be instituted.

In the case of hypotension, dopamine, noradrenalin or dobutamine may be used together with appropriate positioning of the patient. Likewise, in myocardial insufficiency treatment should be either dopamine, dobutamine, cardiac glucosides or 10-20 ml of a 10% solution of calcium gluconate. Second or third degree AV block should be treated with atropine or isoprenaline and if necessary a pace maker should be used.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Verapamil is a Class 4 anti-arrhythmic agent which acts on supraventricular arrhythmias through interfering with calcium conductants.

5.2 Pharmacokinetic properties

Verapamil is almost completely absorbed from the gastro-intestinal tract but is subject to very considerable first-pass metabolism in the liver. The plasma half-life is about 7 hours following oral administration and that of its active metabolite which is norverapamil is about nine hours.

Verapamil acts within minutes of intravenous administration but its effects may only last for about half-an-hour. It may require two hours to act after oral administration with peak effect after five hours.

Verapamil is extensively bound to plasma proteins. The drug is mainly excreted by the kidneys in the form of its metabolites, but some is also excreted in the bile and in the faeces.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize Starch
Lactose
Gelatin
Colloidal Anhydrous Silica
Talc
Magnesium Stearate
Opaspray K-IF-3048
Hydroxypropylmethylcellulose 2190
Ethylcellulose
Diethylphthalate

6.2 Incompatibilities

None known.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store below 25 deg C in a dry place in well closed containers.

6.5 Nature and contents of container

High density polystyrene with polythene lids and/or polypropylene containers with polypropylene or polythene lids and polyurethane/polythene inserts.

Pack sizes: 100 and 500

6.6 Special precautions for disposal

Not applicable.

7 MARKETING AUTHORISATION HOLDER

Chelonia Healthcare Limited
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