SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Timolol maleate 10 mg tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains timolol maleate 10 mg.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet.

White, round, flat, with a score mark on one side and engraved with “V Bet” on the other side.

The tablet can be divided into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Timolol maleate 10 mg tablets are indicated in angina pectoris due to ischaemic heart disease, for the treatment of hypertension and to reduce mortality and reinfarction in patients surviving acute myocardial infarction. Timolol maleate 10 mg tablets are also indicated in the prophylactic treatment of migraine in order to reduce the number of attacks.

4.2 Posology and method of administration

Posology

The lowest possible dosage should be given first in order to be able to identify cardiac decompensation or bronchial phenomena at an early stage; this is especially important in the elderly. Subsequent increases in dose should take place slowly, (e.g. once a week) under control or on the basis of clinical effect.

For angina:

The recommended dose range is 5 - 30 mg twice daily. The initial dose should be 5 mg twice daily, increasing the daily dose by 10 mg not more frequently than every 3 to 4 days to achieve optimum results.

Hypertension:

The recommended dose range is 10 - 60 mg daily. Most hypertensive patients will be controlled by 10 - 30 mg timolol which can be administered once daily or in two divided doses if preferred. Doses in excess of 30 mg daily should be given in two equally divided doses. The dose of Timolol maleate 10 mg tablets may need adjustment when used in conjunction with other antihypertensive drugs.

After myocardial infarction:

Start with 5 mg (½ tablet) twice daily for two days. If there are no adverse effects, increase dosage to 10 mg twice daily and maintain at this dose.

For the prophylactic treatment of migraine:

10 to 20 mg once daily or in two divided doses.

Dosage in the elderly:

Initiate treatment with lowest adult dose and thereafter adjust according to response.

Paediatric population:

The safety and efficacy of Timolol maleate 10 mg tablets in children has not been established. No data are available.

Method of administration

For oral use

4.3 Contraindications

Hypersensitivity to timolol or to any of the excipients.

Heart failure, unless adequately controlled, sinus bradycardia (<45 - 50 bpm) or heart block. Cardiogenic shock. History of bronchospasm and bronchial asthma. Chronic

obstructive pulmonary disease. Patients receiving monoamine oxidase inhibitors. Pregnancy. Sick sinus syndrome (including sino-atrial block), severe peripheral vascular disease or Raynaud's disease. Prinzmetal's angina. Untreated phaeochromocytoma. Metabolic acidosis. Hypotension. Severe peripheral circulatory disturbances.

4.4 Special warnings and precautions for use

Cardiovascular

Although Timolol maleate 10 mg tablets have no direct myocardial depressant activity, the continued depression of sympathetic drive through beta blockade may lead to cardiac failure in patients with latent cardiac insufficiency. All patients should be observed for evidence of cardiac failure and, if it occurs, then treatment with beta blockers should be gradually withdrawn. If it is not possible to withdraw beta blocker treatment, then digitalisation and diuretic therapy should be considered.

In patients with cardiovascular diseases (e.g. coronary heart disease, Prinzmetal’s angina and cardiac failure) and hypotension, therapy with beta-blockers should be critically assessed and the therapy with other active substances should be considered. Patients with cardiovascular diseases should be watched for signs of deterioration of these diseases and of adverse reactions.

Beta blockers should not be used in patients with untreated congestive heart failure. This condition should first be stabilised.

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, replacement therapy should be initiated at the same time, to prevent exacerbation of angina pectoris.

Beta blockers 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.

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.

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

Respiratory disorders:

Respiratory reactions, including death due to bronchospasm in patients with asthma have been reported following administration of some beta-blockers.

Timolol should be used with caution, in patients with mild/moderate chronic obstructive pulmonary disease (COPD) and only if the potential benefit outweighs the potential risk.

Metabolic/endocrine

Timolol maleate 10 mg tablets should be administered with caution to patients with impaired renal function or impaired hepatic function. Patients with liver or kidney insufficiency may need a lower dosage.

Timolol maleate 10 mg tablets may be used safely in diabetes. It may, however, interfere with the cardiovascular and possibly the metabolic responses to hypoglycaemia and, therefore, should be used with caution in diabetic patients treated with insulin or oral hypoglycaemic agents as well as patients subject to spontaneous hypoglycaemia. Beta-blockers could further increase the risk of severe hypoglycaemia when used concurrently with sulfonylureas. Diabetic patients should be advised to carefully monitor blood glucose levels. (see Section 4.5).

Beta-blockers should be administered with caution in patients subject to spontaneous hypoglycaemia or to patients with labile diabetes, as beta blockers may mask the symptoms of thyrotoxicosis or hypoglycaemia. Beta-blockers may also mask the signs of hyperthyroidism.

Corneal diseases

Beta-blockers may induce dryness of eyes. Patients with corneal diseases should be treated with caution.

Other beta-blocking agents

The known effects of systemic beta-blockade may be potentiated when timolol maleate is given to the patients already receiving a systemic betablocking agent. The response of these patients should be closely observed. The use of two topical beta-adrenergic blocking agents is not recommended (see section 4.5).

Anaphylactic reactions

While taking beta-blockers, patients with history of atopy or a history of severe anaphylactic reaction to a variety of allergens may be more reactive to repeated challenge with such allergens and unresponsive to the usual dose of adrenaline used to treat anaphylactic reactions.

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

Surgical anaesthesia

Beta-blockers may block systemic β-agonist effects e.g. of adrenaline. The anaesthesiologist should be informed when the patient is receiving timolol maleate.

Other warnings

Patients with a history of psoriasis should take beta blockers only after careful consideration.

There have been reports of skin rashes and/or dry eyes associated with the use of beta-adrenergic blocking drugs. The reported incidence is rare 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. Cessation of therapy with the beta blocker should be gradual although withdrawal symptoms with timolol are infrequent.

The following statement will appear on the label of this product: `Do not take this medicine if you have a history of wheezing or asthma'.

4.5 Interaction with other medicinal products and other forms of interaction

The depressant effect of beta blocking drugs on myocardial contractility and on intracardiac conduction may be increased by concomitant use with other drugs having similar effects. Serious effects have been reported with verapamil, disopyramide, lignocaine and tocainide and may be anticipated with diltiazem, quinidine, amiodarone and any of the class 1 antiarrhythmic agents. Special care is necessary when any of these agents are given intravenously in patients who are beta blocked.

Concurrent administration of digitalis glycosides may increase the atrio-ventricular conduction time.

Beta blockers increase the risk of `rebound hypertension' when taken with clonidine. When clonidine is used in conjunction with non selective beta blockers such as timolol, treatment with clonidine should be continued for some time after treatment with the beta blocker has been discontinued.

Concomitant administration of tricyclic antidepressants, barbiturates and phenothiazines, dihydropyridine derivatives such as nifedipine or antihypertensive agents may increase the blood pressure lowering effect.

Beta blockers may intensify the blood sugar lowering effect of insulin and oral antidiabetic drugs. The concomitant use of beta-blockers with sulfonylureas could increase the risk of severe hypoglycaemia. (see Section 4.4).

CYP2D6 inhibitors (e.g. quinidine, SSRIs)

Potentiated systemic beta-blockade (e.g. decreased heart rate, depression) has been reported during combined treatment with CYP2D6 inhibitors (e.g. quinidine, fluoxetine, paroxetine) and timolol.

Anaesthesia

The anaesthesiologist should be informed when the patient is receiving a beta blocking agent. Concomitant use of beta blockers and anaesthetics may attenuate reflex tachycardia and increase the risk of hypotension.

The withdrawal of beta blocking drugs prior to surgery is not necessary in the majority of patients. If beta blockade is interrupted in preparation for surgery, therapy should be discontinued at least 24 hours beforehand.

Continuation of beta blockade reduces the risk of arrhythmias during induction and intubation, however the risk of hypertension may be increased. Anaesthetic agents such as ether, cyclopropane and trichloroethylene should not be used whereas halothane, isoflurane, nitrous oxide, intravenous induction agents, muscle relaxants, narcotic analgesics and local anaesthetic agents are all compatible with beta adrenergic blockade. Local anaesthetics with added vasoconstrictors, e.g. adrenaline, should be avoided. The patient may be protected against vagal reactions by intravenous administration of atropine.

The bioavailability of Timolol maleate 10 mg tablets will be increased by co-administration with cimetidine or hydralazine and reduced with rifampicin.

Timolol maleate 10 mg tablets may be prescribed with vasodilation, but increased gastro-intestinal blood flow may affect absorption and metabolism of timolol.

Alcohol induces increased plasma levels of hepatically metabolised beta blockers such as timolol.

Some prostaglandin synthetase inhibiting drugs have been shown to impair the antihypertensive effect of beta blocking drugs.

The effect of sympathomimetic agents, e.g. isoprenaline, salbutamol, will be reduced by concomitant use of beta blockers. In addition, sympathomimetics may counteract the effect of beta blocking agents.

The adverse vasoconstrictor effects of ergot preparations may be potentiated during the treatment of migraine with beta blocking drugs.

Caution is recommended when Timolol maleate 10 mg tablets are administered to patients on catecholamine depleting drugs such as reserpine or guanethidine.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no adequate data for the use of timolol maleate in pregnant women. Timolol maleate should not be used during pregnancy unless clearly necessary.

Epidemiological studies have not revealed malformative effects but show a risk for intra uterine growth retardation when beta-blockers are administered by the oral route. In addition, signs and symptoms of beta-blockade (e.g. bradycardia, hypotension, respiratory distress and hypoglycaemia) have been observed in the neonate when beta-blockers have been administered until delivery. If Timolol is administered until delivery, the neonate should be carefully monitored during the first days of life.

Breast-feeding

Timolol maleate appears in breast milk (milk: plasma ratio 0.8). Breast feeding is therefore not recommended during administration of this product.

4.7 Effects on ability to drive and use machines

No studies on the effect of this medicinal product on the ability to drive have been conducted.
While driving vehicles or operating different machines, it should be taken into account that occasionally visual disturbances may occur including refractive changes, diplopia, ptosis, frequent episodes of mild and transient blurred vision and occasional episodes of dizziness or fatigue.

4.8 Undesirable effects

System Organ Class	Rare ≥ 1/10,000, < 1/1000	Frequency Not Known
Immune system disorders		Systemic lupus erythematosus; systemic allergic reactions including urticaria; localized and generalized rash; pruritus; anaphylactic reaction
Metabolism and nutrition disorders		Hypoglycaemia.
Psychiatric disorders		Psychotic disorder; hallucination; depression; disorientation; confusional state; nightmare; insomnia; sleep disorder; memory loss
Nervous system disorders		Paraesthesia; dizziness; headache; somnolence; syncope, cerebrovascular accident; cerebral ischaemia; increases in signs and symptoms of myasthenia gravis
Eye disorders	Dry eye	Visual impairment; signs and symptoms of ocular irritation (e.g. burning stinging; itching; tearing, redness); blepharitis, keratitis; blurred vision; decreased corneal sensitivity; corneal erosion, ptosis; diplopia
Ear and labyrinth disorders		Vertigo
Cardiac disorders		Atrioventricular block; bradycardia; cardiac failure; cyanosis; chest pain; palpitations; oedema; arrhythmia; congestive heart failure; cardiac arrest
Vascular disorders		Hypotension; Raynaud's phenomenon; increase of an existing intermittent claudication; peripheral coldness
Respiratory, thoracic and mediastinal disorders		Dyspnoea; bronchospasm (in patients with bronchial asthma or a history of asthmatic complaints); cough
Gastrointestinal disorders	Retroperitoneal fibrosis	Dyspepsia; vomiting; nausea; diarrhoea; dysgeusia; dry mouth; abdominal pain
Skin and subcutaneous tissue disorders	Dermatitis allergic; dermatitis psoriasiform; rash erythematous	Alopecia; angioedema; psoriaform rash or exacerbation of psoriasis,

		skin rash
Musculoskeletal and connective tissue disorders	Arthralgia	Myalgia
Reproductive system and breast disorders		Sexual dysfunction (such as impotence); decreased libido
General disorders and administration site conditions		Fatigue; weakness
Investigations		Antinuclear antibody increased

Reporting of suspected adverse reactions
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 via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Poisoning due to an overdose of Timolol maleate 10 mg tablets may lead to severe hypotension, sinus bradycardia, atrioventricular block, heart failure, cardiogenic shock, cardiac arrest, bronchospasm, impairment of consciousness, coma, occasionally hyperkalaemia. The first manifestations usually appear 20 minutes to 2 hours after drug ingestion.

Treatment should include close monitoring of cardiovascular, respiratory and renal function and blood glucose and electrolytes. Further absorption may be prevented by induction of vomiting, gastric lavage or administration of activated charcoal if ingestion is recent. Studies have shown that timolol maleate cannot be removed by haemodialysis.

Cardiovascular complications, such as hypotension, should should be treated symptomatically, which may require the use of sympathomimetic agents, (e.g. noradrenaline, metariminol), atropine or inotropic agents, (e.g. dopamine, dobutamine). Temporary pacing may be required for AV block. Isoprenaline hydrochloride or a pacemaker should be used. Glucagon can reverse the effects of excessive beta blockade, given in a dose of 1-10 mg intravenously.

Symptomatic bradycardia should be treated with atropine sulphate, 0.25 to 2 mg intravenously, should be used to induce vagal blockade. If bradycardia persists, intravenous isoprenaline hydrochloride should be administered cautiously. In refractory cases, the use of a cardiac pacemaker should be considered.

Acute cardiac failure should be treated with conventional therapy with digitalis, diuretics and oxygen should be instituted immediately. In refractory cases, the use of intravenous aminophylline is recommended. This may be followed, if necessary, by glucagon, which has been found useful.

Intravenous B2-stimulants, e.g. terbutaline, may be required to relieve bronchospasm. Isoprenaline hydrochloride can also be given. Concomitant therapy with aminophylline may be considered.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Cardiovascular system, Beta blocking agents, non-selective, timolol , ATC code: C07AA06

Timolol maleate 10 mg tablets are a beta adrenergic receptor blocking agent. The competitive antagonism of adrenergic transmitters at beta receptors blocks beta sympathomimetic activity particularly in the heart, the bronchi and blood vessels.

Timolol maleate 10 mg tablets have been shown to be a highly specific beta adrenergic blocking drug and it does not block the chronotropic or inotropic effects of calcium, glucagon, theophylline or digitalis. It does not have significant local anaesthetic or direct myocardial depressant activity or any significant intrinsic beta adrenergic stimulant effect.

Timolol maleate 10 mg tablets reduce heart rate and force of myocardial contraction and, therefore, myocardial oxygen consumption. Modification of the cardiovascular responses to stress or exercise is therapeutically useful in the treatment of angina pectoris.

The beta blocking action of Timolol maleate 10 mg tablets is also of therapeutic value in hypertension, although the exact mechanism of action is unclear.

5.2 Pharmacokinetic properties

Timolol maleate is rapidly and nearly completely absorbed following oral administration. Beta blocking activity is apparent within 30 minutes of administration and the duration of action, though dependent on dose, has been shown to last for up to 24 hours. Dose proportionality has been established. Plasma half-life is approximately 2.7-5.0 hours with a peak plasma concentration occurring approximately 2 hours post dose. Timolol undergoes significant hepatic metabolism, but "first pass metabolism" is low.
5% of timolol is excreted unchanged by the kidneys.
These pharmacokinetic parameters are unchanged in hypertensive patients and following multiple dosages.
The rate of timolol metabolism varies between individuals. Poor metabolisers (approximately 10%) show higher plasma levels and slower elimination of timolol than extensive metabolisers. Within individuals, however, plasma concentrations and half-life are reproducible. As the therapeutic response and some adverse effects are related to plasma concentrations of timolol, poor metabolisers may require lower than normal doses.

5.3 Preclinical safety data

Timolol has low toxicity and mutagenicity and reproduction and fertility studies have not demonstrated evidence of changes relevant to the dosage used in man.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose
Pregelatinised starch
Magnesium stearate.

6.2 Incompatibilities

None known.

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

Aluminium blister packs or amber glass bottles with high density polyethylene screw cap and desiccant, containing 30 or 100 tablets.
Not all pack sizes may be marketed

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Generics (U.K.) Limited T/A Viatris,
Station Close,
Potters Bar,
EN6 1TL,
United Kingdom.

8. MARKETING AUTHORISATION NUMBER(S)

PL 04569/1773

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

13/02/2025

10 DATE OF REVISION OF THE TEXT

08/05/2026