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TRITACE® 2.5 Tablets
TRITACE® 5 Tablets
Ramipril

SANOFI

Composition
Each tablet Tritace® 2.5 contains, as active ingredient, 2.5 mg ramipril.
Each tablet Tritace® 5 contains, as active ingredient, 5 mg ramipril.
Excipients: Methylhydroxypropylcellulose, pregelatinized maize starch, microcrystalline cellulose, sodium stearyl fumarate, yellow ferric oxide (Tritace 2.5 only), red ferric oxide (Tritace 5 only).
Not all presentation is available in all countries.

Properties
Ramiprilat, the active metabolite of ramipril, is a potent and long-acting angiotensin converting enzyme (ACE) inhibitor.
Administration of Tritace results in a vasodilatation and, especially in hypertensive patients, in a reduction of blood pressure.
The blood-pressure-lowering effect of a single dose occurs within 1 – 2 hours after intake, reaching its peak within 3 - 6 hours, and usually lasts 24 hours.
Tritace is also effective in the treatment of congestive heart failure.
Further, in patients demonstrating clinical signs of congestive heart failure after an acute myocardial infarction, Tritace has been shown to decrease the mortality risk (including the risks of sudden death, of progression to severe/resistant heart failure and of failure-related hospitalisation).
Tritace, when administered on a preventive basis, significantly reduces the incidence of myocardial infarction, stroke or cardiovascular deaths in patients with an increased cardiovascular risk attributable to vascular diseases (such as manifest coronary heart disease, or a history of stroke or of peripheral vascular disease) or to diabetes mellitus with at least one additional risk factor (microalbuminuria, hypertension, elevated total cholesterol levels, low high-density lipoprotein cholesterol levels, smoking). Moreover, it reduces total mortality as well as the need for revascularisations, and delays the start and the progression of congestive heart failure. In diabetic and non-diabetic patients, it significantly reduces the occurrence of microalbuminuria and diminishes the risk of development of nephropathy.
These effects occur both in hypertensive and in normotensive patients.
In patients with non-diabetic nephropathy, Tritace decreased the rate of progression of renal insufficiency and of the development of end-stage renal failure and therewith the need for dialysis or renal transplantation.

Non-diabetic or diabetic nephropathy

Non-diabetic nephropathy:

In overt, mostly non-diabetic (13% diabetic subjects included) nephropathy, the pivotal REIN Study (Ramipril Efficacy In Nephropathy) (N=166) has demonstrated statistically significant decreases in the rate of progression of renal insufficiency and the development of end stage renal failure. The populations studied in this placebo controlled trial included normotensive patients, patients with uncontrolled mild to moderate hypertension (DBP>90mm Hg) and patients with controlled mild to moderate hypertension. For those with uncontrolled hypertension, the target blood pressure was pre-defined (DBP <90mm Hg) and, if this was not achieved with study medication (Tritace or placebo) alone, additional antihypertensives were added. The improvements observed are more dramatic with poorer (elevated) baseline proteinuria (≥3g/24 hours) but are also observed at lower baseline proteinuria (>1 and <3g/24 hours). At this level of proteinuria, subgroup analysis in the REIN study indicated that only patients with worse (lower) GFR (<45mL/Min/1.73m^2) received statistically significant benefits in end stage renal failure. The results of the REIN study are summarized below:

Patient Proteinuria Baseline (N)	Endpoint		Ramipril + conventional therapy	Placebo + conventional therapy	P-value
Proteinuria 1-3g/24hr (N=186)	Secondary endpoint: ESRF (end-stage renal failure) overall and by baseline GFR	Overall	9 (9.1%)	18 (20.7%)	0.01
		>45 mL/min/1.73m^2	2 (3.3%)	1 (2.4%)	Not reported
		≤45 mL/min/1.73m^2	7 (17.9%)	17 (37%)	0.037
	Secondary endpoint: Progression to proteinuria ≥ 3g/day		15 (15.2%)	27 (31%)	0.005

	Primary endpoint: Monthly reduction in GFR (mL/min/1.73m^2)		0.26	0.29	0.59 (comparison)
Proteinuria ≥3g/24hr (N=166)	Primary endpoint: Change in monthly GFR (mL/min/1.73m^2 overall and by baseline proteinuria	Overall	-0.54	-0.88	0.038
		3 to <4.5 g/24hr	-0.53	-0.70	Not reported
		4.5 to <7 g/24hr	-0.47	-0.99	Not reported
		>7 g/24hr	-0.64	-1.44	Not reported
	Secondary endpoint: ESRF or DOC (end stage renal Failure or doubling of creatinine)		18 (23.1%)	40 (45.5%)	0.02 (difference)

The improvement in these key endpoints was observed to increase with time, to be maintained long term and to apply to both hypertensive and non-hypertensive patients. A delay of approximately three months was seen prior to detection of the beneficial effects of ramipril, suggesting the value of early treatment.

Diabetic nephropathy:

Studies in over diabetic nephropathy, particularly the ACE II (angiotensin converting enzyme II study) have demonstrated that both low and high dose Tritace therapy can retard proteinuria and maintain renal health (maintain GFR, creatinine levels and creatinine clearance). The ACE II study, which was an open label follow up to the ACE I study with captopril, investigated the effect of intensive (target MAP ≤92mm Hg ; N=63) versus moderate (target MAP ≥100 to ≤107 mm Hg ; N=66) blood pressure control with Tritace on renal function. While the study observed no significant differences between these moderate and intensive BP control groups, there was no observed deterioration of renal function in this high risk population throughout the two year study (no statistically significant change in serum creatinine or creatinine and a significant improvement in proteinuria). The trial therefore demonstrates the benefit of tRitace in maintaining the renal health of diabetic patients. These results are presented below:

Characteristic (N = 129)	Change from baseline	P-value
Primary endpoint: Creatinine clearance		
24 hr Creatinine clearance (mL/min)	0.14	0.09
Secondary endpoint: Serum creatinine (mg/dL)	0.06	0.43
Secondary endpoint: Proteinuiria	-0.19	0.02

Indications

- Hypertension
- Congestive heart failure
- Treatment of patients who - within the first few days after an acute myocardial infarction - have demonstrated clinical signs of congestive heart failure
- For reducing the risk of myocardial infarction, stroke, cardiovascular death or need for revascularisation procedures in patients of 55 years or more who have clinical evidence of cardiovascular disease (previous MI, unstable angina or multivessel CABG or multivessel PTCA), stroke or peripheral vascular disease.
- For reducing the risk of myocardial infarction, stroke, cardiovascular death or need for revascularisation procedures in diabetic patients of 55 years or more who have one or more of the following clinical findings: hypertension (systolic blood pressure > 160mmHg or diastolic blood pressure > 90mmHg); high total cholesterol (>5.2 mmol/L); low HDL (<0.9 mmol/L); current smoker; known microalbuminuria; clinical evidence of previous vascular disease.
- Prevention of progressive renal failure in patients with persistent proteinuria in excess of 1g/day

Contraindications

Tritace must not be used in patients with
- hypersensitivity to ramipril, any other ACE inhibitor, or to any of the excipients (see “Composition”)
- a history of angioedema (risk of precipitating angioedema; see also “Adverse reactions”)
- concomitantly with sacubitril/valsartan therapy (see “Interaction). Do not initiate Tritace until sacubitril/valsartan is eliminated from the body. In case of switch from Tritace to sacubitril/valsartan, do not start sacubitril/valsartan until Tritace is eliminated from the body.
- blood-flow-reducing narrowing (haemodynamically relevant stenosis) of the renal artery, bilateral or unilateral in the single kidney (risk of fall in blood pressure and renal failure)
- low blood pressure or labile circulatory condition (risk of fall in blood pressure and renal failure).

Since severe rapid-onset and allergy-like (anaphylactoid) hypersensitivity reactions may occur, treatment with ACE inhibitors in conjunction with extracorporeal treatments leading to contact of blood with negatively charged surfaces must be avoided.
The latter include dialysis or haemofiltration with certain high-flux membranes (e.g. polyacrylonitril membranes) and low-density lipoprotein apheresis with dextran sulfate.

- concomitant use of aliskiren-containing medicines in patients with diabetes or with moderate to severe renal impairment (creatinine clearance < 60 ml/min)
- during pregnancy
- with angiotensin II receptor blockers in patients with diabetic nephropathy

Pregnancy

Tritace must not be taken during pregnancy. Therefore, pregnancy must be excluded before starting treatment. Pregnancy must be avoided where treatment with ACE inhibitors is indispensable.
If a pregnancy is planned, treatment with ACE inhibitors must be discontinued, i.e., replaced by another form of treatment.
If pregnancy occurs during treatment, medication with Tritace must be substituted as soon as possible with a treatment regimen which excludes ACE inhibitors. Otherwise there is a risk of harm to the fetus.

Lactation

Because insufficient information is available regarding the use of ramipril during breastfeeding, ramipril is not recommended and alternative treatment with better established safety profiles during breastfeeding are preferable, especially while nursing a newborn or preterm infant.

Special warnings and precautions

Treatment with Tritace requires regular medical supervision.

Dual blockage of the renin-angiotensin-aldosterone system by combining Tritace with angiotensin II receptor blockers or aliskiren is not recommended since there is an increased risk of hypotension, hyperkalemia and changes in renal function compared to monotherapy (see “Interactions”).
If dual blockade therapy is considered absolutely necessary, this should only occur under specialist supervision and subject to frequent close monitoring of renal function, electrolytes and blood pressure.
The use of Tritace in combination with aliskiren is contraindicated in patients with diabetes mellitus or renal impairment (creatinine clearance < 60 ml/min) (see “Contraindications”).
Tritace and angiotensin II receptor blockers should not be used concomitantly in patients with diabetic nephropathy.

Angioedema of the face, extremities, lips, tongue, glottis or larynx, and intestinal angioedema have been reported in patients treated with ACE inhibitors. If angioedema occurs during treatment (see "Adverse Reactions"), Tritace must be discontinued immediately and - if the tongue, glottis or larynx are involved - emergency measures taken. Emergency treatment of life-threatening angioedema includes immediate administration of epinephrine (subcutaneous or slow intravenous injection) accompanied by monitoring of ECG and blood pressure. Hospitalization of the patient is advisable with observation for at least 12 to 24 hours and discharge only upon complete resolution of the symptoms.

Angioedema –Intestinal

Intestinal angioedema has been reported in patients treated with ACE inhibitors. These patients presented with abdominal pain (with or without nausea or vomiting); in some cases facial angioedema also occurred. The intestinal angioedema symptoms resolved after stopping the ACE inhibitor.

Patients with a hyper-stimulated renin angiotensin system must be treated with particular caution. ACE inhibition puts such patients at risk of an acute pronounced fall in blood pressure and deterioration of renal function, especially when an ACE inhibitor or - in combination therapy - a medicine that promotes fluid excretion (diuretic) is given for the first time or for the first time at an increased dose. Therefore, at the start of treatment with Tritace or after the first dose of an additional diuretic, as well as after every first increased dose thereof, blood pressure must be closely monitored until such time as no further acute reduction in blood pressure is expected.
Significant activation of the renin angiotensin system is to be expected for example, in patients:
- with severe, and particularly with malignant hypertension. The initial phase of treatment requires special medical supervision
- with heart failure, particularly if severe or if treated with other potentially blood-pressure-lowering medicines. In severe heart failure, the initial phase of treatment requires special medical supervision
- with blood-flow-reducing (haemodynamically relevant) left-ventricular inflow or outflow impediment (e.g., narrowing of the aortic or mitral valve). The initial phase of treatment requires special medical supervision
- with blood-flow-reducing narrowing (haemodynamically relevant stenosis) of the renal artery. The initial phase of treatment requires special medical supervision. Concomitant treatment with a diuretic may have to be discontinued - pre-treated with diuretics. Where discontinuation or reduction of the dose of the diuretic is not possible, the initial phase of treatment requires special medical supervision - in whom fluid or salt deficiency exist or may develop (as a result of inadequate fluid or salt intake, or as a result of, for example, diarrhoea, vomiting or excessive sweating in cases where salt and fluid replacement is inadequate). Generally, dehydration, reduced blood volume (hypovolaemia), or salt deficiency should be corrected before initiating treatment (in patients with heart failure, however, such corrective action must be carefully weighed against the risk of volume overload).

When such conditions have become clinically relevant, treatment with Tritace must be started or continued only if appropriate steps are taken concurrently to prevent an excessive fall in blood pressure and deterioration of renal function (see also ‘Dosage’).
Also at particular risk from a pronounced fall in blood pressure are, e.g., patients with haemodynamically relevant stenoses of the coronary arteries or of the blood vessels supplying the brain. Such patients as well require special medical supervision in the initial phase of treatment.
In patients with impaired liver function, response to treatment with Tritace may be either increased or reduced.

In addition, in patients with severe liver cirrhosis with oedema and/or ascites, the renin angiotensin system may be significantly activated; therefore, particular caution must be exercised in treating such patients (see also above and under 'Dosage').
Some elderly patients may be particularly responsive to ACE inhibitors.
Renal function should be evaluated at the beginning of treatment (see also "Dosage").
Renal function should be monitored, particularly in the initial weeks of treatment. Particularly careful monitoring is required in patients with heart failure, in patients with renovascular disease (including those with haemodynamically relevant unilateral renal artery stenosis, in whom even a small increase in serum creatinine may be indicative of unilateral loss of renal function), in patients with impairment of renal function, or in kidney transplant patients.
Serum potassium should be monitored regularly. More frequent monitoring of serum potassium is required in patients with impaired renal function.
White blood cell counts should be monitored so that a possible excessive reduction in white blood cells (leucopenia) can be detected. Monitoring should be more frequent in the initial phase of treatment and in patients with impaired renal function, concomitant connective tissue disease (collagen disease such as lupus erythematosus or scleroderma), or in patients treated with other medicines that may alter the blood picture (see "Interactions"). The blood picture must be checked if possible signs of reduced white blood cell or platelet counts occur (see "Adverse reactions").
An increased risk of angioedema is possible with concomitant use of other drugs which may cause angioedema (see "Contraindications" and "Interactions").
Driving
Certain adverse reactions (e.g. some symptoms of a reduction in blood pressure such as light-headedness, dizziness) may impair the ability to concentrate and react, and, therefore, constitute a risk in situations where these abilities are of particular importance (e.g. operating a vehicle or machinery).

Adverse reactions

Adverse reactions frequency is defined using the following convention:
Very common (≥1/10); common (≥1/100) to 1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000), not known (cannot be estimated from the available data).
Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

	Common	*Uncommon*	*Rare*	*Very rare*	*Not known*
Cardiac disorders		*Myocardial ischaemia including angina pectoris or myocardial infarction, tachycardia, arrhythmia, palpitations, oedema peripheral*			
Blood and lymphatic system disorders		*Eosinophilia*	*White blood cell count decreased (including neutropenia or agranulocytosis), red blood cell count decreased, haemoglobin decreased, platelet count decreased*		*Bone marrow failure, pancytopenia, haemolytic anaemia*
Nervous system disorders	*Headache, dizziness (lightheadedness)*	*Vertigo paraesthesia ageusia (loss of taste), dysgeusia (taste disturbances)*	*Tremor, balance disorder*		*Cerebral ischaemia including ischaemic stroke and transient ischaemic attack, psychomotor skills impaired (impaired reactions), burning sensation, parosmia (smell disturbances)*
Eye disorders		*Visual disturbance including blurred vision*	*Conjunctivities*		
Ear and labyrinth disorders			*Hearing impaired, tinnitus*		
Respiratory, thoracic and mediastinal	*Non-productive tickling cough, bronchitis, sinusitis*	*Bronchospasm including asthma aggravated, nasal*			

disorders	*dyspnoea*	*congestion*			
Gastrointestinal disorders	*Gastrointestinal inflammation (inflammatory reactions of the gastrointestinal tract), digestive disturbances, abdominal discomfort, dyspepsia, diarrhoea, nausea, vomiting*	*Fatal pancreatitis (cases of fatal outcome have been very exceptionally reported with ACE inhibitors), pancreatic enzymes increased, small bowel angioedema, abdominal pain upper including gastritis, constipation, dry mouth*	*Glossitis*		*Aphtous stomatitis (inflammatory reactions of the oral cavity)*
Renal and urinary disorders		*Renal impairment including renal failure acute, urine output increased, worsening of a pre-existing proteinuria blood urea increased, blood creatinine increased*			
Skin and subcutaneous tissue disorders	*Rash in particular maculo-papular*	*Angioedema with fatal outcome (maybe/become life threatening, rarely severe course can cause fatal obstruction); pruritus, hyperhidrosis (sweating)*	*Exfoliative dermatitis, urticaria, onycholysis*	*Photosensitivity reaction*	*Toxic epidermal necrolysis, Stevens-Johnson syndrome, erythema multiforme, pemphigus psoriasis aggravated, dermatitis psoriasiform, pemphigoid or lichenoid exanthema or enanthema, alopecia*
Musculoskeletal and connective tissue disorders	*Muscle spasms (muscle cramps), myalgia*	*Arthralgia*			
Endocrine disorders					*Syndrome of inappropriate antidiuretic hormone secretion (SIADH)*
Metabolism and nutrition disorders	*Blood potassium increased*	*Anorexia, decreased appetite*			*Blood sodium decreased*
Vascular disorders	*Hypotension, orthostatic blood pressure decreased (disturbed orthostatic regulation), syncope*	*Flushing*	*Vascular stenosis, hypoperfusion (exacerbation of perfusion disturbances), vasculitis*		*Raynaud's phenomenon*
General disorders and administration site conditions	*Chest pain, fatigue*	*Pyrexia (fever)*	*Asthenia (weakness)*		
Immune system disorders					*Anaphylactic or anaphylactoid reactions (severe anaphylactic and anaphylactoid reactions to insect*

					venoma is increased under ACE inhibition), antinuclear antibody increased
Hepatobiliary disorders		*Hepatic enzymes and/or bilirubin conjugated increased*	*Jaundice cholestatic, hepatocellular damage*		*Acute hepatic failure, cholestatic or cytolytic hepatitis (fatal outcome has been very exceptional)*
Reproductive system and breast disorders		*Transient erectile impotence, libido decreased*			*Gynaecomastia*
Psychiatric disorders		*Depressed mood, anxiety, nervousness, restlessness, sleep disorder including somnolence (drowsiness)*	*Confusional state*		*Disturbance in attention*

Interactions

The concomitant use of ACE inhibitors with sacubitril/valsartan is contraindicated as this increases the risk of angioedema (see ‘‘Contraindications”).

Extracorporeal treatments involving blood contact with negatively charged surfaces carry the risk of severe anaphylactoid reactions (see ‘‘Contraindications”).

The combination of Tritace with aliskiren-containing medicines is contraindicated in patients with diabetes mellitus or moderate renal impairment and is not recommended in other patients. Clinical trial data has shown that dual blockade of the renin-angiotensin-aldosterone-system (RAAS) through the combined use of ACE-inhibitors, angiotensin II receptor blockers or aliskiren is associated with a higher frequency of adverse events such as hypotension, hyperkalemia and decreased renal function (including acute renal failure) compared to the use of a single RAAS-acting agent (see “Contraindications” and “Special warning and precautions”).

The use of Tritace in combination with an angiotensin II receptor blockers is contraindicated in patients with diabetic nephropathy and is not recommended in other patients (see “Contraindications” and “Special warning and precautions”).

When potassium salts, potassium-retaining diuretics or other medicinal products that may increase kalaemia are given concurrently, a rise in serum potassium concentration, sometimes severe, may occur.

Concomitant treatment with potassium-retaining diuretics (e.g. spironolactone), potassium salts or other medicinal products that may increase kalaemia must be accompanied by close monitoring of serum potassium.

When antihypertensive agents (e.g. diuretics) or other medicines with blood-pressure-lowering potential (e.g. nitrates, tricyclic antidepressants, anaesthetics) are used concomitantly, potentiation of the antihypertensive effect is to be anticipated (concerning diuretics, see also ‘‘Special warnings and precautions”, “Adverse reactions”, and “Dosage”). Serum sodium should be regularly monitored in patients receiving diuretics.

Vasopressor sympathomimetics (e.g. epinephrine, norepinephrine) may reduce the antihypertensive effect. Therefore, blood pressure should be monitored particularly closely.

Allopurinol, immunosuppressants, corticosteroids, procainamide, cytostatics, and other medicines that may alter the blood picture increase the likelihood of blood picture changes (see “Special warnings and precautions”).

ACE inhibitors may reduce lithium excretion, possibly increasing its levels in serum and the risk of its toxic effects. Therefore, lithium levels must be monitored.

ACE inhibitors may potentiate the effect of antidiabetic agents (e.g. insulin or sulfonylurea derivatives). In isolated cases, this may lead to an excessive reduction in blood sugar levels (hypoglycaemic reactions).

Therefore, in the initial phase of combined administration, blood sugar levels should be monitored particularly closely.

An increased incidence of angioedema was found in patients taking ACE inhibitors and vildagliptin.

An increased incidence of angioedema was observed in patients taking ACE inhibitors and mTOR inhibitors (mammalian target of rapamycin inhibitors).

Neprilysin (NEP) inhibitors: An increased risk of angioedema has been reported with concomitant use of ACE inhibitors and NEP inhibitors (such as racecadotril)(see “Warning”).

Concurrent administration of certain medicines for the control of pain and inflammation (nonsteroidal anti-inflammatory drugs), such as acetylsalicylic acid or indomethacin, may weaken the antihypertensive effect. Moreover, combined use may increase serum potassium and the risk of a deterioration of renal function.

Concomitant use of heparin may lead to an increase in serum potassium concentration.

Tritace may potentiate the effect of alcohol.

Increased dietary salt intake may weaken the antihypertensive effect.

Anaphylactic and anaphylactoid reactions to insect venoma - and, possibly, other allergens - are increased under ACE inhibition (see “Adverse reactions”).

Dosage

The dosage is based on the desired effect and on how the patient tolerates the medicine. Therapy with Tritace is usually long-term therapy; the doctor determines the duration of treatment individually for each patient.

Treatment of hypertension

The recommended initial dose is 2.5 mg once daily. Depending on the response, the dose may be increased. Any increase should be implemented by doubling the dose at intervals of 2 to 3 weeks. The usual maintenance dose is 2.5 to 5 mg daily, the maximum dose is 10 mg daily.
In impaired renal function, i.e., a creatinine clearance between 50 and 20 ml/min per 1.73 m2 body surface area, the initial dose is generally 1.25 mg and the maximum daily dose is 5 mg. When creatinine clearance cannot be measured, it can be calculated based on the serum creatinine level using the following formula (Cockcroft's equation):

Men: Creatinine clearance (ml/min) =
body weight in kg x (140 - age in years)
72 x serum creatinine in mg/dl

Women: Multiply the product of the above equation by 0.85.
In patients with incompletely corrected fluid or salt deficiency, those with severe hypertension, as well as in those for whom a hypotensive reaction would constitute a particular risk (e.g. patients with haemodynamically relevant stenoses of the coronary arteries or of the blood vessels supplying the brain) and in the elderly, a reduced initial dose of 1.25 mg daily must be considered.
In patients pre-treated with a diuretic, consideration must be given to discontinuing the diuretic for at least 2 to 3 days or - depending on the duration of action of the diuretic - longer before starting treatment with Tritace, or at least to reducing the diuretic dose. The doctor will decide in each individual case whether such discontinuation or dose reduction is possible and how long it should last. The initial dose in such patients is generally 1.25 mg Tritace.
In impaired liver function, response to treatment may be either increased or reduced. Therefore, treatment must be initiated only under close medical supervision. The maximum daily dose is 2.5 mg.

Treatment of congestive heart failure

The recommended initial dose is 1.25 mg once daily. Depending on the response, the dose may be increased. Any increase should be implemented by doubling the dose at intervals of 1 to 2 weeks. The maximum daily dose is 10 mg. The required daily dose, if equalling or exceeding 2.5 mg, may be taken as a single dose or in two separate doses.
In impaired liver or renal function and in patients pre-treated with a diuretic, dosage recommendations for Tritace are identical to those given above in *Treatment of hypertension*. The recommendations given there in conjunction with diuretic pre-treatment also apply.

Treatment after myocardial infarction

The recommended initial dose is 5 mg daily, divided into two single doses of 2.5 mg each, one in the morning and one in the evening. If this dose is not well tolerated, 1.25 mg should be taken twice daily over two days. In either event, depending on the response, the dose may then be increased. If the dose cannot be increased to 2.5mg twice a day treatment should be withdrawn. Any increase should be implemented by doubling the dose at intervals of 1 to 3 days. As treatment progresses, the total daily dose may be taken as a single dose. The maximum daily dose is 10 mg.
Sufficient experience is still lacking in the treatment of patients with severe (NYHA IV) heart failure immediately after myocardial infarction.
Treatment, if nevertheless given, should be started with 1.25 mg once daily, and increased only with particular caution.
In patients with impaired liver or renal function, with incompletely corrected fluid or salt deficiency, or with severe hypertension, and in those for whom a hypotensive reaction would constitute a particular risk (e.g. patients with haemodynamically relevant stenoses of the coronary arteries or of the blood vessels supplying the brain), as well as in those pre-treated with a diuretic and in the elderly, the recommendations are identical to those given above in *Treatment of hypertension*.

Reducing the risk of myocardial infarction, stroke or cardiovascular death and/or the need for revascularisation procedures:

The recommended initial dose is 2.5 mg once daily. Depending on the tolerability, the dose is gradually increased.
The increase should be implemented by doubling the dose after one week. Three weeks later, it should be doubled again to the usual maintenance dose of 10 mg.
In patients with impaired liver or renal function, with incompletely corrected fluid or salt deficiency, or with severe hypertension, and in those for whom a hypotensive reaction would constitute a particular risk (e.g. patients with haemodynamically relevant stenoses of the coronary arteries or of the blood vessels supplying the brain), as well as in those pre-treated with a diuretic and in the elderly, the recommendations are identical to those given above in *Treatment of hypertension*.

Progressive renal failure in patients with persistent proteinuria in excess of 1g/day

The recommended initial dose is 1.25mg Tritace once daily. This should be doubled at intervals of 2-3 weeks, depending on how the drug is tolerated. There are no efficacy data regarding doses above 5mg/day in patients with nephropathy.
In hypertensive patients, a target diastolic blood pressure of < 90mm Hg should be pursued.
In patients pre-treated with a diuretic, consideration must be given to discontinuing the diuretic for at least 2-3 days or longer (depending on duration of action) or at least consideration should be given to reducing the dose, before initiating Tritace.

Administration

The tablets must be swallowed without chewing and with sufficient amounts of liquid (approx. 1/2 glass). They may be taken before, during, or after a meal.

Overdose

Overdosage may cause excessive peripheral vasodilatation (with marked hypotension, shock), bradycardia, electrolyte disturbances, and renal failure.
Primary detoxification: e.g., gastric lavage, administration of adsorbents, sodium sulfate (if possible during the first 30 minutes). In case of hypotension, administration of a1-adrenergic agonists (e.g. norepinephrine, dopamine) and angiotensin II (angiotensinamide) must be considered in addition to volume and salt substitution.

Expiry date

Do not use later than the date of expiry.

Keep medicines out of the reach of children.

Presentation

28 tablets

Manufactured by:-
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