RENITEC
Merck Sharp & Dhome

1. NAME OF THE MEDICINAL PRODUCT
RENITEC 5 mg Tablets
RENITEC 10 mg Tablets
RENITEC 20 mg Tablets
RENITEC 40 mg Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
RENITEC 5 mg
Each tablet contains 5 mg of enalapril maleate.
RENITEC 10 mg
Each tablet contains 10 mg of enalapril maleate.
RENITEC 20 mg
Each tablet contains 20 mg of enalapril maleate.
RENITEC 40 mg
Each tablet contains 40 mg of enalapril maleate. For excipients, see 6.1.

3. PHARMACEUTICAL FORM
Tablets.
RENITEC 5-mg tablets are triangular, white, with the code MSD 712; the tablet has been scored.
RENITEC 10-mg tablets are triangular, reddish brown, with the code MSD 713; the tablet has been scored.
RENITEC 20-mg tablets are triangular, pale orange, with the code MSD 714; the tablet has been scored.
RENITEC 40-mg tablets are triangular, yellow, with the code MSD 715; the tablet has not been scored.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
• Treatment of Hypertension
• Treatment of Symptomatic Heart Failure
• Prevention of Symptomatic Heart Failure in patients with Asymptomatic Left Ventricular Dysfunction (ejection fraction  <35%)
(See Section 5.1 Pharmacodynamic properties)

4.2 Posology and method of administration
The absorption of Tablets RENITEC is not affected by food.

The dose should be individualized according to patient profile (see 4.4 Special warnings and special precautions for use) and blood pressure response.

Hypertension
The initial dose is 5 to maximally 20 mg, depending on the degree of hypertension and the condition of the patient (see below). RENITEC is given once daily. In mild hypertension, the recommended initial dose is 5 to 10 mg. Patients with a strongly activated renin-angiotensin-aldosterone system (e.g., renovascular hypertension, salt and/or volume depletion, cardiac decompensation, or severe hypertension) may experience an excessive blood pressure fall following the initial dose. A starting dose of 5 mg or lower is recommended in such patients and the initiation of treatment should take place under medical supervision.

Prior treatment with high dose diuretics may result in volume depletion and a risk of hypotension when initiating therapy with enalapril. A starting dose of 5 mg or lower is recommended in such patients. If possible, diuretic therapy should be discontinued for 2-3 days prior to initiation of therapy with RENITEC. Renal function and serum potassium should be monitored.

The usual maintenance dose is 20 mg daily. The maximum maintenance dose is 40 mg daily.

Heart Failure/Asymptomatic Left Ventricular Dysfunction
In the management of symptomatic heart failure, RENITEC is used in addition to diuretics and, where appropriate, digitalis or beta-blockers. The initial dose of RENITEC in patients with symptomatic heart failure or asymptomatic left ventricular dysfunction is 2.5 mg, and it should be administered under close medical supervision to determine the initial effect on the blood pressure. In the absence of, or after effective management of, symptomatic hypotension following initiation of therapy
with RENITEC in heart failure, the dose should be increased gradually to the usual maintenance dose of 20 mg, given in a single dose or two divided doses, as tolerated by the patient. This dose titration is recommended to be performed over a 2 to 4 week period. The maximum dose is 40 mg daily given in two divided doses.

Use in pediatrics
There is limited clinical trial experience of the use of RENITEC in hypertensive pediatric patients (see 4.4 Special warnings and special precautions for use, 5.1 Pharmacodynamic properties and 5.2 Pharmacokinetic properties).

For patients who can swallow tablets, the dose should be individualized according to patient profile and blood pressure response. The recommended initial dose is 2.5 mg in patients 20 to <50 kg and 5 mg in patients ≥50 kg. RENITEC is given once daily. The dosage should be adjusted according to the needs of the patient to a maximum of 20 mg daily in patients 20 to <50 kg and 40 mg in patients ≥50 kg. (See 4.4 Special warnings and special precautions for use.)

RENITEC is not recommended in neonates and in pediatric patients with glomerular filtration rate <30 ml/min/1.73 m², as no data are available.

4.3 Contraindications
- Hypersensitivity to enalapril, to any of the excipients or any other ACE inhibitor
- History of angioedema associated with previous ACE inhibitor therapy
- Hereditary or idiopathic angioedema
- Second and third trimesters of pregnancy (see 4.6 Pregnancy and lactation).

4.4 Special warnings and special precautions for use

Symptomatic Hypotension
Symptomatic hypotension is rarely seen in uncomplicated hypertensive patients. In hypertensive patients receiving RENITEC, symptomatic hypotension is more likely to occur if the patient has been volume-depleted, e.g., by diuretic therapy, dietary salt restriction, dialysis, diarrhea or vomiting (see 4.5 Interaction with other medicaments and other forms of interaction and 4.8 Undesirable effects). In patients with heart failure, with or without associated renal insufficiency, symptomatic hypotension has
Renal failure has been reported in association with enalapril and has been mainly in patients with severe heart failure or underlying renal disease, including renal artery stenosis. If recognized promptly and treated appropriately, renal failure when associated with therapy with enalapril is usually reversible. Some hypertensive patients, with no apparent pre-existing renal disease have developed increases in blood urea and creatinine when enalapril has been given concurrently with a diuretic. Dosage reduction of enalapril and/or discontinuation of the diuretic may be required. This situation should raise the possibility of underlying renal artery stenosis (see 4.4 Special warnings and special precautions for use, Renovascular hypertension).

Renovascular hypertension
There is an increased risk of hypotension and renal insufficiency when patients with bilateral renal artery stenosis or stenosis of the artery to a single functioning kidney are treated with ACE inhibitors. Loss of renal function may occur with only mild changes in serum creatinine. In these patients, therapy should be initiated under close medical supervision with low doses, careful titration, and monitoring of renal function.

Kidney Transplantation
There is no experience regarding the administration of RENITEC in patients with a recent kidney transplantation. Treatment with RENITEC is therefore not recommended.

Hepatic failure
Rarely, ACE inhibitors have been associated with a syndrome that starts with cholestatic jaundice and progresses to fulminant hepatic necrosis and (sometimes) death. The mechanism of this syndrome is not understood. Patients receiving ACE inhibitors who develop jaundice or marked elevations of hepatic enzymes should discontinue the ACE inhibitor and receive appropriate medical follow-up.

Neutropenia/Agranulocytosis
Neutropenia/agranulocytosis, thrombocytopenia and anemia have been reported in patients receiving ACE inhibitors. In patients with normal renal func-
tion and no other complicating factors, neutropenia occurs rarely. Enalapril should be used with extreme caution in patients with collagen vascular disease, immunosuppressant therapy, treatment with allopurinol or procainamide, or a combination of these complicating factors, especially if there is pre-existing impaired renal function. Some of these patients developed serious infections which in a few instances did not respond to intensive antibiotic therapy. If enalapril is used in such patients, periodic monitoring of white blood cell counts is advised and patients should be instructed to report any sign of infection.

Hypersensitivity/Angioneurotic Edema
Angioneurotic edema of the face, extremities, lips, tongue, glottis and/or larynx has been reported in patients treated with angiotensin converting enzyme inhibitors, including RENITEC. This may occur at any time during treatment. In such cases, RENITEC should be discontinued promptly and appropriate monitoring should be instituted to ensure complete resolution of symptoms prior to dismissing the patient. In those instances where swelling has been confined to the face and lips the condition generally resolved without treatment, although antihistamines have been useful in relieving symptoms.

Angioneurotic edema associated with laryngeal edema may be fatal. Where there is involvement of the tongue, glottis or larynx, likely to cause airway obstruction, appropriate therapy, which may include subcutaneous epinephrine solution 1:1000 (0.3 ml to 0.5 ml) and/or measures to ensure a patent airway, should be administered promptly.

Black patients receiving ACE inhibitors have been reported to have a higher incidence of angioedema compared to non-blacks.

Patients with a history of angioedema unrelated to ACE inhibitor therapy may be at increased risk of angioedema while receiving an ACE inhibitor. (Also see 4.3 Contraindications.)

Anaphylactoid Reactions during Hymenoptera Desensitization
Rarely, patients receiving ACE inhibitors during desensitization with hymenoptera venom have experienced life-threatening anaphylactoid reactions. These reactions were avoided by temporarily withholding ACE-inhibitor therapy prior to each desensitization.

Anaphylactoid Reactions during LDL Apheresis
Rarely, patients receiving ACE inhibitors during low density lipoprotein (LDL)-apheresis with dextran sulfate have experienced life-threatening anaphylactoid reactions. These reactions were avoided by temporarily withholding ACE-inhibitor therapy prior to each apheresis.

Hemodialysis Patients
Anaphylactoid reactions have been reported in patients dialyzed with high-flux membranes (e.g., AN 69®) and treated concomitantly with an ACE inhibitor. In these patients consideration should be given to using a different type of dialysis membrane or a different class of antihypertensive agent.

Diabetic patients
In diabetic patients treated with oral antidiabetic agents or insulin, glycemic control should be closely monitored during the first month of treatment with an ACE inhibitor. (See 4.5 Interaction with other medicinal products and other forms of interaction, Antidiabetics.)

Cough
Cough has been reported with the use of ACE inhibitors. Characteristically, the cough is nonproductive, persistent and resolves after discontinuation of therapy. ACE inhibitor-induced cough should be considered as part of the differential diagnosis of cough.

Surgery/Anesthesia
In patients undergoing major surgery or during anesthesia with agents that produce hypotension, enalapril blocks angiotensin II formation secondary to compensatory renin release. If hypotension occurs and is considered to be due to this mechanism, it can be corrected by volume expansion.

Hyperkalemia
Elevations in serum potassium have been observed
Use of enalapril is not recommended during breast feeding.

Ethnic differences
As with other angiotensin converting enzyme inhibitors, enalapril is apparently less effective in lowering blood pressure in black people than in non-blacks, possibly because of a higher prevalence of low-renin states in the black hypertensive population.

4.5 Interaction with other medicinal products and other forms of interaction

Potassium sparing diuretics or potassium supplements
ACE inhibitors attenuate diuretic induced potassium loss. Potassium sparing diuretics (e.g. spironolactone, triamterene or amiloride), potassium supplements, or potassium-containing salt substitutes may lead to significant increases in serum potassium. If concomitant use is indicated because of demonstrated hypokalemia they should be used with caution and with frequent monitoring of serum potassium (see 4.4 Special warnings and special precautions for use).

Diuretics (thiazide or loop diuretics)
Prior treatment with high dose diuretics may result in volume depletion and a risk of hypotension when initiating therapy with enalapril (see 4.4 Special warnings and special precautions for use). The hypotensive effects can be reduced by discontinuation of the diuretic, by increasing volume or salt intake or by initiating therapy with a low dose of enalapril.

Other antihypertensive agents
Concomitant use of these agents may increase the hypotensive effects of enalapril. Concomitant use with nitroglycerine and other nitrates, or other vasodilators, may further reduce blood pressure.

Lithium
The combination of lithium and enalapril is generally not recommended (see 4.5 Interaction with other medicinal products and other forms of interaction).

Lactose
RENITEC contains lactose and therefore should not be used by patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption. RENITEC contains less than 200 mg of lactose per tablet.

Pregnancy and lactation
Enalapril should not be used during the first trimester of pregnancy. RENITEC is contraindicated in the second and third trimesters of pregnancy (see 4.3 Contraindications). When pregnancy is detected, enalapril treatment should be discontinued as soon as possible (see 4.6 Pregnancy and lactation).
lithium toxicity with ACE inhibitors. Use of enalapril with lithium is not recommended, but if the combination proves necessary, careful monitoring of serum lithium levels should be performed (see 4.4 Special warnings and special precautions for use).

Tricyclic antidepressants / Antipsychotics / Anesthetics / Narcotics
Concomitant use of certain anesthetic medicinal products, tricyclic antidepressants and antipsychotics with ACE inhibitors may result in further reduction of blood pressure (see 4.4 Special warnings and special precautions for use).

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)
Chronic administration of NSAIDs may reduce the antihypertensive effect of an ACE inhibitor. NSAIDs and ACE inhibitors exert an additive effect on the increase in serum potassium, and may result in a deterioration of renal function. These effects are usually reversible. Rarely, acute renal failure may occur, especially in patients with compromised renal function such as the elderly or dehydrated.

Sympathomimetics
Sympathomimetics may reduce the antihypertensive effects of ACE inhibitors.

Antidiabetics
Epidemiological studies have suggested that concomitant administration of ACE inhibitors and anti-diabetic medicines (insulins, oral hypoglycemic agents) may cause an increased blood-glucose-lowering effect with risk of hypoglycemia. This phenomenon appeared to be more likely to occur during the first weeks of combined treatment and in patients with renal impairment.

Alcohol
Alcohol enhances the hypotensive effect of ACE inhibitors.

Acetyl salicylic acid, thrombolytics and β-blockers
Enalapril can be safely administered concomitantly with acetyl salicylic acid (at cardiology doses), thrombolytics and β-blockers.

4.6 Pregnancy and lactation

Pregnancy
Enalapril should not be used during the first trimester of pregnancy. When a pregnancy is planned or confirmed the switch to an alternative treatment should be initiated as soon as possible. Controlled studies with ACE inhibitors have not been done in humans, but a limited number of cases with first trimester exposure have not appeared to manifest malformations consistent with human fetotoxicity as described below.

Enalapril is contraindicated during the second and third trimesters of pregnancy.

Prolonged enalapril exposure during the second and third trimesters is known to induce human fetotoxicity (decreased renal function, oligohydramnios, skull ossification retardation) and neonatal toxicity (renal failure, hypotension, hyperkalemia). (Also see 5.3 Preclinical safety data.)

Should exposure to enalapril have occurred from the second trimester of pregnancy, ultrasound check of renal function and skull is recommended.

Infants whose mothers have taken RENITEC should be closely observed for hypotension, oliguria and hyperkalemia. Enalapril, which crosses the placenta, has been removed from the neonatal circulation by peritoneal dialysis with some clinical benefit, and theoretically may be removed by exchange transfusion.

Lactation
Enalapril and enalaprilat are excreted in breast milk but their effect on the nursing infant has not been determined. Consequently, use of enalapril is not recommended if breast-feeding.

4.7 Effects on ability to drive and use machines

When driving vehicles or operating machines it should be taken into account that occasionally dizziness or weariness may occur.

4.8 Undesirable effects

Undesirable effects reported for enalapril include:

[Very common (>1/10); common (>1/100, <1/10);
Uncommon (>1/1,000, <1/100); rare (>1/10,000, <1/1,000); very rare (<1/10,000), including isolated reports.

**Blood and the lymphatic system disorders:**
*Uncommon:* anemia (including aplastic and hemolytic)
*Rare:* neutropenia, decreases in hemoglobin, decreases in hematocrit, thrombocytopenia, agranulocytosis, bone marrow depression, pancytopenia, lymphadenopathy, autoimmune diseases

**Metabolism and nutrition disorders:**
*Uncommon:* hypoglycemia (see 4.4 Special warnings and special precautions for use, Diabetic patients)

**Nervous system and psychiatric disorders:**
*Common:* headache, depression
*Uncommon:* confusion, somnolence, insomnia, nervousness, paresthesia, vertigo
*Rare:* dream abnormality, sleep disorders

**Eye disorders:**
*Very common:* blurred vision

**Cardiac and vascular disorders:**
*Very common:* dizziness
*Common:* hypotension (including orthostatic hypotension), syncope, myocardial infarction or cerebrovascular accident, possibly secondary to excessive hypotension in high risk patients (see 4.4 Special warnings and special precautions for use), chest pain, rhythm disturbances, angina pectoris, tachycardia
*Uncommon:* orthostatic hypotension, palpitations
*Rare:* Raynaud’s phenomenon

**Respiratory, thoracic and mediastinal disorders:**
*Very common:* cough
*Common:* dyspnea
*Uncommon:* rhinorrhea, sore throat and hoarseness, bronchospasm/asthma
*Rare:* pulmonary infiltrates, rhinitis, allergic alveolitis/eosinophilic pneumonia

**Gastrointestinal disorders:**
*Very common:* nausea,
*Common:* diarrhea, abdominal pain, taste alteration

*Uncommon:* ileus, pancreatitis, vomiting, dyspepsia, constipation, anorexia, gastric irritations, dry mouth, peptic ulcer
*Rare:* stomatitis/aphthous ulcerations, glossitis
*Very rare:* intestinal angioedema

**Hepatobiliary disorders:**
*Rare:* hepatic failure, hepatitis – either hepatocellular or cholestatic, hepatitis including necrosis, cholestasis (including jaundice)

**Skin and subcutaneous tissue disorders:**
*Common:* rash, hypersensitivity/angioneurotic edema: angioneurotic edema of the face, extremities, lips, tongue, glottis and/or larynx has been reported (see 4.4 Special warnings and special precautions for use)

*Uncommon:* diaphoresis, pruritus, urticaria, alopecia
*Rare:* erythema multiforme, Stevens-Johnson syndrome, exfoliative dermatitis, toxic epidermal necrolysis, pemphigus, erythroderma

A symptom complex has been reported which may include some or all of the following: fever, serositis, vasculitis, myalgia/myositis, arthralgia/arthritis, a positive ANA, elevated ESR, eosinophilia, and leukocytosis. Rash, photosensitivity or other dermatologic manifestations may occur.

**Renal and urinary disorders:**
*Uncommon:* renal dysfunction, renal failure, proteinuria
*Rare:* oliguria

**Reproductive system and breast disorders:**
*Uncommon:* impotence
*Rare:* gynecomastia

**General disorders and administration site conditions:**
*Very common:* asthenia
*Common:* fatigue
*Uncommon:* muscle cramps, flushing, tinnitus, malaise, fever

**Investigations:**
*Common:* hyperkalemia, increases in serum creatinine
After absorption, enalapril is hydrolyzed to enalaprilat, which inhibits ACE. Inhibition of ACE results in decreased plasma angiotensin II, which leads to increased plasma renin activity (due to removal of negative feedback of renin release), and decreased aldosterone secretion. **ACE is identical to kininase II.** Thus RENITEC may also block the degradation of bradykinin, a potent vasodepressor peptide. However, the role that this plays in the therapeutic effects of RENITEC remains to be elucidated.

While the mechanism through which RENITEC lowers blood pressure is believed to be primarily suppression of the renin-angiotensin-aldosterone system, RENITEC is antihypertensive even in patients with low-renin hypertension.

Administration of RENITEC to patients with hypertension results in a reduction of both supine and standing blood pressure without a significant increase in heart rate. Symptomatic postural hypotension is infrequent. In some patients the development of optimal blood pressure reduction may require several weeks of therapy. Abrupt withdrawal of RENITEC has not been associated with rapid increase in blood pressure.

Effective inhibition of ACE activity usually occurs 2 to 4 hours after oral administration of an individual dose of enalapril. Onset of antihypertensive activity was usually seen at one hour, with peak reduction of blood pressure achieved by 4 to 6 hours after administration. The duration of effect is dose-related. However, at recommended doses, antihypertensive and hemodynamic effects have been shown to be maintained for at least 24 hours.

In hemodynamic studies in patients with essential hypertension, blood pressure reduction was accompanied by a reduction in peripheral arterial resistance with an increase in cardiac output and little or no change in heart rate. Following administration of RENITEC there was an increase in renal blood flow; glomerular filtration rate was unchanged. There was no evidence of sodium or water retention. However,
failure due to systolic dysfunction (ejection fraction <35%). 2569 patients receiving conventional treatment for heart failure were randomly assigned to receive either placebo (n=1284) or enalapril (n=1285). There were 510 deaths in the placebo group (39.7%) as compared with 452 in the enalapril group (35.2%) (reduction in risk, 16%; 95% CI, 5 - 26%; p=0.0036). There were 461 cardiovascular deaths in the placebo group as compared with 399 in the enalapril group (risk reduction 18%, 95% CI, 6 - 28%, p<0.002), mainly due to a decrease of deaths due to progressive heart failure (251 in the placebo group vs 209 in the enalapril group, risk reduction 22%, 95% CI, 6 - 35%). Fewer patients died or were hospitalized for worsening heart failure (736 in the placebo group and 613 in the enalapril group; risk reduction, 26%; 95% CI, 18 - 34%; p<0.0001). Overall in SOLVD study, in patients with left ventricular dysfunction, RENITEC reduced the risk of myocardial infarction by 23% (95% CI, 11 – 34%; p<0.001) and reduced the risk of hospitalization for unstable angina pectoris by 20% (95% CI, 9 – 29%; p<0.001).

There is limited experience of the use in hypertensive pediatric patients >6 years. In a clinical study involving 110 hypertensive pediatric patients 6 to 16 years of age with a body weight ≥20 kg and a glomerular filtration rate >30 ml/min/1.73 m², patients who weighed <50 kg received either 0.625, 2.5 or 20 mg of enalapril daily and patients who weighed ≥50 kg received either 1.25, 5 or 40 mg of enalapril daily. Enalapril administration once daily lowered trough blood pressure in a dose-dependent manner. The dose-dependent antihypertensive efficacy of enalapril was consistent across all subgroups (age, Tanner stage, gender, race). However, the lowest doses studied, 0.625 mg and 1.25 mg, corresponding to an average of 0.02 mg/kg once daily, did not appear to offer consistent antihypertensive efficacy. The maximum dose studied was 0.58 mg/kg (up to 40 mg) once daily. The adverse experience profile for pediatric patients is not different from that seen in adult patients.
5.2 Pharmacokinetic properties

Absorption
Oral enalapril is rapidly absorbed, with peak serum concentrations of enalapril occurring within one hour. Based on urinary recovery, the extent of absorption of enalapril from oral enalapril tablet is approximately 60%. The absorption of oral RENITEC is not influenced by the presence of food in the gastrointestinal tract.

Following absorption, oral enalapril is rapidly and extensively hydrolysed to enalaprilat, a potent angiotensin converting enzyme inhibitor. Peak serum concentrations of enalaprilat occur about 4 hours after an oral dose of enalapril tablet. The effective half-life for accumulation of enalaprilat following multiple doses of oral enalapril is 11 hours. In subjects with normal renal function, steady-state serum concentrations of enalaprilat were reached after 4 days of treatment.

Distribution
Over the range of concentrations which are therapeutically relevant, enalaprilat binding to human plasma proteins does not exceed 60%.

Biotransformation
Except for conversion to enalaprilat, there is no evidence for significant metabolism of enalapril.

Elimination
Excretion of enalaprilat is primarily renal. The principal components in urine are enalaprilat, accounting for about 40% of the dose, and intact enalapril (about 20%).

Renal impairment
The exposure of enalapril and enalaprilat is increased in patients with renal insufficiency. In patients with mild to moderate renal insufficiency (creatinine clearance 40-60 ml/min) steady state AUC of enalaprilat was approximately two-fold higher than in patients with normal renal function after administration of 5 mg once daily. In severe renal impairment (creatinine clearance ≤ 30 ml/min), AUC was increased approximately 8-fold. The effective half-life of enalaprilat following multiple doses of enalapril maleate is prolonged at this level of renal insufficiency and time to steady state is delayed. (See 4.2 Posology and method of administration.)

Enalaprilat may be removed from the general circulation by hemodialysis. The dialysis clearance is 62 ml/min.

Children and adolescents
A multiple dose pharmacokinetic study was conducted in 40 hypertensive male and female pediatric patients aged 2 months to ≤ 16 years following daily oral administration of 0.07 to 0.14 mg/kg enalapril maleate. There were no major differences in the pharmacokinetics of enalaprilat in children compared with historic data in adults. The data indicate an increase in AUC (normalised to dose per body weight) with increased age; however, an increase in AUC is not observed when data are normalised by body surface area. At steady state, the mean effective half-life for accumulation of enalaprilat was 14 hours.

5.3 Preclinical safety data
Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and carcinogenic potential. Reproductive toxicity studies suggest that enalapril has no effects on fertility and reproductive performance in rats, and is not teratogenic. In a study in which female rats were dosed prior to mating through gestation, an increased incidence of rat pup deaths occurred during lactation. The compound has been shown to cross the placenta and is secreted in milk. Angiotensin converting enzyme inhibitors, as a class, have been shown to be fetotoxic (causing injury and/or death to the fetus) when given in the second or third trimester.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

RENITEC 5 mg tablets:
sodium bicarbonate (E500), lactose, pregelatinized starch, maize starch, magnesium stearate (E470B)

RENITEC 10 mg tablets:
sodium bicarbonate (E500), lactose, pregelatinized starch, maize starch, magnesium stearate (E470B)
starch, maize starch, magnesium stearate (E470B), red ferric oxide (E172)

**RENITEC 20 mg tablets:**
sodium bicarbonate (E500), lactose, pregelatinized starch, maize starch, magnesium stearate (E470B), red ferric oxide (E172), yellow ferric oxide (E172)

**RENITEC 40 mg tablets:**
sodium bicarbonate (E500), lactose, pregelatinized starch, maize starch, magnesium stearate (E470B), yellow ferric oxide (E172)

6.2 Incompatibilities
Not applicable

6.3 Shelf life
Tablets of 5, 10, and 20 mg three years and tablets 40 mg two and a half years in the blister.
The expiry date is mentioned after “Do not use after” on the package and on the blister after exp., followed by month and year.

6.4 Special precautions for storage
Do not store above 30°C. Store in the original package.

6.5 Nature and contents of container
RENITEC: Boxes with three blisters with 10 tablets each.

6.6 Instructions for use and handling
No special requirements.

7. MARKETING AUTHORIZATION HOLDER
MERCK SHARP & DOHME B.V.
P.O. Box 581
2003 PC Haarlem

8. MARKETING AUTHORIZATION NUMBER
Entered in the register under RVG 10575 (tablets 5 mg), RVG 10852 (tablets 10 mg), RVG 10576 (tablets 20 mg) and RVG 10853 (tablets 40 mg).

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF AUTHORIZATION
Date of first authorization: 11 January 1985
Date of renewal: 1 November 2004.

10. DATE OF (PARTIAL) REVISION OF THE TEXT
31 May 2005.