SCHEDULING STATUS

S3

PROPRIETARY NAME AND DOSAGE FORM

RENITEC® 2,5 Tablet

RENITEC® 5 Tablet

RENITEC® 10 Tablet

RENITEC® 20 Tablet

COMPOSITION

Each RENITEC 2,5 tablet contains 2,5 mg enalapril maleate, MSD.

Each RENITEC 5 tablet contains 5 mg enalapril maleate, MSD.

Each RENITEC 10 tablet contains 10 mg enalapril maleate, MSD.

Each RENITEC 20 tablet contains 20 mg enalapril maleate, MSD.

RENITEC tablets contain sugar.

Excipients: sodium hydrogen carbonate, maize starch, pregelatinised starch, magnesium stearate, lactose monohydrate. In addition the 10 mg and 20 mg tablet contains iron oxide red (E172) and iron oxide yellow (E172) – 20 mg tablet only.

PHARMACOLOGICAL CLASSIFICATION

A 7.1.3 Vascular medicines - other hypotensives

PHARMACOLOGICAL ACTION

Enalapril maleate, is the maleate salt of enalapril, a derivative of two amino acids, L-alanine and L-proline. Following oral absorption, enalapril maleate, is hydrolysed to enalaprilat, which is a specific, long-acting, non-sulphydryl angiotensin converting enzyme inhibitor.

CLINICAL PHARMACOLOGY

Enalapril lowers blood pressure in patients with hypertension and improves the signs and symptoms associated with chronic heart failure.

PHARMACODYNAMICS

Mechanism of action

Angiotensin converting enzyme (ACE) is a peptidyl dipeptidase which catalyzes the conversion of angiotensin I to the pressor substance angiotensin II. 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.

In some patients the development of optimal blood pressure reduction may require several weeks of therapy.

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 haemodynamic effects have been shown to be maintained for at least 24 hours.

Antihypertensive treatment with enalapril leads to a significant regression of left ventricular hypertrophy with preservation of left ventricular systolic performance.

In haemodynamic 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 enalapril there was an increase in renal blood flow; glomerular filtration rate was unchanged. There was no evidence of sodium or water retention. However, in patients with low pre-treatment glomerular filtration rates, the rates were usually increased.

Chronic administration of enalapril to patients with essential hypertension and renal insufficiency may be associated with improvements in renal function, evidenced by increased glomerular filtration rate.

In short term clinical studies in diabetic and nondiabetic patients with renal disease, decreases in albuminuria and urinary excretion of IgG and total urinary protein were seen after the administration of enalapril.

Haemodynamic changes seen during intravenous therapy with enalaprilat are similar to those seen with oral enalapril maleate.

When given together with thiazide-type diuretics, the blood pressure-lowering effects of enalapril are at least additive. Enalapril may reduce or prevent the development of thiazide-induced hypokalaemia.

In patients with heart failure on therapy with digitalis and diuretics, treatment with oral or injection enalapril was associated with decreases in peripheral resistance and blood pressure. Cardiac output increased, while heart rate (usually elevated in patients with heart failure) decreased. Pulmonary capillary wedge pressure was also reduced. Exercise tolerance and severity of heart failure, as measured by New York Heart Association criteria, improved. These actions continued during chronic therapy.

In patients with mild to moderate heart failure, enalapril retarded progressive cardiac dilatation/enlargement and failure, as evidenced by reduced left ventricular end diastolic and systolic volumes and improved ejection fraction

Clinical data have shown that enalapril reduced the frequency of ventricular dysrhythmias in patients with heart failure, although the underlying mechanisms and clinical significance are not known.

PHARMACOKINETICS

Protein binding

Enalaprilat binding to human plasma, over the range of concentrations which are therapeutically relevant, does not exceed 60 %.

Pharmacokinetics and Metabolism

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 is approximately 60 %.

Following absorption, oral enalapril is rapidly and extensively hydrolysed to enalaprilat, a potent angiotensin converting enzyme inhibitor. Similar peak serum concentrations of enalaprilat occur about 4 hours after an oral dose of enalapril. Excretion of enalaprilat is primarily renal. The principal components in urine are enalaprilat, accounting for about 40 % of the dose, and intact enalapril. Except for conversion to enalaprilat, there is no evidence for significant metabolism of enalapril. The serum concentration profile of enalaprilat exhibits a prolonged terminal phase, apparently associated with binding to ACE. In subjects with normal renal function, steady state serum concentrations of enalaprilat were achieved by the fourth day of administration of oral enalapril. The effective half-life for accumulation of enalaprilat following multiple doses of oral enalapril is 11 hours. The absorption of oral enalapril is not influenced by the presence of food in the gastrointestinal tract. The extent of absorption and hydrolysis of enalapril are similar for the various doses in the recommended therapeutic range.

Studies in dogs indicate that enalapril crosses the blood-brain barrier poorly, if at all: enalaprilat does not enter the brain. Multiple doses of oral enalapril in rats do not result in accumulation in any tissues. Milk of lactating rats contains radioactivity following administration of ^{14}C enalapril maleate. Radioactivity was found to cross the placenta following administration of ^{14}C enalapril maleate to pregnant hamsters.

INDICATIONS

RENITEC is indicated in:

- Hypertension

Treatment of hypertension

- Heart failure

RENITEC is indicated for the treatment of symptomatic congestive heart failure, in combination with diuretics and when appropriate digoxin. In these patients RENITEC improves symptoms, increases survival, and decreases the frequency of hospitalisation.

- Asymptomatic Left Ventricular Dysfunction

In clinically stable asymptomatic patients with left ventricular dysfunction (ejection fraction less than or equal to 35 %), RENITEC may decrease the rate of development of overt heart failure and may decrease the incidence of hospitalisation for heart failure

CONTRA-INDICATIONS

- Sensitivity to any of the components of RENITEC
- A history of angioedema related to previous therapy with ACE inhibitors or angiotensin receptor blockers (ARB's): These patients must never again be given these medicines.
- Hereditary or idiopathic angioedema
- Hypertrophic obstructive cardiomyopathy (HOCM)
- Severe renal function impairment (creatinine clearance less than 30 ml/min)
- Bilateral renal artery stenosis
- Renal artery stenosis in patients with a single kidney
- Aortic stenosis
- Concomitant therapy with potassium sparing diuretics such as spironolactone, triamterene, amiloride
- Porphyria
- Lithium therapy: Concomitant administration with RENITEC may lead to toxic blood concentration of lithium.
- Pregnancy and lactation (see PREGNANCY AND LACTATION)

WARNINGS

Should a woman become pregnant while receiving RENITEC, the treatment must be stopped promptly and switched to a different medicine. Should a woman contemplate pregnancy the doctor should institute alternative medication.

See **CONTRA-INDICATIONS** and **PREGNANCY AND LACTATION**

INTERACTIONS

Antihypertensive Therapy

The combination of RENITEC with other antihypertensive medicines may increase the antihypertensive effect, especially in combination with diuretics.

The combination of RENITEC with beta-adrenergic blocking agents and methyldopa or calcium entry blockers, potentiates the hypotensive effects of RENITEC.

Ganglionic blocking agents or adrenergic blocking agents, combined with RENITEC, should only be administered with careful observation of the patient.

Because of lack of experience, concomitant treatment of RENITEC with calcium antagonists is not recommended.

Serum Potassium – see also **SPECIAL PRECAUTIONS**, Hyperkalaemia

Risk factors for the development of hyperkalaemia include renal insufficiency, diabetes mellitus and concomitant use of potassium-sparing diuretics (e.g. spironolactone, epleronone, triamterene or amiloride), potassium supplements, or potassium-containing salt substitutes.

In patients with renal failure, the administration of RENITEC may lead to elevation of serum potassium. The use of potassium supplements, potassium-sparing diuretics, or potassium-containing salt substitutes particularly in patients with impaired renal function may lead to a significant increase in serum potassium. If concomitant use of RENITEC and the above-mentioned agents is deemed appropriate, they should be used with caution and with frequent monitoring of serum potassium.

Antidiabetics

Epidemiological studies have suggested that concomitant administration of ACE inhibitors and antidiabetic medicines (insulins, oral hypoglycaemic agents) may cause an increased blood-glucose-lowering effect with risk of hypoglycaemia. This phenomenon appeared to be more likely to occur during the first weeks of combined treatment and in patients with renal impairment. In diabetic patients treated with oral antidiabetic agents or insulin, glycaemic control should be closely monitored for hypoglycaemia.

Serum Lithium

The lithium elimination may be reduced. Therefore the lithium levels of serum should be carefully compared if lithium salts are to be administered.

Non-Steroidal Anti-inflammatory Drugs including Selective Cyclooxygenase-2 Inhibitors

Non-steroidal anti-inflammatory drugs (NSAIDs) including selective cyclooxygenase-2 inhibitors (COX-2 inhibitors) may reduce the effect of RENITEC. Therefore, the antihypertensive effect of ACE inhibitors may be attenuated by NSAIDs including selective COX-2 inhibitors.

In patients with compromised renal function who are being treated with non-steroidal anti-inflammatory drugs including selective cyclooxgenase-2 inhibitors, the co-administration of RENITEC may result in a further deterioration of renal function. These effects are usually reversible.

Gold

Nitritoid reactions (symptoms include facial flushing, nausea, vomiting and hypotension) have been reported rarely in patients on therapy with injectable gold (sodium aurothiomalate) and concomitant ACE inhibitor therapy including enalapril.

Other Medicines

There are no clinically significant pharmacokinetic interactions between enalapril maleate and the following compounds: hydrochlorothiazide, furosemide, digoxin, timolol, methyldopa and warfarin. Propranolol co administered with enalapril maleate reduces serum enalaprilat concentrations, but this does not appear to be of any clinical significance. Since cimetidine does not interact with enalapril maleate in animals, it is not anticipated that an interaction will occur in humans.

PREGNANCY AND LACTATION

See **CONTRA-INDICATIONS** and **WARNINGS.**

In an epidemiological study, infants whose mothers had taken an ACE inhibitor medicine during the first trimester of pregnancy had an increased risk of major congenital malformations including of the

cardiovascular and neurological system compared with infants whose mothers had not undergone first trimester exposure to ACE inhibitor medicines.

ACE-inhibitors such as RENITEC can cause foetal and neonatal morbidity and mortality when administered to pregnant women during the 2nd and 3rd trimesters. ACE-inhibitors pass through the placenta and can be presumed to cause disturbance in foetal blood pressure regulatory mechanisms. Oligohydramnios, which may result in limb contractures, craniofacial deformities and hypoplastic lung development, as well as hypotension, hyperkalaemia, oliguria and anuria in newborns have been reported after administration of ACE-inhibitors such as RENITEC in the second and third trimester. Cases of defective skull ossification have been observed. Prematurity and low birth mass can occur.

Infants whose mothers have taken RENITEC should be closely observed for hypotension, oliguria and hyperkalaemia. These adverse effects to the embryo and foetus do not appear to have resulted from intra-uterine ACE-inhibitor such as RENITEC exposure limited to the first trimester.

RENITEC, which crosses the placenta, has been removed from the neonatal circulation by peritoneal dialysis with some clinical benefit.

Breastfeeding Mothers

Enalapril and enalaprilat are secreted in human milk. Caution should be exercised if RENITEC is given to a breastfeeding mother

DOSAGE AND DIRECTIONS FOR USE

Since its absorption is not affected by food, RENITEC tablets may be administered before, during or after meals.

Treatment for Hypertension

The initial dose is 10 mg to 20 mg depending on the degree of hypertension and is given once daily. In mild hypertension the recommended initial dose is 10 mg daily. For other degrees of hypertension the initial dose

is 20 mg daily. The usual maintenance dose is one 20 mg tablet taken once daily. The dosage should be adjusted according to the needs of the patient.

Concomitant Diuretic Therapy in Hypertension

Symptomatic hypotension may occur following the initial dose of RENITEC; this is more likely in patients who are being treated currently with diuretics. Caution is recommended, therefore, since these patients may be volume or salt depleted. The diuretic therapy should be discontinued for 2-3 days prior to initiation of therapy with RENITEC. If this is not possible, the initial dose of RENITEC should be low (5 mg or less) to determine the initial effect on the blood pressure. Dosage should then be adjusted according to the needs of the patient.

Dosage in Renal Insufficiency

Generally, the intervals between the administration of enalapril should be prolonged and/or the dosage reduced.

Enalaprilat is dialysable

Renal Status	**Creatinine Clearance ml/min**	**Initial Dose mg/day**
Mild to moderate Impairment	Less than 80, greater than 30	2,5 - 5

Heart Failure / Asymptomatic Left Ventricular Dysfunction

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 may be performed over a 2 to 4 week period, or more rapidly if indicated by the presence of residual signs and symptoms of heart failure. In patients with symptomatic heart failure, this dosage regimen was effective in reducing mortality.

Blood pressure and renal function should be monitored closely before and after starting treatment with RENITEC (see **SPECIAL PRECAUTIONS**) because hypotension and consequent renal failure have been reported. In patients treated with diuretics, the dosage should be reduced if possible before beginning treatment with RENITEC. The appearance of hypotension after the initial dose of RENITEC does not imply that hypotension will recur during chronic therapy with RENITEC and does not preclude continued use of RENITEC.

Serum potassium also should be monitored (see **INTERACTIONS**).

SIDE EFFECTS AND SPECIAL PRECAUTIONS

SIDE EFFECTS

Very common (≥1/10); common (≥1/100, < 1/10), uncommon (≥1/1,000, <1/100); rare (≥1/10,000, < 1/1000); very rare (<1/10,000) including isolated reports.

Blood and lymphatic disorders:

Rare: decreased haemoglobin, decreased haematocrit

Metabolism and nutrition disorders:

Common: hyperkalaemia

Uncommon: hyponatraemia, cases of hypoglycaemia in diabetic patients on oral antidiabetic agents or insulin have been reported (see **INTERACTIONS**)

Nervous system and psychiatric disorders:

Common: headache, depression, taste alteration

Uncommon: confusion, somnolence, insomnia, nervousness, paraesthesia, vertigo

Rare: dream abnormality

Eye disorders:

Very common: blurred vision

Ear and labyrinth disorders:

Uncommon: tinnitus

Cardiac and vascular disorders:

Very common: dizziness (more frequently reported side effect),

Common: hypotension (including orthostatic hypotension), syncope, myocardial infarction or cerebrovascular accident, possibly secondary to excessive hypotension in high risk patients (see **SPECIAL PRECAUTIONS**), chest pain, rhythm disturbances, angina pectoris

Uncommon: orthostatic hypotension, palpitations, flushing

Rare: Raynaud's phenomenon

Respiratory, thoracic and mediastinal disorders:

Very common: cough

Common: dyspnoea

Uncommon: rhinorrhoea, sore throat, hoarseness, bronchospasm/asthma

Rare: pulmonary infiltrates

Gastrointestinal disorders:

Very common: nausea

Common: diarrhoea, abdominal pain

Uncommon: ileus, pancreatitis, vomiting, dyspepsia, constipation, anorexia

Rare: stomatitis, glossitis.

In very rare cases intestinal angio-oedema has been reported with angiotensin converting enzyme inhibitors including enalapril, a component of RENITEC.

Hepatobiliary disorders:

Rare: hepatic failure, hepatitis-either hepatocellular of cholestatic, jaundice

Skin and subcutaneous tissue disorders:

Common: rash, angioedema (which may be fatal), of the face, extremities, lips, tongue, glottis and/or larynx have been reported (see **SPECIAL PRECAUTIONS**)

Uncommon: diaphoresis, pruritus, urticaria, alopecia

Rare: erythema multiforme, Stevens-Johnson syndrome, exfoliative dermatitis, toxic epidermal necrolysis, pemphigus.

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

Musculoskeletal and connective tissue disorders:

Uncommon: muscle cramps

Renal and urinary disorders:

Uncommon: renal dysfunction, renal failure

Rare: oliguria

Reproductive system and breast disorders:

Uncommon: Impotence

General disorders and administration site disorders:

Very common: asthenia

Common: fatigue

Investigations:

Common: increases in serum creatinine

Uncommon: increases in blood urea

Rare: elevations of liver enzymes and/or bilirubin.

These are usually reversible upon discontinuation of RENITEC.

SPECIAL PRECAUTIONS

Symptomatic Hypotension

Symptomatic hypotension may occur in patients with uncomplicated hypertension. Hypotension is more likely to occur if the patient has been volume-depleted, e.g. by diuretic therapy, dietary salt restriction, dialysis, diarrhoea or vomiting (see **INTERACTIONS** and **SIDE EFFECTS**). In patients with heart failure, with or without associated renal insufficiency, symptomatic hypotension has been observed. This is most likely to occur in those patients with more severe degrees of heart failure, as reflected by the use of high doses of loop diuretics, hyponatraemia or functional renal impairment. In these patients, therapy should be started under medical supervision and the patients should be followed closely whenever the dose of RENITEC and/or diuretic is adjusted. Similar considerations may apply to patients with ischaemic heart or cerebrovascular disease in whom an excessive fall in blood pressure could result in myocardial infarction or cerebrovascular accident.

If hypotension occurs, the patient should be placed in the supine position and, if necessary, should receive an intravenous infusion of 0,9 % sodium chloride. A transient hypotensive response is not a contra-indication to further doses, which can be given usually without difficulty once the blood pressure has increased after volume expansion.

In some patients with congestive heart failure who have normal or low blood pressure, additional lowering of systemic blood pressure may occur with RENITEC. This effect is anticipated, and usually is not a reason to discontinue treatment. If hypotension becomes symptomatic, a reduction of dose or discontinuation of RENITEC may be necessary.

Symptomatic postural hypotension is infrequent

Aortic Stenosis/Hypertrophic Cardiomyopathy

RENITEC should be given with caution to patients with obstruction in the outflow tract of the left ventricle.

Renal Function Impairment

Patients with renal insufficiency may require reduced and/or less frequent doses of RENITEC. Careful dose titration and monitoring of renal function should be done (see **DOSAGE AND DIRECTIONS FOR USE**).

Some patients with no apparent pre-existing renal disease have developed minor and usually transient increases in blood urea and serum creatinine when RENITEC has been given concomitantly with a diuretic. Dosage reduction of RENITEC and/or discontinuation of the diuretic may be required.

Hypersensitivity/Angioedema

Angioedema 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. Even in those instances where swelling of only the tongue is involved, without respiratory distress, patients may require prolonged observation since treatment with antihistamines and corticosteroids may not be sufficient.

Fatalities have been reported due to angioedema associated with laryngeal oedema or tongue oedema. Patients with involvement of the tongue, glottis or larynx are likely to experience airway obstruction. Where there is involvement of the tongue, glottis or larynx, which are likely to cause airway obstruction, appropriate therapy which may include subcutaneous epinephrine solution 1:1 000 (0,3 ml to 0,5 ml) and/or measures to ensure a patent airway, should be administered promptly.

Black patients receiving ACE – inhibitors, including RENITEC, 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 RENITEC (also see **CONTRA-INDICATIONS**).

Anaphylactoid Reactions during Hymenoptera Desensitisation

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

Haemodialysis Patients (see **CONTRA-INDICATIONS**)

Anaphylactoid reactions have been reported in patients dialyzed with high-flux membranes and treated concomitantly with an ACE-inhibitor, including RENITEC. In these patients consideration should be given to using a different type of dialysis membrane or a different class of antihypertensive agent (see **CONTRA-INDICATIONS**).

Cough

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

Surgery/Anaesthesia

In patients undergoing major surgery or during anaesthesia 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.

Hyperkalaemia – see also **INTERACTIONS,** Serum Potassium

Risk factors for the development of hyperkalaemia include renal insufficiency, diabetes mellitus, and concomitant use of potassium-sparing diuretics (e.g., spironolactone, eplerenone, triamterene, or amiloride), potassium supplements, or potassium-containing salt substitutes.

The use of potassium supplements, potassium-sparing diuretics, or potassium-containing salt substitutes particularly in patients with impaired renal function may lead to a significant increase in serum potassium. Hyperkalaemia can cause serious, sometimes fatal, dysrhythmias.

If concomitant use of RENITEC and any of the above-mentioned agents is deemed appropriate, they should be used with caution and with frequent monitoring of serum potassium.

Hypoglycaemia

Diabetic patients treated with oral antidiabetic agents or insulin starting an ACE inhibitor should be told to closely monitor for hypoglycaemia, especially during the first month of combined use (see **INTERACTIONS**).

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.

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.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

Limited data are available for over dosage in humans. The most prominent feature of over dosage reported to date is marked hypotension, beginning some six hours after ingestion of tablets, concomitant with blockade of the renin-angiotensin system, and stupor.

The recommended treatment of over dosage is intravenous infusion of normal saline solution. If available, angiotensin II infusion may be beneficial. If ingestion is recent, induce emesis.

Enalaprilat may be removed from the general circulation by haemodialysis (see **SPECIAL PRECAUTIONS**, Haemodialysis Patients)

IDENTIFICATION

RENITEC 2,5 is a white, oval-shaped tablet, one side flat, scored and engraved MSD 14, other side concave and scored.

RENITEC 5 is a white, barrel-shaped tablet, engraved "RENITEC" on one side, scored on reverse.

RENITEC 10 is a rust-red, barrel-shaped tablet, engraved "RENITEC" on one side, scored on reverse.

RENITEC 20 is a peach, barrel-shaped tablet, engraved "RENITEC" on one side, scored on reverse.

PRESENTATION

RENITEC 2,5 tablets are available in packs of 14.

RENITEC 5, 10 and 20 tablets are available in packs of 28.

STORAGE INSTRUCTIONS

Store in a dry place at or below 25 °C. Protect from light.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBERS

RENITEC 2,5: 28/7.1.3/0665

RENITEC 5: T/7.1.3/164

RENITEC 10: T/7.1.3/165

RENITEC 20: T/7.1.3/166

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

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