IRISH MEDICINES BOARD ACTS 1995 AND 2006

MEDICINAL PRODUCTS(CONTROL OF PLACING ON THE MARKET)REGULATIONS,2007

(S.I. No.540 of 2007)

PA0408/068/002
Case No: 2046050

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

Ranbaxy Ireland Limited

Spafield, Cork Road, **Cashel**, **Co. Tipperary**, **Ireland**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Quinapril Ranbaxy 10 mg film-coated tablets

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **01/08/2008** until **31/07/2013**.

Signed on behalf of the Irish Medicines Board this

_____

A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Quinapril Ranbaxy 10mg film-coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 10mg quinapril (as hydrochloride).

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Film-coated tablet

White to off-white oval tablets with a film coating. The codes 'Q' and '10' are imprinted on one face of the tablet on either side of the break line. The other face of the tablet also has a break line.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Essential hypertension and decompensated heart failure.

4.2 Posology and method of administration

For oral administration

The absorption of quinapril is not affected by the presence of food. Tablets should be swallowed whole with a glass of water.

Essential hypertension
Monotherapy:
The recommended initial dose of quinapril is 10 mg once daily. The dose may be increased depending on the clinical effect. In general, the dose may be increased if the desired therapeutic effect at a given dosage is not achieved within 3 to 4 weeks. The normal maintenance dose is 20 to 40 mg per day.
Quinapril should be administered as a single dose or in two separate doses. A single daily dose is suitable for most patients.

Concurrent use with diuretics:
Symptomatic hypotension may occur once treatment with quinapril has started. This occurs more frequently in those patients being treated with diuretics. Care is therefore recommended here as these patients may have volume or sodium depletion.
Where possible treatment with diuretics should be stopped 2 to 3 days before commencing treatment with quinapril. For hypertensive patients for whom treatment with diuretics cannot be stopped, treatment with quinapril should be started at a dose of 2.5 mg. Kidney function and serum potassium need to be monitored. The maintenance dose of quinapril should be adapted to blood pressure response. Treatment with diuretics may be resumed where necessary. (Refer also to sections 4.4 and 4.5).

Decompensated Heart failure
Quinapril should be given as supplement to, or in combination with a diuretic and/or digitalis, when appropriate.

Treatment may be initiated in outpatient care. However, in patients with severe or unstable heart failure, reduced renal function, hypovolaemia, hyponatraemia, or systolic blood pressure <90 mmg Hg treatment should be initiated in hospital. This is also applicable for concomitant treatment with other vasodilating agents and high dose loop diuretics (> 80 mg furosemide), and for patients aged 70 years or over. The patient should be carefully monitored during the first two weeks and always when the dose of quinapril or diuretic is changed.

Initially a dose of 2.5 mg is administered, after which the patient is closely monitored for symptomatic hypotension. The Quinapril dose may gradually be titrated up to 40 mg/day divided in 2 doses. Patients are usually maintained effectively on doses of 10-20 mg/day given twice daily. Patients with mild to moderate heart failure, who have been haemodynamicaly stable on a daily dose of 20 mg divided in 2 doses for at least a month, may also be given the dose once daily.

Renal Impairment
The initial dose of quinapril needs to be decreased for patients with renal impairment since the plasma concentration of quinaprilat increases at a reduced creatinine clearance. The following initial doses are recommended:

Creatinine clearance (ml/min)	**Recommended initial day dose (mg)**
>60	10
30-60	5
10-30	2.5

Currently no information is available regarding patients with creatinine clearance below 10 ml/min, including dialysis patients.
Dialysis has no observable effect on the elimination of quinaprilat. A change in dose should be considered if an insufficient response is being achieved within 3 months.

Use in the elderly
Given that kidney function tends to decline with age this should also be taken into consideration with elderly patients. Treatment should therefore be started at 5 mg quinapril once daily.

Use in children and adolescents:
Effectiveness and safety of quinapril has not been determined for children and adolescents. Use of the product is therefore not recommended for these age-groups.

4.3 Contraindications

- Hypersensitivity to quinapril, to one or more of the excipients or to other ACE inhibitors.
- Medical history of angio-oedema associated with previous treatment with ACE inhibitors.
- Hereditary or idiopathic angio-oedema.
-2nd and 3rd trimester of pregnancy (see section 4.4 and 4.6).

4.4 Special warnings and precautions for use

Intestinal angioedema:
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 there was no prior history of facial angioedema and C-1 esterase levels were normal. The angioedema was diagnosed by procedures including abdominal CT scan or ultrasound, or at surgery, and symptoms resolved after stopping the ACE inhibitor. Intestinal angioedema should be included in the differential diagnosis of patients on ACE inhibitors presenting with abdominal pain.

Symptomatic hypotension
Symptomatic hypotension is rarely observed in patients with uncomplicated hypertension. Hypotension is more likely to occur in hypertensive patients with quinapril who are exhibiting volume depletion (for instance, through treatment with diuretics, salt-restricted diet, dialysis, diarrhoea or vomiting) or serious renin-dependent hypertension (refer to 4.5 Interactions with other drugs and other types of interaction and 4.8 Side-effects).

Symptomatic hypotension has been observed in patients with cardiac myopathies associated either with or without renal insufficiency. The risk of this is increased for patients with serious cardiac myopathies, as is apparent from the increased use of loop diuretics, hyponatraemia or reduced renal function. The start of treatment and dose modifications must be closely monitored in patients with an increased risk of symptomatic hypotension. Similar considerations apply for patients with ischaemic heart disease or cerebrovascular disease, where a significant drop in blood pressure could lead to a myocardial infarction or cerebrovascular accident.

If hypotension arises the patient should be confined to bed, and if necessary, an intravenous infusion of a physiological salt solution should be administered. A transient hypotensive response does not contraindicate subsequent doses, which may be administered without any problems as soon as blood pressure rises.

Aortic and mitral valve stenosis /hypertrophic cardiomyopathy

Quinapril, as with other ACE inhibitors, should be administered with care to patients with mitral valve stenosis or obstruction to left ventricular ejection, such as aortic stenosis and hypertrophic cardiomyopathy.

Renal insufficiency
In the event of renal insufficiency (creatinine clearance < 60 ml/min) the initial dose of quinapril should be adapted to the patient's creatinine clearance (refer to 4.2 Posology and method of administration) and subsequently according to the patient's response to treatment. Routine monitoring of potassium and creatinine forms part of the normal medical treatment of these patients.

Increases in blood urea and serum creatinine values have been observed in some patients being treated with ACE inhibitors with bilateral stenoses of the renal artery or with a single stenosis of the renal artery in a single kidney, which in general were reversible once treatment was stopped. This was particularly observable in patients with renal insufficiency. If there is a concurrent incidence of renovascular hypertension there is an increased risk of serious hypotension or renal insufficiency. For these patients treatment should be started with low doses and careful dose titration under strict medical supervision. Since treatment with diuretics may act to promote the occurrence of the above phenomena, this should be stopped and renal function monitored during the first weeks of treatment with quinapril.

Some hypertensive patients with no manifest prior renal disease may develop a rise in blood urea and serum creatinine values, which are normally limited and of a transient nature, particularly when quinapril is concurrently administered with diuretics. This is more observable with patients with prior renal insufficiency. It may be necessary to reduce the dose and/or stop treatment with diuretics and/or quinapril.

Kidney transplantation
There are no data available concerning administration of quinapril to patients with recent kidney transplants. Treatment with quinapril is therefore not recommended.

Haemodialysis patients
Anaphylactic reactions have been reported in patients who require dialysis with high-flux membranes, who are concurrently being treated with an ACE inhibitor. For these patients use of other types of dialysis membranes or other classes of anti-hypertensives should be considered.

Hypersensitivity / angio-oedema
In rare cases angio-oedema to the face, the extremities, lips, tongue, glottis and/or larynx have been reported in patients being treated with ACE inhibitors, including quinapril. This may occur at any time during treatment. In these cases use of quinapril should be stopped immediately, and appropriate treatment and monitoring should be instigated to ensure that the symptoms have fully disappeared before the patient is discharged. It may be necessary to observe patients for a long period of time, even in cases where only swelling in the tongue occurs in the absence of respiratory problems, as treatment with anti-histamines and corticosteroids may be insufficient.

In very rare cases, deaths have been reported as a result of angio-oedema in combination with laryngeal or tongue oedema. Patients experiencing oedema to the tongue, glottis or larynx will have a greater risk of respiratory tract obstructions, in particular patients who have previously undergone surgery to the respiratory tract.

Emergency treatment should be started immediately in these cases. This may consist of administration of adrenalin and/or maintaining an open airway. The patient must be placed under strict medical supervision until the symptoms have fully and permanently disappeared.

ACE inhibitors cause a higher incidence of angio-oedema in negroid patients compared to non-negroid patients.

Patients with a medical history of angio-oedema not associated with treatment with ACE inhibitors may run a higher risk of angio-oedema when treated with ACE inhibitors (refer to 4.3 Contraindications).

Anaphylactic reactions during LDL (low-density lipoprotein) aphaeresis
In rare cases life-threatening anaphylactic reactions have occurred in patients using ACE inhibitors during LDL aphaeresis with dextran sulphate. These reactions were avoided by temporarily interrupting treatment with ACE inhibitors for each aphaeresis.

Desensitisation
Some patients who were using ACE inhibitors during desensitisation treatment (e.g. hymenoptera poisoning) demonstrated long-term anaphylactic reactions. Reactions were avoided for these patients by temporarily stopping ACE inhibitors, but returned when the drug was inadvertently re-administered.

Hepatic insufficiency
ACE inhibitors are rarely associated with a syndrome that starts with cholestatic icterus and evolves into fulminant hepatic necrosis and (occasionally) death. The mechanisms underlying this syndrome are not known. Patients using ACE inhibitors who develop jaundice or exhibit a significant rise in liver enzymes must stop use of ACE inhibitors and need to receive an appropriate medical follow-up.

Neutropenia/Agranulocytosis
Neutropenia/Agranulocytosis, thrombocytopenia and anaemia have been reported with patients receiving ACE inhibitors. Neutropenia rarely occurs for patients with normal renal function and no other complicating factors. Neutropenia and agranulocytosis are reversible once ACE inhibitor treatment has been stopped. Quinapril must be administered with the uppermost care to patients with abnormalities in vascular collagen who are being treated with immunosuppressants, allopurinol or procainamide, or a combination of these complex factors, particularly in the event of prior renal insufficiency. Some of these patients have developed serious infections, which in some cases did not respond to intensive treatment with antibiotics. Periodic monitoring of white blood cell count is recommended if quinapril is being used for these patients, and the patient should be asked to report any sign of infection.

Ethnic differences
Similar to other ACE inhibitors, quinapril may be less effective in reducing blood pressure in negroid patients compared to non-negroid patients, possibly as a result of a higher prevalence of low renin levels in the hypertensive negroid population.

Coughing
Coughing is reported with the use of ACE inhibitors. This cough is non-productive, persistent and disappears once treatment is stopped. Coughs induced by ACE inhibitors should be considered as the differential diagnosis of coughing.

Surgery/Anaesthesia
Quinapril may block the production of angiotensin II, secondary to compensatory release of renin, in patients undergoing significant surgery or who have been administered anaesthetics which may induce hypotension. In the event of hypotension, this may be corrected by volume expansion, if it is expected to be a consequence of this mechanism.

Hyperkaliaemia
Increased levels of serum potassium have been observed in some patients being treated with ACE inhibitors, including quinapril. Patients who are at risk of hyperkaliaemia include those with renal insufficiency, diabetes mellitus, patients who are concurrently using potassium-sparing diuretics, potassium supplements or salt substitutes containing potassium, or patients who are using other drugs that are associated with an increase in serum potassium levels (e.g. heparin).

Regular monitoring of serum potassium levels is recommended should concurrent use of the above drugs be considered necessary (refer to section 4.5 Interactions with other drugs and other types of interactions).

Diabetics
Blood-sugar levels need to be closely monitored during the first month of treatment with ACE inhibitors in diabetics being treated with oral anti-diabetics or insulin (refer to 4.5 Interactions with other drugs and other types of interactions).

Lithium
In general the combination of lithium and quinapril is not recommended (refer to 4.5 Interactions with other drugs and other types of interactions).

Pregnancy:
Ace inhibitors should not be initiated during pregnancy. Unless continued ACE inhibitor therapy is considered essential, patients planning pregnancy should be changed to alternative anti-hypertensive treatments which have an established safety profile for use in pregnancy. When pregnancy is diagnosed, treatment with ACE inhibitors should be stopped immediately, and, if appropriate, alternative therapy should be started.(see sections 4.3 and 4.6)

Use of quinapril is not recommended in breastfeeding mothers.

4.5 Interaction with other medicinal products and other forms of interaction

Tetracyclines
Quinapril Ranbaxy 10 mg film-coated tablets contains magnesium which forms a chelate complex with tetracyclines reducing their absorption. This combination must be avoided.

Potassium-sparing diuretics or potassium supplements
ACE inhibitors reduce potassium loss induced by diuretics. Potassium-sparing diuretics (e.g. spironolactone, triamterene or amiloride), potassium supplements or salt substitutes containing potassium may lead to a significant increase in serum potassium levels. If concurrent use is indicated due to proven hypokalaemia, ACE inhibitors need to be used with care, through frequent monitoring of serum potassium levels (refer to 4.4 Special warnings and precautions for use).

Diuretics (thiazides or loop diuretics)
Prior treatment with high doses of diuretics may lead to volume depletion and a risk of hypotension when treatment with quinapril is started (refer to 4.4 Special warnings and precautions for use). Hypotensive effects may be reduced by stopping diuretics, increasing volume or salt intake or starting treatment with quinapril at a lower dose.

Lithium
A reversible increase in lithium levels and lithium toxicity has been reported during concurrent use of lithium and ACE inhibitors. Concurrent use of thiazide diuretics may increase the risk of lithium toxicity, and increases the already high risk of lithium toxicity with ACE inhibitors. Use of quinapril in combination with lithium is not recommended, however serum lithium levels should be closely monitored, if the combination is necessary (refer to 4.4 Special warnings and precautions for use).

Tricyclic antidepressants / Anti-psychotics / Anaesthetics / Narcotics
Concurrent use of ACE inhibitors with certain anaesthetics, tricyclic anti-depressants and anti-psychotics may lead to further reductions in blood pressure (refer to 4.4 Special warnings and precautions for use).

Non-steroidal anti-inflammatory drugs (NSAID)
Chronic administration of NSAIDs may reduce the anti-hypertensive effect of ACE inhibitors. NSAIDs and ACE inhibitors have an additive effect on the increase in serum potassium levels, which may lead to deterioration in kidney function. These effects are reversible in general. Renal insufficiency may arise in rare cases, in particular for patients with disrupted renal function, such as the elderly or de-hydrated patients.

Sympathomimetics
Sympathomimetics may reduce the anti-hypertensive effects of ACE inhibitors.

Anti-diabetics
Epidemiological studies suggest that concurrent administration of ACE inhibitors and anti-diabetics (insulin, oral hypoglycaemic agents) may give rise to a significant reduction in blood glucose with a risk of hypoglycaemia. This phenomenon appears to occur more frequently during the first weeks of combination therapy and with patients with renal insufficiency.

Trimethoprim
Serious hyperkaliaemia has been reported during concurrent administration of ACE inhibitors and trimethoprim.

Antacids
Antacids reduce the biological availability of ACE inhibitors.

Allopurinol, cytostatic and immunosuppressive agents, systemic corticosteroids or procainamide: concomitant administration with ACE inhibitors may lead to an increased risk for leucopenia.

Alcohol, barbiturates or narcotics: potentiation of orthostatic hypotension may occur.

Other hypertensive drugs: there may be an additive effect or potentiation.

4.6 Pregnancy and lactation

Pregnancy
The use of ACE inhibitors is not recommended during the first trimester of pregnancy (see section 4.4).The use of ACE inhibitors is contra-indicated during the 2nd and 3rd trimester of pregnancy (see section 4.3 and 4.4).
Epidemiological evidence regarding the risk of teratogenicity following exposure to ACE inhibitors during the first trimester of pregnancy has not been conclusive; however a small increase in risk cannot be excluded. Unless continued ACE inhibitor therapy is considered essential, patients planning pregnancy should be changed to alternative anti-hypertensive treatments which have an established safety profile for use in pregnancy. When pregnancy is diagnosed, treatment with ACE inhibitors should be stopped immediately, and, if appropriate, alternative therapy should be started.
ACE inhibitor therapy 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, hyperkalaemia). (See also 5.3 'Preclinical safety data'). Should exposure to ACE inhibitor have occurred from the second trimester of pregnancy, ultrasound check of renal function and skull is recommended. Infants whose mothers have taken ACE inhibitors should be closely observed for hypotension (see also section 4.3 and 4.4).

Lactation
Quinaprilat is excreted in breast milk. Use of quinaprilat is not recommended in women who are breastfeeding. (See section 5.3)

4.7 Effects on ability to drive and use machines

No data are available regarding the effect of quinapril on driving ability. The possible incidental occurrences of dizziness and tiredness should be taken into account when driving and operating machinery.

4.8 Undesirable effects

The following undesirable effects have been observed during treatment with quinapril and other ACE inhibitors. In this section frequencies of undesirable effects are defined as follows: 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).

Disorders of blood and lymphatic system:
Occasional: haemolytic anaemia, thrombocytopenia
Uncommon: neutropenia (refer to section 4.4)
Rare: agranulocytosis, WBC abnormalities

Psychological disorders:
Uncommon: Sleep disturbance, nervousness
Rare: Depression, confusion, drowsiness

Nervous system disorders:
Common: Dizziness, headache
Uncommon: Paraesthesia, syncope, somnolence
Rare: Neuropathy, cerebral haemorrhage, transient ischaemic attacks
Unknown: disorders of balance

Visual disorders:
Rare: Amblyopia, visual disturbances

Disorders of balance organs and ears:
Rare: Tinnitus
Uncommon: Vertigo

Cardiac disorders:
Uncommon: Palpitations, chest pain, tachycardia, angina pectoris, asystole, myocardial infarction

Vascular disorders:
Common: Hypotension
Uncommon: Vasodilation, Orthostatic hypotension

Disorders of the respiratory system, chest and mediastinum:
Common: Cough, upper respiratory tract infections, dyspnoea, pharyngitis, sinusitis,
Rare: Bronchial spasm, deterioration of asthma, rhinitis, eosinophilic pneumonitis, Bronchitis

Gastro-intestinal disorders:
Common: Nausea, vomiting, diarrhoea
Uncommon: Dyspepsia, abdominal pain, dry mouth, flatulence, gastritis, glossitis, ileus
Rare: Taste disturbances, constipation, pancreatitis
Unknown: Intestinal angioedema

Skin and subdermal disorders:
Uncommon: Exanthema, pruritus, urticaria, exfoliative dermatitis, rash,
Rare: Alopecia, photosensitivity, Pemphigus, psoriasis-like exanthema, Stevens-Johnson syndrome, toxic epidermal necrolysis erythema multiforme, angioneurotic oedema (refer to sections 4.3 and 4.4).
Unknown: Oedema

Musculo-skeletal and connective tissue disorders:
Rare: Myalgia, arthralgia, back pain

Renal and urinary tract disorders:
Rare: Kidney function disorders
Uncommon: urinary tract infections, dysuria, urination urge

Reproductive system and breast disorders:
Rare: Impotence

Hepatobiliary Disorders:
Very rare: Liver function disorders, Cholestatic icterus
Rare: Hepatitis
Uncommon: Hepatic insufficiency

Metabolism and Nutrition Disorders:
Common: Hyperkalaemia

General disorders:
Common: Fatigue
Uncommon: Fever, anaphylactoid reaction

Rare incidences of agranulocytosis have been reported, as well as a syndrome consisting of fever, serositis, myalgia, arthralgia/arthritis, positive ANA titres, increase in ESR, eosinophilia and leucocytosis. Gynaecomastia and vasculitis have been reported in use of other ACE inhibitors and it cannot be concluded that these undesirable effects are class specific.

Laboratory results: Temporary increases in serum creatinine levels and urea levels have been reported, particularly in association with concurrent treatment with diuretics. A slight reduction in haemoglobin and haematocrit has been reported in use of other ACE inhibitors. It may not be concluded that these observations are class specific

Investigations: Decrease in platelets and white cell count as well as elevation of liver enzymes and serum bilirubin. Cases of haemolytic anaemia have been reported in patients with a congential deficiency of G-6-PDH

4.9 Overdose

Symptoms
Symptoms of an overdose are severe hypotension, shock, stupor, bradycardia, electrolyte disturbances and renal insufficiency.

Treatment
Measures should be taken to prevent absorption (e.g. gastric lavage, adsorbents and sodium sulphate within 30 minutes of ingestion) and speed-up elimination if ingestion occurred quite recently. If hypotension arises the patient should be placed in the shock position and quickly administered salt and volume supplements. Treatment with angiotensin II should be considered. Bradycardia or serious vagal reactions should be treated with an administration of atropine. Use of a pacemaker may be considered.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: ACE inhibitors. ATC code: C09AA06.

Quinapril hydrochloride is the hydrochloride salt of quinapril. This molecule has 3 chiral centres and is a pure stereo-isomer.

Quinapril is a pro-drug, which is hydrolysed into the active metabolite quinaprilat, a potent long-acting angiotensin converting enzyme (ACE) inhibitor in plasma and tissue. ACE catalyses the conversion of angiotensin I to angiotensin II, a potent vasoconstrictor. Inhibition of ACE leads to a lowered concentration of angiotensin II and a reduced aldosterone secretion; the metabolism of bradykinin is also possibly inhibited.

In clinical trials quinapril appeared to be neutral on the surface of lipids and had no effect on glucose metabolism. Quinapril reduces the total peripheral and renal arterial resistance. In general there are no significant relevant changes in renal blood flow or glomerular filtration ratio. Quinaprilat leads to a reduction in blood pressure in lying, standing and sitting positions. The maximum effect is achieved after 2-4 hours when used at the recommended doses. In some patients it may take between 2 and 4 weeks before the maximum effect on blood pressure reduction is achieved. In experimental hypertension models in animals a reduction in left ventricular hypertrophy was observed with use of quinapril. Details are not available for morbidity/mortality.

Quinapril may, where necessary, be administered with other blood pressure reducing agents. Concurrent use with thiazide diuretics increases the blood pressure reducing effect of quinapril.

Administration of quinapril to patients with decompensated heart failure reduces peripheral vascular resistance, mean arterial pressure, systolic and diastolic blood pressure and pulmonary capillary wedge pressure; heart minute volume increases.

5.2 Pharmacokinetic properties

The biological availability of the active metabolite, quinaprilat, is 30-40% of the administered oral dose of quinapril. Maximum plasma levels are achieved after approximately 2 hours. Quinapril absorption is not influenced by concurrent intake of food, but food that is extremely rich in fat may reduce intake. Approximately 97% of the drug is bound to plasma proteins. Quinaprilat has a half-life of 3 hours during repeated administration. The steady state is reached within 2-3 days. Quinaprilat is primarily excreted unchanged through the kidneys. Clearance amounts to 220 ml/min. Dialysis does not significantly affect quinapril elimination. Quinapril was not recovered in the dialysate in patients with renal insufficiency; approximately 2.5% of the metabolite quinaprilat dose was recovered after peritoneal dialysis and 5.4% after haemodialysis.
For patients with renal insufficiency the half-life is extended and the plasma concentration of quinaprilat increased (refer to 4.2 Posology and method of administration). A lower concentration of quinaprilat was determined in patients with serious hepatic insufficiency as a consequence of the reduced hydrolysis of quinapril.

5.3 Preclinical safety data

Pre-clinical data do not demonstrate any particular risk to humans based on conventional studies of pharmacological safety, repeated dose toxicity, genotoxicity and carcinogenic capability. Reproductive toxicity studies suggest that quinapril has no negative effects on fertility and reproductive capacity in rats and that it has no teratogenic effect. Milk quinaprilat concentrations were 3-5% of the plasma concentrations 3-5 hr after dosing. The group of ACE inhibitors appear to have foetal toxic effects (causing lesions and/or death of foetus) when administered in the second or third trimester.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:
micro-crystalline cellulose (E 460),
crospovidone, (type A)
magnesium carbonate (heavy) (E 504),
magnesium stearate (E 470B),
povidone K-30 (E 1201).

Film-coating:
lecithin (E 322),
poly(vinyl alcohol),
talc (E 553B),
titanium dioxide (E171)

xanthan gum (E 415).

6.2 Incompatibilities

Not applicable

6.3 Shelf Life

2 years.

6.4 Special precautions for storage

Do not store above 25°C

6.5 Nature and contents of container

Blister OPA/Aluminium/PVC/Aluminium

Packets of 28, 30, 50, 98 or 100 coated tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Ranbaxy Ireland Ltd.
Spafield
Cork Road
Cashel
Co. Tipperary

8 MARKETING AUTHORISATION NUMBER

PA0408/068/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 1st August 2008

10 DATE OF REVISION OF THE TEXT