APPROVED PROFESSIONAL INFORMATION

SCHEDULING STATUS:

S3

PROPRIETARY NAME (AND DOSAGE FORM):

KWINCO 10/12,5 mg (Tablet)

KWINCO 20/12,5 mg (Tablet)

COMPOSITION:

KWINCO 10/12,5 mg:

Each film coated tablet contains quinapril hydrochloride equivalent to quinapril 10 mg and hydrochlorothiazide 12,5 mg. Contains lactose.

Other ingredients for **KWINCO** are crospovidone, lactose monohydrate, magnesium carbonate, magnesium stearate and povidone. The coating ingredients are hydroxypropyl cellulose, hypromellose, iron oxide red, iron oxide yellow, macrogol/PEG 400 and titanium dioxide.

KWINCO 20/12,5 mg:

Each film coated tablet contains quinapril hydrochloride equivalent to quinapril 20 mg and hydrochlorothiazide 12,5 mg. Contains lactose.

Other ingredients for **KWINCO** are crospovidone, lactose monohydrate, magnesium carbonate, magnesium stearate and povidone. The coating ingredients are hydroxypropyl cellulose, hypromellose, iron oxide red, iron oxide yellow, macrogol/PEG 400 and titanium dioxide.

PHARMACOLOGICAL CLASSIFICATION:

A: 7.1.3 Vascular medicines - other hypotensives.

PHARMACOLOGICAL ACTION:

Pharmacodynamics:

KWINCO is a fixed-combination tablet that combines an angiotensin- converting enzyme (ACE) inhibitor, quinapril hydrochloride, and a thiazide diuretic, hydrochlorothiazide. Quinapril hydrochloride

is the hydrochloride salt of quinapril, the ethyl ester of a long-acting nonsulfhydryl, specific angiotensin-converting enzyme (ACE) inhibitor. Quinapril is rapidly de-esterified to quinaprilat (quinapril diacid, the principal metabolite).

Quinapril reduces vascular resistance; mean arterial pressure, systolic and diastolic blood pressure. With chronic treatment, hydrochlorothiazide reduces peripheral vascular resistance, mean arterial pressure, and systolic and diastolic blood pressure.

Hydrochlorothiazide acts on the kidneys to increase the excretion of sodium and chloride and an accompanying volume of water. Hydrochlorothiazide also increases the loss of potassium, bicarbonate and other electrolytes via the urine, and it decreases calcium excretion.

Hydrochlorothiazide increases plasma renin activity (PRA), increases aldosterone secretion, and decreases serum potassium.

Pharmacokinetics:

Quinapril:

Peak plasma quinapril concentrations are observed within one hour following oral administration. Based on recovery of quinapril and its metabolites in urine, the extent of absorption is approximately 60 %. Quinapril absorption is not influenced by food. Following absorption, quinapril is de-esterified to its major active metabolite, quinaprilat, a potent ACE-inhibitor, and to minor inactive metabolites. Quinapril has an apparent half-life of approximately one hour. Peak plasma quinaprilat concentrations are observed approximately two hours following an oral dose of quinapril. Quinaprilat is eliminated primarily by renal excretion and has an elimination half-life of three hours, and a terminal half-life of approximately 25 hours. The excretion of quinapril and quinaprilat in patients with renal insufficiency is decreased. The elimination of quinaprilat is reduced in elderly patients (> 65 years) and correlates well with the diminished renal function which occurs in the elderly (see "**DOSAGE AND DIRECTIONS FOR USE**"). Quinaprilat concentrations are reduced in patients with alcoholic cirrhosis due to impaired de-esterification of quinapril. Studies in rats indicate that quinapril and its metabolites do not cross the blood-brain barrier.

Hydrochlorothiazide:

After oral administration of hydrochlorothiazide, diuresis begins within 2 hours, peaks in about 4 hours, and lasts about 6 to 12 hours. When plasma levels have been followed for at least 24 hours,

the plasma half-life has been observed to vary between 4 to 15 hours. At least 61 % of the oral dose is eliminated unchanged within 24 hours. Hydrochlorothiazide crosses the placental but not the blood-brain barrier.

Hydrochlorothiazide is excreted unchanged by the kidney.

INDICATIONS:

KWINCO is indicated for the treatment of mild to moderate hypertension in patients who have been stabilised on the individual components given in the same proportions.

CONTRA-INDICATIONS:

- Hypersensitivity to any of the components of **KWINCO**.
- Because of the hydrochlorothiazide component, **KWINCO** is contra-indicated in patients with hypersensitivity to other sulphonamide – derived medicines.
- A history of angioedema related to previous therapy with ACE inhibitors or angiotensin receptor blockers (ARBs): such patients must never again be given these medicines.
- Hereditary or idiopathic angioedema.
- Hypertrophic obstructive cardiomyopathy (HOCM).
- Anuria or severe renal function impairment (creatinine clearance < 30 ml/min) – hydrochlorothiazide may produce cumulative effects or precipitate azotaemia.
- 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.
- **KWINCO** is a fixed dose combination tablet containing a thiazide diuretic and ACE inhibitor, and therefore should not be given to patients with Addison's disease. Lithium therapy: Concomitant administration with **KWINCO** may lead to toxic blood concentrations of lithium.

- **KWINCO** is contra-indicated throughout pregnancy and during lactation (see "**WARNINGS AND SPECIAL PRECAUTIONS**" and "**PREGNANCY AND LACTATION**").

WARNINGS AND SPECIAL PRECAUTIONS

WARNINGS:

Should a woman become pregnant while receiving KWINCO, the treatment should be stopped promptly and switched to a different class of medicine. (See "CONTRA-INDICATIONS" and "PREGNANCY AND LACTATION").

Should a woman contemplate pregnancy, the doctor should consider alternative medication.

- Patients with electrolyte imbalances – the condition may be exacerbated. The correction of electrolyte imbalance prior to administration of **KWINCO** is recommended.
- Patients with allergy or bronchial asthma – hypersensitivity reactions to hydrochlorothiazide may be more likely in these patients.

Special Precautions:

Quinapril:

Angioedema: Angioedema which may be fatal has been reported in patients treated with **KWINCO**. If laryngeal stridor or angioedema of the face, tongue, or glottis occurs, treatment with **KWINCO** should be discontinued immediately, the patient treated in accordance with accepted medical care, and carefully observed until the swelling disappears. In instances where swelling is confined to the face and lips, the condition generally resolves without treatment; antihistamines may be useful in relieving symptoms. Angioedema associated with laryngeal involvement may be fatal. Where there is involvement of the tongue, glottis, or larynx likely to cause airway obstruction, emergency therapy including but not limited to subcutaneous epinephrine (adrenaline) injection 1:1 000 (0,3 to 0,5 ml), should be promptly instituted (see "**SIDE-EFFECTS**").

Patients with a history of angioedema unrelated to ACE-inhibitor therapy may be at increased risk of angioedema while receiving **KWINCO**.

Anaphylactoid reactions during desensitisation: Patients receiving ACE-inhibitors during desensitising treatment with hymenoptera venom have sustained life-threatening anaphylactoid

reactions. In the same patients, these reactions may be avoided when ACE-inhibitors are temporarily withheld, but they may reappear upon inadvertent re-challenge.

Hypotension: Symptomatic hypotension is a possible consequence of therapy in salt/volume depleted patients, such as those previously treated with diuretics or patients on dialysis (see "**INTERACTIONS**", and "**SIDE-EFFECTS**").

In patients at risk of excessive hypotension, including those with congestive heart failure, therapy should be started under close medical supervision. These patients should be followed closely for the first 2 weeks of treatment and whenever the dosage of antihypertensive medication is increased (see "**DOSAGE AND DIRECTIONS FOR USE**").

The patient should be placed in the supine position and, if necessary, normal saline may be administered intravenously, if symptomatic hypotension occurs. A transient hypotensive response is not a contra-indication to further doses; however, lower doses of quinapril or reduced concomitant diuretic therapy should be considered.

Neutropenia/Agranulocytosis: In patients with uncomplicated hypertension, ACE-inhibitors have been associated with agranulocytosis and bone marrow depression. Periodic monitoring of white blood cell counts in patients with collagen vascular disease and/or renal disease should be considered.

Impaired renal function: As a consequence of inhibiting the renin-angiotensin-aldosterone system, changes in renal function may be anticipated in susceptible individuals. In patients with severe heart failure whose renal function may depend on the activity of the renin-angiotensin-aldosterone system, treatment with **KWINCO** may be associated with oliguria and/or progressive azotaemia and rarely acute renal failure and/or death.

In clinical studies in hypertensive patients with unilateral or bilateral renal artery stenosis, increases in blood urea and serum creatinine have been observed.

Some patients with hypertension or heart failure with no apparent pre-existing renal vascular disease have developed increases in blood urea and serum creatinine, when quinapril has been given concomitantly with a diuretic. This is more likely to occur in patients with pre-existing renal impairment. Dosage reduction and/or discontinuation of any diuretic and/or quinapril may be required.

Renal function should be closely monitored in patients with renal impairment.

ACE-inhibitors have been associated with hypoglycaemia in diabetic patients on insulin or oral hypoglycaemic agents; closer monitoring of diabetic patients may be required.

Hyperkalaemia and potassium-sparing diuretics: Patients on quinapril alone may have increased serum potassium levels. When administered concomitantly, quinapril may reduce the hypokalaemia induced by thiazide diuretics. Quinapril has not been studied as concomitant therapy with potassium-sparing diuretics. Because of the risk of further potentiating increases in serum potassium, combination therapy with potassium-sparing diuretics is contra-indicated (see "**CONTRA-INDICATIONS**"). With **KWINCO**, which contains both an ACE-inhibitor and a diuretic, the addition of a potassium-sparing diuretic is contra-indicated.

Surgery/anaesthesia: In patients undergoing anaesthesia with agents that produce hypotension, quinapril may block 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.

Hydrochlorothiazide:

Hydrochlorothiazide such as in **KWINCO** should not be used in patients with severe renal disease since uraemia may result. Cumulative medicine effects may develop in patients with impaired renal function (see "**CONTRA-INDICATIONS**").

Hydrochlorothiazide such as in **KWINCO** should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte balance may precipitate hepatic coma.

In patients with or without a history of allergy or bronchial asthma, sensitivity reactions may occur.

Exacerbation or activation of systemic lupus erythematosus has been reported.

Serum electrolyte evaluation should be performed at appropriate intervals to detect possible electrolyte imbalance.

All patients receiving hydrochlorothiazide therapy (such as in **KWINCO**) should be observed for clinical signs of fluid or electrolyte imbalance, including hyponatraemia, hypochloraemic alkalosis, and hypokalaemia. Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Warning signs or symptoms of fluid and electrolyte imbalance, irrespective of cause, include dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscle fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbances such as nausea and vomiting.

Hypokalaemia may develop, especially with brisk diuresis, when severe cirrhosis is present, or after prolonged therapy. Interference with adequate oral electrolyte intake will also contribute to hypokalaemia. Hypokalaemia may cause cardiac dysrhythmia and may also sensitise or exaggerate the response of the heart to the toxic effects of digoxin, for example, increased ventricular irritability. Because quinapril reduces the production of aldosterone, concomitant therapy with quinapril attenuates the diuretic-induced potassium loss (see "**INTERACTIONS**", **Agents Increasing Serum Potassium**).

Although any chloride deficit is generally mild and usually does not require specific treatment, chloride replacement may sometimes be required in the treatment of metabolic alkalosis.

In hot weather, dilutional hyponatraemia may occur in oedematous patients. Appropriate therapy is water restriction, rather than administration of salt, except in rare instances when the hyponatraemia is life threatening. In actual salt depletion, appropriate replacement is the therapy of choice.

Hyperuricaemia may occur or gout may be precipitated in certain patients receiving hydrochlorothiazide therapy.

In diabetic patients dosage adjustments of insulin or oral hypoglycaemic agents may be required.

Hyperglycaemia may occur with hydrochlorothiazide, such as in **KWINCO**. Thus, latent diabetes mellitus may become manifest during therapy.

The antihypertensive effects of **KWINCO** may be enhanced in the post-sympathectomy patient.

If progressive renal impairment becomes evident, it may be necessary to withhold or discontinue diuretic therapy.

Hydrochlorothiazide has been shown to increase urinary magnesium excretion, which may cause hypomagnesaemia.

Hydrochlorothiazide may decrease urinary calcium excretion. Hydrochlorothiazide may cause intermittent and slight serum calcium elevation in the absence of known calcium metabolism disorders. Marked hypercalcaemia may be evidence of hidden hyperparathyroidism. Hydrochlorothiazide and thus **KWINCO** should be discontinued before performing tests for parathyroid function.

Increases in cholesterol and triglyceride levels may be associated with hydrochlorothiazide therapy.

Hydrochlorothiazide decreases the serum PBI levels without signs of thyroid disturbance.

Paediatric use: Safety and efficacy in children have not been established.

Elderly use: Elderly patients exhibited increased AUC and peak levels for quinaprilat compared to values observed in younger patients; this appeared to be related to decreased renal function rather than age itself. No overall differences in effectiveness or safety were observed between older and younger patients, however, greater sensitivity of some older individuals cannot be ruled out.

KWINCO contains lactose and should not be administered to patients with rare hereditary problems, or a history of galactose intolerance, lapp lactase deficiency or glucose-galactose malabsorption.

Ability to drive and use machinery:

The ability to engage in activities such as operating machinery or operating a motor vehicle may be impaired due to dizziness and fatigue.

INTERACTIONS:

Quinapril:

Tetracycline:

Simultaneous administration of tetracycline with quinapril reduced the absorption of tetracycline by approximately 28 % to 37 % in subjects. Decreased absorption is due to the presence of magnesium carbonate as an excipient in **KWINCO**. This interaction should be considered when contemplating concurrent **KWINCO** and tetracycline therapy.

Lithium:

Increased serum lithium levels and symptoms of lithium toxicity have been reported in patients receiving concomitant lithium and ACE inhibitory therapy. With **KWINCO**, which includes a diuretic, the risk of lithium toxicity may be increased (see "**CONTRA-INDICATIONS"**).

Other agents:

When quinapril was administered concomitantly with propranolol, hydrochlorothiazide, digoxin or cimetidine, no clinically important pharmacokinetic interactions occurred. When quinapril and warfarin were given together, no change in prothrombin complex activity occurred.

Concomitant diuretic therapy:

Patients on diuretics, especially those on recently instituted diuretic therapy, may experience an excessive reduction of blood pressure after initiation of therapy with quinapril. In patients in whom a

diuretic is continued, medical supervision should be provided up to two hours after the initial dosage of **KWINCO** (see "**WARNINGS AND SPECIAL PRECAUTIONS**" and "**DOSAGE AND DIRECTIONS FOR USE**").

Agents increasing serum potassium:

Since **KWINCO** contains quinapril, the addition of a potassium-sparing diuretic is not recommended.

Hydrochlorothiazide:

When administered concurrently, the following medicines may interact with hydrochlorothiazide:

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

Anti-diabetic medicines (oral hypoglycaemic agents and insulin): Dosage adjustments of the anti-diabetic medicine may be required.

Other antihypertensive medicines: Additive effect or potentiation.

Corticosteroids, ACTH: Intensified electrolyte depletion, particularly hypokalaemia.

Pressor amines, (e.g. noradrenaline): Possible decreased response to pressor amines, but not sufficient to preclude their use.

Skeletal muscle relaxants, nondepolarising (e.g. tubocurarine): Possible increased responsiveness to the muscle relaxant.

Lithium: should not be given with diuretics. Diuretic agents reduce the renal clearance of lithium and add a high risk of lithium toxicity (see "**CONTRA-INDICATIONS**").

Non-steroidal Anti-inflammatory Medicines: In some patients, the administration of a non-steroidal anti-inflammatory agent can reduce the diuretic, natriuretic, and antihypertensive effects of loop, potassium-sparing, and thiazide diuretics. Therefore, when **KWINCO** and non-steroidal anti-inflammatory agents are used concomitantly, the patient should be observed closely to determine if the desired effect of **KWINCO** is obtained.

Beta2-agonists: Enhancement of potassium – depleting effect of hydrochlorothiazide.

PREGNANCY AND LACTATION:

Pregnancy: Both components of **KWINCO** cross the placenta. **KWINCO** is contra-indicated throughout pregnancy.

KWINCO passes through the placenta and can be presumed to cause disturbance in fetal blood pressure regulatory mechanisms. Oligohydramnios as well as hypotension, oliguria and anuria in new-borns, have been reported after administration of **KWINCO** in the second and third trimester. Cases of defective skull ossification have been observed. Prematurity and low birth mass can occur. In addition, the use of **KWINCO** during the first trimester of pregnancy has been associated with an increased risk of birth defects, in particular of the cardiovascular and central nervous system (See "**CONTRA-INDICATIONS**" and "**WARNINGS AND SPECIAL PRECAUTIONS**").

ACE – inhibitors and ARB's, including **KWINCO** can cause fetal morbidity and death when given to pregnant women.

When pregnancy is established **KWINCO** should be discontinued as soon as possible and monitoring of the fetal development should be performed on a regular basis. In women planning to become pregnant, ACE – inhibitors (including **KWINCO**) should not be used. Women of child-bearing age should be made aware of the potential risks of ACE – inhibitors (including **KWINCO**).

Breastfeeding Mothers: Because quinapril and its metabolites as well as hydrochlorothiazide are secreted in human breast milk, **KWINCO** should not be used by breastfeeding women.

DOSAGE AND DIRECTIONS FOR USE:

Effective blood pressure control is usually achieved with a daily dose of 10/12,5 mg to a maximum of 20/25 mg.

Dosage Adjustment in Renal Impairment: **KWINCO** should not be used as initial therapy in patients with severe renal impairment (creatinine clearance < 30 ml/min).

KWINCO is not recommended for patients with hepatic impairment.

SIDE-EFFECTS:

Adverse experiences that have occurred have been limited to those that have been previously reported with quinapril or hydrochlorothiazide.

The most frequent clinical adverse experiences were headache, dizziness, cough, and fatigue. See "**WARNINGS AND SPECIAL PRECAUTIONS**" regarding angioedema and excessive hypotension or syncope. Adverse experiences by bodily systems reported during treatment with **KWINCO** include the following:

Infections and Infestations:

Less frequent: Viral infection.

Blood and the lymphatic system disorders:

Frequency not known: Haemolytic anaemia.

Immune system disorders:

Angioedema has been reported in patients receiving quinapril (see **"WARNINGS AND SPECIAL PRECAUTIONS**").

Psychiatric disorders:

Frequent: Somnolence, insomnia.

Nervous system disorders:

Frequent*:* Headache, dizziness.

Less frequent*:* Vertigo, paraesthesia, nervousness, syncope.

Cardiac disorders:

Frequent*:* Chest pain.

Less frequent*:* Tachycardia, palpitations.

Vascular disorders:

Frequent*:* Vasodilation

Frequency not known: Postural hypotension.

Respiratory, thoracic and mediastinal disorders:

Frequent: Coughing, rhinitis, upper respiratory infection, bronchitis, pharyngitis.

Less frequent*:* Dyspnoea, sinusitis.

Gastro-intestinal disorders:

Frequent*:* Nausea and/or vomiting, abdominal pain, dyspepsia, diarrhoea.

Less frequent*:* Flatulence, dry mouth or throat, constipation.

Frequency not known*:* Pancreatitis.

Skin and subcutaneous tissue disorders:

Less frequent: Alopecia, pruritus, rash.

Frequency not known*:* Erythema multiforme, exfoliative dermatitis, pemphigus.

Renal and urinary disorders:

Less frequent*:* Impotence, urinary tract infection.

Frequency not known*:* Urinary abnormality, dysuria, urinary frequency.

Musculoskeletal, connective tissue and bone disorders:

Frequent*:* Myalgia, back pain.

Less Frequent: Arthralgia.

Frequency not known*:* Muscle cramps.

General disorders and administrative site conditions:

Frequent*:* Fatigue, asthenia.

Less frequent: Peripheral oedema, fever.

Frequency not known*:* Malaise.

Investigations:

Serum electrolytes: (see "**WARNINGS AND SPECIAL PRECAUTIONS**").

Frequent*:* Creatinine, blood urea: increases (> 1,25 times the upper limit of normal) in serum creatinine and blood urea.

Serum uric acid, glucose, magnesium, cholesterol, triglyceride, protein-bound iodine (PBI), parathyroid function tests and calcium: (see "**WARNINGS AND SPECIAL PRECAUTIONS**").

Other adverse reactions that have been reported with the individual components are listed below:

Quinapril:

Psychiatric disorders:

The following side-effects have been reported, but frequencies are unknown*:* Insomnia.

Nervous system disorders:

Frequent*:* Headache.

The following side-effects have been reported, but frequencies are unknown*:* Dizziness, depression.

Cardiac disorders:

The following side-effects have been reported, but frequencies are unknown*:* Angina pectoris.

Vascular disorders:

The following side-effects have been reported, but frequencies are unknown: Hypotension.

Respiratory, thoracic and mediastinal disorders:

Frequent*:* Coughing.

The following side-effects have been reported, but frequencies are unknown*:* Rhinitis, dyspnoea

Gastro-intestinal disorders:

Less frequent*:* Diarrhoea, nausea

The following side-effects have been reported, but frequencies are unknown: Vomiting, dyspepsia.

Musculoskeletal, connective tissue and bone disorders:

The following side-effects have been reported, but frequencies are unknown*:* Myalgia, back pain.

General disorders and administrative site conditions:

Less frequent*:* Fatigue.

The following side-effects have been reported, but frequencies are unknown*:* Increased perspiration.

Investigations:

Frequent*:* Quinapril: Hyperkalaemia.

Hydrochlorothiazide:

Blood and lymphatic system disorders:

Less frequent*:* Agranulocytosis, thrombocytopenia.

The following side-effects have been reported, but frequencies are unknown*:* Leukopenia, aplastic anaemia, haemolytic anaemia.

Immune system disorders:

Less frequent*:* Urticaria.

The following side-effects have been reported, but frequencies are unknown*:* Purpura, anaphylactic reactions.

Psychiatric disorders:

The following side-effects have been reported, but frequencies are unknown*:* Restlessness.

Eye disorders:

The following side-effects have been reported, but frequencies are unknown*:* Xanthopsia.

Respiratory, thoracic and mediastinal disorders:

The following side-effects have been reported, but frequencies are unknown: Respiratory distress including pneumonitis and pulmonary oedema

Gastro-intestinal disorders:

Less frequent*:* Pancreatitis, anorexia.

The following side-effects have been reported, but frequencies are unknown*:* Gastric irritation, cramping, sialadenitis, constipation.

Hepato-biliary disorders:

Less frequent: Jaundice (intrahepatic cholestatic jaundice)

Skin and subcutaneous tissue disorders:

Hydrochlorothiazide: Stevens-Johnson syndrome.

Less frequent: Photosensitivity

The following side-effects have been reported, but frequencies are unknown: Necrotising angiitis (vasculitis and cutaneous vasculitis)

Musculoskeletal, connective tissue and bone disorders:

The following side-effects have been reported, but frequencies are unknown*:* Muscle spasm.

Renal and urinary disorders:

The following side-effects have been reported, but frequencies are unknown*:* Renal failure, renal dysfunction, interstitial nephritis (see "**WARNINGS AND SPECIAL PRECAUTIONS**").

General disorders and administrative site conditions:

The following side-effects have been reported, but frequencies are unknown: Weakness.

Investigations:

Frequency not known: Hydrochlorothiazide: Hypokalaemia, hyponatraemia, hypochloremic alkalosis, and chloride deficits secondary to thiazide therapy, hyperuricaemia, hypomagnesaemia, hypercalcaemia and hyperglycaemia, increases in cholesterol and triglyceride levels, decreases in serum PBI levels.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Quinapril/Hydrochlorothiazide:

No data is available with respect to overdosage in humans. Treatment is symptomatic and supportive consistent with established medical care. Therapy with **KWINCO** should be discontinued and the patient observed closely.

Quinapril:

No data is available with respect to overdosage in humans.

The most likely clinical manifestation would be symptoms attributable to severe hypotension, which would usually be treated by infusion of intravenous normal saline solution.

Haemodialysis and peritoneal dialysis have little effect on the elimination of quinapril and quinaprilat.

Hydrochlorothiazide:

The most common signs and symptoms observed are those caused by electrolyte depletion (hypokalaemia, hypochloraemia, hyponatraemia) and dehydration resulting from excessive diuresis. If digoxin has also been administered, hypokalaemia may accentuate cardiac dysrhythmias.

IDENTIFICATION:

KWINCO 10/12,5 mg:

Pink coloured, scored, oval shaped, biconvex, film-coated tablets debossed with 'D' on scored side and '18' on other side.

KWINCO 20/12,5 mg:

Pink coloured, triangular, biconvex, film-coated tablets debossed with 'D' and '19' on either sides of a score line on one side and plain on the other side.

PRESENTATION:

KWINCO 10/ 12,5 mg:

Blister Packs:

Tablets are packed in blister packs (composed of polyamide/silver coloured aluminium foil/PVC film and a peelable printed white paper laminated silver-coloured aluminium backing foil). Each blister contains 10 tablets.

Pack size: 30's – Each carton contains 3 blisters of 10 tablets each.

KWINCO 20/12,5 mg:

Blister Packs:

Tablets are packed in blister packs (composed of polyamide/silver coloured aluminium foil/PVC film and a peelable printed white paper laminated silver-coloured aluminium backing foil). Each blister contains 10 tablets.

Pack size: 30's – Each carton contains 3 blisters of 10 tablets each.

HDPE Container Pack:

Tablets are packed in white opaque HDPE containers.

Pack size: 30's: One HDPE container of 30 tablets.

STORAGE INSTRUCTIONS:

Store in a cool (at or below 25 °C), dry place. Protect from light.

Do not remove the blisters from the carton until required.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

KWINCO 10/ 12,5 mg: 43/7.1.3/1046

KWINCO 20/12,5 mg: 43/7.1.3/1047

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

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