PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

[Pr]Auro-Quinapril

Quinapril Tablets USP

Tablets, 5 mg, 10 mg, 20 mg and 40 mg quinapril (as quinapril hydrochloride), Oral

Angiotensin Converting Enzyme Inhibitor

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CANADA

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Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

Auro-Quinapril (quinapril hydrochloride) is indicated for:

- **Hypertension:** treatment of essential hypertension. It is usually administered in association with other drugs, particularly thiazide diuretics.

- **Congestive Heart Failure:** treatment of congestive heart failure as adjunctive therapy when added to diuretics and/or digitalis glycosides.

The safety and efficacy of quinapril hydrochloride in renovascular hypertension has not been established; therefore, use in this condition is not recommended.

Treatment with Auro-Quinapril should be initiated under close medical supervision.

1.1 Pediatrics (<18 years of age)

Pediatrics (<18 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

1.2 Geriatrics (> 65 years of age)

Of the total number of subjects in clinical studies of quinapril hydrochloride, 21% were ≥65 years old. (There was no distinction between patients >65 or >75 years.) No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience did not identify differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

2 CONTRAINDICATIONS

Auro-Quinapril is contraindicated in:

- Patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.

- Patients with a history of angioedema related to previous treatment with an angiotensin converting enzyme (ACE) inhibitor (see 7 WARNINGS AND PRECAUTIONS, Immune, Head and Neck Angioedema)

- Combination with sacubitril/valsartan due to increased risk of angioedema. Auro-Quinapril must not be initiated until at least 36 hours have elapsed following

discontinuation of sacubitril/valsartan therapy. If treatment with Auro-Quinapril is stopped, sacubitril/valsartan therapy must not be initiated until 36 hours after the last dose of Auro-Quinapril.

- Women who are pregnant, intend to become pregnant, or of childbearing potential who are not using adequate contraception (see 7 WARNINGS AND PRECAUTIONS, 7.1 Special Populations, 7.1.1 Pregnant Women and 8 ADVERSE REACTIONS).

- Nursing women (see 7 WARNINGS AND PRECAUTIONS, 7.1 Special Populations, 7.1.2 Breast-feeding).

- Combination with aliskiren-containing medicines in patients with:
  - diabetes mellitus (type 1 or type 2),
  - moderate to severe kidney insufficiency (GFR < 60 mL/min/1.73 m^2),
  - hyperkalemia (> 5mMol/L) or
  - congestive heart failure who are hypotensive (see 7 WARNINGS AND PRECAUTIONS, Cardiovascular, Dual blockade of the Renin-Angiotensin System (RAS) and Renal, Renal Impairment, and 9 DRUG INTERACTIONS, 9.4 Drug-Drug Interactions, Aliskiren-containing medicines and Angiotensin receptor blockers (ARBs)).

- Combination with angiotensin receptor blockers (ARBs) in patients with:
  - diabetes mellitus (type 1 or type 2) with end organ damage,
  - moderate to severe kidney insufficiency (GFR < 60 mL/min/1.73m2),
  - hyperkalemia (> 5mMol/L) or
  - congestive heart failure who are hypotensive (see 9 DRUG INTERACTIONS, Angiotensin receptor blockers (ARBs)).

- Patients with the rare hereditary condition of galactose intolerance, glucose-galactose malabsorption or Lapp lactase deficiency as Auro-Quinapril contains lactose (see 7 WARNINGS AND PRECAUTIONS, Sensitivity/Resistance).

3 SERIOUS WARNINGS AND PRECAUTIONS BOX

Serious Warnings and Precautions
When used in pregnancy, angiotensin converting enzyme (ACE) inhibitors can cause injury or even death of the developing fetus. When pregnancy is detected, Auro-Quinapril should be discontinued as soon as possible

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

Dosage of Auro-Quinapril (quinapril hydrochloride) must be individualized.

4.2 Recommended Dose and Dosage Adjustment

Hypertension

Initiation of therapy requires consideration of recent antihypertensive drug treatment, the extent of blood pressure (BP) elevation and salt restriction. The dosage of other antihypertensive agents being used with Auro-Quinapril may need to be adjusted.

Monotherapy:

The recommended initial dose of Auro-Quinapril in patients not on diuretics is 10 mg once daily. An initial dose of 20 mg once daily can be considered for patients without advanced age, renal impairment, or concomitant heart failure and who are not volume depleted (see 7 WARNINGS AND PRECAUTIONS, Cardiovascular, Hypotension). Dosage should be adjusted according to BP response, generally at intervals of 2-4 weeks. A dose of 40 mg daily should not be exceeded.

In some patients treated once daily, the antihypertensive effect may diminish towards the end of the dosing interval. This can be evaluated by measuring BP just prior to dosing to determine whether satisfactory control is being maintained for 24 hours. If it is not, either 2x daily administration with the same total daily dose, or an increase in dose should be considered. If BP is not controlled with Auro-Quinapril alone, a diuretic may be added. After the addition of a diuretic, it may be possible to reduce the dose of Auro-Quinapril.

Concomitant Diuretic Therapy:

Symptomatic hypotension occasionally may occur following the initial dose of quinapril hydrochloride and is more likely in patients who are currently being treated with a diuretic. The diuretic should, if possible, be discontinued for 2-3 days before beginning therapy with Auro-Quinapril to reduce the likelihood of hypotension depleted (see 7 WARNINGS AND PRECAUTIONS, Cardiovascular, Hypotension). If the diuretic cannot be discontinued, an initial dose of 5 mg Auro-Quinapril should be used with careful medical supervision for several hours and until BP has stabilized. The dosage of Auro-Quinapril should subsequently be titrated (as described above) to the optimal response.

Dosing Adjustment in Renal Impairment:
For use in hemodialysis patients, see 7 WARNINGS and PRECAUTIONS, Immune, Anaphylactoid Reactions during Membrane Exposure. Quinapril should be administered on days when dialysis is not performed.

Starting doses should be reduced according to the following guidelines:

Creatinine Clearance (mL/min)	Maximum Recommended Initial Dose (mg)
>60	10
30-60	5
10-30	2.5
<10	Insufficient data for dosage recommendation

Patients should subsequently have dosage titrated (as described above) to the optimal response.

Dosage in the Elderly (>65 years):

The recommended initial dosage of Auro-Quinapril is 10 mg once daily (depending on renal function), followed by titration (as described above) to the optimal response.

Congestive Heart Failure

Auro-Quinapril is indicated as adjunctive therapy to diuretics, and/or cardiac glycosides. Therapy should be initiated under close medical supervision. BP and renal function should be monitored, both before and during treatment with Auro-Quinapril, because severe hypotension and, more rarely, consequent renal failure have been reported (see 7 WARNINGS AND PRECAUTIONS, Cardiovascular, Hypotension).

Initiation of therapy requires consideration of recent diuretic therapy and the possibility of severe salt/volume depletion. If possible, the dose of diuretic should be reduced before beginning treatment, to reduce the likelihood of hypotension. Serum potassium should also be monitored (see 7 WARNINGS AND PRECAUTIONS and 9 DRUG INTERACTIONS).

The recommended starting dose is 5 mg once daily, to be administered under close medical supervision to determine the initial effect on BP. After the initial dose, the patient should be observed for ≥2 hours, or until the pressure has stabilized for ≥1 additional hour (see 7 WARNINGS AND PRECAUTIONS, Cardiovascular, Hypotension). This dose may improve symptoms of heart failure but increases in exercise duration have generally required higher doses. Therefore, if the initial dosage of Auro-Quinapril is well tolerated or after effective management of symptomatic hypotension following initiation of therapy, the dose should then be increased gradually to 10 mg once daily, then 20 mg once daily, and to 40 mg per day given in 2 equally divided doses, depending on the patient's response. The maximum daily dose is 40 mg.

The dose titration may be done at weekly intervals, as indicated by the presence of residual signs or symptoms of heart failure.

Renal Impairment or Hyponatremia:

Kinetic data indicate that Quinapril hydrochloride elimination is dependent on the level of renal function. The recommended initial dose of Quinapril hydrochloride is 5 mg in patients with a creatinine clearance of 30- 60 mL/min and 2.5 mg in patients with a creatinine clearance of 10-30 mL/min. There is insufficient data for dosage recommendation in patients with a creatinine clearance <10 mL/min. If the initial dose is well tolerated, Auro-Quinapril may be administered the following day as a 2x daily regimen. In the absence of excessive hypotension or significant deterioration of renal function, the dose may be increased at weekly intervals based on clinical and hemodynamic response (See 7 WARNINGS AND PRECAUTIONS and 8 ADVERSE REACTIONS).

4.3 Administration

See 4 DOSAGE AND ADMINISTRATION, 4.2 Recommended Dose and Dosage Adjustment

4.4 Missed Dose

A patient missing a dose should take it as soon as they remember to. If it is almost time for the next dose, the missed dose should be skipped. The patient should be cautioned against taking two doses concomitantly to “make up” for the missed dose.

5 OVERDOSAGE

No data are available regarding overdosage with quinapril hydrochloride. The most likely clinical manifestation would be symptoms attributable to severe hypotension, which should be normally treated by intravenous volume expansion with 0.9% sodium chloride. Hemodialysis and peritoneal dialysis have little effect on the elimination of quinapril and quinaprilat.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 1 – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength / Composition	All Non-medicinal Ingredients
Oral	Tablet: 5,10, 20 and 40 mg	Colloidal silicon dioxide, Crospovidone, Lactose Monohydrate, Magnesium carbonate, Magnesium stearate and Povidone. Opadry -Y-5-9020 Brown contains hydroxy propyl methyl cellulose, hydroxy propyl cellulose, titanium dioxide, PEG 400, Iron oxide red

Auro-Quinapril (quinapril hydrochloride) tablets are supplied as follows:

Auro-Quinapril 5 mg: Contains Brown coloured, oval shaped film coated Tablets, debossed with "5" and "2" on either side of the Scoreline on one side and "H" on other side. Tablet is free from physical defects. HDPE bottle packs: 100's count

Auro-Quinapril 10 mg: Contains Brown coloured, triangular shaped film coated Tablets, debossed with "53" on one side and "H" on other side. Tablet is free from physical defects. HDPE bottle packs: 100's count.

Auro-Quinapril 20 mg: Contains Brown coloured, circular shaped film coated Tablets, debossed with "D" on one side and "16" on other side. Tablet is free from physical defects. HDPE bottle packs: 100's count.

Auro-Quinapril 40 mg: Contains Brown coloured, oval shaped film coated Tablets, debossed with "D" on one side and "17" on other side. Tablet is free from physical defects. HDPE bottle packs: 100's count.

7 WARNINGS AND PRECAUTIONS

Please see 3 SERIOUS WARNINGS AND PRECAUTIONS BOX.

Cardiovascular

Dual blockade of the Renin-Angiotensin System (RAS)

Dual blockade of the Renin-Angiotensin System (RAS): There is evidence that co-administration of angiotensin converting enzyme (ACE) inhibitors, such as quinapril hydrochloride, or of angiotensin receptor antagonists (ARBs) with aliskiren increases the risk of hypotension, syncope, stroke,

hyperkalemia and deterioration of renal function, including acute renal failure, in patients with diabetes mellitus (type 1 or type 2) and/or moderate to severe kidney insufficiency (GFR < 60 mL/min/1.73 m2). Therefore, the use of Auro-Quinapril in combination with aliskiren-containing drugs is contraindicated in these patients (see 2 CONTRAINDICATIONS).

Further, co-administration of ACE inhibitors, including quinapril hydrochloride, with other agents blocking the RAS, such as ARBs or aliskiren-containing drugs, is generally not recommended in other patients, since such treatment has been associated with an increased incidence of severe hypotension, renal failure, and hyperkalemia. Administration should be limited to individually defined cases with close monitoring of renal function and blood potassium levels (see 2 CONTRAINDICATIONS).

Hypotension

Symptomatic hypotension has occurred after administration of quinapril hydrochloride, usually after the first or second dose or when the dose was increased. It is more likely to occur in patients who are volume depleted by diuretic therapy, dietary salt restriction, dialysis, diarrhea, or vomiting. In patients with ischemic heart or cerebrovascular disease, an excessive fall in blood pressure could result in a myocardial infarction or cerebrovascular accident (See 8 ADVERSE REACTIONS). Because of the potential fall in blood pressure in these patients, therapy with Auro-Quinapril should be started under close medical supervision (see 4 DOSAGE AND ADMINISTRATION). Such patients should be followed closely for the first weeks of treatment and whenever the dose of Auro-Quinapril is increased. In patients with severe congestive heart failure, with or without associated renal insufficiency, excessive hypotension has been observed and may be associated with oliguria and/or progressive azotemia, and rarely with acute failure and/or death.

If hypotension occurs, the patient should be placed in supine position and, if necessary, receive an intravenous infusion of 0.9% sodium chloride. A transient hypotensive response is not a contraindication to further doses which usually can be given without difficulty once the blood pressure has increased after volume expansion. However, lower doses of Auro-Quinapril and/or reduced concomitant diuretic therapy should be considered.

Valvular Stenosis

There is concern on theoretical grounds that patients with aortic stenosis might be at particular risk of decreased coronary perfusion when treated with vasodilators because they do not develop as much afterload reduction.

Driving and Operating Machinery

The ability to engage in activities such as operating machinery or operating a motor vehicle may be impaired, especially when initiating quinapril therapy.

Exercise caution when driving or operating a vehicle or potentially dangerous machinery.

Endocrine and Metabolism

Hyperkalemia

Elevated serum potassium (>5.7 mMol/L) was observed in approximately 2% of patients receiving quinapril hydrochloride. In most cases these were isolated values which resolved despite continued therapy. Hyperkalemia was a cause of discontinuation of therapy in <0.1% of hypertensive patients. Risk factors for the development of hyperkalemia include renal insufficiency, diabetes mellitus, and the concomitant use of agents to treat hypokalemia,

potassium-sparing diuretics, potassium supplements, potassium-containing salt substitutes, or other drugs known to raise serum potassium levels. Because of the risk of hyperkalemia it is advised that combination therapy be initiated with caution and the patient's serum potassium levels be closely monitored (see 7 WARNINGS AND PRECAUTIONS, Monitoring and Laboratory Test, Hyperkalemia, 8 ADVERSE REACTIONS, and 9 DRUG INTERACTIONS, 9.4 Drug-Drug Interactions, Agents Increasing Serum Potassium, Trimethoprim-containing products).

Hyponatraemia and SIADH

Syndrome of Inappropriate Anti-diuretic Hormone (SIADH) and subsequent hyponatraemia has been observed in some patients treated with other ACE inhibitors. It is recommended that serum sodium levels be monitored regularly in the elderly and in other patients at risk of hyponatraemia.

Hypoglycemia and Diabetes

ACE inhibitors may reduce insulin resistance and may lead to hypoglycemia in diabetic patients on insulin or oral hypoglycemic agents; closer monitoring of diabetic patients may be required.

Hematologic

Neutropenia/Agranulocytosis

Agranulocytosis and bone marrow depression have been caused by ACE inhibitors. Agranulocytosis did occur during quinapril hydrochloride treatment in 1 patient with a history of neutropenia during previous captopril therapy. Periodic monitoring of white blood cell counts should be considered, especially in patients with collagen vascular disease and/or renal disease.

Hepatic/Biliary/Pancreatic

Patients with Impaired Liver Function

Hepatitis (hepatocellular and/or cholestatic), elevations of liver enzymes and/or serum bilirubin have occurred during therapy with other ACE inhibitors in patients with or without pre-existing liver abnormalities. In most cases the changes were reversed on discontinuation of the drug.

Elevations of liver enzymes and/or serum bilirubin have been reported for quinapril hydrochloride (see 8 ADVERSE REACTIONS). Should the patient receiving Auro-Quinapril experience any unexplained symptoms particularly during the first weeks or months of treatment, it is recommended that a full set of liver function tests and any other necessary investigation be carried out. Discontinuation of Auro-Quinapril should be considered when appropriate.

There are no adequate studies in patients with cirrhosis and/or liver dysfunction. Auro-Quinapril should be used with particular caution in patients with pre-existing liver abnormalities. In such patients baseline liver function tests should be obtained before administration of the drug and close monitoring of response and metabolic effects should apply.

Auro-Quinapril (quinapril), when combined with a diuretic 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. The metabolism of quinapril to quinaprilat is normally dependent upon hepatic esterase. Quinaprilat concentrations are reduced in patients with alcoholic cirrhosis due to impaired de-esterification of quinapril.

Immune

Hypersensitivity to ACE inhibitor

Head and Neck Angioedema

Head and neck angioedema has been reported in patients treated with quinapril hydrochloride. Angioedema associated with laryngeal involvement may be fatal. If laryngeal stridor or angioedema of the face, tongue, or glottis occurs, Auro-Quinapril should be discontinued immediately, the patient treated appropriately 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, although antihistamines may be useful in relieving symptoms. Where there is involvement of the tongue, glottis or larynx, likely to cause airway obstruction, appropriate therapy (including but not limited to 0.3 to 0.5 mL of subcutaneous epinephrine solution 1:1000) should be administered promptly (see 8 ADVERSE REACTIONS).

The incidence of angioedema during ACE inhibitor therapy has been reported to be higher in black than in non-black patients.

Patients taking a concomitant mTOR inhibitor (e.g. temsirolimus), DPP-4 inhibitor (e.g. sitagliptin) or neutral endopeptidase (NEP) inhibitor may be at increased risk for angioedema. Caution should be used when either initiating ACE inhibitor therapy in patients already taking a mTOR, DPP-4 inhibitor or NEP inhibitor or vice versa (see 9 DRUG INTERACTIONS).

Patients with a history of angioedema related or unrelated to ACE inhibitor therapy may be at increased risk of angioedema while receiving an ACE inhibitor (see 2 CONTRAINDICATIONS).

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.

Anaphylactoid Reactions during Membrane Exposure

Anaphylactoid reactions have been reported in patients dialysed with high-flux membranes (e.g.: polyacrylonitrile [PAN]) and treated concomitantly with an ACE inhibitor. Dialysis should be stopped immediately if symptoms such as nausea, abdominal cramps, burning, angioedema, shortness of breath and severe hypotension occur. Symptoms are not relieved by antihistamines. In these patients consideration should be given to using a different type of dialysis membrane or a different class of antihypertensive agents.

Anaphylactoid Reactions during LDL Apheresis

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

Anaphylactoid Reactions during Desensitization

There have been isolated reports of patients experiencing sustained life threatening anaphylactoid reactions while receiving ACE inhibitors during desensitizing treatment with hymenoptera (bees, wasps) venom. In the same patients, these reactions have been avoided when ACE inhibitors were temporarily withheld for at least 24 hours, but they have reappeared upon inadvertent rechallenge to an ACE inhibitor.

Nitritoid Reactions-Gold

Nitritoid reactions (symptoms include facial flushing, nausea, vomiting and symptomatic hypotension) have been reported rarely in patients on therapy with injectable gold (sodium aurothiomalate) and concomitant ACE inhibitor therapy including quinapril hydrochloride (see 9 DRUG INTERACTIONS).

Monitoring and Laboratory Tests

Hematology**:**

Periodic monitoring of white blood cell counts should be considered, especially in patients with collagen vascular disease and/or renal disease (see 7 WARNINGS AND PRECAUTIONS, Hematologic, Neutropenic/Agranulocytisis).

Hyperkalemia**:**

Patients with renal insufficiency, diabetes mellitus or concomitantly taking agents to treat hypokalemia may be at increased risk of developing hyperkalemia. Serum potassium should be monitored regularly (see 2 CONTRAINDICATIONS, 7 WARNINGS AND PRECAUTIONS, Endocrine and Metabolism, Hyperkalemia).

Hyponatraemia: (see 7 WARNINGS AND PRECAUTIONS, Endocrine and Metabolism, Hyponatraemia and SIADH). It is recommended that serum sodium levels be monitored regularly in the elderly and in other patients at risk of hyponatraemia.

Creatinine and Blood Urea Nitrogen: Increases (>1.25x the upper limit of normal) in serum creatinine and blood urea nitrogen (BUN) were observed in 2% each of patients treated with quinapril hydrochloride alone. Increases were more likely to occur in patients receiving concomitant diuretic therapy than in those on quinapril hydrochloride alone (see 7 WARNINGS AND PRECAUTIONS, Renal, Renal Impairment). These increases often reversed on continued therapy. In controlled studies of heart failure, increases in BUN and serum creatinine were observed in 11% and 8%, respectively, of patients treated with quinapril hydrochloride. Most often, these patients were receiving diuretics with or without digitalis. Use of Auro-Quinapril should include appropriate assessment of renal function.

Hepatic: Elevations of liver enzymes and/or serum bilirubin have occurred in patients receiving quinapril hydrochloride. If a patient receiving Auro-Quinapril experience any unexplained symptoms, particularly during the first weeks or months of treatment, a full set of liver function tests and any other investigation should be carried out. Discontinuation of Auro-Quinapril should be considered when appropriate. In patients with pre-existing liver abnormalities, baseline liver function tests should be obtained before administration of the drug and response and metabolic effects should be closely monitored (see 7 WARNINGS AND PRECAUTIONS, Hepatic/Biliary/Pancreatic, Patients with Impaired Liver Function).

Peri-Operative Considerations

Surgery/Anaesthesia

In patients undergoing major surgery or during anaesthesia with agents that produce hypotension, quinapril hydrochloride will 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.

Renal

Renal Impairment

The use of ACE inhibitors, including quinapril hydrochloride, with ARBs or aliskiren-containing drugs is contraindicated in patients with moderate to severe kidney insufficiency (GFR < 60

mL/min/1.73m2) (see 2 CONTRAINDICATIONS and 9 DRUG INTERACTIONS, 9.4 Drug-Drug Interactions, Aliskiren-containing medicines and Angiotensin receptor blockers (ARBs)).

As a consequence of inhibiting the renin-angiotensin-aldosterone system (RAAS), changes in renal function have been seen in susceptible individuals. In patients whose renal function may depend on the activity of the RAAS, such as patients with bilateral renal artery stenosis, unilateral renal artery stenosis to a solitary kidney, or severe congestive heart failure, treatment with agents that inhibit this system has been associated with oliguria, progressive azotemia, and rarely, acute renal failure and/or death. In susceptible patients, concomitant diuretic use may further increase risk (see 4 DOSAGE AND ADMINISTRATION and 8 ADVERSE REACTIONS).

Use of Auro-Quinapril should include appropriate assessment of renal (see 4 DOSAGE AND ADMINISTRATION and 8 ADVERSE REACTIONS).

Respiratory

Cough

Cough has been reported with the use of ACE inhibitors, including quinapril. Characteristically, the cough is dry and persistent and usually disappears only after withdrawal or lowering of the dose of quinapril hydrochloride. ACE inhibitor-induced cough should be considered as part of the differential diagnosis of the cough.

Sensitivity/Resistance

Due to the presence of lactose, patients with hereditary problems of galactose intolerance, glucose-galactose malabsorption or the Lapp lactase deficiency should not take Auro-Quinapril (see 2 CONTRAINDICATIONS).

Skin

Psoriasis and Aggravation of Psoriasis

Psoriasis or aggravation of psoriasis have been reported in patients receiving ACE inhibitors. Quinapril should be used with caution in patients, especially those with a medical history or family history of psoriasis. Consider discontinuation of quinapril if clinically significant psoriasis or psoriasis aggravation occurs.

7.1 Special Populations

7.1.1 Pregnant Women

Quinapril is contraindicated in pregnancy (see 2 CONTRAINDICATIONS and 8 ADVERSE

REACTIONS). ACE inhibitors can cause fetal and neonatal morbidity and mortality when administered to pregnant women. Several dozen cases have been reported in the world literature. When pregnancy is detected, Auro-Quinapril should be discontinued as soon as possible.

The use of ACE inhibitors during the second and third trimesters of pregnancy has been associated with fetal and neonatal injury including hypotension, neonatal skull hypoplasia, anuria, reversible or irreversible renal failure, and death. Oligohydramnios has also been reported, presumably resulting from decreased fetal renal function; oligohydramnios in this setting has been associated with fetal limb contractures, craniofacial deformation, and hypoplastic lung development.

Prematurity, and patent ductus arteriosus and other structural cardiac malformations, as well as neurologic malformations have also been reported, following exposure in the first trimester of pregnancy.

Infants with a history of in utero exposure to ACE inhibitors should be closely observed for hypotension, oliguria, and hyperkalemia. If oliguria occurs, attention should be directed toward support of blood pressure and renal perfusion. Exchange transfusion or dialysis may be required as a means of reversing hypotension and/or substituting for impaired renal function, however; limited experience with those procedures has not been associated with significant clinical benefit.

If oligohydramnios is observed, a non-stress test (NST), and/or a biophysical profiling (BPP) may be appropriate, depending upon the week of pregnancy. If concerns regarding fetal well- being still persist, a contraction stress testing (CST) should be considered. Patients and physicians should be aware, however, that oligohydramnios may not appear until after the fetus has sustained irreversible injury.

Animal Data: No fetotoxic or teratogenic effects were observed in rats at doses as high as 300 mg/kg/day (180x the maximum daily human dose), despite maternal toxicity at 150 mg/kg/day. Offspring body weights were reduced in rats treated late in gestation and during lactation with doses of ≥25 mg/kg/day. Quinapril hydrochloride was not teratogenic in rabbits; however, maternal and embryo toxicity were seen in some rabbits at 1 mg/kg/day.

No adverse effects on fertility or reproduction were observed in rats at dose levels ≤100 mg/kg/day (60x the maximum daily human dose) (see 16 NON-CLINICAL TOXICOLOGY, Table 5).

7.1.2 Breast-feeding

The presence of concentrations of ACE inhibitor has been reported in human milk. The use of Auro-Quinapril is contraindicated during breast-feeding (see 2 CONTRAINDICATIONS).

7.1.3 Pediatrics (<18 years of age)

No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

7.1.4 Geriatrics (>65 years of age)

Of the total number of subjects in clinical studies of quinapril hydrochloride, 21% were ≥65 years old. (There was no distinction between patients >65 or >75 years.) No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function (see 4 DOSAGE AND ADMINISTRATION and 8 ADVERSE REACTIONS).

Elderly patients exhibited increased area under the plasma concentration time curve and peak levels for quinaprilat compared to values observed in younger patients; this appeared to relate to decreased renal function rather than to age itself.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

This information is not available for this drug product.

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials; therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

Hypertension

Quinapril hydrochloride monotherapy was evaluated for safety in 2005 hypertensive patients, including 313 elderly patients, enrolled in placebo-controlled clinical trials. There was no increase in the incidence of adverse events (AEs) in elderly patients given the same daily dosages. Quinapril hydrochloride was evaluated for long-term safety in >1100 patients treated for ≥1 year. AEs were usually mild and transient in nature.

The most serious AE was angioedema (0.1%). Renal insufficiency (1 case), agranulocytosis (1 case) and mild azotemia (2 cases in CHF patients) have been reported. Myocardial infarction and cerebrovascular accident occurred, possibly secondary to excessive hypotension in high risk patients (see 7 WARNINGS AND PRECAUTIONS, Cardiovascular, Hypotension).

The most frequent AEs in controlled clinical trials were headache (8.1%), dizziness (4.1%), cough (3.2%), fatigue (3.2%), rhinitis (3.2%), nausea and/or vomiting (2.3%), and abdominal pain (2.0%).

Discontinuation of therapy because of AEs was required in 4.7% of patients treated with quinapril hydrochloride in placebo-controlled trials.

Congestive Heart Failure (CHF)

Out of the 1108 patients with CHF, 605 (55%) experience ≥1 AE. In controlled clinical trials, 525 of these patients were evaluated for safety. The frequencies of AEs were similar for both sexes as well as for younger (< 65 years) and older (> 65 years) patients.

The most serious non-fatal AEs/reactions were angioedema (0.1%), chest pain of unknown origin (0.8%), angina pectoris (0.4%), hypotension (0.1%) and impaired renal function (see 7 WARNINGS AND PRECAUTIONS, Renal, Renal Impairment). Myocardial infarct and cerebrovascular accident occurred (see 7 WARNINGS AND PRECAUTIONS, Cardiovascular, Hypotension). Rare cases of eosinophilic pneumonitis have been reported. Hepatitis or hepatic failure have rarely been observed with other ACE inhibitors.

The most frequent AEs in controlled clinical trials were dizziness (11.2%), cough (7.6%), chest pain (6.5%), dyspnea (5.5%), fatigue (5.1%), and nausea/vomiting (5.0%).

Discontinuation due to AEs in controlled clinical trials was required for 41 (8.0%) patients. Hypotension (0.8%) and cough (0.8%) were the most common reasons for withdrawal.

AEs occurring in ≥ 0.5% of 2005 hypertensive patients treated with quinapril hydrochloride monotherapy and in 525 patients with CHF treated with quinapril hydrochloride as adjunctive therapy, in controlled clinical trials, are presented in the table below:

Table 2 Adverse Events in Patients (≥0.5%) with Hypertension and Congestive Heart Failure in Controlled Clinical Trials (Irrespective of Causal Relationship)

	Hypertension[1] % Patients (N=2005)	**Congestive Heart Failure[2]** % Patients (N=525)
Cardiovascular		
Hypotension	1.0	3.4
Angina Pectoris	0.2	2.3

	Hypertension[1] % Patients (N=2005)	Congestive Heart Failure[2] % Patients (N=525)
Palpitation	0.4	1.3
Tachycardia	0.2	1.1
Myocardial infarct	-	0.6
Arrhythmia	0.1	0.6
Eye disorders		
Amblyopia	0.3	1.3
Abnormal Vision	0.1	0.6
Gastrointestinal Disorders		
Nausea and/or vomiting	2.3	5.0
Abdominal pain	2.0	2.5
Diarrhea	1.9	3.4
Dyspepsia	1.9	1.5
Dry mouth or throat	0.4	0.8
Unusual Taste	0.1	0.8
Taste Loss	0.2	0.6
General disorders and administration site conditions		
Chest Pain	1.2	6.5
Fatigue	3.2	5.1
Headache	8.1	3.2
Back Pain	1.3	1.7
Asthenia	1.0	1.7
Peripheral Edema	0.9	1.5
Generalized Edema	0.7	0.2
Musculoskeletal and connective tissue disorders		
Myalgia	1.2	2.9
Nervous System Disorders		
Dizziness	4.1	11.2
Insomnia	1.3	1.1
Paresthesia	1.0	1.3
Nervousness	1.0	0.2
Somnolence	0.9	0.6
Syncope	0.3	0.6
Vertigo	0.4	0.8
Depression	0.6	1.0
Renal and Urinary Disorders		
Impotence	0.5	0.2
Respiratory, Thoracic and Mediastinal Disorders		
Cough	3.2	7.6
Dyspnea	0.9	5.5

	Hypertension[1] % Patients (N=2005)	Congestive Heart Failure[2] % Patients (N=525)
Hemoptysis	-	0.6
Rhinitis	3.2	2.5
Skin and subcutaneous tissue disorders		
Rash	0.6	1.9
Sweating increased	0.8	1.1
Pruritus	0.6	0.4
[1] Quinapril hydrochloride monotherapy [2] Quinapril hydrochloride as adjunctive therapy to diuretic and/or digitalis.		

8.3 Less Common Clinical Trial Adverse Reactions

AEs occurring in <0.5% of patients with hypertension or CHF include:

Blood and lymphatic system disorders:	Agranulocytosis, anemia, including hemolytic anemia
Cardiovascular disorders:	Atrial flutter, cerebrovascular accident, heart failure vasodilatation, ventricular tachycardia
Ear and labyrinth disorders:	Tinnitus
Gastrointestinal disorders:	Anorexia, bloody stools, constipation, GI hemorrhage, tongue
General disorders and administration site conditions:	Allergy, chill, dehydration, face edema, weight increase
Musculoskeletal and connective tissue disorders:	Arthritis
Nervous system disorders:	Amnesia, anxiety, arthralgia, confusion
Renal and urinary disorders:	Dysuria, impaired renal function, polyuria
Respiratory, thoracic and mediastinal disorders:	Asthma, hoarseness
Skin and subcutaneous tissue disorders:	Dermatitis, eczema, Stevens-Johnson syndrome, urticaria, psoriasis

Clinical adverse experiences probably, possibly, or definitely related, or of uncertain relationship to therapy occurring in 0.5% to < 1.0% of the patients treated with quinapril (with or without concomitant diuretic) in controlled or uncontrolled clinical trials and less frequent events seen in clinical trials or post-marketing experience (indicated by a *) included:

Blood and lymphatic system disorders:	Thrombocytopenia*, hemolytic anemia*
Cardiovascular disorders:	Postural hypotension*, syncope*, vasodilation
Congenital, familial and genetic disorders:	Fetal/neonatal injury including: anuria, hypotension, oligohydramnios, skull hypoplasia, reversible or irreversible renal

	failure, and death (see 2 CONTRAINDICATIONS, 7 WARNINGS AND PRECAUTIONS, Pregnant Women)
Gastrointestinal disorders:	Flatulence, pancreatitis*
General disorders and administration site conditions:	Anaphylactoid reaction*; photosensitivity reaction*, edema (peripheral and generalized)
Musculoskeletal and connective tissue disorders:	Arthralgia
Renal and urinary disorders:	Urinary tract infection
Skin and subcutaneous tissue disorders:	Alopecia*, exfoliative dermatitis*, pemphigus*

8.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data

Clinical Trial Findings

This information is not available for this drug product.

8.5 Post-Market Adverse Reactions

Blood and lymphatic system disorders: Thrombocytopenia, hemolytic anemia Cardiovascular disorders: Postural hypotension, syncope
General disorders and administration site conditions: Anaphylactoid reaction; photosensitivity reaction
Skin and subcutaneous tissue disorders: Alopecia, exfoliative dermatitis, pemphigus

See 8 ADVERSE REACTIONS, 8.3 Less Common Clinical Trial Adverse Reactions

9 DRUG INTERACTIONS

9.1 Serious drug interactions

Concomitant use with sacubitril/valsartan is contraindicated due to an increased risk of angioedema (see 2 CONTRAINDICATIONS; 7 WARNINGS & PRECAUTIONS; 9.4 Drug-drug interactions.

9.3 Drug-Behavioural Interactions

Alcohol use should be avoided when taking Auro-Quinapril as it can cause orthostatic hypotension

9.4 Drug-Drug Interactions

The drugs listed in this table are based on either drug interaction case reports or studies, or potential interactions due to the expected magnitude and seriousness of the interaction (i.e., those identified as contraindicated).

Table 3 - Established or Potential Drug-Drug Interactions

[Proper/Common name]	Source of Evidence	Effect	Clinical comment
Adrenergic neuron blocking agents (e.g. MAO inhibitors, chlorpromazine)	---		These agents affect sympathetic activity and should be used with caution. Beta-adrenergic blocking drugs add some further antihypertensive effect to quinapril hydrochloride.
Agents Increasing Serum Potassium e.g. potassium sparing diuretics, potassium supplements	---	Since quinapril hydrochloride decreases aldosterone production, elevation of serum potassium may occur.	Potassium sparing diuretics such as spironolactone, triamterene or amiloride, potassium supplements or other drugs known to raise serum potassium levels should be given with caution and with frequent monitoring of serum potassium, since they may lead to a significant increase in serum potassium. Salt substitutes which contain potassium should also be used with caution.
Aliskiren- containing medicines	CT	Dual blockade of the renin-angiotensin-aldosterone system by combining an ACE inhibitor with aliskiren-containing medicines is not recommended since there is an increased risk of hypotension, syncope, stroke, hyperkalemia and changes in renal function, including renal failure.	The use of quinapril hydrochloride in combination with aliskiren- containing medicines is contraindicated in patients with diabetes mellitus (type 1 or type 2), moderate to severe kidney insufficiency (GFR < 60 mL/min/1.73 m^2), hyperkalemia (> 5mMol/L) or congestive heart failure who are hypotensive It is not recommended in other patients (see 2 CONTRAINDICATIONS, 7 WARNINGS AND PRECAUTIONS, Cardiovascular, Dual blockade of the Renin-Angiotensin System (RAS))

[Proper/Common name]	Source of Evidence	Effect	Clinical comment
Angiotensin receptor blockers (ARBs)	CT	Dual blockade of the renin-angiotensin-aldosterone system by combining an ACE inhibitor with ARBs is not recommended since there is an increased risk of hypotension, syncope, stroke, hyperkalemia and changes in renal function, including renal failure.	The use of quinapril hydrochloride in combination with ARBs is contraindicated in patients with diabetes and end organ damage, moderate to severe kidney insufficiency (GFR < 60 mL/min/1.73 m^2), hyperkalemia (> 5mMol/L) or congestive heart failure who are hypotensive. It is not recommended in other patients (see 2 CONTRAINDICATIONS, 7 WARNINGS AND PRECAUTIONS, Cardiovascular, Dual blockade of the Renin-Angiotensin System (RAS))
Antidiabetic agents (e.g. insulin, oral hypoglycemic agents)	CT	ACE inhibitors may reduce insulin resistance and may lead to hypoglycemia in diabetic patients on insulin or oral hypoglycemic agents.	Monitor closely diabetic patients (see 7 WARNINGS AND PRECAUTIONS, Endocrine and Metabolism, Hypoglycemia and Diabetes).
Anti-neoplastic drugs e.g. cyclo-phosphamide	C, CT	Increased hematotoxicity and/or immunosuppression may result from a combined effect of cyclophosphamide and ACE inhibitors. ACE inhibitors can cause leukopenia. Pancytopenia is a known ADR of the combination of cyclophosphamide and ACE inhibitors.	Patients receiving such combinations must be monitored closely for signs of toxicity to permit timely intervention

[Proper/Common name]	Source of Evidence	Effect	Clinical comment
Concomitant Diuretic Therapy	---	Patients concomitantly taking ACE inhibitors and diuretics, and especially those in whom diuretic therapy was recently instituted, may occasionally experience an excessive reduction of blood pressure after initiation of therapy.	The possibility of hypotensive effects after the first dose of quinapril hydrochloride can be minimized by either discontinuing the diuretic or increasing the salt intake (except in patients with heart failure) prior to initiation of treatment with quinapril hydrochloride. If it is not possible to discontinue the diuretic, the starting dose of Auro-Quinapril should be reduced and the patient should be closely observed for several hours following initial dose and until blood pressure has stabilized (see 7 WARNINGS AND PRECAUTIONS, Cardiovascular, Hypotension and 4 DOSAGE AND ADMINISTRATION).
DDP-IV inhibitors (linagliptin, saxagliptin, sitagliptin)	---	Patients taking concomitant DPP-4 inhibitor therapy may be at increased risk for angioedema.	Caution should be used when either initiating ACE inhibitor therapy in patients already taking a DPP-4 inhibitor or *vice versa* (see 7 WARNINGS AND PRECAUTIONS, Immune, Head and Neck Angioedema).
Gold	C	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 quinapril hydrochloride (see 7 WARNINGS AND PRECAUTIONS, **Immune, Nitritoid Reactions-Gold**).	
Lithium	---	As with other drugs which eliminate sodium, the lithium elimination may be reduced.	The serum lithium levels should be monitored carefully if lithium salts are to be administered.

[Proper/Common name]	Source of Evidence	Effect	Clinical comment
Neutral endopeptidase (NEP) inhibitor	---	ACE inhibitors are known to cause angioedema. This risk may be elevated when used concomitantly with a neutral endopeptidase inhibitor	Caution should be used when either initiating ACE inhibitor therapy in patients already taking a neutral endopeptidase inhibitor or *vice versa* (see 7 WARNINGS AND PRECAUTIONS, Immune, Head and Neck Angioedema).
Non-Steroidal Anti-Inflammatory Drugs (NSAID) including selective cyclooxygenase-2 inhibitors (COX-2 inhibitors)	CT	In patients who are elderly, volume- depleted (including those on diuretic therapy), or with compromised renal function, co-administration of NSAIDs, including selective COX-2 inhibitors, with ACE inhibitors, including quinapril, may result in deterioration of renal function, including possible acute renal failure. These effects are usually reversible. The antihypertensive effect of ACE inhibitors, including quinapril may be attenuated by NSAIDs.	Closely monitor renal function, serum potassium and blood pressure in patients receiving quinapril and NSAID therapy. Dose adjustment may be required.
Other Antihypertensive Agents	CT	The antihypertensive effect of quinapril hydrochloride is augmented by antihypertensive agents that cause renin release (e.g. diuretics).	
mTOR inhibitors (e.g. sirolimus, everolimus, temsirolimus)	CT	An increased incidence of angioedema was observed in patients taking ACE inhibitors and mTOR inhibitors (mammalian target of rapamycin inhibitors)	Caution should be used when either initiating ACE inhibitor therapy in patients already taking mTOR inhibitors or vice versa (see 7 WARNINGS AND PRECAUTIONS, Immune, Head and Neck Angioedema).

[Proper/Common name]	Source of Evidence	Effect	Clinical comment
Sacubitril/ Valsartan (e.g. ENTRESTO™)		Increased risk of angioedema	Quinapril hydrochloride must not be initiated until at least 36 hours have elapsed following discontinuation of sacubitril/valsartan therapy. If treatment with quinapril hydrochloride is stopped, sacubitril/valsartan therapy must not be initiated until 36 hours after the last dose of quinapril hydrochloride. (See 2 CONTRAINDICATIONS)
Tetracycline	---	Concomitant administration of tetracycline with quinapril hydrochloride reduced the absorption of tetracycline in healthy volunteers (by 28- 37%) due to the presence of magnesium carbonate as an excipient in the formulation.	This interaction should be considered with concomitant use of quinapril hydrochloride and tetracycline or other drugs which interact with magnesium.
Trimethoprim-containing products (sulfamethoxazole /trimethoprim)	C	In patients who are elderly or have compromised renal function, co-administration of an ACE inhibitor with sulfamethoxazole/trimethoprim has been associated with severe hyperkalemia, likely due to the hyperkalemic effects of trimethoprim.	Quinapril and trimethoprim-containing products should only be co-administered with caution and with appropriate monitoring of serum potassium.

Legend: C = Case Study; CT = Clinical Trial; T = Theoretical

9.5 Drug-Food Interactions

The rate and extent of quinapril absorption are diminished moderately (approximately 25-30%) when quinapril hydrochloride tablets are administered during a high-fat meal (see 4 DOSAGE AND ADMINISTRATION). However, no effect on quinapril absorption occurs when taken during a regular meal.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Quinapril hydrochloride is a nonpeptide, nonsulphydryl inhibitor of angiotensin converting enzyme (ACE), which is used in the treatment of hypertension.

ACE is a peptidyl dipeptidase that catalyzes the conversion of angiotensin I to the vasoconstrictor angiotensin II. After absorption, quinapril is rapidly de-esterified to quinaprilat (quinapril diacid), its principal active metabolite. Its primary mode of action is to inhibit circulating and tissue ACE, thereby decreasing vasopressor activity and aldosterone secretion. Although the decrease in aldosterone is small, it results in a small increase in serum K+ (see 7 WARNINGS AND PRECAUTIONS). Removal of angiotensin II negative feedback on renin secretion leads to increased plasma renin activity. Although quinapril hydrochloride had antihypertensive activity in all races studied, black hypertensive patients (usually a low-renin hypertensive population) had a smaller average response to ACE inhibitor monotherapy than non-black patients.

ACE is identical to kininase II. Thus, quinapril may interfere with the degradation of bradykinin, a potent peptide vasodilator. However, it is not known whether this system contributes to the therapeutic effects of quinapril hydrochloride.

In animal studies, the antihypertensive effect of quinapril outlasts its inhibitory effect on circulating ACE. Tissue ACE inhibition more closely correlates with the duration of antihypertensive effects and this may be related to enzyme binding characteristics.

In Vitro Studies:
Quinapril was shown to be an inhibitor of angiotensin converting enzyme (ACE) in both plasma and tissue. In assays utilizing human plasma as sources of ACE, the diacid form of quinapril (quinaprilat) exhibited greater inhibition of ACE activity than quinapril (6.4 x 10-10M and 8.4 x 10-8M, respectively). In rabbit and rat aortic strips, quinapril (10-7M, 10-5M) specifically suppressed the contractile responses elicited by angiotensin I (50% contraction at approximately 10-7M and 10-6M angiotensin I, respectively), but had no effect on contractions induced by angiotensin II and potassium chloride.

In Vivo Studies:

Following oral dosing of quinapril, captopril or enalapril (0.1-3 mg/kg) to conscious normotensive rats, plasma ACE inhibition was assessed in vivo by the decrease in pressor

response to intravenous (IV) angiotensin I, angiotensin II, norepinephrine and bradykinin. Quinapril produced a dose-dependent reduction (44% at 0.1 mg/kg, 81% at 0.3 mg/kg) of angiotensin I (0.32 µg/kg IV) pressor response and potentiated the response to bradykinin (154% after 0.3 mg/kg quinapril), but had no effect on angiotensin II and norepinephrine responses. Quinapril was equipotent to captopril and enalapril, but had a longer duration of action than captopril. In the conscious dog, oral administration of quinapril (0.1- 3 mg/kg) resulted in plasma ACE inhibition comparable to that of enalapril and captopril.

In human subjects, quinapril at single oral doses of 10-20 mg/day produced 95-100% inhibition of plasma ACE activity at 0.5 hour post dose, with >80% inhibition persisting at 24 hours post dose. Multiple oral doses of quinapril to humans for 12-weeks (20-80 mg/day) confirmed the inhibitory effect on plasma ACE and showed that it produces corresponding decreases in angiotensin II with significant increases in plasma renin activity. Once or 2x daily dosing did not alter the results.

10.2 Pharmacodynamics

Hypertension

Administration of 10-40 mg of quinapril hydrochloride to patients with essential hypertension results in a reduction of both sitting and standing BP with minimal effect on heart rate. Antihypertensive activity commences within 1 hour with peak effects usually achieved by 2-4 hours after dosing. Achievement of maximum BP lowering effects may require 2 weeks of therapy in some patients. At the recommended doses, antihypertensive effects are maintained throughout the 24-hour dosing interval in most patients. While the dose response relationship is relatively flat, a dose of 40 mg was somewhat more effective at trough than 10-20 mg, and 2x daily dosing tended to give a somewhat lower BP than 1x daily dosing with the same total daily dose. The antihypertensive effect of quinapril hydrochloride was maintained during long-term therapy with no evidence of loss of effectiveness.

Hemodynamic assessments in patients with essential hypertension indicate that BP reduction produced by quinapril is accompanied by a reduction in total peripheral resistance and renal vascular resistance with little or no change in heart rate and cardiac index. There was an increase in renal blood flow which was not significant. Little or no change in glomerular filtration rate (GFR) or filtration fraction was observed.

Quinapril has been shown to reduce microalbuminuria in patients with essential hypertension independently of changes in systemic BP.

When quinapril hydrochloride is given together with thiazide-type diuretics, the antihypertensive effects are approximately additive.

Congestive heart failure

Administration of quinapril hydrochloride to patients with congestive heart failure (CHF) reduces peripheral vascular resistance, systolic and diastolic BP, pulmonary capillary wedge pressure, and increases cardiac output. The onset of effects was observed within 1 hour and maximal effects occurred at 1.25- 4 hours after administration of quinapril hydrochloride. Peak hemodynamic effects correlated well with peak plasma levels of quinaprilat (1- 4 hours after administration).

Exercise tolerance was improved with quinapril hydrochloride therapy.

The effect of quinapril hydrochloride on survival in patients with heart failure has not been evaluated.

10.3 Pharmacokinetics

Absorption:
Following oral administration of quinapril hydrochloride, peak plasma concentrations of quinapril occur within 1 hour. Based on the recovery of quinapril and its metabolites in urine, the extent of absorption is ≥60%.

Distribution:
Approximately 97% of either quinapril or quinaprilat circulating in plasma is bound to proteins.

Metabolism:
Following absorption, quinapril is de-esterified to its major active metabolite, quinaprilat (quinapril diacid) a potent ACE inhibitor, and to minor inactive metabolites. Quinapril has an apparent half-life in plasma of approximately 1 hour. Peak plasma quinaprilat concentrations occur approximately 2 hours after an oral dose of quinapril hydrochloride.

Elimination:
Quinaprilat is eliminated primarily by renal excretion and has an effective accumulation half-life of approximately 3 hours. Quinaprilat has an elimination half-life in plasma of approximately 2 hours with a prolonged terminal phase of 25 hours.

Pharmacokinetic studies in patients with end-stage renal disease on chronic hemodialysis or continuous ambulatory peritoneal dialysis indicate that dialysis has little effect on the elimination of quinapril and quinaprilat.

The disposition of quinapril and quinaprilat in patients with renal insufficiency is similar to that in patients with normal renal function until creatinine clearance is ≤60 mL/min. With creatinine clearance <60 mL/min, peak and trough quinaprilat concentrations increase, apparent half-life increases, and time to steady state may be delayed. The elimination of quinaprilat may be reduced in elderly patients (>65 years) and in those with heart failure; this reduction is attributable to decrease in renal function (see 4 DOSAGE AND ADMINISTRATION). Quinaprilat concentrations are reduced in patients with alcoholic cirrhosis due to impaired

de- esterification of quinapril.

The rate and extent of quinapril absorption are diminished moderately (approximately 25-30%) when quinapril hydrochloride tablets are administered during a high-fat meal. However, no effect on quinapril absorption occurs when taken during a regular meal.

Studies in rats indicate that quinapril and its metabolites do not cross the blood-brain barrier.

Special Populations and Conditions

- **Geriatrics** Therapeutic effects appear to be the same for elderly (>65 years of age) and younger adult patients given the same daily dosages, with no increase in AEs in elderly patients.

- **Ethnic Origin** The antihypertensive effect of ACE inhibitors is generally lower in black than in non-black patients

11 STORAGE, STABILITY AND DISPOSAL

Store at controlled room temperature, 15-30^{o}C. Protect from light and Moisture. Dispense in well-closed containers.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

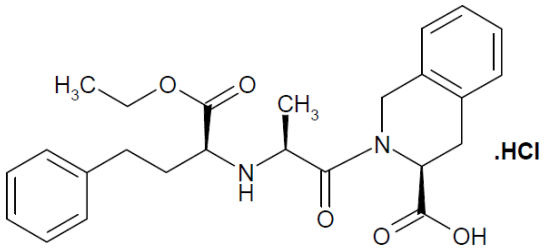
Proper Name: Quinapril Hydrochloride

Chemical Name: 3-Isoquinolinecarboxylic acid, 2-[2-[[1-(ethoxycarbonyl) 3 phenylpropyl] amino]-1-oxopropyl]-1,2,3,4-tetrahydro-monohydrochloride, [3S [2[R*(R*)],3R*]]

Molecular Formula: $C_{25}H_{30}N_2O_5$.HCl

Molecular Weight: 474.98 g /mol

Molecular Structure:



Description: Quinapril hydrochloride is a white or almost white or slightly pink powder. Freely soluble in water and in ethanol (96%) Very slightly soluble in acetone.

Melting Point: Crystals from ethyl acetate-toluene 120-130°C, Also white crystalline solid from acetonitrile 119-121.5°C.

14 CLINICAL TRIALS

14.1 Clinical Trials by Indication

This information is not available for this drug product.

14.2 Comparative Bioavailability Studies

A double blind, balanced, randomized, two-treatment, two-sequence, two-period, crossover, single-dose, oral bioequivalence study of Auro-Quinapril (quinapril hydrochloride) 40 mg tablet (Auro Pharma Inc.) and ACCUPRIL (quinapril hydrochloride) 40 mg tablet (Pfizer Canada Inc.) was conducted in healthy, adult, South Asian, male subjects who completed the study is presented in the following table.

SUMMARY TABLE OF THE COMPARATIVE BIOAVAILABILITY DATA

Quinapril (1 x 40 mg) From measured data Geometric Mean Arithmetic Mean (CV %)				
Parameter	Test[1]	Reference[2]	% Ratio of Geometric Means	90% Confidence Interval
AUC_T (ng•h/mL)	461.18 490.72 (35.7)	448.10 476.63 (37.0)	102.9	97.3 – 108.8
AUC_I (ng•h/mL)	471.39 500.57 (35.1)	457.50 485.59 (36.4)	103.0	97.5 – 108.8
C_{max} (ng/mL)	522.17 584.04 (45.6)	506.95 570.46 (46.6)	103.0	93.3 - 113.8
T_{max}[3] (h)	0.50 (0.25 – 1.50)	0.50 (0.25 – 1.50)		
$T_{½}$[4] (h)	0.92 (24.8)	0.86 (21.3)		

[1]Auro-Quinapril (Quinapril Hydrochloride) tablets, 40 mg (Auro Pharma Inc.).
[2] Accupril® (Quinapril Hydrochloride) tablets, 40 mg of (Pfizer Canada Inc.).
[3] Expressed as the median (range) only.
[4] Expressed as the arithmetic mean (CV %) only

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

Quinapril showed a low order of acute toxicity. Clinical signs of toxicity in both mice and rats

were depression or hypoactivity, prostration and ataxia. Peak mortality occurred within 24 hours in oral studies and within 15 minutes in IV studies. Asymptomatic oral dose levels were 500 mg/kg in mice and 1000 mg/kg in rats.

In the dog study, escalating oral doses of 50-400 mg/kg were given over 13-consecutive days. Vomiting occurred after doses of ≥150 mg/kg. BPs decreased with increasing dose. At 400 mg/kg, the female had elevated creatinine and blood urea nitrogen (BUN) levels, decreased sodium and chloride levels, and granular casts in the urine. Gastric erosions and ulcers were seen in both animals and renal tubular dilatation was noted in the female.

The results of quinapril toxicity from, chronic, reproductive, genetic and carcinogenicity studies are given in Tables 4-7, respectively. Table 8 summarizes the results of toxicity studies with quinaprilat, the major active metabolite of quinapril.

Table 4: Chronic Toxicity Studies of Quinapril					
Species	**Duration (Week)**	**No. of Animals/ Sex / Group**	**Route**	**Doses (mg/kg/day)**	**Results**
Rat	57[1]	30	PO	UC[2], VC[2], 10, 50, 100	No drug-related deaths; transient post-dose salivation, body weight gain suppression, increased BUN, decreased glucose, increased plasma renin level, decreased heart weight, JGA hypertrophy and hyperplasia with increased granules; degenerative changes in kidneys.
Dog	52	4	PO	VC, 10, 50, 100	No deaths; elevation of plasma renin and liver enzyme levels, focal areas of chronic active inflammation in the liver at 100 mg/kg; gastric erosion at 50 mg/kg, and hypertrophy / hyperplasia of renal JGA.

[1] 52 weeks treatment plus 4 weeks without treatment for some animals

[2] UC = Untreated Control; VC = Vehicle Control; BUN = blood urea nitrogen; JGA = juxtaglomerular apparatus.

Table 5: Reproductive Toxicology Studies of Quinapril

Species	No. of Animals/ Sex/Group	Route	Doses (mg/kg/day)	Duration of Dosing	Results
Fertility:					
Rat	12 Male 24 Female	PO	VC[1], 10, 50, 100	Males-60 days prior to mating Females-14 days prior to mating until weaning of offspring	No effects on fertility, no adverse effects on F1offspring parameters, and no teratogenic effects.
Teratology:					
Rat	5 Female	PO	100, 200, 400, 600, 800	Days 6 to 15 of gestation	No teratogenicity. Maternal deaths at 600 and 800 mg/kg; decreased fetal body weights at ≥200 mg/kg.
Rat	20 Female	PO	UC[1], VC, 50, 150, 300	Days 6 to 15 of gestation	No fetotoxic or teratogenic effects. Reversible maternal toxicity.
Rabbit	5-7 Female	PO	10, 15, 25, 50, 100, 200, 400	Days 6 to 18 of gestation	Severe materno- and fetotoxicity.

Rabbit	5 Female	PO	VC, 1, 2, 4, 6, 8	Days 6 to 18 of gestation	Abortions and maternal deaths at 4, 6, and 8 mg/kg; materno- and fetotoxicity at doses >1 mg/kg.
Rabbit	14 Female	PO	VC 0.5, 1.0, 1.5	Days 6 to 18 of gestation	Not teratogenic. Maternal weight loss; increased incidence of Post implantation loss (embryotoxicity) at 1.0 and 1.5 mg/kg.
Perinatal/ Postnatal:					
Rat	20 Female	PO	VC, 25, 75, 150	Day 15 of gestation to Day 20 of lactation	Reduction in offspring body weights from birth to Day 21 postnatally at 25, 75, and 150 mg/kg.

1 UC = Untreated Control; VC = Vehicle Control

Table 6: Genetic Toxicology Studies of Quinapril

Test	Dosage Range	Results
Mutagenicity		
1) *In Vitro* a) Initial cytotoxicity in *Salmonella* strain	≤10,000 µg/plate	Non-cytotoxic.
b) Mutagenesis assay in *Salmonella*	625-10,000 µg/plate	Negative-with or without metabolic activation.
2) *In Vitro* a) Initial cytotoxicity assay	≤44,300 µg/mL	Cytotoxic at ≥1400 µg/mL.
b) Point mutation assay in Chinese hamster lung cells	175-1400 µg/mL	Negative - did not manifest direct acting or promutagen activity.
Cytogenetics		
1) *In Vitro* a) Initial cytotoxicity assay	≤44,300 µg/mL	Cytotoxic at concentrations >700 µg/mL.
b) Sister chromatid exchange (SCE) assay in Chinese hamster ovary cells	10.94-1400 µg/mL	No increase in SCE at toxicity-limited doses ≤700 µg/mL in the presence of metabolic activation or ≤1400 µg/mL in the absence of metabolic activation.
2) *In Vitro* a) Initial cytotoxicity assay	≤2700 µg/mL	Cytotoxic at ≥1200 µg/mL.
b) Structural chromosomal aberration (SCA) assay in Chinese hamster lung cells	800-1800 µg/mL	Slight, statistically significant increase in SCA with metabolic activation; not considered biologically significant.
3) *In Vivo* a) Mouse micronucleus assay	1-1430 µg/kg	Not clastogenic; no increased frequency of micronuclei.

Table 7: Carcinogenicity Studies of Quinapril

Species	Duration (Week)	No. of Animals/ Sex/Group	Route	Doses (mg/kg/day)	Results
Mouse	104	50	PO	UC[1], VC[1], 5, 35, 75	No evidence of tumorigenic potential. Reduced heart weight, nephritis, and JGA hypertrophy/hyperplasia.
Rat	104	65	PO	UC, VC, 10, 50, 100	No evidence of tumorigenic potential. Reduced RBC, JGA hypertrophy/hyperplasia and renal degenerative changes.

[1] UC = Untreated Control; VC= Vehicle Control; JGA = juxtaglomerular apparatus; RBC = red blood cell count

Table 8: Toxicity Studies of Quinaprilat

Species	Duration (Week)	No. of Animals/ Sex/Group	Route	Doses (mg/kg/day)	Results
A. Acute Studies:					
Mouse	Single-dose	10	IV	VC[1], 250, 500, 1000	No deaths; MLD >1000 mg/kg. No clinical or gross pathological changes.
Rat	Single-dose	10	IV	VC, 50, 100, 200, 300, 400	No deaths; MLD >400 mg/kg. No clinical or gross pathological changes.
Dog	Escalating doses	1	IV	Escalating; 1-240	No deaths; MLD >240 mg/kg. Reduced food consumption, weight loss, and slight increase in myeloid to erythroid ratio.
B. Subacute Studies:					
Rat	2	5	IV	VC, 25, 50, 100, 200	No deaths, clinical signs or adverse pathological findings.
Rat	4	10	IV	VC, 20, 100, 200	No drug-related deaths or clinical signs; reduced heart weights.
Dog	2	1	IV	VC, 10, 50, 100	Sporadic increases in heart rate.
Dog	4	3	IV	VC, 10, 50, 100	No clinical or gross pathologic findings; JGA hypertrophy/hyperplasia.

C. Genotoxicity Studies:

Test	Dosage range	Results
Mutagenicity		
In Vitro:		
a) Initial cytotoxicity in Salmonella	≤1200 µg/plate	Non-cytotoxic
b) Mutagenesis assay in Salmonella	75-1200 µg/plate	Negative-with or without metabolic activation

[1] VC = Vehicle Control; MLD = median lethal dose; JGA = juxtaglomerular apparatus

17 SUPPORTING PRODUCT MONOGRAPHS

1. PrACCUPRIL® Tablets 5 mg, 10 mg, 20 mg and 40 mg, submission control 266170, Product Monograph, Pfizer Canada ULC (Dec 12, 2022).

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

[Pr]Auro-Quinapril

Quinapril Tablets

Read this carefully before you start taking **Auro-Quinapril** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Auro-Quinapril**.

Serious Warnings and Precautions

Pregnancy

Auro-Quinapril should not be used during pregnancy. Taking **Auro-Quinapril** can cause injury or even death to your baby. If you discover that you are pregnant while taking Auro-Quinapril stop the medication and contact your healthcare professional as soon as possible.

What is Auro-Quinapril used for?

- High Blood Pressure (Hypertension): Auro-Quinapril lowers high blood pressure. It can be used alone or together with a diuretic ("water pill").
- Congestive Heart Failure: Auro-Quinapril is used for congestive heart failure (a condition where the heart is unable to pump enough blood for the body`s needs), when it is combined with either a diuretic ("water pill") and/or digitalis glycosides (drugs which help the heart beat more normally).

How does Auro-Quinapril work?

Auro-Quinapril is an angiotensin converting enzyme (ACE) inhibitor. You can recognize ACE inhibitors because their medicinal ingredient ends in '-PRIL'.

This medicine does not cure your disease. It helps to control it. Therefore, it is important to continue taking Auro-Quinapril regularly even if you feel fine.

What are the ingredients in Auro-Quinapril?

Medicinal ingredients: Quinapril hydrochloride

Non-medicinal ingredients: Colloidal silicon dioxide, Crospovidone, Lactose Monohydrate, Magnesium carbonate, Magnesium stearate and Povidone. Opadry -Y-5-9020 Brown contains hydroxy propyl methyl cellulose, hydroxy propyl cellulose, titanium dioxide, PEG 400, and iron oxide red

Auro-Quinapril comes in the following dosage forms:

Tablets; 5 mg, 10 mg, 20 mg, 40 mg

Do not use Auro-Quinapril if you:

- Are allergic to quinapril hydrochloride or to any non-medicinal ingredient in the formulation.
- Have experienced an allergic reaction (angioedema) with swelling of the hands, feet, or ankles, face, lips, tongue, throat, or sudden difficulty breathing or swallowing, to any ACE inhibitor or without a known cause. Be sure to tell your healthcare professional that this has happened to you.
- Have been diagnosed with hereditary angioedema: an increased risk of getting an allergic reaction that is passed down through families. This can be triggered by different factors, such as surgery, flu, or dental procedures.
- Are taking ENTRESTO™ (sacubitril/valsartan), due to the increased risk of serious allergic reaction which causes swelling of the face or throat (angioedema) when taken with Auro-Quinapril.
- Are pregnant or intend to become pregnant. Taking Auro-Quinapril during pregnancy can cause injury and even death to your baby.
- Are breastfeeding. Auro-Quinapril passes into breast milk.
- Have renovascular hypertension (a form of high blood pressure that affects the blood vessels leading to the kidney's).
- Are taking aliskiren-containing medicines, such as Rasilez, **and** have one of the following conditions:
  - Diabetes
  - Kidney disease
  - High levels of potassium
  - Congestive heart failure combined with hypotension.
- Are taking an angiotensin receptor blocker (ARB), another medicine to treat your high blood pressure, **and** have one of the following conditions:
  - Diabetes with end organ damage
  - Kidney disease
  - High levels of potassium
  - Congestive heart failure combined with hypotension.

  You can recognize ARBs because their medicinal ingredient ends in "-**SARTAN**".
- Have one of the following rare hereditary diseases:
  - Galactose intolerance
  - Lapp lactase deficiency, a type of lactose intolerance
  - Glucose-galactose malabsorption

  Because lactose is a non-medicinal ingredient in Auro-Quinapril.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Auro-Quinapril. Talk about any health conditions or problems you may have, including if you:

- Are allergic to any drug used to lower blood pressure.
- Have a condition causing your body's immune system to attack your own tissues (collagen vascular disease)
- Have recently received or are planning to get allergy shots for bee or wasp stings.
- Have narrowing of an artery or a heart valve.
- Have had a heart attack or stroke.
- Have heart failure.
- Have diabetes, liver or kidney problems.
- Are on dialysis or receiving LDL apheresis (treatment to remove "bad cholesterol" from the blood).
- Are dehydrated or suffer from excessive vomiting, diarrhea, or sweating.
- Are taking a salt substitute that contains potassium, potassium supplements, or a potassium-sparing diuretic (a specific kind of "water pill").
- Are taking an antibiotic containing trimethoprim.
- Are on a low-salt diet.
- Are receiving gold (sodium aurothiomalate) injections.
- Are less than 18 years old.
- Are taking a neutral endopeptidase inhibitor. The combination with Auro-Quinapril is not recommended.
- Are taking a medicine that contains aliskiren, such as Rasilez or an angiotensin receptor blocker (ARB). The combination with Auro-Quinapril is not recommended.
- Are taking anti-cancer (temsirolimus, everolimus), anti-rejection (sirolimus) or anti-diabetic (gliptins) drugs. Use of ACE inhibitors, such as Auro-Quinapril, with these drugs may increase the chance of having an allergic reaction.
- Have a medical history or family history of psoriasis (rash with itchy, scaly patches usually on the knees, elbows truck and scalp).

Other warnings you should know about:
You may become sensitive to the sun while taking Auro-Quinapril. Exposure to sunlight should be minimized until you know how you respond.
If you are going to have surgery and will be given an anesthetic, be sure to tell your healthcare professional that you are taking Auro-Quinapril.

Driving and using machines: Before you perform tasks, which may require special attention, wait until you know how you respond to Auro-Quinapril. Dizziness, light-headedness, or fainting can especially occur after the first dose and when the dose is increased. Exercise caution when driving or operating a vehicle or potentially dangerous machinery.

Development or worsening symptoms of psoriasis:

Auro-Quinapril can cause or worsen psoriasis (rash with itchy, scaly patches usually on the knees, elbows truck and scalp). Talk to your healthcare professional if you experience symptoms of psoriasis or worsening psoriasis.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with Auro-Quinapril:

- Agents increasing serum potassium, such as a salt substitute that contains potassium, potassium supplements, a potassium-sparing diuretic (a specific kind of "water pill") or sulfamethoxazole/trimethoprim.
- Alcohol
- Allopurinol used to treat gout.
- Anti-cancer drugs, including cyclophosphamide, methotrexate and temsirolimus and everolimus
- Anti-rejection drugs, such as sirolimus (Rapamune)
- Anti-diabetic drugs including insulin and oral medicines (e.g. metformin, gliptins, sulfonylureas)
- Blood pressure-lowering drugs, including diuretics ("water pills"), aliskiren-containing products (e.g. Rasilez), angiotensin receptor blockers (ARBs) (in addition to Auro-Quinapril)
- Gold for the treatment of rheumatoid arthritis.
- Lithium used to treat bipolar disease
- Neutral endopeptidase (NEP) inhibitor used to treat heart failure
- Nonsteroidal anti-inflammatory drugs (NSAIDs), used to reduce pain and swelling. Examples include ibuprofen, naproxen, and celecoxib.
- Tetracycline (a type of antibiotic)

How to take Auro-Quinapril:

Usual dose:

Take Auro-Quinapril exactly as prescribed. It is recommended to take your dose at about the same time every day.

Usual Adult Dose:

High Blood Pressure (Hypertension)

For patients NOT taking a diuretic ("water pills"): The recommended starting dose is 10 mg once a day.
For patients ALSO taking a diuretic ("water pill"): The recommended starting dose is 5

mg once a day.

Congestive Heart Failure

The recommended starting dose is 5 mg once a day.

Overdose:

If you think you, or a person you are caring for, have taken too much Auro-Quinapril, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you have forgotten to take your dose during the day, take it as soon as you remember. If it is almost time for the next dose, the missed dose should be skipped. You carry on with the next dose at the usual time. Do NOT double dose.

What are possible side effects from using Auro-Quinapril?

These are not all the possible side effects you may have when taking Auro-Quinapril. If you experience any side effects not listed here, tell your healthcare professional.

Side effects may include:

- Dizziness, headache, trouble sleeping
- drowsiness, fatigue, weakness
- cough, stuffy and runny nose
- abdominal pain, diarrhea, indigestion, nausea, vomiting
- back pain

Auro-Quinapril can cause abnormal blood test results. Your healthcare professional will decide when to perform blood tests and will interpret the results.

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
COMMON			
Low blood pressure: dizziness, fainting, light-headedness may occur when you go from lying or sitting to standing up.	✓		
Increased levels of potassium in the blood: irregular heartbeat,			

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
muscle weakness and generally feeling unwell		✓	
UNCOMMON			
Allergic reaction, including angioedema: rash, hives, swelling of the face, lips, tongue or throat, difficulty swallowing or breathing			✓
Kidney disorder: change in frequency of urination, nausea, vomiting, swelling of extremities, fatigue		✓	
Liver disorder: yellowing of the skin or eyes, dark urine, abdominal pain, nausea, vomiting, loss of appetite		✓	
Electrolyte imbalance: weakness, drowsiness, muscle pain or cramps, irregular heartbeat		✓	
Tachycardia: fast heartbeat		✓	
Edema: swelling of hands, ankles or feet		✓	
Rash, red patches on skin, including a skin disorder called psoriasis	✓		
RARE			
Decreased platelets: bruising, bleeding, fatigue and weakness		✓	
Decreased white blood cells: infections, fatigue, fever, aches, pains, and flu-like symptoms		✓	
Chest Pain, heart attack			✓
Shortness of breath	✓		
Coughing up blood			✓
High nitrogen compound found in blood (Azotemia): rapid heart rate, high blood pressure, fatigue, confusion, light headedness, dizziness, decreased urine production			✓

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store Auro-Quinapril at room temperature, between 15° and 30°C. Protect from light and moisture. Keep in well closed container.
Keep Auro-Quinapril out of the reach and sight of children.

If you want more information about Auro-Quinapril

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; the manufacturer's website www.auropharma.ca, or by calling 1-855-648-6681.
- This leaflet was prepared by Auro Pharma Inc.,

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