

health is inextricably linked to the health and vitality of our families, communities, and societies.”

— Jim Hollingworth, MD
Goderich, Ont

Reference

1. Worton KS. Green medicine. Environmental impact of health care [Platform]. *Can Fam Physician* 1995; 41:977-80.

Farm-related injuries taken seriously

The article by Dr Young¹ clearly illustrates the seriousness of farm-related injuries and deaths in rural Manitoba.

The original research leading to this article was completed while Dr Young was enrolled in the Parkland Family Practice Residency Program in Dauphin, Man. The study exemplifies the high-quality research carried out by family practice residents across the country.

It is important for family physician teachers to support and nurture these activities because this type of research is crucial in attempting to answer the many relevant questions in family medicine.

— James Goertzen, MD, CCFP
Dauphin, Man

Reference

1. Young SK. Agriculture-related injuries in the parkland region of Manitoba. *Can Fam Physician* 1995;41:1190-7.



Therapeutic Classification

Angiotensin Converting Enzyme Inhibitor

Indications And Clinical Use

Mild to moderate essential hypertension. May use alone or in combination with thiazide diuretics. Use not recommended in congestive heart failure or renovascular hypertension as safety and efficacy not established. Safety and efficacy of concomitant use with antihypertensive agents other than thiazide diuretics not established. When used in pregnancy during the second and third trimesters, ACE inhibitors can cause injury or even death of the developing fetus. When pregnancy is detected 'Inhibace' should be discontinued as soon as possible.

Contraindications

Hypersensitivity to this product and history of angioedema related to previous treatment with an angiotensin converting enzyme inhibitor.

Warnings

Angioedema: Angioedema has been reported. Discontinue, institute appropriate therapy without delay, and follow carefully until the swelling subsides. When tongue, glottis or larynx involved, administer subcutaneous adrenaline (0.5 mL 1:1000) promptly when indicated. Patients with history of angioedema unrelated to ACE inhibitor may be at increased risk.

Hypotension: Symptomatic hypotension has been reported, after first dose or with dose increased. More likely with sodium or volume depletion. Patients with congestive heart failure may experience excessive hypotension and should start therapy under close medical supervision and be followed for the first two weeks of treatment and when increasing the dose of 'Inhibace' and/or diuretic.

Neutropenia/Agranulocytosis: Leucopenia and neutropenia have been reported. Monitor white blood cell counts periodically.

Use in Pregnancy: ACE inhibitors can cause fetal and neonatal morbidity and mortality when administered to pregnant women. Discontinue as soon as possible if pregnancy detected. Consult product monograph for situations in which treatment should be discontinued, and for infants with a history of in utero exposure.

Precautions

Impaired Renal Function: Use with caution. Monitor patients closely before and during therapy. Dosage reduction and/or discontinuation of concomitant diuretic and/or cilazapril may be required. In patients with severe heart disease, treatment with ACE inhibitors may result in hypotension, azotemia and acute renal failure and/or death. Increases in blood urea nitrogen and creatinine observed in patients with renal artery stenosis. Increases in blood urea nitrogen and creatinine observed with concomitant use of diuretic.

Anaphylactoid Reactions during Membrane Exposure: Anaphylactoid reactions have been reported in patients dialysed with high-flux (beta-2-microglobulin) membranes. Dialysis should be stopped immediately.

Anaphylactoid Reactions during Desensitization: Most cases of anaphylactoid reactions in patients experiencing sustained life-threatening anaphylactoid reactions receiving ACE inhibitors during desensitizing treatment with venom (bees and wasps) venom.

Hypertension: Elevated serum potassium levels may be observed in some patients. Monitor serum potassium levels in patients with additional risk factors.

Valvular Stenosis: Patients with bicuspid aortic valve and/or depressed coronary perfusion.

Surgery/Anesthesia: Arterial hypotension may result.

Impaired Liver Function: Mild to moderate elevations in liver enzymes and/or serum bilirubin reported during clinical trials. Liver function tests, other necessary investigations and clinical course should be considered. No studies in patients with cirrhosis and/or cholestasis. Use with caution.

Cough: Consider possible drug involvement in diagnosis.

Nursing Mothers: Not known. Use with caution.

Pediatric Use: Safety and efficacy not established. Not recommended.

Elderly: Greater sensitivity to hypotension.

Drug Interactions

Diuretic Therapy: Occurrence of hypotension. Minimize discontinuing diuretic or increasing dose of diuretic at initiation of treatment with 'Inhibace' and/or reducing initial dose of diuretic.

Agents Increasing Serum Potassium: Serum potassium has been reported. Use potassium sparing diuretics with caution. Monitor frequently.

Agents Causing Renin Release: Antihypertensive effect is augmented.

Agents Affecting Sympathetic Activity: Use with caution.

Inhibitors of Endogenous Prostaglandin Synthesis: Indomethacin may reduce the antihypertensive effect of cilazapril but there is no evidence of attenuation of blood pressure lowering effects of cilazapril when its administration precedes the administration of the NSAID.

Digoxin: No pharmacodynamic or pharmacokinetic interaction.

Lithium Salts: Lithium elimination may be reduced. Therefore, monitor serum lithium levels.

Adverse Reactions

The most frequent adverse reactions (2,586 hypertensive participants) reported in controlled clinical trials were: headache (5.1%), dizziness (3.0%), fatigue (2.1%), cough (1.8%) and constipation (1.3%). 2.4% discontinued. The most severe adverse reactions reported in hypertensive patients were angioedema/face edema (0.1%), postural hypotension (0.3%), systolic hypertension (2.1%), myocardial infarction (0.1%), cerebrovascular accident (0.04%), hyperkalemia (0.09%), and thrombocytopenia (0.04%). Adverse reactions occurring in <1% of the patients controlled clinical trials were: neutropenia 0.4%, changes in liver function enzymes 0.1% - 1.1%, abnormal function tests 0.6% or less, hypotension (>5.5 mEq/L) 0.7%, serum creatinine >2 mg/dL 1.3%, pruritus 0.1%.

Dosage and Administration

Initial Dosage: Initial dose 2.5 mg once daily. Usual dose range 2.5 mg to 5 mg per day. Dosage should be adjusted if blood pressure control is not maintained for 24 hours, consider increasing to the same total daily dose or an increased dose, maximum 5 mg once daily.

Diuretic-treated Patients: If blood pressure is not controlled with diuretic alone, a non-potassium-sparing diuretic may be added. Start diuretic 2-3 days before 'Inhibace'. Start 'Inhibace' once diuretic has been administered. Adjust the dose of diuretic to individual response.

Elderly (Over 65 Years): Start with 1.25 mg once daily with caution.

Dosage in Renal Impairment (Including peritoneal dialysis):

Creatinine Clearance (mL/min): Initial Dose of 'Inhibace' 1.25 mg once daily. If creatinine clearance is >40 mL/min, increase to 2.5 mg once daily. If creatinine clearance is 30-40 mL/min, increase to 5 mg once daily. If creatinine clearance is <30 mL/min, increase to 2.5 mg once daily. If creatinine clearance is <15 mL/min, increase to 1.25 mg once or twice a week according to blood pressure response.

Dose Adjustment in Hypertension: Initiate treatment with caution.

Initial Dose: 2.5 mg once daily. If blood pressure is not controlled, increase to 5 mg once daily.

Usual Dose: 2.5 mg once daily.

Maximum Dose: 5 mg once or twice a week according to blood pressure response.

Product Monograph available upon request.

Availability

'Inhibace' (cilazapril) is available in film-coated tablets containing:
1 mg cilazapril: white, oval shaped, single scored biconvex tablets, imprinted CL 1.
2.5 mg cilazapril: pinkish-brown, oval shaped, single scored biconvex tablets, imprinted CL 2.5.
5 mg cilazapril: reddish-brown, oval shaped, single scored biconvex tablets, imprinted CL 5.

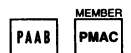
Bottles of 100 tablets.

Schedule F Drug.

Product Monograph available upon request.

References

1. Clozel JP, et al. Vascular protection with cilazapril in hypertension. *J Cardiovasc Pharmacol* 1992;19(suppl 5):286-33s.
2. Clozel JP, et al. Effects of chronic ACE inhibition on cardiac hypertrophy and coronary vascular reverse in spontaneously hypertensive rats with developed hypertension. *J of Hypertension* 1989;7:267-275.
3. Clozel JP, et al. Decreases of vascular hypertrophy in four different types of arteries in spontaneous hypertensive rats. *Am J Med* 1989;87(suppl 6B):92s-95s.
4. Inhibace® Product Monograph.
5. Locourcière Y et al. Antihypertensive effects of cilazapril, 2.5 and 5 mg, once daily versus placebo on ambulatory blood pressure following single- and repeat-dose administration. *J Cardiovasc Pharmacol* 1991;18:219-223.
6. Jackson B, Cabela R, Johnston C. Angiotensin converting enzyme (ACE), characterization by 125I-AK351A binding studies of plasma and tissue ACE during variation of salt status in the rat. *J of Hypertension* 1986;4:759-765.
7. Higashimura K, Garte J, Holzemann G, Inagami T. Significance of vascular renin for local generation of angiotensins. *Hypertension* 1991;17(3):270-277.
8. Based on 1994 Price Lists and Ontario Drug Benefit Formulary with January 15, 1995 Supplement and 1995 Quebec Formulary.



© 1995, Hoffmann-La Roche Limited
Registered Trademark of Hoffmann-La Roche Limited
Mississauga, Ontario L5N 6L7