

TARGACEPT

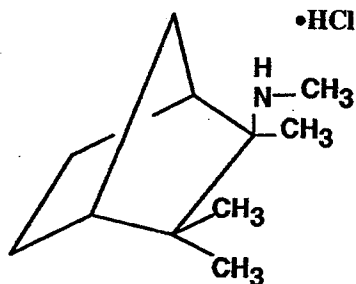
TABLETS

INVERSINE®

(MECAMYLAMINE HCl)

DESCRIPTION

INVERSINE® (Mecamylamine HCl) is a potent, oral antihypertension agent and ganglion blocker, and is a secondary amine. It is N,2,3,3-tetramethyl-bicyclo [2.2.1] heptan-2-amine hydrochloride. Its empirical formula is $C_{11}H_{21}N \cdot HCl$ and its structural formula is:



It is a white, odorless, or practically odorless, crystalline powder, is highly stable, soluble in water and has a molecular weight of 203.75.

INVERSINE is supplied as tablets for oral use, each containing 2.5 mg mecamylamine HCl. Inactive ingredients are acacia, calcium phosphate, D&C Yellow 10, FD&C Yellow 6, lactose, magnesium stearate, starch, and talc.

CLINICAL PHARMACOLOGY

Mecamylamine reduces blood pressure in both normotensive and hypertensive individuals. It has a gradual onset of action (1/2 to 2 hours) and a longlasting effect (usually 6 to 12 hours or more). A small oral dosage often produces a smooth and predictable reduction of blood pressure. Although this antihypertensive effect is predominantly orthostatic, the supine blood pressure is also significantly reduced.

Pharmacokinetics and Metabolism

Mecamylamine is almost completely absorbed from the gastrointestinal tract, resulting in consistent lowering of blood pressure in most patients with hypertensive cardiovascular disease. Mecamylamine is excreted slowly in the urine in the unchanged form. The rate of its renal elimination is influenced markedly by urinary pH. Alkalinization of the urine reduces, and acidification promotes, renal excretion of mecamylamine.

Mecamylamine crosses the blood-brain and placental barriers.

INDICATIONS AND USAGE

For the management of moderately severe to severe essential hypertension and in uncomplicated cases of malignant hypertension.

CONTRAINDICATIONS

INVERSINE should not be used in mild, moderate, labile hypertension and may prove unsuitable in uncooperative patients. It is contraindicated in coronary insufficiency or recent myocardial infarction.

INVERSINE should be given with great discretion, if at all, when renal insufficiency is manifested by a rising or elevated BUN. The drug is contraindicated in uremia. Patients receiving antibiotics and sulfonamides should

generally not be treated with ganglion blockers. Other contraindications are glaucoma, organic pyloric stenosis or hypersensitivity to the product.

WARNINGS

Mecamylamine, a secondary amine, readily penetrates into the brain and thus may produce central nervous system effects. Tremor, choreiform movements, mental aberrations, and convulsions may occur rarely. These have occurred most often when large doses of INVERSINE were used, especially in patients with cerebral or renal insufficiency.

When ganglion blockers or other potent antihypertensive drugs are discontinued suddenly, hypertensive levels return. In patients with malignant hypertension and others, this may occur abruptly and may cause fatal cerebral vascular accidents or acute congestive heart failure. When INVERSINE is withdrawn, this should be done gradually and other antihypertensive therapy usually must be substituted. On the other hand, the effects of INVERSINE sometimes may last from hours to days after therapy is discontinued.

PRECAUTIONS

General

The patient's condition should be evaluated carefully, particularly as to renal and cardiovascular function. When renal, cerebral, or coronary blood flow is deficient, any additional impairment, which might result from added hypotension, must be avoided. The use of INVERSINE in patients with marked cerebral and coronary arteriosclerosis or after a recent cerebral accident requires caution.

The action of INVERSINE may be potentiated by excessive heat, fever, infection, hemorrhage, pregnancy, anesthesia, surgery, vigorous exercise, other antihypertensive drugs, alcohol, and salt depletion as a result of diminished intake or increased excretion due to diarrhea, vomiting, excessive sweating, or diuretics.

During therapy with INVERSINE, sodium intake should not be restricted but, if necessary, the dosage of the ganglion blocker must be adjusted.

Since urinary retention may occur in patients on ganglion blockers, caution is required in patients with prostatic hypertrophy, bladder neck obstruction, and urethral stricture.

Frequent loose bowel movements with abdominal distention and decreased borborygmi may be the first signs of paralytic ileus. If these are present, INVERSINE should be discontinued immediately and remedial steps taken.

Information for patients

INVERSINE may cause dizziness, lightheadedness, or fainting, especially when rising from a lying or sitting position. This effect may be increased by alcoholic beverages, exercise, or during hot weather. Getting up slowly may help alleviate such a reaction.

Drug Interactions

Patients receiving antibiotics and sulfonamides generally should not be treated with ganglion blockers.

The action of INVERSINE may be potentiated by anesthesia, other antihypertensive drugs and alcohol.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals have not been performed to evaluate the effects upon fertility, mutagenic or carcinogenic potential of INVERSINE.

Pregnancy

Pregnancy Category C. Animal reproduction studies have not been conducted with INVERSINE. It is not known whether INVERSINE can cause fetal harm when given to a pregnant woman or can affect reproductive capacity. INVERSINE should be given to a pregnant woman only if clearly needed.

Nursing Mothers

Because of the potential for serious adverse reactions in nursing infants from INVERSINE, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

