MECAMYLAMINE HYDROCHLORIDE

Generic	Brand	HICL	GCN	Exception/Other
MECAMYLAMINE HCL	VECAMYL		1471	

This drug requires a written request for prior authorization.

GUIDELINES FOR USE

1. Does the patient have a diagnosis of moderately severe to severe essential (or primary) hypertension or uncomplicated malignant hypertension?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

2. Has the patient tried or does the patient have a contraindication to three of the following: angiotensin converting enzyme (ACE) inhibitor or ACE-I combination, angiotensin receptor blocker (ARB) or ARB combination, Beta Blocker, or Calcium Channel Blocker?
   PAC NOTE: These drugs include: benazepril, benazepril-HCTZ, captopril, captopril-HCTZ, enalapril, enalapril-HCTZ, fosinopril, fosinopril-HCTZ, lisinopril, lisinopril-HCTZ, quinapril, ramipril, moexipril, moexipril-HCTZ, perindopril erbumine, quinapril, quinapril-HCTZ, trandolapril, trandolapril/verapamil, losartan, losartan-HCTZ, irbesartan, irbesartan-HCTZ, olmesartan, olmesartan-HCTZ, olmesartan-amlodipine-HCTZ, valsartan, valsartan-HCTZ, diltiazem HCL, diltiazem sustained release (generics only), verapamil, verapamil sustained release (generics only), atenolol, atenolol-chlorthalidone, bisoprolol, bisoprolol-HCTZ, carvedilol, metoprolol tartrate, nadolol, acebutolol, betaxolol, labetalol, metoprolol succinate, metoprolol-HCTZ, pindolol, propranolol, propranolol-HCTZ, sotalol, timolol maleate, or nebivolol.

   If yes, **approve for 12 months by GPID.**
   If no, do not approve.
   DENIAL TEXT: See the denial text at the end of the guideline.

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MECAMYLAMINE HYDROCHLORIDE

GUIDELINES FOR USE

DENIAL TEXT: Approval requires that Vecamyl be used for the management of moderately severe to severe essential (or primary) hypertension or in uncomplicated cases of malignant hypertension; and a trial or a contraindication to at least three of the following: angiotensin converting enzyme (ACE) inhibitor or ACE-I combination, angiotensin receptor blocker (ARB) or ARB combination, Beta Blocker, or Calcium Channel Blocker, such as benazepril, benazepril-HCTZ, captopril, captopril-HCTZ, enalapril, enalapril-HCTZ, fosinopril, fosinopril-HCTZ, lisinopril, lisinopril-HCTZ, quinapril, ramipril, moexipril, moexipril-HCTZ, perindopril erbumine, quinapril, quinapril-HCTZ, trandolapril, trandolapril/verapamil, losartan, losartan-HCTZ, irbesartan, irbesartan-HCTZ, olmesartan, olmesartan-HCTZ, olmesartan-amlodipine-HCTZ, valsartan, valsartan-HCTZ, diltiazem HCL, diltiazem sustained release (generics only), verapamil, verapamil sustained release (generics only), atenolol, atenolol-chlorthalidone, bisoprolol, bisoprolol-HCTZ, carvedilol, metoprolol tartrate, nadolol, acebutolol, betaxolol, labetalol, metoprolol succinate, metoprolol-HCTZ, pindolol, propranolol, propranolol-HCTZ, sotalol, timolol maleate, or nebivolol.

RATIONALE

To ensure appropriate use aligned with FDA approved indication.

Therapy is usually started with one 2.5 mg tablet of Vecamyl twice a day. This initial dosage should be modified by increments of one 2.5 mg tablet at intervals of not less than 2 days until the desired blood pressure response occurs (the criterion being a dosage just under that which causes signs of mild postural hypotension).

The average total daily dosage of Vecamyl is 25 mg, usually in three divided doses. However, as little as 2.5 mg daily may be sufficient to control hypertension in some patients. Since the blood pressure response to antihypertensive drugs is increased in the early morning, the larger dose should be given at noontime and perhaps in the evening.

Vecamyl joins several different agents used in the treatment of hypertension. The most commonly prescribed drug classes for primary hypertension include thiazide-type diuretics, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), calcium channel blockers, and beta blockers; all of which have generic formulations available. Each category of antihypertensive agent has similar levels of efficacy in lowering the blood pressure, producing a good antihypertensive response in 30 to 50 percent of patients. Malignant hypertension most often occurs in patients with long-standing uncontrolled hypertension, many of whom have discontinued antihypertensive therapy. The oral drug of choice in uncomplicated malignant hypertension is the ACE inhibitor, captopril, since it can substantially lower the BP within 10 to 30 minutes for most patients and has a relatively short duration that facilitates dose titration.

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MECAMYLAMINE HYDROCHLORIDE

RATIONALE (CONTINUED)
In more recent years, there has been considerable interest in evaluating Vecamyl for the treatment of other clinical indications, including smoking cessation and depression. The principal focus of research on other clinical indications largely involves Vecamyl's potent blockade of brain nicotinic receptors at doses that do not have a significant effect on parasympathetic function (2.5-10 mg/day). Recently Vecamyl was studied as an add-on treatment to existing anti-depressants. However, it failed two short-term Phase 3 clinical trials in 2011, showing no significant difference in patients when compared to a placebo.

The package insert for Vecamyl does not include any clinical trials as it was approved using an abbreviated new drug application (ANDA) of the innovator product, Inversine (mecamylamine). The distribution of Inversine was discontinued in 2009. Approved on March 1, 1956, Inversine was available prior to the 1962 amendments to the Federal Food, Drug, and Cosmetic Act (commonly referred to as the Kefauver-Harris Amendments) which established a framework requiring drug manufacturers to prove scientifically that a medication was not only safe, but effective. Since drugs approved between 1938 and 1962 were approved only on the grounds of safety, the FDA's Drug Efficacy Study Implementation (DESI) program has been retrospectively evaluating the effectiveness of these medications.

The Journal of the American Medical Association published a study in 1957 examining the effects of mecamylamine alone on 17 patients with sustained blood pressure above 150/100 mm Hg. Each patient was initiated on mecamylamine 2.5mg twice daily before undergoing a set dose titration. Treatment response was defined as a decrease in mean blood pressure by at least 20 mm Hg or a reduction of blood pressure to the normotensive level (defined by the investigators as less than 150/100 mm Hg). A little more than half of this small group responded to mecamylamine alone. Among the responders, the average dose was 34mg daily. However, there were some patients, who despite doubling this average dose, did not respond satisfactorily to mecamylamine.

Vecamyl is contraindicated in those with coronary insufficiency or recent myocardial infarction, uremia, glaucoma, organic pyloric stenosis as well as patients with hypersensitivity to the product.

Vecamyl should be given with great discretion, if at all, in patients with renal insufficiency. Patients receiving antibiotics and sulfonamides should generally not be treated with ganglion blockers such as Vecamyl.

Vecamyl should not be used in mild, moderate, labile hypertension and may prove unsuitable in uncooperative patients. When ganglion blockers or other potent antihypertensive drugs are discontinued suddenly, hypertensive levels return. For some patients, particularly those with malignant hypertension, this may occur abruptly and may cause fatal cerebral vascular accidents or acute congestive heart failure. Vecamyl should be gradually discontinued and substituted with other antihypertensive therapy.

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MECAMYLAMINE HYDROCHLORIDE

RATIONALE (CONTINUED)
At therapeutic antihypertensive doses (30 to 90 mg per day), Vecamyl has parasympathetic-blocking activity which results in side effects such as constipation, urinary retention, dryness of the mouth and skin, dilation of the pupils, and loss of visual accommodation in some patients. Since urinary retention may occur, caution is required in patients with prostatic hypertrophy, bladder neck obstruction, and urethral stricture. Vecamyl should be discontinued immediately if a patient is showing signs of paralytic ileus (for example frequent loose bowel movements with abdominal distention and decreased bowel sounds).

Since Vecamyl readily penetrates into the brain, it can cause central nervous system effects such as tremor, choreiform movements, mental aberrations, and convulsions. Although rare in nature, these effects have occurred most often when large doses of Vecamyl were used, especially in patients with cerebral or renal insufficiency.

Vecamyl is pregnancy category C. Because of the potential for serious adverse reactions in nursing infants from Vecamyl, 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.

FDA APPROVED INDICATIONS
For the management of moderately severe to severe essential (or primary) hypertension and in uncomplicated cases of malignant hypertension.

REFERENCES

- Vecamyl [Prescribing Information]. Fort Collins, CO: Manchester Pharmaceuticals; February 2012.
- UpToDate, Inc. Choice of therapy in primary (essential) hypertension: Recommendations. UpToDate [database online]. Waltham, MA. Available at http://www.uptodate.com/home/index.html. Updated March 25, 2013.
- UpToDate, Inc. Malignant hypertension and hypertensive encephalopathy in adults. UpToDate [database online]. Waltham, MA. Available at http://www.uptodate.com/home/index.html. Updated July 17, 2012.
- Shytle RD, Penny, E, et. al. Mecamylamine (Inversine): an old antihypertensive with new research directions. Journal of Human Hypertension. 2002; (16): 453-457.
- The Death of TC-5214. Available at http://scienceleftuntitled.wordpress.com/2012/05/11/the-death-of-tc-5214/ Accessed on May 9, 2013.
- Kefauver-Harris Amendments Revolutionized Drug Development. Updated on October 10, 2012. Available at http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm322856.htm# Accessed on May 9, 2013.
- Moyer, John; Heider, Charles; Dennis, Edward. Mecamylamine (inversine) in the treatment of hypertension. JAMA. 1957;164(17):1879-1886. Available at http://www.uptodate.com/home/index.html. Updated February 25, 2013.

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STANDARD COMMERCIAL DRUG FORMULARY
PRIOR AUTHORIZATION GUIDELINES

MECAMYLAMINE HYDROCHLORIDE

Library	Commercial	NSA
Yes	Yes	No

Part D Effective: N/A
Commercial Effective: 10/01/13
Created: 05/13
Client Approval: 08/13
P&T Approval: 08/13