mecamylamine (Vecamyl®)

EOCCO POLICY

Policy Type: PA Pharmacy Coverage Policy: EOCCO232

Description

Mecamylamine (Vecamyl) is an orally administered sympathetic ganglionic blocker, which blocks cholinergic stimuli at nicotinic receptors leading to blood vessels dilation and reduction in blood pressure.

Length of Authorization

- Initial: 12 months
- Renewal: 12 months

Quantity Limits

Product Name	Dosage Form	Indication	Quantity Limit
Mecamylamine (Vecamyl)	2.5 mg tablet	Moderately severe to severe hypertension	300 tablets/30 days
		Uncomplicated malignant hypertension	

Initial Evaluation

I. Mecamylamine (Vecamyl) may be considered medically necessary when the following criteria are met:
   A. Member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with, a cardiologist; **AND**
   C. A diagnosis of **Moderately severe to severe hypertension OR Uncomplicated malignant hypertension** when the following are met:
      1. Treatment with at least one agent from FIVE of the following classes of antihypertensive agents has been ineffective or not tolerated (Note, if a class of agents is contraindicated, a trial and failure of at least five agents or combinations thereof from the remaining groups is required):
         i. Thiazide diuretics (e.g. hydrochlorothiazide)
         ii. Angiotensin-converting enzyme inhibitors (e.g. lisinopril, captopril, benazepril)
         iii. Angiotensin II receptor antagonists (e.g. losartan, valsartan)
         iv. Beta blockers (e.g. metoprolol)
         v. Calcium channel blockers (e.g. amlodipine, diltiazem)

vi. Direct renin inhibitors (e.g. aliskiren)
vii. Other (e.g. clonidine, hydralazine, doxazosin) **AND**

2. Treatment with at least one parenteral antihypertensive agent (e.g. IV nitroprusside, nicardipine, clevidipine, labetalol) has been ineffective, contraindicated, or not tolerated.

II. Mecamylamine (Vecamyl) is considered investigational when used for all other conditions, including but not limited to:
   A. Major depressive disorder (MDD)
   B. Giles de la Tourette's syndrome
   C. Hyperreflexia
   D. Nicotine dependence

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Member has exhibited improvement or stability of disease symptoms [e.g. reduction in blood pressure].

Supporting Evidence

I. Mecamylamine (Vecamyl) is a nicotinic parasympathetic ganglionic blocker, which prevents stimulation of postsynaptic receptors by acetylcholine released from presynaptic nerve endings. The hypotensive effect of mecamylamine (Vecamyl) is attributed to reduction in sympathetic tone, vasodilation, and reduced cardiac output. It is considered a nonselective antagonist that easily passes through the blood-brain barrier, and thus, having the potential to affect nicotinic acetylcholine receptors in the central nervous system.
II. Mecamylamine (Vecamyl) is FDA approved for use in patients 18 years of age and older. Efficacy and safety of this drug are not established in the pediatric population.
III. Mecamylamine (Vecamyl) 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.

IV. The package insert for mecamylamine (Vecamyl) does not include any clinical trials as it was approved using an abbreviated new drug application (ANDA) of the innovator product, mecamylamine (Inversine). Approved on March 1, 1956, Inversine was available prior to the 1962 amendments to the Federal Food, Drug, and Cosmetic Act, which led to inclusion of Inversine as an approved DESI drug; however, the distribution of Inversine was discontinued in 2009.

V. An observational clinical study (N=17) in 1957 examined the effects of mecamylamine monotherapy for blood pressure reduction from baseline (>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). Response rate to mecamylamine was reported to be 52% at average 34 mg/day dose, while the other half of subject population (non-responders) had no blood pressure reductions despite doubling the average dose.

VI. Mecamylamine (Vecamyl) is not an acceptable alternative agent to consider for supplemental use after first-line antihypertensive agents have failed to provide adequate response. More predictably effective agents with proven effects on morbidity and mortality and with safer side effect profiles have replaced mecamylamine for use in both essential and accelerated hypertension.

VII. It should be noted that parenteral antihypertensives (e.g. IV nitroprusside, nicardipine, clevipine, labetalol etc.) are most often used in the initial treatment of malignant hypertension due to their faster onset of action. Trial of a parenteral antihypertensive agent is warranted before consideration of mecamylamine (Vecamyl) as the next therapeutic agent.

VIII. The Clinical Practice Guidelines from the American College of Cardiology/American Heart Association Task Force (2017) do not include ganglionic blockers (e.g. mecamylamine (Vecamyl)) as a recommended primary or secondary treatment option. The Evidence-Based Guideline for the Management of High Blood Pressure in Adults from the panel members of the eighth joint national committee (2014) advise selection among four specific medication classes (thiazide type diuretics, calcium channel blockers, angiotensin-converting enzyme inhibitors, or angiotensin receptor blockers) as initial treatment and inclusion of other classes (e.g. beta blockers, direct renin inhibitors, alpha1 blockers, centrally acting drugs and direct vasodialator) as secondary choices in treatment.

Investigational or Not Medically Necessary Uses

I. Major depressive disorder (MDD)

A. The principal focus of research on mecamylamine largely involves its potent blockade of nicotinic receptors in central nervous system at doses that do not have a significant effect on parasympathetic function (2.5-10 mg/day). Recently mecamylamine was studied via two short-term, phase III clinical trials, as an add-on treatment to existing antidepressant agents. These trials did not show significant difference in treatment groups compared to a placebo.

II. Giles de la Tourette's syndrome and Hyperreflexia

A. Use of mecamylamine for the treatment of Giles de la Tourette's syndrome and hyperreflexia has been studied in retrospective case studies and the quality of evidence in these settings is considered low.

III. Nicotine dependence

A. A randomized, double-blind, placebo controlled clinical trial (N=48) assessed efficacy of mecamylamine in combination with transdermal nicotine patches as compared to placebo in combination with nicotine patch. Although this study reported greater abstinence rates in treatment group at week 7 (50% versus 16%), the trial was not adequately powered to analyze effect size and the primary outcome assessment was based on patient self-reporting. Additionally, all subjects received transdermal nicotine, which confounded the outcomes assessment. Mecamylamine has not been FDA-approved in this setting.

References

1. Vecamyl [Prescribing Information]. Fort Collins, CO: Manchester Pharmaceuticals; July 2015.
2. Shytle RD, Penny, E, et. al. Mecamylamine (Inversine): an old antihypertensive with new research directions. Journal of Human Hypertension. 2002; (16): 453-457.
3. The Death of TC-5214. Kefauver-Harris Amendments Revolutionized Drug Development. Updated on October 10, 2012. Available at http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm322856.
4. Moyer, John; Heider, Charles; Dennis, Edward. Mecamylamine (Inversine) in the treatment of hypertension. JAMA. 1957;164(17):1879-1886.
5. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults. JACC,. 2018; 71, e127-248.

Policy Implementation/Update:

Action and Summary of Changes	Date
Transition of old criteria document to the policy format; added requirement of drug being prescribed by a specialist; removed criteria for validation of contraindications before treatment start; added E/I uses; added supporting evidence	05/2021
Criteria created	09/2013