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THE PRESCRIBER e-LETTER

Clobazam (Onfi) for Lennox-Gastaut Syndrome

Clobazam (Onfi) is a schedule IV benzodiazepine that was recently granted FDA approval for the adjunctive treatment of Lennox-Gastaut syndrome in patients two years of age and older. Lennox-Gastaut syndrome is a severe form of epilepsy that can cause debilitating seizures, characterized by multiple seizure types. Often, these seizures present within the first seven years of life. Treatment may consist of the use of various anti-epileptic agents. Those agents with FDA approval for the treatment of Lennox-Gastaut syndrome include rufinamide (Banzel), divalproex sodium (Depakote), lamotrigine (Lamictal), and topiramate (Topamax). Clinical trials have demonstrated that treatment with clobazam results in a decreased weekly rate of drop seizures and non-drop seizures when compared to placebo. Currently, the National Institute for Clinical Excellence guidelines on the treatment of epilepsy list clobazam as a first- or second-line treatment option for most types of epilepsy.

The table below provides a comparison of the monthly cost of some of the agents that can be used in the treatment of Lennox-Gastaut. As a result of the availability of effective, less costly alternatives, clobazam has been added to the MassHealth Drug List requiring PA as of March 12, 2012.

Medication	Cost/30 days
Banzel (rufinamide) tablets	$222.00-$1,773.60
Depakote (divalproex sodium) # tablets and ER tablets	$42.37-$215.40
Lamictal (lamotrigine) # tablets	$12.60-$21.30
ONFI (clobazam) tablets	$98.70-$787.80
Topamax (topiramate) # tablets	$10.50-$21.00

This is a brand-name drug with an FDA "A"-rated generic equivalent. PA is required for the brand, unless a particular form of that drug does not have an FDA "A"-rated generic.

Hereditary Angioedema Agents

Hereditary angioedema (HAE) is a rare disorder that is caused by an absence or a dysfunction of the c1 esterase inhibitor, which is a key regulator of the Factor XII/kallikrein proteolytic cascade that leads to bradykinin production. Symptoms of HAE include episodic, nonpruritic, localized, subcutaneous and submucosal swelling that can occur in attacks of varying intensity and severity.

Short-term prophylaxis may be used in anticipation of a medical procedure or a period of stress that might trigger an attack. Long-term prophylaxis should be considered in patients who experience more than one severe event per month, those who are disabled more than five days per month, or in anyone that has experienced a laryngeal attack. The agents that can be used for prophylaxis include: human c1 esterase inhibitor (Cinryze), danazol, oxandrolone, and methyltestosterone. Agents that can be used for the treatment of an acute attack include: icatibant (Firazyr), human c1 esterase inhibitor (Berinert), and ecallantide (Kalbitor).

The table below provides a comparison of the cost associated with some of these agents when used for prophylaxis or an acute attack. MassHealth recognizes that both purified human c1 esterase inhibitor (Cinryze) and purified human c1 esterase inhibitor (Berinert) may be used for self-administration and therefore removed the requirement that these products only be available if dispensed through the administering prescriber. However, due to the high cost of these agents both will require PA as of March 26, 2012.

Medication	Cost/30 Days Prophylaxis	Cost/Dose for Acute Attack
Berinert (human c1 esterase inhibitor)	NA	$5,975.55
Cinryze (human c1 esterase inhibitor)	$31,689.42-$45,270.60	NA
Firazyr (icatibant)	NA	$7,140.00
Kalbitor (ecallantide)	NA	$8,767.50

The Prescriber e-Letter is an update designed to enhance the transparency and efficiency of the MassHealth drug prior-authorization (PA) process and the MassHealth Drug List. Each issue will **highlight** key clinical **information and updates** to the **MassHealth Drug List**. The Prescriber E-Letter was prepared by the MassHealth Drug Utilization Review Program and the MassHealth Pharmacy Program.

Recent MassHealth Drug List Updates

Drug/Drug Class	Addition/Deletion/Change	Rationale
Antidiarrheal agents	Change in PA status; **requires PA,** opium tincture and atropine/difenoxin (Motofen)	Due to the abuse potential with opium tincture and the availability of less costly generic alternatives, both opium tincture and atropine/difenoxin will require PA.
asparaginase *Erwinia chrysanthemi* (Erwinaze)	Addition; **requires PA^** ^This drug is available through the health care professional who administers the drug. Medicaid does not pay for this drug to be dispensed through a retail pharmacy.	Asparaginase *Erwinia chrysanthemi* is FDA approved as part of a multi-agent chemotherapeutic regimen for the treatment of patients with acute lymphoblastic leukemia who have developed hypersensitivity to *E. coli*-derived asparaginase. Due to the very specific indication for this agent and its high cost, asparaginase *Erwinia chrysanthemi* requires PA and is available only through the health care professionals who administer the drug.
bevacizumab (Avastin)	Change in PA status; **requires PA**	Bevacizumab is a vascular endothelial growth factor-specific angiogenesis inhibitor FDA approved for use in treating: metastatic colorectal cancer, with intravenous 5-fluorouracil-based chemotherapy; non-squamous non-small cell lung cancer with carboplatin and paclitaxel for first-line treatment of unresectable, locally advanced, recurrent or metastatic disease; glioblastoma; and metastatic renal cell carcinoma with interferon alfa. In December 2011, the FDA removed the indication of metastatic breast cancer from the bevacizumab label. As a result, in order to ensure this agent is used for FDA approved indications, bevacizumab will require PA.
clobazam (ONFI)	Addition; **requires PA**	ONFI (clobazam) is benzodiazepine (schedule IV) indicated for the adjunctive treatment of seizures associated with LGS in patients 2 years of age or older. Due to the availability of less costly alternatives, clobazam requires PA.
donepezil (Aricept) 10 mg tablet	Change in PA status; **requires PA if quantity > 60 units/month**	Donepezil is an acetylcholinesterase inhibitor FDA approved for the treatment of Alzheimer's dementia. Due to the cost of the 23 mg dosage form of donepezil (Aricept), the generic 10 mg tablets will be available in quantities up to 60 units per month. Quantities > 60 units/month require PA.
fluocinolone oil, otic drops	Addition	Fluocinolone oil, otic drops are the new "A" rated generic to DermOtic. This new generic formulation does not require PA.
fluoxetine 60 mg tablet	Addition; **requires PA**	Due to the availability of less costly, lower strengths of the generic fluoxetine (e.g., 10 mg and 20 mg capsules), this strength of fluoxetine requires PA.
Hereditary angioedema (HAE) agents	Change in PA status; **requires PA,** human c1 esterase inhibitor (Berinert), human c1 esterase inhibitor (Cinryze)	C1 esterase inhibitor (Berinert) is FDA approved for the treatment of acute abdominal, facial, or laryngeal attacks of HAE in adult and adolescent patients. This agent can be self-administered by appropriately trained patients. C1 esterase inhibitor (Cinryze) is FDA approved for routine prophylaxis against angioedema attacks in adolescent and adult patients with HAE. MassHealth realizes that these agents may be used for self administration and therefore removed the requirement that these products only be available if dispensed through the administering prescriber. However, due to the high cost of these agents, both will require PA.

Please send any suggestions or comments to: PrescriberELetter@state.ma.us

Recent MassHealth Drug List Updates (cont.)

Drug/Drug Class	Addition/Deletion/Change	Rationale
methylphenidate 20 mg, 30 mg, and 40 mg capsules	Addition**; requires PA if quantity > 60 units/month**	Methylphenidate 20 mg, 30 mg, and 40 mg capsules are the new "A"-rated generic to Ritalin LA. To ensure proper dose consolidation when applicable, this agent requires PA if quantities > 60 units/month.
naltrexone (Vivitrol) injection	Change in PA status; does not require PA	Naltrexone injection is an opioid antagonist that is indicated for the treatment of alcohol dependence in patients who are able to abstain from alcohol in an outpatient setting prior to initiating treatment with naltrexone and it is also indicated for the prevention of relapse to opioid dependence, following opioid detoxification. A recent review of utilization within the MassHealth population has indicated appropriate use of this product and therefore it does not require PA.
naltrexone powder	Change in PA status; **requires PA**	In order to limit the use of this agent to compound off-label, low-dose naltrexone formulations, naltrexone powder will require PA.
piperacillin/tazobactam	Addition	Piperacillin/tazobactam is the new "A" rated generic to Zosyn. This new generic formulation does not require PA.
ruxolitinib (Jakafi)	Addition; **requires PA**	Ruxolitinib is a kinase inhibitor FDA approved for the treatment of high-risk myelofibrosis, including primary myelofibrosis, post-polycythemia vera myelofibrosis and post-essential thrombocythemia myelofibrosis. Due to the high-cost of ruxolitinib and the availability of less costly alternatives (i.e., hydroxyurea), ruxolitinib requires PA.
tiotropium (Spiriva)	Change in PA status; **requires PA if quantity > 30 units/month**	Tiotropium is FDA approved for the long-term, once-daily maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD) and for reducing COPD exacerbations. Tiotropium is administered as two inhalations from one 18 mcg capsule (one unit) once daily. To ensure tiotropium is being used at the FDA approved dosing, PA will be required for quantities > 30 units/month.

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