January 2014, Volume 6, Issue 1

THE PRESCRIBER e-LETTER

Preventing Pediatric Osteoporosis in High-Risk Patients: Knowing the Risks

Osteoporosis is a disease characterized by low bone mass and deterioration of bone tissue leading to increased bone fragility. While osteoporosis is not a common diagnosis in children and adolescents, it has become an increasingly important medical concern in this age group.

Although there is no systematically collected data, reports suggest that pediatric patients affected by particular chronic conditions and those taking certain medications may be at risk for secondary osteoporosis. For example, the overall incidence of fractures in children with cerebral palsy has been reported to range from 15.5% to as high as 39%. Additional common diseases that may lead to the development of osteoporosis include chronic systemic disease/malignancy, cystic fibrosis, Duchenne muscular dystrophy, eating disorders, inflammatory bowel disease, juvenile idiopathic arthritis, leukemia, organ and bone marrow transplantation, rheumatological conditions, nephrotic syndrome, conditions that reduce mobility, systemic lupus erythematosus, dermatomyositis, and disordered puberty conditions such as thalassaemia major or gonadal damage due to radiotherapy/ chemotherapy. Osteotoxic medications associated with increased risk include antiepileptics, cyclosporine, glucocorticoids, gonadotropin-releasing hormone analogs, heparin, lithium, medroxyproges-terone acetate, methotrexate, and sucralfate.

Currently no consensus guidelines are available for the treatment of osteoporosis in pediatric patients. In general, approaches to reduce or eliminate the risk factors for low bone mass and ensure the lowest doses of osteotoxic medications are important. Therapeutic interventions include calcium, vitamin D, antiresportive medications, and, when possible, low-impact weight-bearing exercises.

The goal of the osteoporosis initiative is to provide prescribers with the risk factors associated with the development of pediatric osteoporosis.

These materials are general recommendations only; specific clinical decisions should be made by the treating clinician based on an individual patient's clinical condition.

For additional information, please visit the MassHealth Drug List website at https://masshealthdruglist.ehs.state.ma.us/MHDL/

Updated Opioid High-Dose Limits

Opioid misuse and abuse is a major public health concern in Massachusetts and across the United States. MassHealth currently requires prior authorization (PA) to exceed certain dose limits for most opioid formulations. The dose limits were developed based on analysis of opioid utilization within the MassHealth population.

As part of the continuous monitoring of drug utilization within the MassHealth population, and in light of opioid misuse concerns, the MassHealth Pharmacy Program has conducted an analysis of both opioid utilization and recent published medical literature. Although there is no one single definition of "high-dose" opioid therapy, a review of clinical studies and guidance indicates that the highest daily dose of morphine allowed in randomized opioid trials was 240 mg/day, and the highest average dose was 120 mg/day.

Given this information, MassHealth will be implementing lower dose limits for opioids beginning in March 2014. PA will be required for doses exceeding these limits, which are available for your reference in the table below.

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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.

Long-acting			
Drug	**Dose Limits**		**Quantity Limit**
	Current	**New**	
Avinza (morphine extended-release)*	**> 360 mg/day**	**> 240 mg/day**	**> 1 capsule/day**
Dolophine, Methadose (methadone)† ‡	**> 120 mg/day**	**> 60 mg/day**	**N/A**
Duragesic (transdermal fentanyl)* ‡	**> 200 µg/hr**	**> 75 µg/hr**	**> 10 patches/ month**
Exalgo (hydromorphone extended-release)*	**> 60 mg/day**	**> 64 mg/day§**	**> 4 tablets/day**
Kadian (morphine extended-release)* ‡	**> 360 mg/day**	**> 240 mg/day**	**> 1 capsule/day**
Levo-Dromoran (levorphanol)‡	**> 32 mg/day**	**> 8 mg/day**	**> 4 tablets/day**
MS Contin, Oramorph SR (morphine controlled-release)‡	**> 360 mg/day**	**> 240 mg/day**	**N/A**
Opana ER (oxymorphone extended-release)* ‡	**> 120 mg/day**	**> 80 mg/day**	**> 2 tablets/day**
OxyContin (oxycodone controlled-release)*	**> 240 mg/day**	**> 160 mg/day**	**> 3 tablets/day**

Short-acting		
Drug	**Dose Limits**	
	Current	**New**
Codeine‡	**> 360 mg/day**	**Unchanged**
Demerol® (meperidine)* ‡	**> 750 mg/day**	**Removed****
Dilaudid® (hydromorphone)† ‡	**> 60 mg/day**	**> 64 mg/day**
Morphine immediate-release† ‡	**> 360 mg/day**	**> 240 mg/day**
Opana® (oxymorphone immediate-release)* † ‡	**> 120 mg/day**	**> 80 mg/day**
Oxycodone immediate-release‡	**> 240 mg/day**	**> 160 mg/day**

*Both brand and generic (if available) require PA, even within dose and quantity limits; PA criteria available at www.mass.gov/masshealth/pharmacy.
†Dose limits apply to both oral and injectable formulation.
‡Available generically.
§Increased limit due to available tablet strengths.
**PA required for all doses.

Recent MassHealth Drug List Updates

Drug/Drug Class	Addition/Deletion/Change	Rationale
acamprosate	Addition; **does not require PA**	Acamprosate is the new "A"-rated generic to Campral. This agent does not require PA.
adenovirus live vaccine DR oral tablet	Addition; **does not require PA**	Adenovirus live vaccine DR oral tablet is indicated for active immunization for the prevention of febrile acute respiratory disease caused by Adenovirus Type 4 and Type 7.
afatinib (GILOTRIF)	Addition; **requires PA**	Afatinib is an EGFR inhibitor indicated for the first-line treatment of patients with metastatic NSCLC whose tumors have EGFR exon 19 deletions or exon 21 substitution (L858R) mutations. Due to the high cost and specific indication, this agent requires PA.

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amantadine	Change in PA status; **does not require PA**	Amantadine is covered without PA given the appropriate utilization and the decrease in cost.
Antifungal topical agents	Change in PA status; **requires PA** nystatin/triamcinolone cream, ointment clotrimazole/betamethasone lotion	Due to the high cost of nystatin/triamcinolone cream and ointment and clotrimazole/betamethasone lotion compared to clotrimazole/betamethasone cream, these agents require PA.
Antiglaucoma agents	Change in PA status; **requires PA** brimonidine (Alphagan P) brinzolamide (Azopt) timolol (Betimol) betaxolol (Betoptic S) brimonidine/timolol (Combigan) timolol (Istalol)	Due to availabilities of less costly alternatives in the respective antiglaucoma agent classes, these agents require PA.
azacitidine	Addition; **does not require PA**	Azacitidine is the new "A"-rated generic to Vidaza. This agent does not require PA.
bedaquiline (Sirturo)	Addition; **requires PA**	Bedaquiline is an antitubercular agent indicated as part of combination therapy in adults with pulmonary multi-drug resistant tuberculosis. Due to the high cost and limited indication as a last line agent, this agent requires PA.
buprenorphine/naloxone tablet (Zubsolv)	Addition; **requires PA**	Buprenorphine/naloxone tablet is indicated for the maintenance treatment of opioid dependence. Due to the availability of generic buprenorphine/naloxone tablets, this agent requires PA.
brinzolamide/brimonidine tartrate ophthalmic suspension (SIMBRINZA)	Addition; **requires PA**	Brinzolamide/brimonidine tartrate is indicated for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension. Due to the low utilization of the individual ingredients and high cost of the combination product, this agent requires PA.
coagulation factor IX, recombinant (RIXUBIS)	Addition; **does not require PA**	Coagulation factor IX (recombinant) is an antihemophilic factor indicated for the control and prevention of bleeding episodes in adults with hemophilia B, perioperative management in adults with hemophilia B, and routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adults with hemophilia B.
cyclosporine (Sandimmune)	Change in PA status; **requires PA for brand name requests**	Cyclosporine is the new "A"-rated generic to Sandimmune. Due to the generic availability of Sandimmune, brand name requests require PA.

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dolutegravir (Tivicay)	Addition; **requires PA >30 units/30 days**	Dolutegravir is an integrase strand transfer inhibitor indicated for the treatment of HIV-1 infection in combination with other antiretroviral agents. To ensure appropriate use, the twice-daily dosing requires PA.
IV iron agents	Change in PA status; **requires PA** dextran (Dexferrum) ferumoxytol (Feraheme) sodium ferric gluconate complex (Ferrlecit) iron sucrose (Venofer)	These injectable products are indicated for iron-replacement products. Due to the high cost associated with these products compared to iron dextran (InFeD), these agents require PA.
enalapril powder for oral solution (Epaned)	Addition; **requires PA**	Enalapril is an angiotensin-converting enzyme inhibitor indicated for the treatment of hypertension.
erlotinib (Tarceva)	Change in PA status; **requires PA**	Erlotinib is an EGFR inhibitor indicated for the first-line treatment of patients with metastatic NSCLC whose tumors have EGFR exon 19 deletions or exon 21 substitution (L858R) mutations, and as maintenance therapy for patients with locally advanced or metastatic NSCLC whose disease has not progressed after four cycles of platinum-based first-line chemotherapy. Due to the high cost and specific indication, this agent requires PA.
esomeprazole strontium	Addition; **requires PA**	Esomeprazole strontium is a branded medication approved based on bioequivalence studies to esomeprazole magnesium. Due to the high cost and availability of less costly alternatives, such as omeprazole, pantoprazole, and lansoprazole, this agent requires PA.
ferric carboxymaltose injection (Injectafer)	Addition; **requires PA**	Ferric carboxymaltose injection is indicated for the treatment of iron deficiency anemia in adult patients who have intolerance or have had an unsatisfactory response to oral iron or who have nondialysis-dependent chronic kidney disease. Due to the high cost compared to iron dextran (InFeD), this agent requires PA.
fluorouracil (Fluoroplex)	Deletion; **removed from MassHealth Drug List**	MassHealth does not pay for drugs that are manufactured by companies that have not signed rebate agreements with U.S. Secretary of Health and Human Services.
fluticasone/vilanterol inhalation powder (BREO ELLIPTA)	Addition; **requires PA**	Fluticasone/vilanterol inhalation powder is a combination inhaled corticosteroid/long-acting beta2-adrenergic agonist indicated for the long-term, once-daily, maintenance treatment of airflow

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		obstruction in patients with chronic pulmonary disease, including chronic bronchitis and/or emphysema. Due to the potential for off-label use in asthma, this agent requires PA.
golimumab for infusion (Simponi ARIA)	Addition; **requires PA**	Golimumab is an intravenous human monoclonal antibody indicated for the treatment of adults with moderately to severely active rheumatoid arthritis in combination with methotrexate. Due to availability of less costly alternatives such as DMARDs and similar cost in comparison to the subcutaneous injection, this agent requires PA.
Hormone replacement therapy	Deletion; **removed from MassHealth Drug List** estradiol (Elestrin) estradiol (Estraderm) estradiol (Femtrace)	The production of these products has been discontinued by the manufacturer and has been removed from the MassHealth Drug List.
Immunomodulators	Change in PA status; **requires PA** azathioprine (Azasan) mycophenolate (Myfortic)	Due to availability of less costly formulations, these agents require PA.
influenza virus vaccine (Flublok)	Addition; **does not require PA**	Influenza virus vaccine is indicated for active immunization against disease caused by influenza virus subtype A and type B contained in the vaccine in persons 18 through 49 years of age.
influenza virus vaccine (FluLaval Quadrivalent)	Addition; **does not require PA**	Influenza virus quadrivalent vaccine is indicated for active immunization for the prevention of disease caused by influenza subtype A viruses and type B viruses contained in the vaccine in persons 3 years of age and older.
malathion (Ovide)	Change in PA status; **requires PA**	Malathion is indicated for the treatment of head lice. Due to increased cost of malathion compared to alternatives, this agent requires PA.
meningococcal groups C and Y and haemophilus b tetanus toxoid conjugate vaccine (MENHIBRIX)	Addition; **does not require PA**	Meningococcal groups C and Y and haemophilus b tetanus toxoid conjugate vaccine is indicated to provide active immunity to prevent invasive disease caused by meningococcal serogroups C and Y and haemophilus influenzae type b.
niacin ER tablet	Addition; does not require PA	Niacin ER is the new "A"-rated generic to Niaspan. This agent does not require PA.
nimodipine capsule	Change in PA status; **requires PA >21 days treatment/year**	Nimodipine is a dihydropyridine calcium channel-blocker indicated for the improvement of neurological outcome by reducing the incidence and severity of ischemic deficits in adult patients with subarachnoid hemorrhage from ruptured

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Drug/Drug Class	Addition/Deletion/Change	Rationale
		intracranial berry aneurysms, regardless of their post-ictus neurological condition. Due to the potential for off-label use, this agent requires PA.
nimodipine oral solution (Nymalize)	Addition; **requires PA >21 days treatment/year**	Nimodipine is a dihydropyridine calcium channel-blocker indicated for the improvement of neurological outcome by reducing the incidence and severity of ischemic deficits in adult patients with subarachnoid hemorrhage from ruptured intracranial berry aneurysms, regardless of their post-ictus neurological condition. Due to the increased cost compared to nimodipine capsules and potential for off-label use, this agent requires PA.
Nonsteroidal anti-inflammatory drugs	Change in PA status; **requires PA** oxaprozin (Daypro) indomethacin suspension (Indocin)	Due to the high cost associated with these products compared to numerous alternative nonsteroidal anti-inflammatory drugs, these agents require PA.
paroxetine mesylate (Brisdelle)	Addition; **requires PA**	Paroxetine mesylate is a selective serotonin re-uptake inhibitor indicated for the treatment of moderate-to-severe vasomotor symptoms associated with menopause. Due to its place in therapy, high cost, and the availability of less costly alternatives, this agent requires PA.
radium RA 223 dichloride (Xofigo)	Addition; **requires PA^** ^This agent is available only through the health care professional who administers the drug. MassHealth does not pay for this drug to be dispensed through a retail pharmacy.	Radium RA 223 dichloride is a radiopharmaceutical indicated for the treatment of symptomatic metastatic castration-recurrent prostate cancer that has metastasized to the bones but not to other organs. In order to ensure this agent is used properly due to the high cost and specific indication, it is available only through the health care professional who administers the drug; it also requires PA.
sitagliptan/simvastatin (Juvisync)	Deletion; **removed from MassHealth Drug List**	The production of this product has been discontinued by the manufacturer and has been removed from the MassHealth Drug List.
sodium fluoride (Prevident)	Deletion; **removed from MassHealth Drug List**	MassHealth does not pay for drugs that are manufactured by companies that have not signed rebate agreements with U.S. Secretary of Health and Human Services.
tacrolimus ER capsules (Astragraf XL)	Addition; **does not require PA**	Tacrolimus ER is indicated for the prophylaxis of organ rejection in patients receiving a kidney transplant.
tazarotene foam (FABIOR)	Addition; **requires PA**	Tazarotene foam is indicated for the topical treatment of acne vulgaris in patients 12 years of age or older. Due to the availability of less costly

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		alternatives, this agent requires PA.
temozolomide	Addition; **does not require PA**	Temozolomide is the new "A"-rated generic to Temodar. This agent does not require PA.
terbinafine topical	Deletion; **removed from MassHealth Drug List**	The production of this product has been discontinued by the manufacturer and has been removed from the MassHealth Drug List.
topiramate ER capsule (Trokendi XR)	Addition; **requires PA**	Topiramate ER is indicated as initial monotherapy in patients 10 years of age and older with partial onset or primary generalized tonic-clonic seizures, and adjunctive therapy in patients 6 years of age and older with partial onset or primary generalized tonic-clonic seizures. Due to the availability of less costly alternatives, this agent requires PA.
trametinib (Mekinist)	Addition; **requires PA**	Trametinib is indicated for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations. Due to the specificity of the FDA-approved indication, cost of therapy in relation to other treatment options, and current place in therapy, this agent requires PA.
Urinary antispasmodics	Change in PA status; **requires PA** tolterodine ER (Detrol LA) solifenacin (Vesicare)	Due to the high cost compared to less costly agent alternatives darifenacin (Enablex) and fesoterodine (Toviaz), these agents now require PA.