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December 2020

THE OMNICARE
HealthLine

Focus on Medications That Rebuild Bone in Osteoporosis

By Richard Kilmartin

Debilitating fractures, often resulting from osteoporosis, greatly impact an individual's quality of life. The anabolic osteoporosis agents (i.e., teriparatide, abaloparatide, romosozumab) are approved to reduce the risk of fracture in those considered to be at very high risk for osteoporotic fracture, including older adults with prior fragility fractures or low bone density scores (i.e., T-score of -2.5 or lower). To safely use them, we must understand their uses and limitations, including potential adverse effects. The following table provides a summary of some basic considerations for the currently available agents.

Medication	Dosing Interval (subcutaneous injection)	Storage	Duration of Therapy
Teriparatide (Forteo)	Daily	• Refrigerate; do not freeze; protect from light • Discard 28 days after first use	No more than 2 years of use in a lifetime
Abaloparatide (Tymlos)	Daily	• Refrigerate; do not freeze • After first use, store at room temperature for up to 30 days	
Romosozumab (Evenity)	Monthly	• Refrigerate; do not freeze; protect from light • May be kept at room temperature in the original carton for up to 30 days	Not to exceed 12 monthly doses

What's different about these anabolic agents compared to older treatments? Most traditional osteoporosis therapies target a reduction in bone loss or turnover, whereas the anabolic osteoporosis agents primarily act by adding new bone. Healthy bone is constantly undergoing a process of regeneration where older bone is resorbed, and new bone is laid down in its place. This balance shifts as we age, creating a relative increase in bone loss. Individuals at the highest risk for fracture may have already lost significant bone at diagnosis, making the anabolic agents' ability to add new bone particularly attractive.

All three anabolic agents are approved for the treatment of osteoporosis in postmenopausal women at high risk for fracture, or who failed or are intolerant to other treatments. Teriparatide is additionally approved for treatment of:

- men with primary or hypogonadal osteoporosis
- men and women with glucocorticoid-induced osteoporosis

As noted in the table above, these medications should not be given indefinitely. Additionally, for teriparatide and abaloparatide, lifetime use is cumulative, including all times when either was given. Therefore, it is important that a history of start dates and durations of therapy be maintained. Anabolic agents do not build bone indefinitely and an important point to remember is that once an anabolic osteoporosis treatment is discontinued, it should be followed by a medication that reduces further bone loss, such as a bisphosphonate

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(e.g., alendronate, risedronate) or denosumab. If follow-up therapy is not used, it is possible that the bone density gains from the anabolic therapy will be lost over time with a resulting increase in fracture risk.

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Those being treated for osteoporosis should receive adequate calcium and vitamin D, through diet or supplements, to maintain bone health during and after therapy. As with any medication, consideration must be given to potential adverse consequences and appropriate monitoring. The table below lists considerations and strategies to promote safe use of anabolic agents.

Medication	Side Effects and Warnings	Monitor for	Strategies to Promote Safe Use
Teriparatide (Forteo) **Abaloparatide (Tymlos)**	• Boxed Warning describing a risk of bone cancer (i.e., osteosarcoma) • Low blood pressure and dizziness, particularly after administration • Nausea • High blood calcium levels	• New and persistent pain, unusual lumps, or unexplained swelling under the skin • Orthostatic hypotension (low blood pressure upon rising) or dizziness	Orthostasis may be minimized by sitting or lying down during administration
Romosozumab (Evenity)	• Boxed Warning describing an increased risk of severe cardiovascular events in those who have had a heart attack or stroke in the past year and in those with cardiovascular risk factors (e.g., obesity, hypertension, kidney disease) • Low blood calcium levels • Severe jawbone problems (osteonecrosis) • Unusual thigh bone fracture	• Signs or symptoms of heart attack or stroke (e.g., chest pain, weakness on one side of the body) • Monitor for development of cardiovascular risk • High or low blood calcium (monitor prior to each dose)	• Notify the dentist of use before dental work is done • Ensure laboratory monitoring is obtained at appropriate intervals, especially in those with kidney disease

Anabolic osteoporosis agents offer another exciting method to treat those at the highest risk of fractures, especially in conjunction with proper monitoring and lifestyle modifications (e.g., adequate calcium and vitamin D, exercise, falls prevention).

Vancomycin Monitoring in Severe MRSA Infections

by Carrie Allen

Due to guidelines that were released earlier this year, you may see a difference in vancomycin monitoring orders for patients who have severe methicillin-resistant *Staphylococcus aureus* (MRSA) infections. Trough-only monitoring with a target of 15 to 20 mg/L is no longer recommended, based on efficacy and nephrotoxicity data in these patients. To reduce the risk of acute kidney injury (AKI) caused by vancomycin, the new guidelines advocate for monitoring a peak and trough, rather than trough only, in those who have serous MRSA infections, such as:

- **Blood stream infections due to central lines**
- **Pneumonia**
- **Osteomyelitis**
- **Sepsis**
- **Device-related osteoarticular infections (e.g., prosthetic devices)**
- **Septic Arthritis**
- **Meningitis**
- **Brain abscess**
- **Endocarditis**
- **Some surgical site infections**

In addition, they recommend using specific calculations to determine the amount of vancomycin the patient has actually been exposed to, which is also called area under the curve (AUC). By evaluating AUC and targeting a range of 400 to 600 mg•h/L, we can determine the best dose of vancomycin to treat the infection, while simultaneously reducing the risk for AKI. Your pharmacist will be able to support you or perform calculations upon request.

Some things to consider as this practice begins to emerge are:

- Ensure you know the indication for use for any patients receiving vancomycin
- If the patient was transferred from another facility, ask if they were monitoring AUC, and to give you those results
- Discuss the ongoing monitoring plan with the prescriber at your facility, as most episodes of AKI develop between 4 to 17 days after initiation
- If AUC monitoring is recommended, ensure samples are drawn at the next available peak and trough time after the 3rd or 4th dose
  - Peaks are ideally drawn 1 to 2 hours after the infusion is completed
  - Troughs are drawn at the end of the dosing interval, approximately 30 minutes prior to the next dose

Finally, it is important to remember that regardless of the type of infection, vancomycin can cause kidney injury in high-risk individuals, such as:

- Critically ill patients receiving concurrent nephrotoxins (e.g., aminoglycosides)
- Patients with unstable renal function (i.e., deteriorating or significantly improving)
- Patients receiving prolonged courses of therapy (i.e., over 3 to 5 days)

The frequency of monitoring should be individualized based on the clinical picture of the patient and the judgement of the prescriber. For example, frequent (e.g., twice weekly) or daily monitoring may be prudent for hemodynamically unstable patients (e.g., those with end-stage renal disease), but once weekly monitoring may be acceptable for hemodynamically stable patients.

The guidelines discussed here are a consensus from the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the Society of Infectious Diseases Pharmacists and are available for free at: https://academic.oup.com/ajhp/article/77/11/835/5810200

New Generic Medications

By Allen Lefkovitz

Generic Name	Brand Name	Date Generic Available
Rufinamide 40 mg/mL Oral Suspension	Banzel® Oral Suspension	11/4/20
Tavaborole 5% Solution	Kerydin® Topical Solution	10/26/20
Tolvaptan* 15 mg Tablet	Samsca™ Tablet	10/19/20
Fosfomycin 3 gram Granules for Oral Solution	Monurol® Granules	10/9/20
Dimethyl Fumarate 120 mg and 240 mg DR Capsule Starter Pack	Tecfidera® Starter Pack	10/5/20
Methylphenidate 10, 15, 20, 30, 40, 50, 60 mg Capsule ER	Aptensio XR™ Capsule ER	10/5/20
Lapatinib 250 mg Tablet	Tykerb® Tablet	10/2/20
Efavirenz/Emtricitabine/Tenofovir 600 mg/200 mg/300 mg Tablet	Atripla® Tablet	10/2/20
Emtricitabine/Tenofovir 200 mg/300 mg Tablet	Truvada® Tablet	10/2/20
Sapropterin 100 mg Tablet	Kuvan® Tablet	10/2/20
Sapropterin 100 mg and 500 mg Powder for Oral Solution Packet	Kuvan® Packet	10/2/20
Tobramycin 300 mg/4 mL Inhalation Solution	Bethkis® Inhalation Solution	9/17/20

* Not an A-rated generic; substitution policies may vary by state and how orders are written

New Drug

by Dave Pregizer

Olinvyk™ Injection

Brand Name (Generic Name)	Olinvyk™ [oh-LIN-vick] (oliceridine) [OH-li-SER-i-deen]
How Supplied	1 mg/mL and 2 mg/2 ml single-dose vials and 30 mg/30 mL single-patient-use vial for patient controlled analgesia (PCA) use only
Therapeutic Class	Opioid agonist (Schedule II controlled substance)
Approved Indication	Management of acute pain, severe enough to require an intravenous opioid analgesic and for which alternative treatments are inadequate
Usual Dosing	Initiate with 1.5 mg IV, with supplemental doses of 0.75 mg IV given one hour after initial dose, then hourly as needed. Individual single doses should not exceed 3 mg and cumulative daily doses should not exceed 27 mg.
Select Drug Interactions	Moderate and strong CYP2D6 and CYP3A4 inhibitors may increase Olinvyk concentrations. Risk of serotonin syndrome with serotonergic drugs. Mixed agonist/antagonist and partial agonist opioids may reduce analgesic effect and/or precipitate withdrawal symptoms.
Most Common Side Effects	Nausea, vomiting, dizziness, headache, constipation, pruritus, and hypoxia
Miscellaneous	Boxed warning regarding risks associated with opioid use. Total daily doses exceeding 27 mg may increase risk for QT interval prolongation.
Website	http://www.Olinvyk.com