# the PRUDENT prescriber

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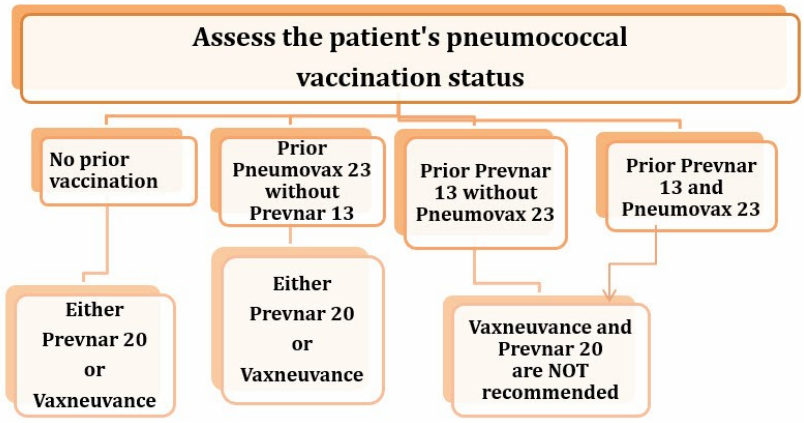
## New Pneumococcal Vaccine Guidelines

Two new vaccines directed toward pneumococcal disease are now available: Prevnar 20 and 15-valent Vaxneuvance.

### Prevnar 20 and Vaxneuvance

- Approved in the summer of 2021 for adults 18 and older.
- Single dose IM injections
- Conjugate vaccines that may well lead to longer lasting immunity than the Pneumovax 23 polysaccharide vaccine.
- Pain at the injection site is the most common side effect. Muscle pain, fatigue, headache and joint pain were also noted.
- Both vaccines cover the same 13 serotypes as Prevnar 13. Prevnar 20 also covers seven more serotypes which cause about 30% of invasive bacterial disease.
- Vaxneuvance covers two more serotypes than Prevnar 13. These two serotypes cause about 15% of invasive bacterial disease.
- Pneumovax 23 still has broader serotype coverage. Seven to 10% of invasive disease is caused by serotypes found only in Pneumovax 23.

### The CDC recommendations




### MY TAKE

- Although the guidelines do not prefer one strategy over another, using Prevnar 20 ($240) for patients with no prior vaccination or only Pneumovax 23 makes sense. Patients who receive Vaxneuvance ($220) as their initial pneumococcal vaccine also require Pneumovax 23 ($120).
- At this point, there are no data to suggest that giving one of the new vaccines on top of Prevnar 13 ($215) adds any benefit.
- Pushing pneumococcal vaccines in kids represents an indirect, but important protection for adults.
- Download the CDC's user-friendly PneumoRecsVaxADvisor mobile app.

## Pharmaceutical Outrage of the Month:
## Opzelura for Eczema

Opzelura (ruxolitinib) is a new short term or intermittent long-term topical treatment for mild to moderate eczema. This Janus kinase (JAK) inhibitor works by suppressing cytokines resulting in improved itching and decreased inflammation.

Methods: In two trials, 1249 subjects 12 years and older with body surface area of 3-20% and investigator's global assessment (IGA) of 2 - mild (25%) or 3- moderate (75%)eczema were randomized 2:2:1 to treatment with Opzelura (ruxolitinib 1.5%), ruxolitinib cream, 0.75%,or vehicle cream twice daily (BID) for 8 weeks. The primary efficacy endpoint was the proportion of subjects at week 8 achieving treatment success defined as a score of 0 (clear) or 1 (almost clear) with ≥ 2 grade improvement from baseline. Efficacy was also assessed using a ≥ 4-point improvement on a 10 point itch scale.

Efficacy: Curiously, the researchers reported on only 749 of the 1249 enrolled subjects representing 60% of the total enrolled subjects. There were no data reported on those patients who got the half strength ruxolitinib cream. In the two trials, 52% and 51% of the Opzelura groups met the clearing end point as did 15% and 16% of the placebo vehicle cream groups. (NNTs = 2.7 and 2.9, respectively)

Side Effects: The following adverse reactions occurred in these clinical trials in the Opzelura group: one episode each of neutropenia, allergic conjunctivitis, pyrexia, seasonal allergy, herpes zoster, otitis externa, Staphylococcal infection, and acneiform dermatitis.

Cost: A 60 gram tube of Opzelura retails for $2020. (GoodRx March 2022)

### MY TAKE

The pandemic has promoted a useful problem-solving tool for patients and clinicians alike: the benefit-risk ratio. "Should I send my unvaccinated kid to school in the face of the significant Covid-19 outbreak?"

The manufacturers of Opzelura and the FDA were clearly not employing credible decision making in creating and approving this drug. Yes, Opzelura clears skin and stops itching in patients with mild to moderate eczema. Great NNTs! But at what risk? Although only 10% of the cream is systemically absorbed, Opzelura is linked to reports of serious infections (TB, invasive fungal infections and herpes zoster) and skin cancers. It shares the same extensive BLACK BOX warning as the oral Janus kinase inhibitors: major adverse cardiovascular events, an increased incidence of thrombosis and lymphomas.

Should we expose patients to a potentially lethal product for treating mild or moderate skin disease?
And then throw in the egregious pricing at $2020 for a 60gm tube? I don't think so.

The focus for treating eczema should remain with moisturizing topicals and steroids. Teach patients the true benefit-risk ratio of topical steroids. Snuff out steroid phobia!

## Time to Benefit:
## Rethinking Bisphosphonates in Osteoporosis

There is good science (multiple randomized controlled trials {RCTs}) that demonstrates that bisphosphonates lower the risk for fractures in postmenopausal women with osteoporosis. A study from the University of California-San Francisco (JAMA Intern Med 2021 Nov22) attempts to answer the question, "How long do you have to take a bisphosphonate to achieve protection for sustaining a fracture?" "What is the Time to Benefit?"

Methods: The authors analyzed 10 RCTs involving 23,384 postmenopausal women (mean age range 63-74) with documented osteoporosis who were taking either alendronate, risedronate or zoledronic acid. The participants were followed for 12-48 months.

Results:

- Bisphosphonates would need to be given to 100 post- menopausal women with osteoporosis for 12 months to prevent one non-vertebral fracture.
- Bisphosphonates would need to be given to 200 postmenopausal women with osteoporosis for 20 months to prevent one hip fracture.

### MY TAKE

- The benefit from bisphosphonates in the near term is minimal at best. A prudent prescriber would likely **not** start these medications in women with a life expectancy of only a year or two.
- This meta-analysis does suggest that the benefit of bisphosphonate therapy increases in a nearly linear manner with increasing follow-up durations. The number of non-vertebral fractures prevented per 100 postmenopausal women with osteoporosis receiving bisphosphonate therapy increased from 1.0 at 12 months to 1.5 at 18 months.
- The Cochrane Databases of Systematic Reviews from 2008 showed that for every 100 osteoporotic women who took bisphosphonates for three years, six would avoid a fracture of some sort (mostly vertebral) and one would avoid a hip fracture.
- I understand the public health implications of preventing hip fractures. But will most women choose to take a medication for three years that may give them a bellyache knowing that there is only a 1%-6% chance that it will benefit them?

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