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Focus on Shingles and the Shingles Vaccine

By Allen Lefkovitz

Prior to the availability of an effective vaccine, shingles (herpes zoster) affected nearly 1 in 3 persons during their lifetime, one million people each year, and about 50% of adults 85 years or older. The varicella-zoster virus, which causes chickenpox, can lay dormant for many years before taking advantage of a weakened immune system and reactivating, thereby causing shingles. This has led some to refer to shingles as "an unwelcome encore."

Approximately 2 to 4 days before a shingles rash develops, the individual often experiences itching, tingling, or pain at the site. The rash, in addition to being painful, is generally localized on one side of the body, and most often appears in a single stripe-like pattern on the torso or face (along a dermatome). However, in individuals with weakened immune systems, the rash can be more widespread, similar to chickenpox. The rash goes on to develop into fluid-filled blisters that typically crust or scab over in 7 to 10 days, and then gradually resolves in 2 to 4 weeks. Beyond pain and itching, other symptoms of shingles may include fever, headache, chills, sensitivity to light, or an upset stomach. While exposure to someone with shingles does not increase another person's risk of developing shingles, and shingles is only about 20% as infectious as chickenpox, individuals who have never had chickenpox and who have never been vaccinated for chickenpox are at risk of contracting chickenpox. This risk of transmission begins with the appearance of the rash and continues until the lesions crust over. To help lower the risk of spread to others, individuals with shingles should cover their rash, wash their hands often, and avoid touching or scratching the rash whenever possible.

Everyone who has had chickenpox (which includes 99% of individuals born before 1980) is at risk of developing shingles, but those over the age of 50 are at the greatest risk. Other individuals at increased risk of developing shingles (as well as recurrence of shingles) include individuals with weakened immune systems, such as those:

- with cancer, especially leukemia or lymphoma
- with human immunodeficiency virus (HIV)
- who have undergone bone marrow or organ transplantation, or
- who are taking immunosuppressant medications (e.g., corticosteroids, chemotherapy, anti-rejection medications).

The risk of developing shingles as well as shingles-associated complications increases with age. Potential complications of shingles include:

Postherpetic neuralgia (PHN)	**Scarring**
Bacterial skin infections	**Vision and hearing impairment**
Pneumonia	**Stroke or heart attacks**
Brain inflammation (encephalitis)	**Weakness or paralysis**
Social isolation	**Death**

Vaccination provides an opportunity to prevent the pain and suffering associated with shingles. In 2006 the first shingles vaccine, Zostavax, became available, and it reduced the risk of shingles by up to 64%. However, it was a live vaccine with limitations for use in those with a weakened immune system, and its effectiveness decreased significantly during the first 3 years after

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vaccination (i.e., decreased to 18% effective in those age 80 years and older 3 years following vaccination). Due to these limitations, reduced effectiveness, and preferential recommendation of a newer option by the Centers for Disease Control and Prevention (CDC), Zostavax was discontinued by the manufacturer and is no longer available as of November 2020.

The more recent option is Shingrix, a recombinant zoster vaccine (RZV) that does not contain any preservatives (e.g., thimerosal), but does include an adjuvant, AS01B, that is used to reconstitute the vaccine. Adjuvants are included to boost the body's immune response to the vaccine. According to the CDC, 2 doses of Shingrix are 97% effective in preventing shingles in those 50 to 69 years of age, and 91% effective in those 70 years and older. Research has shown that protection from shingles is also maintained at greater than 85% after more than 4 years. Additionally, in those who are vaccinated but still develop shingles, Shingrix is 89% effective in preventing PHN. In fact, in a February 2021 BMJ article entitled "Vaccines for older adults", the authors referred to RZV as "**the benchmark for efficacious vaccines in older people**". These authors also noted that RZV "will substantially reduce the societal costs of herpes zoster in older adults, including the use of antivirals and pain medications, and hospitalization." A summary of the Shingrix vaccine is provided in Figure 1, followed by who should or should not receive it.

Figure 1. Shingrix (RZV)	
Vaccine Type	Recombinant, adjuvanted herpes zoster vaccine
Storage Considerations	The vaccine and adjuvant suspension for reconstitution should be stored in the refrigerator between 36 and 46˚ F. After reconstitution, the vaccine should be used immediately or stored in the refrigerator for up to 6 hours. Discard any vaccine or adjuvant suspension that has been frozen or not used within 6 hours.
Dosing	After reconstitution, inject 0.5 mL intramuscularly in the deltoid region of the upper arm; given as a 2-dose series with the second dose between 2 and 6 months later

WHO SHOULD GET
Healthy adults 50 years of age and older, including individuals who have had shingles before
Have received Zostavax previously*
Receive low-dose immunosuppressive therapy or have recovered from an immunocompromising illness†

WHO SHOULD NOT GET
Have a severe allergy to any component of the vaccine
Currently have shingles
Have a moderate or severe acute illness (e.g., fever ≥ 101.3°F)
Women who are pregnant or breastfeeding

* Use of Shingrix is recommended for all individuals who have received Zostavax previously, especially if Zostavax was given more than 5 years ago or if they were over 70 years of age when vaccinated with Zostavax

† Although not contraindicated, as they continue to review data, CDC currently does not recommend Shingrix for individuals with severe immunocompromising conditions (e.g., HIV with CD4 count < 200 cells/mm^3)

While approved for intramuscular administration, if a dose is incorrectly given subcutaneously, the dose should still be considered valid. Additionally, the timing of the Shingrix vaccine series must be considered. If more than 6 months have elapsed before the second dose is administered, the series does not need to be restarted. However, if the second dose is given less than 4 weeks after the first dose, it should be considered invalid, and an additional dose should be given at least 8 weeks after the invalid dose.

Shingrix may be given with most other adult vaccines (e.g., non-adjuvanted influenza vaccines, pneumococcal vaccines) if administered in different arms. However, CDC currently recommends against giving any other vaccines within 14 days before or after a COVID-19 vaccine, and the use of Shingrix with other adjuvanted vaccines (e.g., Fluad Quadrivalent) has not been studied.

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As Shingrix produces a strong immune response, some individuals may experience more intense adverse effects with either dose than with most other vaccines; however, those side effects generally only affect their ability to do normal activities of daily living for up to 3 days. While most individuals (up to 78%) will have a sore arm and experience redness or swelling at the injection site, CDC emphasizes that "the pain will be less severe than having shingles and the complications from the disease." Individuals who experience discomfort may receive ibuprofen or acetaminophen. Other common adverse effects include headache, shivering, fever, fatigue, or nausea. Serious adverse events are rare, with an incidence of 2 or fewer people per 1 million doses. Unless an individual experienced a severe allergic reaction (e.g., hives, difficulty breathing), 96% of participants in clinical trials were able to receive both doses of Shingrix. As with any vaccine, adverse reactions should be reported to the Vaccine Adverse Event Reporting System [VAERS (https://vaers.hhs.gov/index.html)] whenever possible.

As no vaccine is 100% effective in preventing disease, when shingles does occur, prompt treatment is imperative to minimize the severity and duration of infection as well as the risk of complications. Oral antiviral medications (see table below) are recommended as soon as possible, ideally within 48 to 72 hours after the rash begins. While more severe shingles infection may necessitate use of intravenous therapy, topical antivirals (e.g., acyclovir ointment) are **not** considered effective for the treatment of shingles.

Antiviral	Usual Oral Dosing for Shingles*	Most Common Adverse Effects
acyclovir	800 mg five times daily for 7 to 10 days	Unusual weakness or tiredness, nausea
famciclovir	500 mg three times daily for 7 days	Headache, nausea
valacyclovir	1 gram three times daily for 7 days	Headache, nausea, abdominal pain

* Renal dosage adjustments are necessary. See https://dailymed.nlm.nih.gov/dailymed/ for additional prescribing information

When pain from shingles is mild or moderate, over-the-counter medications such as acetaminophen or ibuprofen may be utilized. Additionally, loose-fitting clothing, wet compresses, calamine lotion, or colloidal oatmeal baths may be used to help relieve itching; however, lesions are best kept clean and dry to avoid risk of bacterial infections. When eye involvement is suspected, prompt ophthalmology consultation is suggested.

PHN is the most common complication of shingles and involves persistent pain where the rash was. This nerve pain can last for weeks, months, or even years, and it may severely impact an individual's quality of life and normal activities. PHN occurs in up to 18% of individuals with shingles, but the risk of PHN (and increased risk of severity and duration) is greatest in older adults. It is estimated that in 15% of people over 50 years of age with shingles, significant pain can persist for at least 3 months.

Although treatment of PHN has varying degrees of success, treatment options may include:

- Topical capsaicin
- Anticonvulsants for neuropathic pain (e.g., gabapentin, pregabalin)
- Tricyclic antidepressants (e.g., nortriptyline)
- Topical anesthetics (e.g., lidocaine)

Second-line treatment options may include short-term opioid therapy (e.g., morphine, oxycodone) and injectable therapy with corticosteroids or local anesthetics.

According to a July 2020 CDC report, only 34.5% of adults 60 years and older had received either type of shingles vaccine, meaning a significant number of older adults remain at risk of shingles. Prevention by vaccination remains the best defense against shingles, PHN, and its other potentially devastating complications. For additional information on shingles and the shingles vaccine please see: www.cdc.gov/shingles and www.immunize.org/zoster/

New Generic Medications

By Allen Lefkovitz

Generic Name	Brand Name	Date Generic Available
Droxidopa 100 mg, 200 mg, and 300 mg Capsule	Northera™ Capsule	2/19/21
Loteprednol Etabonate 0.5% Ophthalmic Gel	Lotemax® Ophthalmic Gel	2/19/21
Glucagon 1 mg Powder for Injection	Glucagon Emergency Kit	2/12/21
Topiramate 25 mg, 50 mg, 100 mg, 150 mg, and 200 mg ER Capsule*	Qudexy® XR Capsule	2/12/21
Imiquimod 3.75% Cream	Zyclara® Cream	2/8/21
Levothyroxine 13 mcg, 25 mcg, 50 mcg, 75 mcg, 88 mcg, 100 mcg, 112 mcg, 125 mcg, 137 mcg, 150 mcg, 175 mcg, and 200 mcg Capsule	Tirosint® Capsule	2/8/21
Epoprostenol 0.5 mg and 1.5 mg Vial for Injection	Veletri® Injection	1/29/21
Emtricitabine/Tenofovir DF 100 mg/150 mg, 133 mg/200 mg, 167 mg/250 mg Tablet	Truvada® Tablet	1/25/21
Zolmitriptan 2.5 mg and 5 mg Nasal Spray*	Zomig® Nasal Spray	1/25/21
Lubiprostone 8 mcg and 24 mcg Capsule*	Amitiza® Capsule	1/15/21

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

New Drug

By Dave Pregizer

Verquvo® Tablet

Brand Name (Generic Name)	Verquvo ® [ver-KYU-voh] (vericiguat) [VER-i-SIG-ue-at]
How Supplied	2.5 mg, 5 mg, and 10 mg tablets
Therapeutic Class	A soluble guanylate cyclase (sGC) stimulator
Approved Indication	To reduce the risk of cardiovascular death and heart failure (HF) hospitalization following a hospitalization for HF or need for outpatient IV diuretics, in adults with symptomatic chronic HF and ejection fraction less than 45%
Usual Dosing	Initiate 2.5 mg orally once daily with food. Double the dose approximately every 2 weeks, as tolerated to achieve a target maintenance dose of 10 mg once daily. Tablets may be crushed and mixed with water.
Select Drug Interactions	Concomitant use with PDE-5 Inhibitors (e.g., sildenafil) is not recommended. Avoid use with other sGC stimulators [e.g., Adempas (riociguat)].
Most Common Side Effects	Hypotension and anemia
Miscellaneous	No dose adjustment with mild or moderate hepatic impairment or eGFR greater than or equal to 15 mL/min/1.73m^2. Boxed Warning for embryo-fetal toxicity.
Website	http://www.verquvo.com