Varicella (Chickenpox) and Zoster (Shingles) Disease
Varicella and Zoster Vaccines

Pink Book Webinar Series 2019

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Varicella Disease
Varicella Zoster Virus

- Herpes virus (DNA)
- Primary infection results in varicella (chickenpox)
- Short survival in environment
Varicella Pathogenesis

- Respiratory transmission of virus
- Replication in nasopharynx and regional lymph nodes
- Primary viremia 4 to 6 days after infection
- Multiple tissues, including sensory ganglia, infected during viremia
Varicella (Chickenpox) Clinical Features

- Incubation period: 14 to 16 days (10–21 days)
- Mild prodrome for 1 to 2 days (adults)
- Rash generally appears first on the head; most concentrated on the trunk
- Successive crops over several days with lesions present in several stages of development
Varicella Complications

- Bacterial infection of lesions
- Hemorrhagic varicella
- CNS manifestations
- Pneumonia (primary viral or secondary bacterial)
- Congenital varicella
- Perinatal varicella
Varicella with a secondary bacterial infection
Increased Risk of Complications of Varicella

- Persons older than 15 years
- Infants younger than 1 year
- Immunocompromised persons
- Newborns of women with rash onset within 5 days before to 48 hours after delivery
Varicella Epidemiology

Reservoir  Human

Transmission  Person to person – respiratory tract secretions
               Direct contact with lesions

Temporal Pattern  Peak in late winter and spring (U.S.)

Communicability  1 to 2 days before until lesions have formed crusts
                 May be longer in immunocompromised
Varicella-containing Vaccines
### Vaccines for the Prevention of Varicella (Chickenpox)

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<th>Product</th>
<th>ACIP Recommended Age Indications</th>
<th>ACIP Abbreviation</th>
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<tr>
<td>Varivax</td>
<td>12 months and older</td>
<td>VAR</td>
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<tr>
<td>ProQuad</td>
<td>12 months through 12 years</td>
<td>MMRV</td>
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Varicella Vaccine
Immunogenicity and Efficacy

- In a pre-licensure clinical trial, 2 doses of vaccine were:
  - 98% effective at preventing any form of varicella
  - 100% effective against severe varicella

- In post-licensure studies, 2 doses of vaccine were:
  - 88% to 98% effective at preventing all varicella

CDC Chickenpox About the Vaccine for Health Care Professionals [www.cdc.gov/vaccines/vpd/varicella/hcp/about-vaccine.html](http://www.cdc.gov/vaccines/vpd/varicella/hcp/about-vaccine.html), accessed 8/13/2018
Varicella-Containing Vaccines: Varivax (Var) and ProQuad (MMRV)

- **Storage:**
  - Lyophilized vaccine: In the freezer between -50°C and -15°C (-58°F and +5°F)
  - Diluent: At room temperature (68°F to 77°F, 20°C to 25°C) or in the refrigerator (36°F to 46°F, 2°C to 8°C)

- **Preparation:** Reconstitute the vaccine with the diluent supplied by the manufacturer just before administering

- **Administration:** Subcut injection
  - Site: Fatty tissue of the anterolateral thigh or upper outer triceps of the arm
  - Needle length and gauge: 5/8-inch, 23- to 25-gauge needle
Varicella Vaccine and Clinical Considerations
Acceptable Evidence of Varicella Immunity

- Written documentation of age-appropriate vaccination
- Laboratory evidence of immunity or laboratory confirmation of varicella disease
- U.S.-born before 1980*
- Health care provider diagnosis or verification of varicella disease
- History of herpes zoster based on health care provider diagnosis

*Birth year immunity criterion does not apply to health care personnel or pregnant women

MMWR 2007;56(RR-4):16-17
ACIP Immunization Recommendations: Young Children

- Routine recommendations:
  - Dose 1 at 12–15 months of age
  - Dose 2 at 4–6 years of age

- Minimum interval between doses is 3 months for children 12 years of age and younger
ACIP Immunization Recommendations: Adolescents and Adults

- Assess all persons 13 years of age and older for evidence of varicella immunity
- Administer 2 doses separated by at least 4 weeks to those without evidence of immunity

- 2nd dose recommended for persons of any age who have only received 1 dose
  - Do not repeat 1st dose because of extended interval between doses
Varicella Vaccination and Health Care Personnel

- Assess all health care personnel for evidence of immunity
- Vaccination is recommended for all susceptible health care personnel
  - Give 2 doses, 4 weeks apart to susceptible persons
- Prevaccination serologic screening might be cost-effective
- Postvaccination testing NOT recommended
Varicella Serology and *Post Vaccination*

- CDC and ACIP do NOT recommend antibody testing *AFTER* varicella vaccination
  - Commercially available laboratory tests for varicella antibody are usually not sufficiently sensitive to detect vaccine–induced antibody
  - Even though they are generally sensitive to deduce antibodies resulting from varicella zoster virus infection
- Documented receipt of 2 doses of varicella vaccine *SUPERSEDES* results of subsequent serologic testing
Varicella Vaccine and Immunocompromised Persons

- Single-antigen varicella vaccine may be administered to persons with isolated humoral immunodeficiency

- Consider varicella vaccination for:
  - HIV-infected children with CD4 count of 15% or higher
  - HIV-infected older children and adults with CD4 count of 200 or higher
Varicella and MMRV Vaccine Contraindications

- Severe allergic reaction to a vaccine component or following a prior dose
- Pregnancy or planned pregnancy within 4 weeks*
- Immunosuppression
- Family history of altered immunocompetence

*ACIP off-label recommendation

MMWR 2007;56(RR-04)

Varicella and MMRV Vaccine Precautions

- Moderate or severe acute illness with or without fever
- Recent blood product
  - Varicella or MMRV vaccines should not be administered for 3–11 months after receipt of antibody-containing blood products
- Receipt of specific antiviral drugs (acyclovir, famciclovir, or valacyclovir) 24 hours before vaccination
  - Avoid use of these antiviral drugs for 14 days after vaccination
- Use of aspirin or aspirin-containing products

MMWR 2007;56(RR-04)
Varicella-Containing Vaccines Precautions

- MMRV only: personal or family (i.e., sibling or parent) history of seizures of any etiology

- These children generally should be vaccinated with separate MMR and varicella vaccines
Varicella Adverse Reactions

- Local reactions (pain, erythema)
  - Varicella:
    - 19% (children)
    - 24% (adolescents and adults)
  - Rash: 3%–4%
  - May be maculopapular rather than vesicular
  - Average 5 lesions

- Systemic reactions not common
Adverse Reactions

MMRV and MMR + VAR

- Fever is more common in the 5–12 days after vaccination with MMRV (22%) than with MMR + VAR (15%)
- Data from CDC Vaccine Safety Datalink sites indicate the rate of febrile seizures following MMRV (9 per 10,000 vaccinated) was approximately 2 times higher than among those receiving MMR + VAR at the same visit (4 per 10,000 vaccinated)
- Merck postlicensure surveillance has identified a similar trend
MMRV Vaccine

- For the first dose of measles, mumps, rubella, and varicella vaccines at age 12–47 months, either MMR vaccine and varicella vaccine or MMRV vaccine may be used.

- Providers who are considering administering MMRV vaccine should discuss the benefits and risks of both vaccination options with the parents or caregivers.

- Unless the parent or caregiver expresses a preference for MMRV vaccine, CDC recommends that separate MMR vaccine and varicella vaccine should be administered for the first dose for children 12–47 months of age.
MMRV Vaccine

- Administer MMRV:
  - For the second dose of measles, mumps, rubella, and varicella vaccines at age 15 months through 12 years
  - For the first dose at age 48 months or older
Zoster Disease
Herpes Zoster (Shingles)

- Reactivation of varicella zoster virus
- Associated with:
  - Aging
  - Immunosuppression
  - Intrauterine exposure
  - Varicella disease younger than 18 months of age
Complications of Herpes Zoster

- Postherpetic neuralgia (PHN)

- Dissemination with generalized skin eruptions and involvement of the central nervous system, lungs, liver, and pancreas

- Ophthalmic zoster
Herpes Zoster

- Approximately 1 million episodes occur annually in the United States
- Lifetime risk of zoster estimated to be 32%
- 50% of persons living until age 85 will develop zoster

CDC Shingles (Herpes Zoster) Overview https://www.cdc.gov/shingles/about/overview.html
Zoster involving the ophthalmic division of the trigeminal nerve
Zoster Vaccines
Vaccines for Prevention of Zoster (Shingles)

<table>
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<tr>
<th>Product (ACIP Abbreviation)</th>
<th>Type</th>
<th>ACIP Age Recommendations</th>
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<tbody>
<tr>
<td>Zostavax (ZVL)</td>
<td>Live, attenuated</td>
<td>60 years of age and older*</td>
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<tr>
<td>Shingrix (RZV)</td>
<td>Inactivated, adjuvanted</td>
<td>50 years of age and older</td>
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*Zostavax is FDA-approved for persons 50 years of and older*
Live Zoster Vaccine (ZVL) Efficacy

- Vaccine recipients 60 to 80 years of age had 51% fewer episodes of zoster
  - Efficacy declines with increasing age
  - Significantly reduces the risk of postherpetic neuralgia
  - Reduces the risk of zoster 69.8% in persons 50 through 59 years of age
RZV Vaccine Efficacy

- **Efficacy for the prevention of zoster:**
  - 96.6% in adults age 50 to 59 years
  - 97.4% in adults age 60 to 69 years
  - 91.3% in adults age 70 years and older

- **The efficacy for the prevention of postherpetic neuralgia (PHN) was:**
  - 91.2% in adults age 50 years and older
  - 88.8% in adults age 70 years and older

CDC Shingrix Information for Healthcare Professionals [https://www.cdc.gov/vaccines/vpd/shingles/hcp/shingrix/about-vaccine.html](https://www.cdc.gov/vaccines/vpd/shingles/hcp/shingrix/about-vaccine.html), accessed 8/12/2018
Zoster Vaccine: Zostavax (ZVL)

- **Storage:**
  - Lyophilized vaccine: In the freezer between -50°C and -15°C (-58°F and +5°F)
  - Diluent: At room temperature (68°F to 77°F, 20°C to 25°C) or in the refrigerator (36°F to 46°F, 2°C to 8°C)

- **Preparation:** Reconstitute the vaccine with the diluent supplied by the manufacturer just before administering

- **Schedule:** 1 dose

- **Administration:** Subcut injection
  - Site: Fatty tissue of the upper outer triceps of the arm
  - Needle length and gauge: 5/8-inch, 23- to 25-gauge needle

Zoster Vaccine: Shingrix (RZV)

- **Storage:** Store vaccine AND diluent in the refrigerator between 2°C and 8°C (36°F and 46°F)
- **Preparation:** Reconstitute the vaccine with the diluent (adjuvant) supplied by the manufacturer just before administering
  - If not used immediately, the reconstituted vaccine may be stored in the refrigerator and use it within 6 hours of reconstitution
  - If not used,
- **Schedule:** 2 doses, 2 to 6 months apart
- **Route:** IM Injection
  - Site: Deltoid or the thigh may be used if necessary
  - Needle gauge and length: 23- to 25-gauge needle, length varies by age/weight
- **RZV may be administered during the same clinical encounter as other vaccines**
Vaccine Supply: Shingrix

- Due to high levels of demand for GSK’s Shingrix vaccine, GSK has implemented order limits and providers have experienced shipping delays.
- Order limits and shipping delays will continue throughout 2019.
- GSK increased the U.S. supply during 2018 and plans to make even more doses available in 2019.

CDC Current Vaccine Shortages and Delays [www.cdc.gov/vaccines/hcp/clinical-resources/shortages.html](http://www.cdc.gov/vaccines/hcp/clinical-resources/shortages.html), accessed 8/27/2019
Clinical Considerations
ACIP Zoster Immunization Recommendations

- Administer 2 doses of Shingrix, 2 to 6 months apart, for adults 50 years of age and older
- Shingrix is preferred to Zostavax for persons 60 years and older
- Whether or not they report a:
  - History of zoster disease
  - Prior dose of Zostavax or varicella vaccine
    - Separate varicella-containing vaccines and Shingrix by at least 8 weeks
  - History of chronic medical condition, unless a contraindication or precaution exists
Zoster Vaccination:
Patients Who Do Not Report A Prior Episode of Varicella

- ACIP considers people born in the United States prior to 1980 immune to varicella
- When vaccinating adults 50 years of age and older, there is no need to:
  - Screen for a history of varicella (chickenpox) infection OR
  - Conduct laboratory testing for serologic evidence of prior varicella infection
  - More than 99% of adults age 50 years and older worldwide have been exposed to varicella zoster virus

*MMWR 2018;67(3):103–108*
Zoster Vaccine and Serology

- **If tested and varicella-negative:**
  - Administer 2 doses of single-antigen varicella vaccine (Varivax) separated by at least 4 weeks
  - Followed by 2 doses of RZV, separated by 2–6 months
    - Separate the 2nd (last) dose of varicella and 1st dose of RZV by at least 8 weeks
RZV Contraindications and Precautions

- History of severe allergic reaction, such as anaphylaxis, to any component of a vaccine or after a previous dose of Shingrix
- Moderate to severe illness, including an acute episode of herpes zoster
  - Shingrix is not a treatment for herpes zoster or postherpetic neuralgia (PHN)
- Shingrix has not been studied in pregnant women or women who are breastfeeding. Providers should consider delaying Shingrix vaccination for these women

CDC Shingrix Recommendations [www.cdc.gov/vaccines/vpd/shingles/hcp/shingrix/recommendations.html](http://www.cdc.gov/vaccines/vpd/shingles/hcp/shingrix/recommendations.html), accessed 8/12/2018
RZV and Immunosuppressive Therapy

- Administer RZV to persons:
  - Taking low-dose immunosuppressive therapy (e.g., <20 mg/day of prednisone or equivalent or using inhaled or topical steroids)
  - Anticipating immunosuppression
  - Who have recovered from an immunocompromising illness

- ACIP has not yet made recommendations regarding administering RZV to persons on moderate to high doses of immunosuppressive therapy

MMWR 2018;67(3):103–108
Zostavax (ZVL) Contraindications

- History of a life-threatening or severe allergic reaction to gelatin, the antibiotic neomycin, or any other component of ZVL
- A weakened immune system because of:
  - HIV/AIDS or another disease that affects the immune system
  - Treatment with drugs that affect the immune system
  - Cancer treatment such as radiation or chemotherapy
  - Cancer affecting the bone marrow or lymphatic system, such as leukemia or lymphoma
- Women who are or might be pregnant
  - Women should not become pregnant until at least 4 weeks* after getting ZVL

*ACIP off-label recommendation
MMWR 2008;57(RR-5)
Zostavax (ZVL) Vaccine Precautions

- Moderate or severe acute illness

- Current treatment with an antiviral drug active against herpes viruses
  - Discontinue at least 24 hours before administration of zoster vaccine
  - Should not be taken for at least 14 days after vaccination

- Recent receipt of a blood product is NOT a precaution
Zostavax (ZVL) Adverse Reactions

- Local reactions—34% (pain, erythema)
- No increased risk of fever
- No serious adverse reactions identified
### RZV (Shingrix) Adverse Reactions

<table>
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<tr>
<th>Reaction</th>
<th>Rate</th>
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<tr>
<td>Local reactions</td>
<td>49%</td>
</tr>
<tr>
<td>Local reactions–Grade 3</td>
<td>9.4%</td>
</tr>
<tr>
<td>Systemic reactions (headache, malaise, fatigue)</td>
<td>45–78%</td>
</tr>
<tr>
<td>Systemic reactions (headache, malaise, fatigue)–Grade 3</td>
<td>11%</td>
</tr>
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*MMWR 2018;67(3):103–108*
Adverse Reactions after Shingrix

- Educate patients regarding:
  - Potential adverse reactions, including injection site and systemic reactions
  - The need for a second dose—even if s/he has an adverse reaction

- Offer comfort measures and strategies
Resources
There is a VIS for:
- RZV (Shingrix)
- Var (Varicella)
- MMRV (ProQuad)
- ZVL (Zostavax)

Give the parent or patient the appropriate VIS for the product that will be administered.

Vaccine Information Statements [https://www.cdc.gov/vaccines/hcp/vis/vis-statements/shingles.html](https://www.cdc.gov/vaccines/hcp/vis/vis-statements/shingles.html), accessed 8/12/2018
Varicella and Zoster Vaccine Resources and References

- Resources and references are available on the webinar web page.

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<td>Epidemiology and Prevention of Vaccine-Preventable Diseases</td>
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**Varicella**
- Ask the Experts-Varicella FAQs: [www.immunize.org/askexperts/experts_var.asp](http://www.immunize.org/askexperts/experts_var.asp)
- CDC Varicella Disease and Vaccination: [www.cdc.gov/chickenpox/hcp/index.html](http://www.cdc.gov/chickenpox/hcp/index.html)
- Chickenpox Infographic: [www.cdc.gov/chickenpox/vaccine-infographic.html](http://www.cdc.gov/chickenpox/vaccine-infographic.html)
- Standing Orders for Administering Varicella Vaccine:

**Zoster**
- Ask the Experts-Zoster FAQs: [www.immunize.org/askexperts/experts_zos.asp](http://www.immunize.org/askexperts/experts_zos.asp)
- CDC Zoster Disease: [www.cdc.gov/shingles/about/index.html](http://www.cdc.gov/shingles/about/index.html)
- CDC Zoster Vaccination: [www.cdc.gov/vaccines/vpd/shingles/hcp/index.html](http://www.cdc.gov/vaccines/vpd/shingles/hcp/index.html)