Varicella (Chickenpox) and Zoster (Shingles) Disease

Varicella and Zoster Vaccines

Pink Book Webinar Series 2018

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Varicella Zoster Virus

- Herpes virus (DNA)
- Primary infection results in varicella (chickenpox)
- Recurrent infection results in herpes zoster (shingles)
- 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
- 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

MMWR 2007;56(RR-04)
Varicella Complications

- Bacterial infection of lesions
- Hemorrhagic varicella
- CNS manifestations
- Pneumonia (primary viral or secondary bacterial)
- Congenital varicella
- Perinatal varicella

Prevaccine era:
- Hospitalization ~3 per 1,000 cases or 1,000/year
- Death ~1 per 60,000 cases or 100/year

MMWR 2007;56(RR-04)
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

MMWR 2007;56(RR-04)
### Varicella Epidemiology

<table>
<thead>
<tr>
<th>Reservoir</th>
<th>Human</th>
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| 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 |

*MMWR 2007;56(RR-04)*
Herpes Zoster (Shingles)

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

*MMWR* 2008;57(RR-5)
Complications of Herpes Zoster

- Dissemination with generalized skin eruptions and involvement of the central nervous system, lungs, liver, and pancreas
- Postherpetic neuralgia (PHN)
- Ophthalmic zoster
Zoster involving the ophthalmic division of the trigeminal nerve
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
ACIP Recommendations: Varicella
# Vaccines for the Prevention of Varicella (Chickenpox)

<table>
<thead>
<tr>
<th>Product</th>
<th>ACIP Recommended Age Indications</th>
<th>ACIP Abbreviation</th>
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</thead>
<tbody>
<tr>
<td>Varivax</td>
<td>12 months and older</td>
<td>VAR</td>
</tr>
<tr>
<td>ProQuad</td>
<td>12 months through 12 years</td>
<td>MMRV</td>
</tr>
</tbody>
</table>
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
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
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
Varicella Vaccination and 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 younger than 13 years of age
Varicella Vaccination and Adolescents and Adults

- All persons 13 years of age and older without evidence of varicella immunity
  - 2 doses separated by at least 4 weeks
- Do not repeat first dose because of extended interval between doses
- Second dose recommended for persons of any age who have only received 1 dose
Varicella Vaccination and Health Care Personnel

- Vaccination is recommended for all susceptible health care personnel
- Prevaccination serologic screening probably cost-effective
- Postvaccination testing not necessary or recommended
- Give 2 doses, 4 weeks apart to susceptible persons
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.
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
**MMRV Vaccine**

- 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.
ACIP Recommendations: Zoster
## Vaccines for Prevention of Zoster (Shingles)

<table>
<thead>
<tr>
<th>Product (ACIP Abbreviation)</th>
<th>Type</th>
<th>ACIP Age Recommendations</th>
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</thead>
<tbody>
<tr>
<td>Zostavax (ZVL)</td>
<td>Live, attenuated</td>
<td>60 years of age and older*</td>
</tr>
<tr>
<td>Shingrix (RZV)</td>
<td>Inactivated, adjuvanted</td>
<td>50 years of age and older</td>
</tr>
</tbody>
</table>

*Zostavax is FDA-approved for persons 50 years of and older*
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 2018.
- GSK has increased the U.S. supply available for 2018 and plans to release doses to all customer types on a consistent and predictable schedule for the rest of 2018.
- Overall, the supply of Shingrix during 2018 is sufficient to support the vaccination of more patients during 2018 than were vaccinated against shingles during 2017.

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 8/12/2018
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

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/ypd/shingles/hcp/shingrix/about-vaccine.html](https://www.cdc.gov/vaccines/ypd/shingles/hcp/shingrix/about-vaccine.html), accessed 8/12/2018
Vaccine Efficacy and Effectiveness against HZ for HZ/su and ZVL, by Age Group, During the First 4± Years Following Vaccination

<table>
<thead>
<tr>
<th>Age Group</th>
<th>HZ/su (ZOE 50/70)</th>
<th>ZVL (RCTs*)</th>
<th>ZVL (Baxter 2017)</th>
<th>ZVL (Izurieta 2017)</th>
</tr>
</thead>
<tbody>
<tr>
<td>50-59 yrs</td>
<td>97</td>
<td>70</td>
<td>64</td>
<td>55</td>
</tr>
<tr>
<td>60-69 yrs</td>
<td>97</td>
<td>55</td>
<td>36</td>
<td>32</td>
</tr>
<tr>
<td>70+ yrs</td>
<td>91</td>
<td>38</td>
<td>48</td>
<td>32</td>
</tr>
</tbody>
</table>

† Median follow-up may be less than 3 yrs: Schmader 2012= 1.3 yrs
^ZOE 50/70= 50-59 and 60-69yr: Lal 2015, 70+yrs: Cunningham 2016
*RCTs= 50-59 yrs: Schmader 2012, 60-69 and 70+ yrs: Oxman 2005,
ACIP Zoster Immunization Recommendations

- Administer 2 doses of Shingrix to immunocompetent persons 50 years of age and older
  - Regardless of previous history of:
    - Vaccination with varicella-containing vaccines—Varivax or Zostavax
    - Zoster disease

- Shingrix is preferred to Zostavax for persons 60 years and older
  - Separate varicella-containing vaccines and Shingrix by at least 8 weeks
Zoster Vaccination: Patients Who Do Not Report A Prior Episode of 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

- ACIP considers people born in the United States prior to 1980 immune to varicella

*MMWR* 2018;67(3):103–108
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 use RZV in these patients
  - Persons on moderate to high doses of immunosuppressive therapy were excluded from RZV efficacy studies
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**

*MMWR 2008;57(RR-5)*
Zostavax (ZVL) Adverse Reactions

- Local reactions–34% (pain, erythema)
- No increased risk of fever
- No serious adverse reactions identified

MMWR 2008;57(RR-5)
## RZV (Shingrix) Adverse Reactions

<table>
<thead>
<tr>
<th>Type of Reactions</th>
<th>Percentage</th>
</tr>
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<tbody>
<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>
</tbody>
</table>

*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

CDC unpublished photo. Used with the permission of the patient.
There is a VIS for:
- ZVL (Zostavax)
- RZV (Shingrix)
- Var (Varicella)
- MMRV (ProQuad)

Give the parent or patient the appropriate VIS for the product that will be administered.
Real-Life Shingrix Administration Errors

- Notes from the Field: Vaccine Administration Errors Involving Recombinant Zoster Vaccine
- 13 (8%) of the 155 reports to VAERS regarding Shingrix documented a vaccine administration error

MMWR 2018;67:20
Shingrix Vaccine Administration Errors

- Vaccine administration errors reported to VAERS include:
  - **Wrong route**: Subcut route rather than the IM
  - **Wrong age**: Administered to persons less than 50 years of age
  - **Wrong vaccine**: Shingrix instead of varicella (Varivax) vaccine
  - **Improper storage**: Administered after frozen storage
  - **Wrong preparation**: Administered the adjuvanted diluent only
  - **Wrong schedule**: Interval violations between doses of Shingrix or a previous dose of varicella-containing vaccine

- **Other errors we have heard about**:
  - Staff unaware of the need for a second dose
  - Staff thinks Zostavax can count toward completing the 2-dose Shingrix series
Resources and references are available on the webinar web page.

Varicella and Zoster Vaccine Resources and References

2018 PINK BOOK WEBINAR SERIES

ACIP recommendations
- Current ACIP varicella vaccine recommendations www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/varicella.html
- Current ACIP MMWR recommendations www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/mmwr.html
- Current ACIP zoster vaccine recommendations www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/shingles.html
- ACIP Update on the use of herpes zoster vaccine www.cdc.gov/mmwr/volumes/67/wr/mm6723a5.htm

Manufacturer's vaccine package inserts (PI)
- VAR (Varivax), Merck & Co., Inc. www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm205582.htm
- MMRV (Provarrix), Merck & Co., Inc. www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm299805.htm
- ZDV (Shingrix), GlaxoSmithKline Biologicals www.fda.gov/downloads/biologicsbiotechnology/vaccines/approvedproducts/ucm581605.pdf
- ZCV (Shingrix), Merck & Co., Inc. www.fda.gov/downloads/biologicsbiotechnology/vaccines/approvedproducts/ucm632811.pdf

Schedule
- 2018 Recommended immunization schedule for persons aged 18 years and younger www.cdc.gov/vaccines/schedules/hcp/child-adolescent.html
- 2018 Recommended immunization schedule for adults 19 years and older www.cdc.gov/vaccines/schedules/hcp/adult.html

Disease
- Chickenpox disease webpage www.cdc.gov/chickenpox/about/
- Information you need to know www.pediatrics.org/content/chickenpox/
- Shingles (Herpes Zoster) www.cdc.gov/shingles/hcp/index.html

Information for health care personnel
- Epidemiology and Prevention of Varicella-Preventable Disease: Varicella chapter www.cdc.gov/vaccines/pubs/pinkbook/chapters.html
- Ask the Experts: varicella questions www.immunize.org/askexperts/experts_var.asp
- Ask the Experts: zoster questions www.immunize.org/askexperts/experts_z.asp
- CDC Zoster Fact Sheet www.cdc.gov/foodsafety/docs/shingles-factsheet-hcp.pdf
- MMWR & varicella vaccine or MMRV vaccine: discussing options with parents www.cdc.gov/vaccines/pdfs/mmwr/vaccination/mmwr-factsheet.pdf
- You Call the Shots: Varicella www.cdc.gov/vaccines/hcp/pubs/shots/MMWR-Postcard-VAR.pdf
- You Call the Shots: Zoster www.cdc.gov/vaccines/hcp/pubs/shots/MMWR-Postcard-ZST.pdf
- Varicella information www.immunize.org/varicella/
- Zoster information www.immunize.org/zoster/