VARIZIG®
VARICELLA ZOSTER
IMMUNE GLOBULIN (HUMAN)

Treatment Guide for VARIZIG

Use in High Risk Individuals After Exposure to Varicella (Chickenpox and Shingles)

INDICATIONS AND USAGE

VARIZIG®, Varicella Zoster Immune Globulin (Human) is indicated for post-exposure prophylaxis of varicella in high risk individuals. High risk groups include:

- immunocompromised children and adults
- newborns of mothers with varicella shortly before or after delivery
- premature infants
- neonates and infants less than one year of age
- adults without evidence of immunity
- pregnant women

VARIZIG administration is intended to reduce the severity of varicella.

KAMADA

Kamada Inc.
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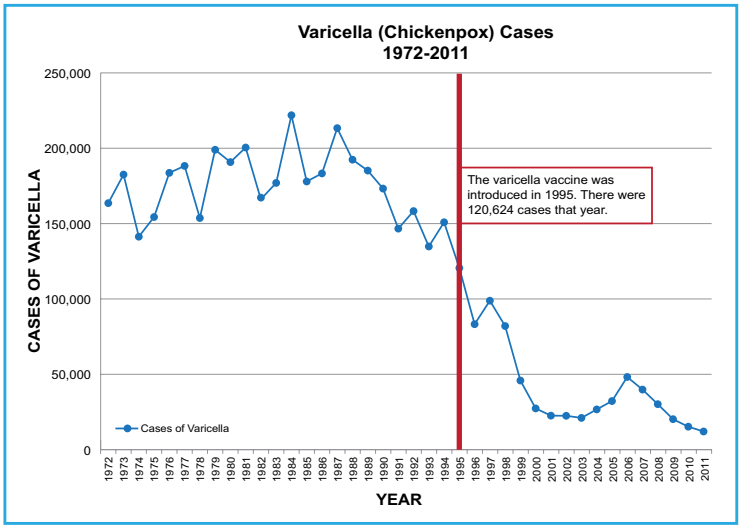
Background

Each year, more than 3.5 million cases of varicella, 9,000 hospitalizations, and 100 deaths are prevented by varicella vaccination in the United States.[1]

Although the use of varicella vaccine has reduced the frequency of chickenpox, the virus has not been eradicated. Chickenpox outbreaks continue to occur even in settings such as schools where most children are vaccinated. (Refer to Varicella Cases, 1972-2011 graph)[2]



CHICKENPOX

In the US, incidence of VZV (Varicella Zoster Virus) infection has decreased dramatically since the introduction of the varicella vaccine in 1995

- Before routine 1-dose varicella vaccination began in 1995, there were an estimated 4 million cases of varicella, 10,000 varicella–related hospitalizations, and 100 deaths annually.[3]
  Now there are fewer than 150K cases of varicella, fewer than 100 hospitalizations, and less than 30 deaths annually
- Prior to June 2006, the Single-dose varicella vaccine effectiveness was approximately 85%[4]
- In June 2006, the Advisory Committee on Immunization Practices recommended a routine second varicella vaccine dose.[4] Effectiveness of 2 doses of the vaccine was 98%,[4] resulting in additional declines in varicella incidence, from 25.4 cases per 100,000 population in 2005–2006 to 3.9 cases per 100,000 population in 2013–2014.[5] Significant declines in varicella outpatient visits (60% decline) and varicella hospitalizations[4]

Suboptimal vaccination rates contribute to outbreaks and increased risk of VZV exposure

- As of 2016, varicella vaccination rates (≥1 dose 19–35 months of age) in the US ranged from 69% to 97%[6]
- Increasing rates of undervaccination and vaccine refusal in recent years are associated with vaccine-preventable disease outbreaks[7]
- Vaccination disparities exist between foreign-born and US-born populations[8]
- Outbreaks of vaccine-preventable diseases are more likely to occur in areas where nonimmunized patients are clustered[9]

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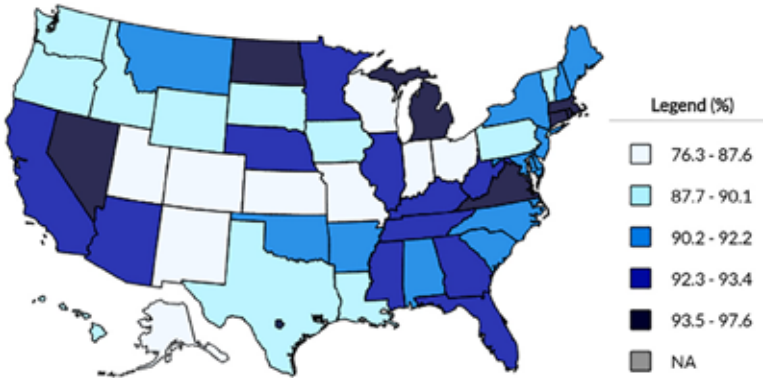
2017 Varicella Vaccination Rates (≥1 Dose) Among Children 19–35 Months of Age, by State, According to CDC Data from the National Immunization Survey-Child (NIS-Child) (Centers for Disease Control and Prevention, 2017a)[6]

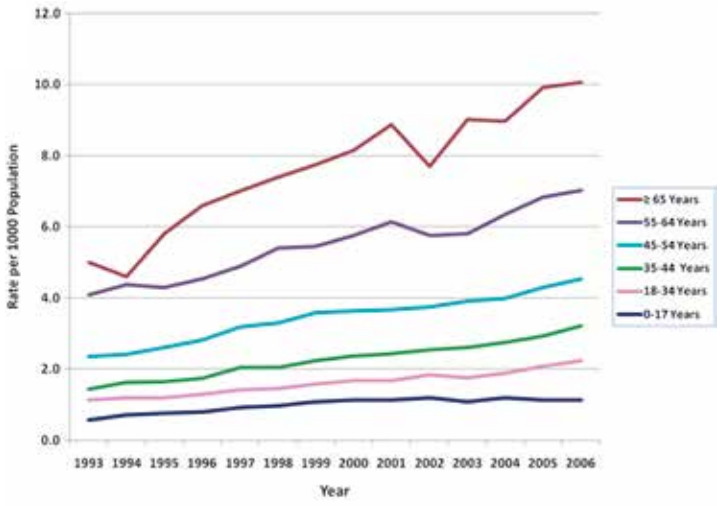


SHINGLES

Incidence of HZ (Herpes Zoster) is increasing among adults in the US[10,11]

- In 2013 there were approximately 1 million cases annually in the US[12]
- Unknown cause for increase; not related to widespread varicella vaccination of children[10,11]

Herpes Zoster Incidence by Age



Annual 1000 persons (in the /1000 persons) by Age Group, MarketScan Enrolled Population, 1993–2006. Denominator data taken from 1993 –2006 MarketScan Population Tables, which contain aggregate enrollment information. Leung et al., Herpes Zoster Incidence Among Insured Persons in the United States, 1993–2006, CID, 2011:52(3); 332-340, by permission of Oxford University Press.

Selected Important Safety Information

The passive transfer of antibodies with immune globulin administration may impair the efficacy of live attenuated virus vaccines such as measles, rubella, mumps and varicella. Defer vaccination with live virus vaccines until approximately three months after VARIZIG®, Varicella Zoster Immune Globulin (Human) administration. Inform the immunizing physician of recent therapy with VARIZIG so that appropriate measures can be taken.

High-Risk Patient Populations

Varicella is likely to be severe in patients whose immunity is compromised, either due to a congenital immunodeficiency, transplantation, or various treatments for malignant or autoimmune disease.[13]

Immunocompromised population and other patient groups are at high risk for severe varicella and complications[14,15,16,17]

- Immunocompromised patients without evidence of immunity to varicella and for those whom vaccine is contraindicated
- Newborn infants whose mothers have signs and symptoms of varicella around the time of delivery (ie, 5 days before to 2 days after)
- Hospitalized premature infants born at ≥28 weeks of gestation whose mothers do not have evidence of immunity to varicella
- Hospitalized premature infants born at <28 weeks of gestation or who weigh ≤1,000 g at birth, regardless of their mothers' evidence of immunity to varicella
- Pregnant women without evidence of immunity

Selected Important Safety Information

Severe hypersensitivity reactions may occur following VARIZIG® administration. Administer VARIZIG, in a setting with appropriate equipment, medication and personnel trained in the management of hypersensitivity, anaphylaxis and shock. In the case of hypersensitivity, discontinue administration of VARIZIG immediately and provide appropriate treatment.

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Potential complications of varicella[4,14,16,18,19]

COMPLICATION	EXAMPLE	ESTIMATED INCIDENCE RATE
Cutaneous	Secondary bacterial infections of skin lesions caused by Staphylococcus or Streptococcus infections	• Most common complication in children, causing hospitalization in 2–3 per 1,000 cases • Less common cutaneous complications include hemorrhagic varicella and purpura fulminans associated with thrombocytopenia and disseminated intravascular coagulation
Pulmonary	Pneumonia	• Radiographic evidence of varicella pneumonia is seen in 3% to 16% of adults • Varicella pneumonia appears to be more severe and more frequent in pregnant women, complicating 10% to 20% of cases
Neurologic	Cerebellar ataxia, encephalitis	• Overall incidence of neurologic complications: 1–3 per 10,000 cases » Cerebellar ataxia: 1 in 4,000 cases » Encephalitis: 1–2 episodes per 10,000 cases » Rare neurologic complications include transverse myelitis, aseptic meningitis, optic neuritis, and Guillain-Barré syndrome
Congenital	Congenital varicella syndrome	• During first 20 weeks of pregnancy baby faces a small risk (0.4% to 2.0%) of a rare group of serious birth defects known as congenital varicella syndrome, which can cause » skin scarring » underdeveloped arms and legs » inflammation of eyes » incomplete brain development • Exposure within 5 days of delivery to 48 hours postpartum: » Baby could be born with or develop a potentially life-threatening infection, neonatal varicella

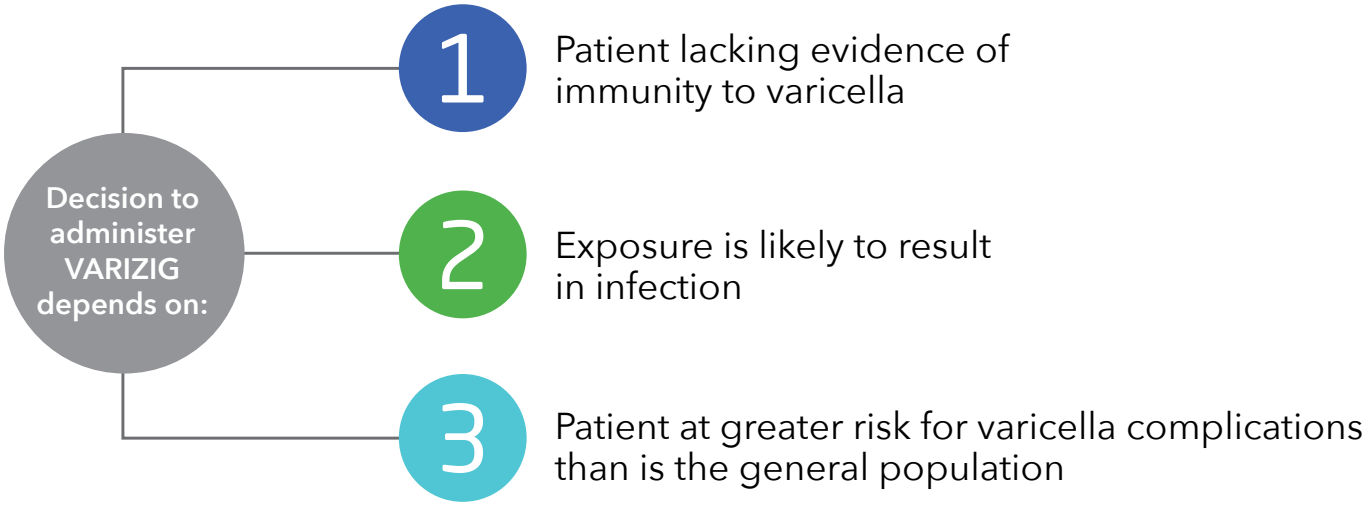
VARIZIG®, Varicella Zoster Immune Globulin (Human)[25] Indications and Usage

VARIZIG®, Varicella Zoster Immune Globulin (Human) is indicated for post-exposure prophylaxis of varicella in high risk individuals. High risk groups include:

- immunocompromised children and adults
- newborns of mothers with varicella shortly before or after delivery
- premature infants ▶ neonates and infants less than one year of age
- adults without evidence of immunity
- pregnant women

VARIZIG administration is intended to reduce the severity of varicella.

Current recommendation according the CDC guidelines for Varicella prevention and treatment[14]



- **Timing**: CDC recommends that VARIZIG should be administered as soon as possible after exposure to varicella-zoster virus and within 10 days.
- **Patients:** VARIZIG is recommended for patients without evidence of immunity to varicella who are at high risk for severe varicella and complications, who have been exposed to chickenpox or shingles, and for whom varicella vaccine is contraindicated.

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MANAGEMENT OF EXPOSURES TO VARICELLA-ZOSTER VIRUS[20, 21, 26, 27]

Significant exposure:

- **Healthy outpatient:** exposure to a household contact or non-transient face-to-face contact indoors with a playmate or other contact
- **Hospital:**
  - **Varicella:** exposure in the same 2 to 4-bed room, face-to-face contact with an infectious staff member or patient, or a visit by a person deemed contagious
  - **Zoster:** Intimate contact (e.g., touching or hugging) with a person deemed contagious
- **Immunosuppressed patients:**[a,b,c]
  - If direct exposure should be closely followed to assure they do not develop symptoms or signs of varicella
- **Newborn**

No → No prophylaxis

Yes → **Does the patient have evidence of immunity to varicella based on one or more of the following:**[e]

- Documentation of age-appropriate vaccination (from CDC yellowbook guidelines)
  - Preschool-aged children (≥12 months through 3 years of age): 1 dose
  - School-aged children (≥4 years of age), adolescents, and adults: 2 doses
- Laboratory evidence of immunity or laboratory confirmation disease
- Birth in the United States before 1980 (not a criterion for health care personnel, pregnant women, and immunocompromised people)
- Diagnosis or verification of a history of varicella or herpes zoster by a health care provider
  - * *If seropositive but immunosuppressed (including patients who may have profound reduction in T-cell function) and have direct exposure they are at risk and should be closely followed to assure they do not develop symptoms or signs of varicella*

Yes → Healthy person

- <12 months of age → No prophylaxis[d]
- ≥12 months of age → Within 5 days of **exposure of rash**
  - **No** → No prophylaxis
  - **Yes** → If no prior dose of varicella vaccine received, administer monovalent varicella vaccine (Varivax),[e] unless contraindicated[j,f]

No →

- **Immunocompromised people**[a,b,c] **(including patients who may have profound reduction in T-cell function)**
- **Seronegative transplant recipients should receive post-exposure prophylaxis after a significant exposure**
- **Pregnant woman**
- **Neonates and Infants**
  - Newborn infant whose mother had onset of chickenpox within 5 days before delivery or within 48 hours after delivery; VARIZIG or IGIV is not indicated if the mother has zoster
  - Hospitalized preterm infant (28 wk or more of gestation) whose mother lacks evidence of immunity against varicella

Within 10 days of exposure

- **No** → No prophylaxis
- **Yes** → **Can VARIZIG be administered within 10 days of exposure?**
  - **No** →
    - Seronegative transplant patient[i]
      - (**) valacyclovir either for a 7-day course of therapy beginning 7-10 days after VZV exposure, or alternatively from day 3 to 28 following exposure
    - IVIG if VARIZIG unavailable
  - **Yes** → **VARIZIG[h],** intramuscularly, 125 units/10 kg body weight (62.5 units if ≤2 kg), up to a maximum of 625 units (ie, 5 vials)

Sources:

- Varicella Zoster virus in solid organ transplantation: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice, 2019.
- The CDC updated Recommendations for Use of VARIZIG - United States, 2013.
- Red-Book: 2021–2024 Report of the Committee on Infectious Diseases.

Footnotes a-j on the next page

Continued from previous page

VARIZIG® indicates Varicella-Zoster Immune Globulin; IGIV, Immune Globulin Intravenous.

a People who receive hematopoietic stem cell transplants should be considered nonimmune regardless of previous history of varicella disease or varicella vaccination in themselves or in their donors.

b Immunocompromised children include those with congenital or acquired T-lymphocyte immunodeficiency, including leukemia, lymphoma, and other malignant neoplasms affecting the bone marrow or lymphatic system; children receiving immuno-suppressive therapy, including ≥2 mg/kg/day of systemic prednisone (or its equivalent) for ≥14 days; all children with human immunodeficiency virus (HIV) infection regardless of CD4+ T-lymphocyte percentage; and all hematopoietic stem cell transplant patients regardless of pretransplant immunity status.

c After close contact with a person who has active varicella or herpes zoster, adolescents and adults with HIV who are susceptible to VZV (particularly those with CD4 counts <200 cells/mm3) should receive VARIZIG as soon as possible (preferably within 96 hours), but up to 10 days after exposure.[28]

d If the exposed person is an adolescent or adult, has chronic illness, or there are other compelling reasons to try to avert varicella, some experts recommend preemptive therapy with oral acyclovir (20 mg/kg per dose administered 4 times per day, with a maximum daily dose of 3200 mg) or oral valacyclovir (if ≥3 months of age; 20 mg/kg per dose administered 3 times per day, with a maximum daily dose of 3000 mg) beginning 7 to 10 days after exposure and continuing for 7 days. If the child is ≥12 months of age, age-appropriate vaccination still is recommended for protection against subsequent exposures, but vaccine should not be administered while antiviral therapy is being administered; if the exposure occurred during an outbreak, 2-dose vaccination is recommended for preschool-aged children younger than 4 years for outbreak control.

e If 1 prior dose of varicella vaccine has been received, a second dose should be administered at ≥4 years of age. If the exposure occurred during an outbreak, a second dose is recommended for preschool-aged children younger than 4 years for outbreak control if at least 3 months have passed after the first dose.

f If post-exposure varicella-zoster immune globulin (VARIZIG) has been administered, an interval of at least 5 months is recommended before varicella vaccination.[28] If post-exposure acyclovir has been administered, an interval of at least 3 days is recommended before varicella vaccination.

g Contraindications include patients who are allergic to a vaccine component, or who are immunocompromised (see above footnote), or pregnant. Caution should be used in patients receiving salicylates. Vaccine may not be as effective if patient has recently received Immune Globulin Intravenous, whole blood, or plasma transfusions, and for this reason, it is recommended that varicella vaccine be withheld for 3 to 11 months, depending on the dose, after administration of these products.

h VARIZIG is manufactured by Emergent BioSolutions Inc. (Winnipeg, Canada), and distributed in the United States by KAMADA Inc. 221 River St. 9th floor Hoboken NJ 07030.

i If VARIZIG and IGIV are not available, some experts recommend preemptive therapy with oral acyclovir (20 mg/kg per dose, administered 4 times per day, with a maximum daily dose of 3200 mg) or oral valacyclovir (if ≥3 months of age; 20 mg/kg per dose, administered 3 times per day, with a maximum daily dose of 3000 mg) beginning 7 to 10 days after exposure and continuing for 7 days. Preemptive oral acyclovir has only been studied in the normal host but sometimes is used in addition to VARIZIG or IGIV in the immunocompromised host.

j The use of antiviral agents as post-exposure prophylaxis has not been evaluated in randomized clinical trials in immunocompromised patients, but should be considered as adjunctive therapy in patients receiving immunoprophylaxis or in patients who were unable to receive immunoprophylaxis prior to 10 days after their exposure. The value of acyclovir as post-exposure prophylaxis has been demonstrated in a study of immunocomponent children and has been suggested to be effective (in addition to VZIG) in a small study of high-risk children which included five kidney transplant recipients.

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DEFINITION OF EXPOSURE[21]

Close contact with an infectious person, such as close indoor contact (e.g., in the same room) or face-to-face contact. Experts differ in their opinion about the duration of contact; some suggest 5 minutes and others up to 1 hour, but do agree that it does not include transitory contact.

TYPES OF EXPOSURE[21]

- Types of exposure to VZV (Chickenpox) that are likely to result in infection include:
  - ✓ Household exposure: Exposure to an infected contact residing in the same household
  - ✓ Playmate: Face-to-face indoor play of 5 minutes or more (some experts suggest >1 hour as the threshold for significant exposure through direct contact)
  - ✓ Hospital exposure
- Types of exposure to HZ (Shingles) that are likely to result in infection include:
  - ✓ Close contact, such as touching or hugging
  - ✓ Transmission has been seen to occur even when an HZ rash is covered.[24]

EVIDENCE OF IMMUNITY TO VARICELLA INCLUDES[4]

- Documentation of age-appropriate vaccination
  - ✓ Preschool-aged children aged ≥12 months: 1 dose
  - ✓ School-aged children, adolescents, and adults: 2 doses (for children who received their first dose at age <13 years and for whom the interval between the 2 doses was ≥28 days, the second dose is considered valid)
- Laboratory evidence of immunity
  - ✓ Laboratory confirmation of disease.
  - ✓ Serologic confirmation of immunity. Commercial assays (IgG) can be used to assess disease-induced immunity, but they lack sensitivity to always detect vaccine-induced immunity (i.e., they might yield false-negative results).
- Birth in the United States before 1980. For healthcare personnel, pregnant women, and immunocompromised persons, birth before 1980 should not be considered evidence of immunity; in such cases, the other criteria of evidence of immunity should be sought.
- Diagnosis or verification of a history of varicella disease and/or Herpes Zoster by a healthcare provider. For typical disease, diagnosis or verification of history of disease can be provided by any healthcare provider. For persons reporting a history of, or reporting with, atypical or mild cases, assessment by a physician or their designee is recommended, and one of the following should be sought: 1) an epidemiologic link to a typical varicella case or laboratory-confirmed case or 2) evidence of laboratory confirmation (if laboratory testing was performed at the time of acute disease). When such documentation is lacking, persons should not be considered as having a valid history of disease because other diseases can mimic mild atypical varicella.
- Diagnosis or verification of a history of herpes zoster by a healthcare provider.

Selected Important Safety Information

VARIZIG®, Varicella zoster immune globulin (human) contains trace amounts of IgA (less than 40 micrograms per milliliter). Patients with known antibodies to IgA have a greater risk of severe hypersensitivity and anaphylactic reactions. VARIZIG is contraindicated in IgA deficient patients with antibodies against IgA and history of hypersensitivity reactions.

Individuals known to have anaphylactic or severe systemic (hypersensitivity) reactions to human immune globulin preparations should not receive VARIZIG. IgA-deficient patients with antibodies against IgA and a history of hypersensitivity may have an anaphylactoid reaction. VARIZIG contains less than 40 micrograms per milliliter of IgA.

Please see full Prescribing Information for full prescribing details.

VARIZIG®, Varicella Zoster Immune Globulin (Human) may help your most vulnerable patients defend against serious disease from varicella exposure.

In an open label expanded access protocol of over 500 high risk individuals that received VARIZIG after exposure to chickenpox or shingles, a low percentage (<10%) developed clinical varicella.[22]

VARIZIG administration is intended to reduce the severity of varicella.

CLINICAL TRIALS[22,23]

High risk individuals received VARIZIG intramuscularly in two clinical trials which included **pregnant women, infants and immunocompromised pediatric and adult patients.**

The table below presents general characteristics of each study.

Clinical studies designed to capture safety, efficacy and pharmacokinetics of VARIZIG

Study ID	Type of information collected	Study Design	Study drug: dosage, route of administration	Study Population
VZ-006	Safety & efficacy	Phase 3, multi-center, randomized, open-label, active controlled study in non-immune pregnant women exposed to VZV	VARIZIG: single dose at 125 IU/ 10 kg IM or 125 IU/ 10 kg IV, up to a maximum dose of 625 IU VZIG: single dose at 125 IU/10 kg IM, up to a maximum dose of 625 IU	Pregnant women, n=57 VZIG IM, n=19 VARIZIG IM, n=17 VARIZIG IV, n=21
VZ-009	Safety & efficacy	Phase 3, open-label, multi-center expanded access program in high risk individuals exposed to VZV	VARIZIG: single dose at 125 IU/10 kg body weight, IM, up to a maximum dose of 625 IU	High-risk individuals, n=621 Non-immune healthy adults, n=5 Immunocompromised adult and pediatric patients, n=299 Infants, n=152 Pregnant women, n=166

VZ-006 STUDY OVERVIEW[22,29]

Conducted in 60 pregnant women without immunity to VZV as confirmed by a latex agglutination test. Of the 60 pregnant patients enrolled in the trial, 57 were included in the per protocol efficacy analysis.

HIGH RISK POPULATION

- Pregnant women, n=57
- VZIG IM, n=19
- VARIZIG IM, n=17
- VARIZIG IV, n=21

EFFICACY ENDPOINT

The primary endpoint for this study was the incidence of varicella in high risk pregnant women treated with VARIZIG® IM or IV or VZIG IM.

Fewer patients treated with VARIZIG developed varicella [IM: n=5 (29%); IV: n=6 (29%)] compared to those treated VZIG IM (n=8, 42%).

The incidence of clinical varicella was similar across all treatment groups with an overall incidence of 33% (19/57). The expected rate of varicella in pregnant women after exposure is approximately 70%.[3] In the subset of 28 subjects with more than 24 hours exposure to varicella, the incidence of clinical varicella in the combined treatment groups was 64%.

The small number of subjects in each treatment stratum and the lack of agreed upon pre-specified hypothesis testing precluded formal statistical comparisons between groups.

There were no severe complications of varicella, including pneumonia, encephalitis or mortality, observed.

SAFETY

The most frequent adverse events overall were pruritus (12%), headache (10%), injection site pain (9%), and nausea (9%). Similar incidences of adverse drug reactions were reported in patients in the standard VZIG group. Other less frequent reactions included myalgia, fatigue, nausea and flushing.

CONCLUSION

Overall, data collected from study VZ-006 indicated that VARIZIG was as efficacious as VZIG in modifying the course of varicella infection in pregnant women without immunity to VZV.

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VZ-009 STUDY OVERVIEW[23, 29]

An expanded access program designed to provide VARIZIG®, Varicella zoster immune globulin (human), to high risk individuals. The objective of the study was to further assess and confirm the safety and efficacy of intramuscular injection of VARIZIG in the prevention or reduction of severity of complications from varicella infections in the indicated high risk populations. 513 subjects had sufficient efficacy data to be included in primary efficacy population.

HIGH RISK POPULATIONS

- Immunocompromised adult and pediatric patients (n=269)
- Infants including newborns, preterm and <1 year (n=105),
- Healthy non-immune adults (n=2)
- Pregnant women (n=137).

EFFICACY ENDPOINT

The primary endpoint was the incidence of clinical varicella (chickenpox) in each high risk population exposed to VZV. 513 subjects had sufficient data to be included in the primary efficacy population. The incidence of varicella is listed in the table below:

High Risk Population	Number of total doses administered*	Incidence of Varicella after treatment
Pregnant Women	137	7.3% (10 people)
Immunocompromised patients	269	4.5% (12 people)
Infants including newborns, preterm and <1 year	105	11.4% (12 people)

* Several people had more than one dose

** 2 healthy non immune adults were excluded from efficacy group

The secondary endpoints included incidence of varicella-related complications (pox count >100, pneumonia, encephalitis and mortality). Overall, complications due to VZV were observed in 4 of 28 cases of clinical varicella in the efficacy population.

- The overall incidence of clinical varicella was 8.8% of high risk individuals exposed to VZV and treated with VARIZIG for all combined populations
- 5 of 35 participants who developed > 100 pox: 2 immunocompromised participants and 3 infants. Each received VARIZIG within 96 hours of exposure to varicella.
  - One infant developed both pox counts > 100 pox and encephalitis.
  - One newborn infant developed both pox counts > 100 and pneumonia.
- None of the 10 evaluable participants with varicella in the robustness population had > 100 pox.
- No pregnant woman developed > 100 pox or had any complications.

- 1 newborn developed disseminated varicella with pneumonia and encephalitis after intrauterine exposure to VZV; this patient received acyclovir treatment at birth and received VARIZIG® 6 days after birth. When this patient began to exhibit evidence of clinical varicella, acyclovir was administered again.
- No participants died because of varicella.

TIMING OF ADMINISTRATION

The comparison of the incidence of varicella in subjects administered VARIZIG, Varicella zoster immune globulin (human) within 96 hours from exposure and the incidence of varicella in subjects administered VARIZIG more than 96 hours (4-10 days) was also performed.

This data showed there was no statistically significant difference between the observed incidences of varicella between the subjects treated with VARIZIG within 96 hours or more than 96 hours (4-10 days) from VZV exposure.

SAFETY

A total of 63 subjects experienced 143 serious AE's, 7 considered related to VARIZIG (nausea, vomiting, convulsion, headache, abortion spontaneous, serum sickness and Varicella). Only 2 serious adverse events (1 serum sickness and 1 isolated case of Varicella) were considered probably related to VARIZIG.

The most common AE (≥ 3% of subjects) was pyrexia; all reports of pyrexia occurred in immunocompromised subjects and only 1 report was considered related to VARIZIG.

CONCLUSION

In this expanded-access program in which the determination of risk, exposure, and clinical outcome was made by each local investigator, the incidence and severity of varicella was low in high-risk subjects after administration of VARIZIG. Although there was no comparator for this study, these results were compared in the context of data before passive immunization was used. When compared to population-specific historical untreated controls VARIZIG likely reduced the incidence of varicella.

Please see full Prescribing Information for full prescribing details.

COMBINED ADVERSE REACTIONS FROM BOTH CLINICAL TRIALS[25]

The most serious adverse drug reactions observed in clinical trials for all subjects and patients (n=601) include pyrexia, nausea, and vomiting. The most common adverse drug reactions (reported by ≥ 1% of subjects) observed in clinical trials for all subjects and patients (n=621) are the following:

- injection site pain (3%),
- headache (2%),
- rash (including terms pruritus, rash, rash erythematous, rash vesicular and urticaria) (1%),
- fatigue (1%),
- chills (1%),
- nausea (1%).

All other adverse drug reactions occurred in less than 1%

Selected Important Safety Information

Because VARIZIG® is made from human plasma, it may carry a risk of transmitting infectious agents, e.g., viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent.1 The plasma donors are screened for the presence of certain infectious agents and the manufacturing process for VARIZIG includes measures to inactivate and remove certain viruses. Despite these measures, products derived from human plasma can still potentially transmit diseases. No cases of transmission of viral diseases, vCJD or CJD have been associated with the use of VARIZIG.

The most common adverse drug reactions observed in clinical trials for all subjects and patients are the following: injection site pain (3%); and headache (2%). Less common adverse drug reactions reported include the following: chills, fatigue, rash and nausea.

Please see full Prescribing Information for full prescribing details.

VARIZIG® [Varicella Zoster Immune Globulin (Human)] dosage and administration[25]

TIMING OF ADMINISTRATION

TREATMENT REQUIRES QUICK ACTION

Administer VARIZIG ideally within 96 hours for greatest effectiveness.

A comparison of the incidence of clinical varicella based on treatment window revealed that treatment between 5 and 10 days post-exposure was no different from treatment within 96 hours.

DOSING

DOSING OF VARIZIG IS BASED ON BODY WEIGHT[25]

Administer a single dose of VARIZIG intramuscularly as recommended in the following table:

Weight of Patient		VARIZIG Dose		Volume to administer* (milliliters)
Kilograms	Pounds	IU	Number of Vials	
≤2.0	≤4.4	62.5	0.5	0.6
2.1-10.0	4.5-22.0	125	1	1.2
10.1-20.0	22.1-44.0	250	2	2.4
20.1-30.0	44.1-66.0	375	3	3.6
30.1-40.0	66.1-88.0	500	4	4.8
≥40.1	≥88.1	625	5	6.0

* Extractable volumes are confirmed using 21 gauge needle as per USP General Chapters <1> Injections.

Minimum dose

62.5 IU for small infants ≤2 kilograms body weight

Maximum dose

625 IU should be administered for all patients greater than 40 kilograms in weight

INTRAMUSCULAR ADMINISTRATION ONLY[25]

Divide the intramuscular dose and administer in two or more injection sites, depending on patient size. Do not exceed 3 milliliters per injection site.

- Inject into the deltoid muscle or the anterolateral aspects of the upper thigh
- Due to the risk of sciatic nerve injury, do not use the gluteal region as a routine injection site - if the gluteal region is used, only use the upper, outer quadrant
- To prevent the transmission of infectious agents from one person to another, use a new disposable sterile syringe and needle for each individual patient

PREPARATION AND HANDLING[25]

- Each vial of VARIZIG® contains a minimum potency of 125 IU in 1.2 mL.
- Bring VARIZIG to room temperature prior to use.
- Inspect VARIZIG for particulate matter and discoloration prior to administration. Do not use if the solution is cloudy or contains particulates.
- VARIZIG is for single use only. Discard any unused portion.

Selected Important Safety Information

Thrombotic events may occur during or following treatment with immune globulin products. Patients at risk include those with a history of atherosclerosis, multiple cardiovascular risk factors, advanced age, impaired cardiac output, coagulation disorders, prolonged periods of immobilization, and/or known/suspected hyperviscosity. Consider baseline assessment of blood viscosity in patients at risk for hyperviscosity including those with cryoglobulins, fasting chylomicronemia/markedly high triacylglycerols (triglycerides), or monoclonal gammopathies.

Please see full Prescribing Information for full prescribing details.

VARIZIG® [Varicella Zoster Immune Globulin (Human)] is Widely Available. To stock VARIZIG: contact your specialty distributor

Check with your distributor to see if a consignment program is available.

Please visit VARIZIG.com for more information.

PRODUCT DESCRIPTION[25]

VARIZIG is supplied as a sterile solution for intramuscular injection and is available in a single-use vial of 125 IU.

NDC Code	Strength	Concentration
 49591-126-51	≥125 IU	104 IU per mL

STORAGE AND HANDLING[22]

Store VARIZIG at 2 to 8°C (36 to 46°F). Do not freeze. Do not use after expiration date.

REIMBURSEMENT CODES

The CPT®, ICD-9-CM and ICD-10-CM codes provided are based on American Medical Association (AMA) or Centers for Medicare and Medicaid Services (CMS) guidelines and are provided for information purposes only. The billing party is solely responsible for appropriate coding of products or services (eg, CPT® coding). As the information provided is not intended to provide specific guidance on billing, and because government and other third-party payor coding requirements change periodically, all coding requirements should be verified directly with the payor being billed.

CPT® Code	90396	Varicella-Zoster Immune Globulin, human, for intramuscular use
ICD-9-CM	V01.71	Contact with or exposure to communicable diseases, varicella
	V05.4	Need for other prophylactic vaccination and inoculation against single diseases, varicella
ICD-10-CM	Z20.820	Contact with and (suspected) exposure to varicella
Temporary J Code		J-9999

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Selected Important Safety Information

Administer VARIZIG via the intramuscular route only. In patients who have severe thrombocytopenia or any coagulation disorder that would contraindicate intramuscular injections, only administer VARIZIG if the expected benefits outweigh the potential risks.

Please see full Prescribing Information for full prescribing details.

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IMPORTANT SAFETY INFORMATION

In patients who have severe thrombocytopenia or any coagulation disorder that would contraindicate intramuscular injections, only administer VARIZIG if the expected benefits outweigh the potential risks. Thrombotic events may occur following treatment with VARIZIG and other immune globulin products. Individuals known to have severe, potentially life-threatening reactions to human globulin should not receive VARIZIG or any other immune globulin (Human). Individuals who are deficient in IgA may have the potential for developing IgA antibodies and have severe, potentially life-threatening allergic reactions. Products made from human plasma may carry a risk of transmitting infectious agents, e.g. viruses and, theoretically, the Creutzfeldt-Jakob disease agent. The most serious adverse drug reactions observed in clinical trials for all subjects and patients include pyrexia, nausea, and vomiting. The most common adverse drug reactions observed in clinical trials for all subjects and patients were injection site pain, headache, chills, fatigue, rash and nausea.

Please see full Prescribing Information for full prescribing details.
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