Vaccinia Immune Globulin IV (Human) (AHFS DI)

Generic Name: Vaccinia Immune Globulin IV (Human)
Brand Information: CNJ-016®

Introduction
Specific immune globulin (hyperimmune globulin).[134] Vaccinia immune globulin IV (VIGIV) contains IgG prepared from plasma of adults immunized with smallpox (vaccinia) vaccine.[1]

Uses
Smallpox Vaccination Complications
Treatment and/or management of certain complications of smallpox vaccination, including eczema vaccinatum, progressive vaccinia, severe generalized vaccinia, vaccinia infection in individuals with certain skin conditions (e.g., burns, impetigo, varicella zoster virus infection, poison ivy, active or extensive eczematous skin lesions), and aberrant vaccinia infection caused by inadvertent autoinoculation to the eyes (except isolated vaccinia keratitis), mouth, or other areas where such infection would constitute a special hazard.[1] Designated an orphan drug by FDA for this use.[9]

Considered first-line treatment for serious complications of smallpox vaccination.[2,3,10,11,12,14,15] Contraindicated in patients with isolated vaccinia keratitis;[1] not recommended for treatment of postvaccinial encephalitis.[1,2,3,11]

If VIGIV alone is inadequate or if VIGIV not readily available, may consider use of certain antivirals (e.g., cidofovir, tecovirimat, brincidofovir) as a secondary treatment after consultation with CDC.[11]

VIGIV is not commercially available but can be obtained through the Strategic National Stockpile for treatment of smallpox vaccine complications in patients with serious clinical manifestations.[11]

Contact state or local health department or CDC Emergency Operations Center at 770-488-7100 for assistance with diagnosis and management of suspected complications of smallpox vaccination.[11]

Mpox
Has been used in the treatment of mpox infection (off-label).[6]

Mpox virus is an orthopoxvirus closely related to the causative agent of smallpox.[6,50] Although no specific treatments are available for human mpox infection, drugs that have shown to be effective against other orthopoxviruses (e.g., cidofovir, tecovirimat, brincidofovir, VIGIV) have been used to treatment severe mpox.[6]

Supportive care and pain control usually sufficient for most patients with an intact immune

system who do not have a skin disease.[6] In patients who require more than supportive care, tecovirimat is typically the first therapy that should be considered.[6] Brincidofovir and VIGIV are additional therapeutics available from the Strategic National Stockpile (SNS) that can be considered in patients who need an additional or alternative treatment to tecovirimat; cidofovir can also be considered.[6] Treatment decisions should be individualized.[6] Healthcare providers may request a clinical consultation with CDC at poxvirus@cdc.gov or 770-488-7100.[6]

CDC states that use of VIGIV may be considered for postexposure prophylaxis of mpox (off-label) in exposed individuals who cannot receive postexposure vaccination with smallpox vaccine because of severe T-cell function immunodeficiency.[6]

Dosage and Administration
General

Patient Monitoring
1. Patients should be closely monitored for adverse effects and vital signs should be evaluated during and immediately following IV infusion of VIGIV.[1]

Premedication and Prophylaxis
1. Ensure that patient is adequately hydrated and assess renal function (e.g., BUN and Scr) prior to administration of VIGIV and at appropriate intervals thereafter.[1]

Administration and Preparation
Administer only by IV infusion.[1]

IV Infusion
Administer through a dedicated IV line.[1] If preexisting catheter must be used, flush line with 0.9% sodium chloride injection before administering VIGIV.[1]

Prior to administration, allow vials of VIGIV to come to room temperature.[1] Thaw frozen vials by placing in a refrigerator (2–8°C) until thawed (approximately 14 hours) or by placing at room temperature for 1 hour followed by water bath (37°C) until completely thawed.[1] Do not thaw in a microwave.[1]

Should appear as a clear to opalescent liquid; do not use if cloudy, discolored, or contains particulates.[1]

May be administered undiluted or may be diluted to no more than 1:2 using 0.9% sodium chloride injection.[1] Data not available regarding compatibility with other infusion solutions.[1] Must start IV infusion within 4 hours after vial is entered.[1] Discard partially used vials.[1] Do not shake vials since shaking may cause foaming.[1]

Rate of Administration
Administer by IV infusion at a rate of ≤2 mL/minute.[1]

Patients weighing <50 kg: Manufacturer recommends a maximum IV infusion rate of 0.04 mL/kg per minute (133.3 units/kg per minute).[1]

Patients with preexisting renal impairment or at increased risk of developing acute renal injury, thrombosis, or volume overload: Administer using minimum concentration and IV infusion rate practicable.[1] Do not exceed recommended infusion rate and closely follow infusion schedule.[1]

If relatively minor adverse effects (e.g., flushing) occur, slow infusion rate.[1]
If more serious reactions (e.g., anaphylaxis, hypotension) occur, discontinue infusion immediately and initiate appropriate therapy.[1]

Dosage
Pediatric Patients
Smallpox Vaccination Complications
Adolescents ≥16 Years of Age: 6000 units/kg IV as a single dose.[1,10] Give as soon as symptoms appear and severe vaccinia-related complication diagnosed.[1]

Depending on severity of symptoms and response to treatment, may consider giving second dose of 6000 units/kg; clinical data regarding repeat doses of VIGIV not available.[1]
If no response to initial dose, may consider a higher dose (e.g., 9000 units/kg).[1,10]

Patients with risk factors for thrombosis: Maximum dosage 12,000 units/kg daily.[1]

Adults
Smallpox Vaccination Complications
Adults ≤65 Years of Age*:* 6000 units/kg IV as a single dose.[1,10] Give as soon as symptoms appear and severe vaccinia-related complication diagnosed.[1]

Depending on severity of symptoms and response to treatment, may consider giving second dose of 6000 units/kg; clinical data regarding repeat doses of VIGIV not available.[1]
If no response to initial dose, may consider a higher dose (e.g., 9000 units/kg).[1,10] In clinical trials in healthy adults, doses up to 24,000 units/kg were well tolerated.[1]

Patients with risk factors for thrombosis: Maximum dosage 12,000 units/kg daily.[1]

Special Populations
Hepatic Impairment
No specific dosage recommendations.[1]

Renal Impairment

No specific dosage recommendations.[1] Use with caution in patients with renal impairment and in those at increased risk of renal dysfunction.[1]

Cautions
Contraindications

1. Isolated vaccinia keratitis.[1]
2. History of anaphylaxis or severe systemic reaction to VIGIV or any other parenteral immune globulin preparation.[1]
3. IgA-deficient individuals with antibodies against IgA and history of IgA hypersensitivity.[1]

Warnings and Precautions
Sensitivity Reactions
Severe immediate hypersensitivity reactions to plasma-derived products may occur.[1] Although acute systemic allergic reactions not reported in clinical trials of VIGIV, administer only in settings where appropriate equipment and personnel trained in the management of acute anaphylaxis are available.[1] If hypotension or an allergic or anaphylactic reaction occurs, immediately discontinue the IV infusion of VIGIV and initiate appropriate supportive treatment as needed.[1,2]

Individuals with IgA deficiency may develop antibodies to IgA; anaphylaxis could occur following administration of plasma-derived products containing IgA.[1] VIGIV contains trace amounts of IgA (≤40 mcg/mL).[1]

Renal Effects
Renal dysfunction, acute renal failure, osmotic nephropathy, proximal tubular nephropathy, and death reported in patients receiving immune globulin IV (IGIV).[1] Most reported cases of renal impairment following administration of IGIV occurred in patients receiving IGIV preparations containing sucrose in daily dosages ≥400 mg/kg.[1] VIGIV does not contain sucrose.[1]

Use VIGIV with caution in patients with preexisting renal impairment and in patients at risk of developing renal impairment (e.g., those with diabetes mellitus, volume depletion, paraproteinemia, or sepsis and those who are >65 years of age or are receiving nephrotoxic drugs).[1]

Data not available to date to identify a maximum safe dose, concentration, and/or IV infusion rate for use of VIGIV in patients at risk of developing renal impairment.[1] If VIGIV used in such patients, administer using minimum infusion rate practicable.[1] Prior to administration, ensure that patients with preexisting renal impairment and patients at increased risk of developing renal impairment are not volume depleted.[1]

Assess renal function (BUN and Scr) prior to and at appropriate intervals after VIGIV.[1]

Periodically monitor renal function and urine output, especially in patients considered at increased risk of developing acute renal failure.[1] If renal function deteriorates, consider discontinuing VIGIV.[1]

Interference with Laboratory Testing
Contains maltose which may cause falsely elevated results in blood glucose determinations that use glucose dehydrogenase pyrroloquinolinequinone (GDH-PQQ) or glucose-dye-oxidoreductase methods.[1] Falsely elevated glucose determinations could result in inappropriate administration of insulin and life-threatening hypoglycemia and there is a risk that true cases of hypoglycemia may go untreated.[1] Use glucose-specific test methods (monitor and test strips) not affected by maltose.[1] If uncertainty exists, contact glucose testing system manufacturer to determine if the system will provide accurate blood glucose determinations in patients receiving VIGIV.[1]

Contains antibodies that may interfere with some serologic tests.[1] Patients receiving immune globulins such as VIGIV may have transitory increases in various passively acquired antibodies that could cause false-positive serologic test results (e.g., Coombs' test).[1]

Thrombosis
Thrombotic events reported in patients receiving IGIV.[1] Patients at risk of thrombotic events include those with a history of cardiovascular risk factors, advanced age, impaired cardiac output, hypercoagulable disorders, prolonged periods of immobilization, history of arterial or venous thrombosis, concomitant use of estrogen-containing preparations, indwelling central vascular catheters, and/or known or suspected hyperviscosity.[1]

Consider potential risks and benefits of VIGIV and weigh against those of alternative therapies.[1] Because of potentially increased risk of thrombosis, consider baseline assessment of blood viscosity in patients at risk for hyperviscosity (e.g., those with cryoglobulins, fasting chylomicronemia/markedly high triacyglycerols [triglycerides], monoclonal gammopathies).[1]

If benefits of VIGIV outweigh potential risks of thrombotic and thromboembolic events, administer VIGIV at minimum concentration available and minimum IV infusion rate practicable and monitor for signs and symptoms of thrombosis.[1] In addition, ensure adequate hydration prior to administration of VIGIV.[1]

Prospective data not available to identify a maximum safe dose, concentration, and/or IV infusion rate if VIGIV used in patients with thrombosis/thromboembolism.[1] Manufacturer states do not exceed VIGIV dosage of 12,000 units/kg daily in patients with thrombotic risk factors.[1]

Hemolysis

VIGIV may contain blood group antibodies that can act as hemolysins and induce in vivo coating of RBCs with immune globulin, causing a positive direct antiglobulin reaction and hemolysis.[1]

Acute hemolysis, consistent with intravascular hemolysis, reported with IGIV; hemolytic anemia can develop subsequent to IGIV therapy due to enhanced erythrocyte sequestration.[1]

Risk factors possibly associated with development of hemolysis following administration of IGIV include high doses (given either as a single dose or in divided doses over several days) and non-O blood group.[1] Although other individual patient factors also hypothesized to increase risk of hemolysis following administration of IGIV (e.g., underlying inflammatory state as may be reflected by, for example, elevated C-reactive protein or erythrocyte sedimentation rate), role of these factors uncertain.[1]

Monitor closely for clinical signs and symptoms of hemolysis, especially in those with risk factors for hemolysis.[1] In patients considered at higher risk, consider appropriate laboratory testing, including measurement of hemoglobin or hematocrit prior to IV infusion of VIGIV and within approximately 36–96 hours after completion of the infusion.[1] Perform additional confirmatory laboratory testing if signs and/or symptoms of hemolysis or a substantial decrease in hemoglobin or hematocrit occurs after the VIGIV infusion.[1]

If a blood transfusion indicated for a patient who developed hemolysis with clinically compromising anemia after receiving VIGIV, perform adequate cross-matching to avoid exacerbating ongoing hemolysis.[1]

Aseptic Meningitis Syndrome
Aseptic meningitis syndrome reported in patients receiving IGIV.[1] Characterized by severe headache, nuchal rigidity, drowsiness, fever, photophobia, painful eye movements, nausea, and vomiting; usually evident within several hours to 2 days after administration of IGIV.[1]

CSF analysis frequently reveals pleocytosis (up to several thousand cells per mm3), predominantly from the granulocytic series, and protein concentrations up to several hundred mg/dL; CSF cultures are negative.[1]

In patients receiving IGIV, aseptic meningitis syndrome reported most frequently in those receiving high total doses (2 g/kg).[1] In comparison, at recommended VIGIV dosage of 6000 units/kg, patient may be exposed to up to 0.18 g/kg of protein.[1]

Aseptic meningitis syndrome generally resolves within several days without sequelae

following discontinuance of IGIV.[1] If signs and symptoms of aseptic meningitis syndrome occur in patients treated with VIGIV, perform thorough neurologic examination (including CSF studies) to rule out other causes of meningitis.[1]

Transfusion-related Acute Lung Injury
Transfusion-related acute lung injury (TRALI; noncardiogenic pulmonary edema) reported in patients receiving IGIV.[1] Typically occurs within 1–6 hours after IGIV infusion and is characterized by severe respiratory distress, pulmonary edema, hypoxemia, normal left ventricular function, and fever.[1]

Monitor for adverse pulmonary reactions.[1] If TRALI is suspected, perform appropriate tests to determine whether antineutrophil antibodies are present in the product or in patient serum.[1] Manage using oxygen therapy with adequate ventilatory support.[1]

Risk of Transmissible Infectious Agents in Plasma-derived Preparations
Because VIGIV is prepared from pooled human plasma, it is a potential vehicle for transmission of human viruses and theoretically may carry a risk of transmitting the causative agent of Creutzfeldt-Jakob disease (CJD).[1]

Although plasma donations used to prepare VIGIV are tested for certain viruses (e.g., HIV, HBV, HCV) and VIGIV undergoes certain procedures (i.e., solvent/detergent viral inactivation, virus filtration, anion-exchange column chromatography) that reduce viral infectious potential, a risk for transmission of infectious agents, including unrecognized blood-borne infectious agents, still remains despite these measures.[1] Report any infection believed to have been transmitted by VIGIV to the manufacturer at 800-768-2304.[1]

Improper Storage and Handling
Improper storage or handling of immune globulins may affect efficacy.[134] Inspect all immune globulins upon delivery and monitor during storage to ensure that the appropriate temperature is maintained.[134] Do not administer VIGIV that has been mishandled or has not been stored at the recommended temperature.[134]

If there are concerns about mishandling, contact the manufacturer or state or local immunization or health departments for guidance on whether VIGIV is usable.[134]

Specific Populations
Pregnancy
Animal reproduction studies not performed.[1] Data not available on use of VIGIV in pregnant women to inform drug-associated risk.[1]

ACIP states there are no known risks associated with use of immune globulins in pregnant women.[134] CDC states VIGIV not indicated for prophylaxis in pregnant women unintentionally vaccinated with smallpox vaccine; however, do not withhold VIGIV if a

pregnant woman develops a smallpox vaccination complication (e.g., eczema vaccinatum).[2]

Lactation
Not known whether VIGIV is distributed into human milk, affects milk production, or affects the breast-fed infant.[1]

Pediatric Use
Safety and efficacy not established in pediatric patients <16 years of age.[1]

Geriatric Use Safety and efficacy not established in geriatric adults >65 years of age.[1]

Renal Impairment
Use with caution and administer at minimum IV infusion rate practicable in patients with preexisting renal impairment and in those at risk of developing renal impairment.[1] This includes, but is not limited to, individuals with diabetes mellitus, volume depletion, paraproteinemia, or sepsis and those who are >65 years of age (off-label) or are receiving nephrotoxic drugs.[1]

Common Adverse Effects
Headache, nausea, rigors, dizziness.[1]

Drug Interactions
Inactivated Vaccines and Toxoids
Inactivated vaccines or toxoids may be administered simultaneously with (at different sites) or at any interval before or after immune globulin preparations, including VIGIV.[134]

Live Vaccines
Antibodies contained in VIGIV may interfere with the immune responses to some live virus vaccines, including measles, mumps, and rubella virus vaccine live (MMR) and varicella virus vaccine live.[1,134] Do not administer live vaccines and immune globulin preparations, including VIGIV, simultaneously.[134] Defer live virus vaccines until approximately 3 months after VIGIV; revaccination with live vaccines indicated if VIGIV administered shortly after the live vaccines.[1]

Stability
Injection, for IV Infusion
Unopened single-use vials: Store frozen (-15°C or lower) or refrigerate at 2–8°C.[1]
Frozen vials that have been thawed by placing in a refrigerator (2–8°C): Must be used within 60 days after thawing.[1]

Does not contain thimerosal or any other preservatives.[1] Begin IV infusion within 4 hours after entering vial; discard partially used vials.[1]

Actions

1. VIGIV is prepared from pooled plasma of healthy adults who received vaccination with smallpox (vaccinia) vaccine and have high titers of antibody against vaccinia virus.[1]
2. Potency of VIGIV (as determined by a plaque reduction neutralization test) is expressed in arbitrary units by comparison to FDA reference standard.[1]
3. Each vial of VIGIV contains approximately 40–80 mg/mL total protein, ≥50,000 units of vaccinia antibody neutralizing activity, and ≤40 mcg/mL of IgA.[1] VIGIV is stabilized with 10% maltose and 0.03% polysorbate 80.[1]
4. Although exact mechanism of action not known, provides passive immunity against vaccinia virus in individuals with certain complications following vaccination with smallpox (vaccinia) vaccine.[1] VIGIV possibly can neutralize vaccinia virus in vivo.[1]

Advice to Patients

1. Advise patients of the risks and benefits of VIGIV.[1]
2. Inform patients that hypersensitivity reactions may occur, especially in individuals with previous reactions to human immune globulin and in individuals with IgA deficiency.[1] Importance of immediately seeking medical attention if symptoms of allergic reaction (e.g., hives, rash, chest tightness, wheezing, shortness of breath, feeling lightheaded or dizzy upon standing) or any other adverse effects (e.g., injection site pain, chills, fever, headache, nausea, vomiting, joint pain) occur.[1]
3. Inform patients that VIGIV contains maltose and may cause falsely elevated glucose readings when blood glucose monitoring systems based on GDH-PQQ or glucose-dyeoxidoreductase
methods used; this could result in inappropriate administration of
insulin and life-threatening hypoglycemia or could mask true hypoglycemia.[1]
Importance of using glucose-specific test methods not affected by maltose.[1]
4. Inform patients that VIGIV is prepared from pooled human plasma.[1] Although improved donor screening and viral-inactivating and purification procedures used in manufacture of plasma-derived preparations have reduced the risk of pathogen transmission, a risk of transmission of human viruses or other pathogens still remains.[1] Importance of reporting any infection believed to have been transmitted by VIGIV.[1]
5. Advise patients that VIGIV may interfere with immune responses to certain live viral vaccines (e.g., MMR, varicella virus vaccine live).[1] Importance of informing clinicians about any recent vaccinations.[1]
6. Advise patients to inform their clinicians of existing or contemplated concomitant therapy, including prescription and OTC drugs, as well as any concomitant illnesses.[1]
7. Advise women to inform their clinicians if they are or plan to become pregnant or plan to breast-feed.[1]
8. Inform patients of other important precautionary information.[1]

advised that decisions regarding use of drugs are complex medical decisions requiring the independent, informed decision of an appropriate health care professional, and that the information contained in the monograph is provided for informational purposes only. The manufacturer's labeling should be consulted for more detailed information. The American Society of Health-System Pharmacists, Inc. does not endorse or recommend the use of any drug. The information contained in the monograph is not a substitute for medical care.

Preparations

Restricted Distribution

VIGIV is stored in the US Strategic National Stockpile (SNS) and is not commercially available in the US.[1,11] The SNS ensures that certain drugs and medical supplies are readily available to prevent or treat specific diseases, including during public health emergencies, and is managed by the US Department of Health and Human Services (HHS) Office of the Assistant Secretary for Preparedness and Response (ASPR).[5] To request a drug from the SNS, state health departments can contact the CDC Emergency Operations Center at 770-488-7100 or the HHS Secretary's Operations Center at 202-619-7800.[17]

Excipients in commercially available drug preparations may have clinically important effects in some individuals; consult specific product labeling for details.

Vaccinia Immune Globulin IV (Human)
Injection, for IV infusion
≥50,000 units (of vaccinia antibody neutralizing activity) per vial
CNJ-016®
Emergent

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