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A New Product (VariZIG™) for Postexposure Prophylaxis of Varicella Available Under an Investigational New Drug Application Expanded Access Protocol

On October 27, 2004, the Advisory Committee on Immunization Practices (ACIP) was informed by the only U.S.-licensed manufacturer of varicella zoster immune globulin (VZIG) (Massachusetts Public Health Biologic Laboratories, Boston, Massachusetts) that the company had discontinued production of VZIG. The supply of the licensed VZIG product is now nearly depleted. In February 2006, an investigational (not licensed) VZIG product, VariZIG™ (Cangene Corporation, Winnipeg, Canada) became available under an investigational new drug application (IND) submitted to the Food and Drug Administration (FDA).* This product can be requested from the sole authorized U.S. distributor, FFF Enterprises (Temecula, California), for patients who have been exposed to varicella and who are at increased risk for severe disease and complications (*1*).

The investigational VariZIG, similar to licensed VZIG, is a purified human immune globulin preparation made from plasma containing high levels of anti-varicella antibodies (immunoglobulin class G [IgG]). Unlike the previous product, the investigational product is lyophilized. When properly reconstituted, VariZIG is approximately a 5% solution of IgG that can be administered intramuscularly. As with any product used under IND, patients must be informed of potential risks and benefits and must give informed consent before receiving the product.

Indications for Use of Investigational VariZIG

Patients without evidence of immunity to varicella (i.e., without history of disease or age-appropriate vaccination) who are at high risk for severe disease and complications, who have been exposed to varicella, and from whom informed consent has been obtained, are eligible to receive the IND application product under an expanded access protocol. The patient groups recommended by ACIP to receive VariZIG include the following:

- Immunocompromised patients.
- Neonates whose mothers have signs and symptoms of varicella around the time of delivery (i.e., 5 days before to 2 days after).
- Premature infants born at ≥28 weeks of gestation who are exposed during the neonatal period and whose mothers do not have evidence of immunity.
- Premature infants born at <28 weeks of gestation or who weigh ≤1,000 g at birth and were exposed during the neonatal period, regardless of maternal history of varicella disease or vaccination.
- Pregnant women.

Varicella vaccine was recommended in 1999 for postexposure prophylaxis of other persons without evidence of varicella immunity and who have no contraindications to vaccination (*2*). The vaccine should be administered preferably within 96 hours and possibly up to 120 hours postexposure. If illness occurs, with or without postexposure vaccination, antiviral treatment (e.g., acyclovir) can be considered for adolescents and adults.

Administration

Investigational VariZIG is expected to provide maximum benefit when administered as soon as possible after exposure, although it can be effective if administered as late as 96 hours after exposure; treatment after 96 hours is of uncertain value. VariZIG should be administered intramuscularly as directed by the manufacturer.

When indicated, health-care providers should make every effort to obtain and administer VariZIG. In situations in which administration of VariZIG does not appear possible within 96 hours of exposure, administration of immune globulin intravenous (IGIV) should be considered as an alternative. IGIV should also be administered

* Available at http://www.fda.gov/cber/infosheets/mphvzig020806.htm.

within 96 hours of exposure. Although licensed IGIV preparations are known to contain anti-varicella antibody titers, the titer of any specific lot of IGIV that might be available is uncertain because IGIV is not routinely tested for anti-varicella antibodies. The recommended IGIV dose for postexposure prophylaxis of varicella is 400 mg/kg, administered once. For pregnant women who cannot receive VariZIG within 96 hours of exposure, clinicians may choose either to administer IGIV or closely monitor the women for signs and symptoms of varicella and institute treatment with acyclovir if illness occurs.

Dosage

Investigational VariZIG is supplied in 125-U vials. The recommended dose is 125 units/10 kg body weight, up to a maximum of 625 units (five vials). The minimum dose is 125 U.

Interval Between Administration of VariZIG and Varicella Vaccine

Any patient who receives investigational VariZIG to prevent varicella subsequently should receive varicella vaccine, provided the vaccine is not contraindicated. Varicella vaccination should be delayed until 5 months after VariZIG administration. Varicella vaccine is not needed if the patient has varicella after administration of VariZIG.

Antiviral Therapy

Any patient who receives investigational VariZIG should be observed closely for signs or symptoms of varicella for 28 days after exposure because VariZIG might prolong the incubation period by ≥1 week. Antiviral therapy should be instituted immediately if signs or symptoms of varicella disease occur. The route and duration of antiviral therapy should be determined by specific host factors, extent of infection, and initial response to therapy.

How to Obtain Investigational VariZIG

Investigational VariZIG is produced by Cangene Corporation (Winnipeg, Canada) and is distributed by FFF Enterprises (Temecula, California). An expanded access protocol under the IND application enables use of investigational VariZIG for patients who meet the protocol's enrollment criteria[†] and who choose to participate. The expanded access protocol has received central institutional review board (IRB) approval. With this central IRB review and approval, FDA does not require an additional approval by the IRB at the treatment site. However, some institutions might require that the institution's IRB be notified before the institution or its physicians participate in a study reviewed by a central IRB. In such cases, notification and any local IRB review may take place before a patient who needs the investigational product is identified. However, if a patient who needs the investigational product is identified before any required local IRB review has taken place, the investigational product may be shipped under the approval of the central IRB while coordination with the institution's IRB is addressed. In any event, all informed consent and other patient protections must still be in place.

Pharmacists and health-care providers who expect to have patients who will need VariZIG may participate in a program that allows them to acquire inventory in advance. VariZIG delivered for inventory will be accompanied by all forms required by the IND expanded access protocol (i.e., release form, protocol, informed consent form, case report forms, investigator brochure, drug accountability form, and contact information for FFF Enterprises and Cangene Corporation); IRB approval (i.e., central or local) should be in place. Providers who identify a patient for whom VariZIG is indicated should contact FFF Enterprises (24-hour telephone, 800-843-7477) and fax the completed release form. FFF Enterprises will review the form to determine patient eligibility and allot a patient number to eligible patients at the time of the call.

Alternatively, if VariZIG is not available on site to the pharmacist or health-care provider, a product release form can be requested directly from FFF Enterprises by calling the 24-hour telephone line. FFF Enterprises will transmit the product release form by e-mail or fax for completion and return. If the patient is eligible, FFF Enterprises will allot a patient number, and investigational VariZIG will be shipped with the required forms. Under normal circumstances, investigational VariZIG can be delivered from the distributor to its destination within 24 hours of request.

References

1. CDC. Prevention of varicella: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1996;45 (No. RR-11):21.
2. CDC. Prevention of varicella: updated recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1999;48(No. RR-6).

[†] A sample release form is available at http://www.fda.gov/cber/infosheets/mphvzig020806form.pdf.