

**SMALLPOX FACT SHEET – *Information for Clinicians and Public Health Professionals*****Medical Management of Smallpox (Vaccinia) Vaccine Adverse Reactions: Vaccinia Immune Globulin and Cidofovir**

Smallpox vaccination (vaccinia) is a generally safe and effective means to prevent smallpox. However, in a number of individuals, smallpox vaccination can result in untoward effects and adverse reactions. The majority of adverse reactions caused by the smallpox vaccine are mild to moderate complications that resolve on their own. Serious reactions are rare, but can be fatal.

There are two medications that may help persons who have certain serious reactions to the smallpox vaccine; vaccinia immune globulin (VIG) and cidofovir. VIG has been extensively used in the past and felt (but not shown in controlled studies) to be effective. Cidofovir may be effective based on studies in animals. Treatment with these medications may require the vaccine recipient to be in the hospital. They are investigational and may cause a number of serious side effects themselves.

Vaccinia Immune Globulin (VIG)

- Vaccinia immune globulin (VIG) is a product used to treat certain serious adverse reactions caused by smallpox vaccine. There are about 2,700 treatment doses of VIG (enough for predicted reactions with more than 27 million people). Additional doses of VIG are being produced this year.
- VIG was produced in the 1960s from plasma obtained from recently vaccinated donors. It contained a high titer of anti-vaccinia neutralizing antibody. Because it contained a high proportion of aggregated protein it was administered solely by the intramuscular route and could not be used intravenously.
- An effort is underway to produce new lots of VIG that will meet the standards for intravenous immune globulin. This IV-VIG will require new recommendations for both dosage and preferred method of administration. The new IV-VIG has a low level of aggregated protein, allowing it to be used by either the IM or IV route. Intravenous VIG will be most likely administered at a lower dose than the intramuscular preparation.

VIG Indications, Precautions and Contraindications

- Historically, VIG has been indicated for accidental implantation involving extensive lesions, eczema vaccinatum, generalized vaccinia, and progressive vaccinia.
- VIG is NOT recommended for mild instances of accidental implantation, mild or limited generalized vaccinia, erythema multiforme, or encephalitis post-vaccination.
- For more information on the adverse reactions mentioned above, go to www.cdc.gov/smallpox.

Concomitant Use of VIG with Vaccination

In some instances, VIG was given concomitantly with vaccination to “prevent” complications in a susceptible person. Not enough is known about the efficacy of this practice to recommend its use. Furthermore, there is currently an insufficient amount of VIG to use prophylactically when the benefits are uncertain.

Dosage

When it was used in the 1950s-1970s, the dosage of VIG varied. In general an initial dose of 0.6 ml/kg body weight was injected intramuscularly and subsequent administration determined by the course of illness.

In severe cases of eczema vaccinatum and progressive vaccinia as much as 1-10 ml/kg was used. These large doses were split into smaller units, and injected at multiple sites spread out over time.

Frequency of Use

Data from a CDC survey indicates that VIG was administered at a rate of 47 uses per 1 million primary vaccinees and 2 uses per million revaccinees.

Cidofovir

Another drug that may be used to treat certain serious smallpox vaccine reactions is cidofovir, an antiviral drug marketed as Vistide.

- Cidofovir is currently licensed for the treatment of CMV retinitis and has demonstrated antiviral activity against poxviruses in vitro, and against cowpox and vaccinia viruses in mice.
- However, its use for the treatment of vaccinia adverse reactions is restricted under an Investigational New Drug (IND) protocol. Under the IND, cidofovir would only be used when VIG was not efficacious.
- Renal toxicity is a known adverse reaction of cidofovir.

Obtaining VIG and Cidofovir

Indications for VIG/cidofovir release

- Vaccinia Immune Globulin (VIG) and cidofovir are indicated for the treatment of certain serious smallpox vaccine adverse events, including progressive vaccinia, eczema vaccinatum, generalized vaccinia (severe form or if underlying illness), and inadvertent inoculation (if judged to be severe due to the number of lesions, toxicity of affected individual, or significant pain). VIG is recommended as the first line of therapy. Cidofovir may be considered as a secondary treatment, and will only be released by CDC after all inventories of VIG have been exhausted, after a patient fails to improve with VIG treatment, or as a last effort for a patient who is otherwise near death.
- VIG and cidofovir are available for civilians through the CDC under Investigational New Drug (IND) protocols for treatment of specific smallpox vaccine reactions. Based on the anticipated number of adverse events resulting from the planned vaccination program for healthcare workers, CDC's supply of VIG should be adequate.
- Physicians at military facilities may request VIG by calling the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) at 301-619-2257 or 888-USA-RIID and asking for the physician on call.

Process for obtaining VIG/cidofovir under Investigational New Drug Protocol (IND)

- Physicians should first contact their State Health Department when seeking consultation for civilian patients experiencing a severe or unexpected adverse event following smallpox vaccination or when requesting VIG or cidofovir. If further consultation is required, or VIG or cidofovir is recommended, the physician will be referred to the **CDC Clinical Information Line (CIL) at 1-877-554-4625**. The nurses staffing the CIL will take basic information and then expedite the call to the CDC Smallpox Vaccine Adverse Events Clinical Consultation Team. The CDC Clinical Consultation Team will provide in-depth consultation and will facilitate VIG or cidofovir release as appropriate.
- According to FDA regulations, VIG or cidofovir released from the CDC must be administered according to their investigational new drug protocols (IND). The IND mandates that the treating physician must become a co-investigator. The responsibilities of the co-investigator are primarily to complete follow-up forms describing the clinical status of the patient being treated with VIG

and/or cidofovir, including the prompt report of any significant adverse reaction in the recipient. Detailed information on the requirements of the IND will be shipped with the products.

- Details on the process for requesting VIG from USAMRIID for vaccinated military personnel with adverse reactions may be obtained at <http://www.smallpox.army.mil/resource/vig.asp?ste=milvax>.

Shipment of VIG/cidofovir

- VIG/cidofovir will be shipped by the National Pharmaceutical Stockpile (NPS). The CDC Smallpox Vaccine Adverse Events Clinical Consultation Team will coordinate the shipment of VIG/cidofovir with NPS. The cost of VIG and cidofovir and the cost of shipping will be covered by the U.S. Government. Arrival of shipments should be expected within 12 hours of the approval for release.

For more information, visit www.cdc.gov/smallpox, or call CDC at 800-CDC-INFO (English and Spanish) or 888-232-6348 (TTY).
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