

7 Chickenpox

HUMAN VARICELLA-ZOSTER IMMUNOGLOBULIN (VZIG) SPECIFIC

Dispensed in vials of: 250mg (minimum 100 i.u./ml) supplied by BPL

Indications

VZIG prophylaxis is recommended for individuals who fulfil **all** of the following three criteria:

- a. A clinical condition which increases the risk of severe varicella: includes immunosuppressed patients (Notes 2), neonates (Notes 3) and pregnant women (Notes 4).
- b. No antibodies to varicella-zoster (VZ) virus. (See The Green Book, Chapter 34. Available at <http://www.dh.gov.uk/PolicyAndGuidance/HealthAndSocialCareTopics/GreenBook/fs/en>) Urgent VZ antibody testing can be performed within 24 hours.
- c. Significant exposure to chickenpox or herpes zoster (see Box 1 below).

Box 1 Definition of a significant exposure of varicella-zoster virus

Three aspects of the exposure are relevant:

Type of varicella-zoster infection in index case: The risk of acquiring infection from an immunocompetent individual with non-exposed zoster lesions (e.g. thoraco-lumbar) is remote. The issue of VZIG should therefore be restricted to those in contact with chickenpox, or the following: disseminated zoster, immunocompetent individuals with exposed lesions (e.g. ophthalmic zoster) or immunosuppressed patients with localised zoster on any part of the body (in whom viral shedding may be greater).

The timing of the exposure in relation to onset of rash in index case: VZIG should normally be restricted to patients exposed to a case of chickenpox or disseminated zoster between 48 hours before onset of rash until crusting has ceased and crusting of all lesions, or day of onset of rash until crusting for those exposed to localised zoster.

Closeness and duration of contact: The following should be used as a guide to the type of exposure, other than maternal/neonatal and continuous home contact, that requires VZIG prophylaxis:

Contact in the same room (e.g. in a house or classroom or a 2-4 bed hospital bay) for a significant period of time (15 minutes or more).

Face to face contact, for example while having a conversation.

In the case of large open wards, where air-borne transmission at a distance has occasionally been reported, the necessity of giving VZIG to all susceptible high-risk contacts should be considered, particularly in paediatric wards where the degree of contact may be difficult to define.

There is no evidence that VZIG is effective in the treatment of severe disease. However, since antibody production can be delayed in immunosuppressed individuals, intravenous commercial preparations of Human normal immunoglobulin (HNIG) may be used to provide an immediate source of antibody.

Where VZIG is not indicated, antiviral treatment may be used for patients in whom attenuation of an attack of chickenpox would be desirable such as those with cystic fibrosis.

Antiviral prophylaxis has been used in immunocompetent children to attenuate an attack of chickenpox (when started within 24 hours of symptoms) but there is no evidence of its effectiveness in immunocompromised and in adults (Box 2 below).

Box 2	<i>Use of antivirals for prophylaxis</i>
Indications:	
For those patients for whom VZIG is not indicated	
Dose:	
Oral acyclovir	
40mg/kg/day in 4 divided doses	
given from days 7 to 14 after exposure	
(Kumagai et al, 1999)	

Dosage and Timing of VZIG

(to be given within 10 days of exposure).

0 – 5 Years	250mg	}	by slow intramuscular injection
6 – 10 Years	500mg		
11 – 14 Years	750mg		
15 years and older	1000mg		

Give second dose if further exposure occurs and three weeks have lapsed since first dose.

Notes

1. If large total doses (>5mls) of intramuscular VZIG are required, it is advisable to administer them in divided doses at different sites.
2. Immunocompromised Patients: (Algorithm 1, page 7-5)

These include:

- a) patients with evidence of severe primary immunodeficiency, for example, severe combined immunodeficiency (SCID), Wiskott-Aldrich syndrome and other combined immunodeficiency syndromes
- b) all patients currently being treated for malignant disease with immunosuppressive chemotherapy or radiotherapy, and for at least six months after terminating such treatment
- c) all patients who have received a solid organ transplant and are currently on immunosuppressive treatment
- d) patients who have received a bone marrow transplant until at least 12 months after finishing all immunosuppressive treatment, or longer where the patient has developed graft-versus-host disease.
- e) all patients receiving systemic high-dose steroids until at least three months after treatment has stopped. This would include children who receive prednisolone, orally or rectally, at a daily dose (or its equivalent) of 2mg/kg/day for at least one week, or 1mg/kg/day for one month. For adults, an equivalent dose is harder to define but immunosuppression should be considered in those who receive 40mg of prednisolone per day for more than one week. Occasionally, there may be individuals on lower doses of steroids who may be immunosuppressed, and are at increased risk from infections.

- f) patients receiving other types of immunosuppressive drugs (e.g. azathioprine, ciclosporin, methotrexate, cyclophosphamide, leflunomide and the newer cytokine inhibitors) alone or in combination with lower doses of steroids. The advice of the physician in charge or immunologist should be sought for at least six months after treatment
- g) patients with immunosuppression due to HIV infection

Patients with gammaglobulin deficiencies who are receiving replacement therapy with intravenous normal immunoglobulin, do not require VZIG.

Determination of VZ immune status

Whenever possible, immunosuppressed contacts should be tested irrespective of their history of chickenpox. However, VZIG administration should not be delayed past 7 days after initial contact while an antibody test is done. Under these circumstances VZIG should be given on the basis of a negative history of chickenpox. If the patient has a positive history of chickenpox, wait for the antibody results. Those with a positive history in whom VZ antibody is not detected by a sensitive assay should be given VZIG.

VZIG is not indicated in immunosuppressed contacts with detectable antibody as the amount of antibody provided by VZIG will not significantly increase VZ antibody titres in those who are already positive. Second attacks of chickenpox can occasionally occur in immunosuppressed VZ antibody positive patients, but these are likely to be related to defects in cell-mediated immunity.

3. Neonates: (Algorithm 2, page 7-6)

VZIG is recommended for the following:

- Infants whose mothers develop chickenpox (but not herpes zoster) in the period 7 days before to 7 days after delivery. VZIG can be given without antibody testing of the infant.

VZIG is not usually required for infants born more than 7 days after the onset of maternal chickenpox or whose mothers develop zoster before or after delivery as these infants will have maternal antibody.

VZIG is also recommended for the following:

- VZ antibody-negative infants exposed to chickenpox or herpes zoster (other than in the mother) in the first 7 days of life.
- VZ antibody-negative infants of any age, exposed to chickenpox or herpes zoster while still requiring intensive or prolonged special care nursing.

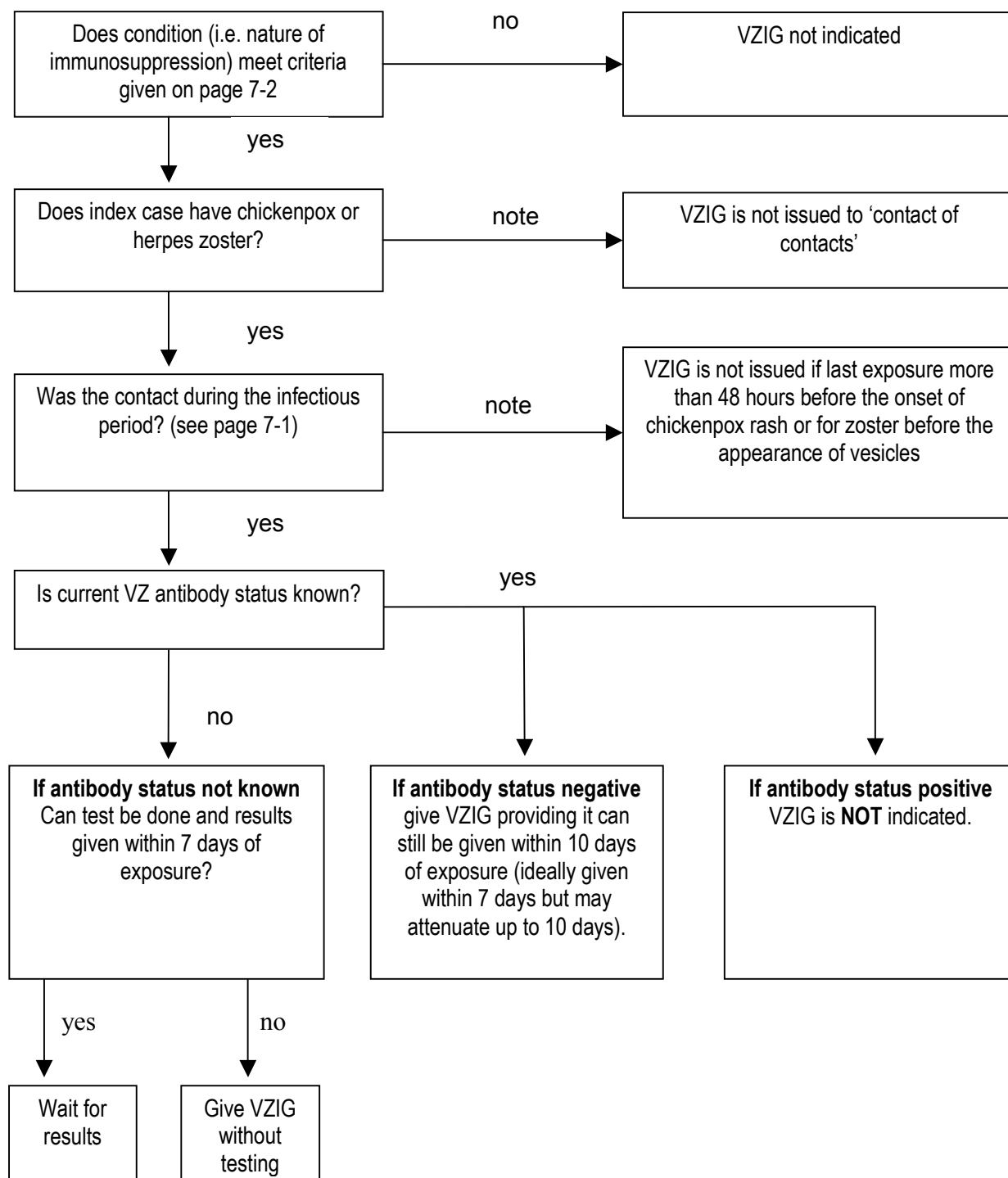
For infants in these two exposure groups who are born before 28 weeks gestation, weighed less than 1000g at birth, are more than 60 days old, or have had repeated blood sampling with replacement by packed red cell infusion, maternal antibody may not be present despite a positive maternal history of chickenpox. It is therefore recommended that where possible, such infants are tested to determine their VZ antibody status in the event of a contact. Other infants whose mothers have a positive history of chickenpox and/or a positive VZ antibody result will usually have maternal antibody and do not require VZIG.

4. Pregnant Women: (Algorithm 3, page 7-7)

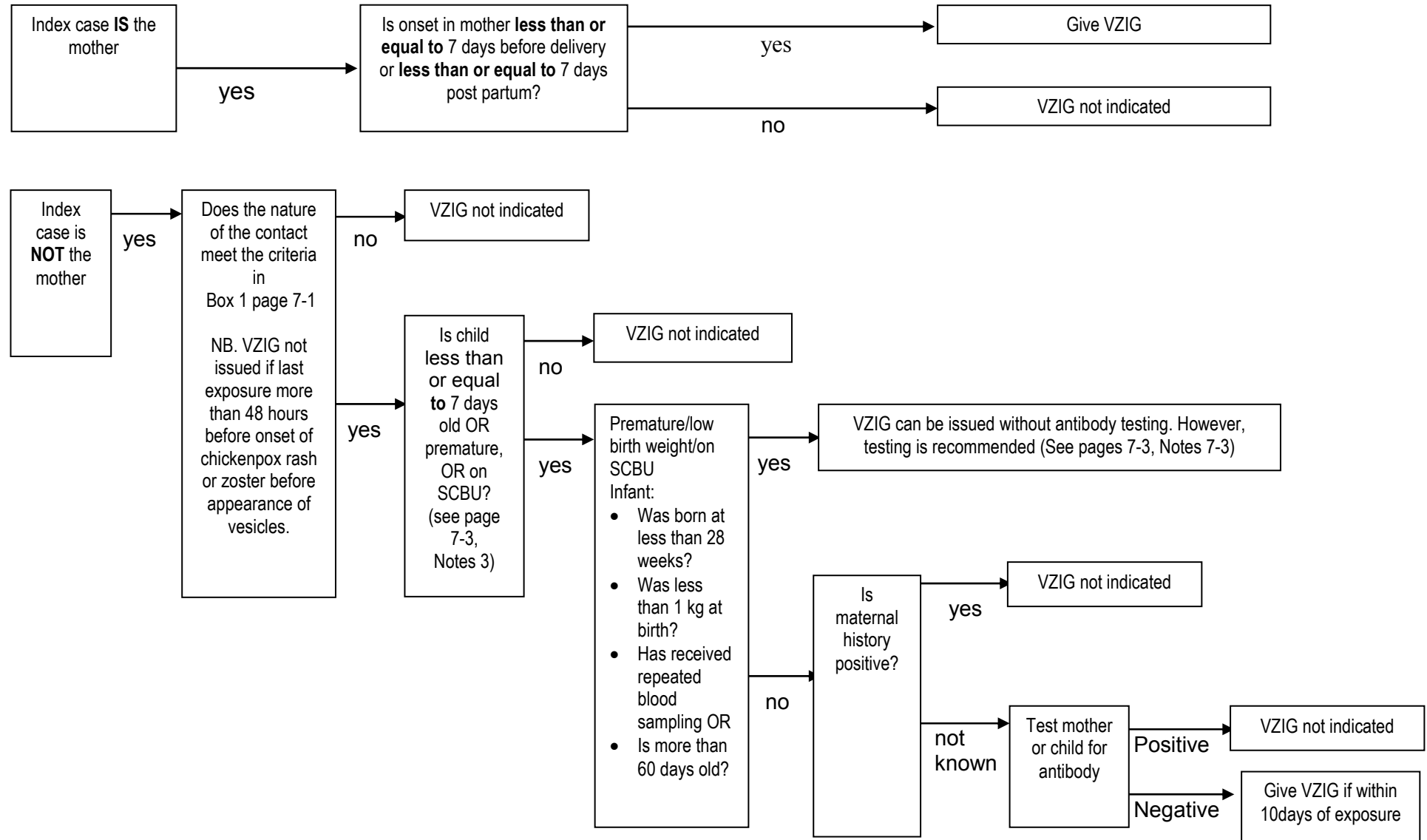
- a) VZIG is recommended for VZ antibody negative pregnant contacts exposed at any stage of pregnancy, providing VZIG can be given within 10 days of contact (for household contacts count from day of onset of rash). However, when supplies of VZIG are short, issues to pregnant women may be restricted.
- b) Pregnant contacts with a positive history of chickenpox do not require VZIG. Those with a negative history must be tested for VZ antibody before VZIG is given. The outcome in pregnant women is not adversely affected if administration of VZIG is delayed up to 10 days after initial contact while a VZ antibody test is done. There is therefore still time to test for VZ antibody even when the woman presents relatively late after contact.

Further information about chickenpox in pregnancy is provided by the Royal College of Obstetrics and Gynaecology at

http://www.rcog.org.uk/resources/Public/pdf/greentop13_chickenpox0907.pdf

Algorithm 1: VZIG algorithm for immunocompromised patients

Algorithm 2: VZIG algorithm for neonates (See page 7-3, Notes 3 definition of a neonate)



Algorithm 3: VZIG algorithm for pregnant women