Varicella Zoster Postexposure Prophylaxis

A) Contents

B) Purpose and Scope

This guideline has been written to help decide on what testing and management is required for individuals exposed to varicella zoster virus. It is based on PHE guidance (Guidelines on post exposure prophylaxis for varicella/shingles April 2022) and adapted for local use. Most, but not every case, will be covered by the document and it is for guidance only.

Post exposure prophylaxis is recommended for individuals who fulfil all of the following 3 criteria-

- significant exposure to chickenpox (varicella) or shingles (zoster) during the infectious period
- at increased risk of severe chickenpox such as immunosuppressed individuals, neonates and pregnant women
- no antibodies to varicella-zoster virus (VZV) – urgent VZV antibody testing can be performed within 24 hours

Note-Over 90% of adults born or brought up in the UK will be immune, and many people with no history will actually have VZ IgG detected when tested. Where possible, any patient in whom prophylaxis is being considered should have their VZV IgG level checked.

In summary-

- Antivirals (acyclovir/valaciclovir) are now recommended for post-exposure prophylaxis for all at risk groups apart from susceptible neonates described below
- Varicella zoster immunoglobulin (VZIG) is recommended for susceptible neonates exposed within one week of delivery (either in utero or post-delivery) and in those for whom oral antivirals are contraindicated (rare). VZIG is a blood-pooled product given by IM injection. In individuals with renal impairment or intestinal malabsorption e.g. inflammatory bowel disease, aciclovir / valaciclovir dose adjustment or VZIG should be considered.

C) Responsibility and Training Requirements

Virology Medics

D) Definitions

See Appendix 2

E) Procedure

Risk assessment

When called about a VZV exposure, assess as per details below and then discuss with a senior virologist:

A. Confirm patient is in an 'at risk' group:

- Immunosuppressed (see Green Book – VZV chapter 34 – for further information)
- Pregnant females
- Neonates (see algorithm 3)

If not in any of the above groups, post exposure prophylaxis is not indicated. If there are other concerns about the patient, consider on a case-by-case basis whether acyclovir / valaciclovir prophylaxis could be given, or if any other infection control measures (e.g. work exclusion) are required.

B. Confirm that a significant exposure has occurred

Three aspects of exposure to VZV during the infectious period are relevant when considering the need for post-exposure prophylaxis (PEP) for a susceptible high risk individual:

a. Type of VZV infection in index case-PEP indicated for at risk individuals exposed to:
   i. **Chickenpox** exposure >15 minutes in same small room (e.g. house, classroom or hospital bay) or face to face contact
   ii. **Shingles in an immunocompetent patient:** direct contact with vesicles or exposure to shingles at an uncovered site e.g. ophthalmic lesions, from rash onset until 5 days after onset of rash.

iii. **Shingles in an immunocompromised patient:** rash at any site of the body, due to greater viral shedding including from the oropharynx (from rash onset until lesions healed).

Confirm how the diagnosis has been made in the index case (exposure source); have they been seen by a health professional or are there plans to be seen; have they had any swabs taken? If in doubt about the diagnosis, ensure appropriate investigations are done.

b. Timing of the exposure-

- The day of exposure is defined as the date of the rash in the index patient if the index is a household contact. If not a household contact then date of first or only contact with the index case 24 hours before the rash appears to 5 days after the onset of rash or until lesions crust.
- PEP should be offered to individuals in the at risk group exposed during the infectious period-24 hours before the rash appears to 5 days after the onset of rash(immunocompetent patient) or until lesions crust(immunocompromised patient)
- Contact with healed/scabbed rash is not considered to be a risk.

c. Closeness and duration of contact- In addition to household contacts, the following contacts in the specified risk groups require PEP:

i. those in the same small room (for example in a house or classroom or a 2 to 4 bed hospital bay) for a significant period of time (15 minutes or more)
ii. face to face contact, for example while having a conversation
iii. immunosuppressed contacts on large open wards, where air-borne transmission at a distance has occasionally been reported, particularly in paediatric wards where the degree of contact may be difficult to define

C. Assess for susceptibility-

- For immunocompetent individuals including pregnant women, a history of previous chickenpox, shingles or 2 doses of varicella vaccine is sufficient evidence of immunity.

  In those without such a history, urgent antibody testing should be undertaken on a recent blood sample (booking blood samples are acceptable for pregnant women if available). PEP should be offered if VZV IgG is < 100mIU/ml.

- For immunosuppressed patients, a history of previous infection or vaccination is not a reliable history of immunity and VZV antibody levels should be checked urgently. Individuals with VZV antibody levels of 150 mIU/ml or greater are unlikely to benefit from VZIG

- Follow appropriate further algorithm: management of pregnant or immunosuppressed or neonatal patients.Discuss with a Virology Consultant (or SpR) and decide whether post exposure prophylaxis is required or not.

Actions to be taken by the Senior Virologist

1. Arrange for VZV IgG test on a serum sample (if results not already available).

2. If aciclovir / valaciclovir post-exposure prophylaxis is advised (see attached algorithms) the requesting clinician should be asked to arrange a prescription to be sent to pharmacy and pharmacy to dispense the prescription for the patient.

3. Where VZIG is recommended:

If the clinician calling is a GP-

Give them the telephone number of RIgS ((Rabies and Immunoglobulin Service, PHE Colindale, London, telephone number 03301281020) and ask them to arrange the issue/delivery of VZIG directly with them.

If the clinician calling is hospital / community based

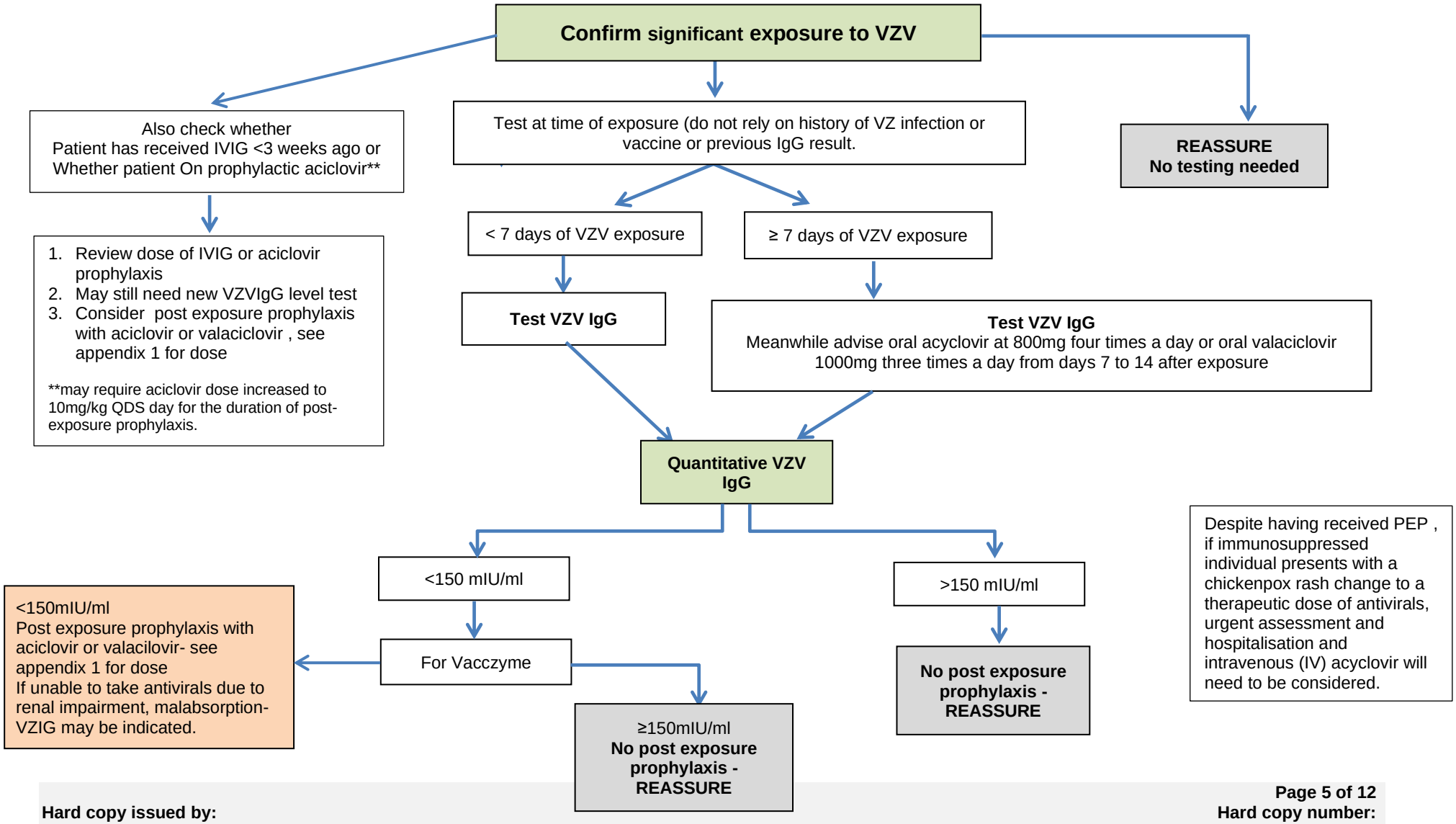
- Telephone RIgS (Rabies and Immunoglobulin Service, PHE Colindale, London, telephone number 03301281020), and arrange for VZIG to be sent to the STH pharmacy. Ask the requesting clinician to send a prescription for it to their respective pharmacy to release the VZIG and arrange for the patient to receive VZIG. To avoid making a repeat phone call you may wish to arrange this with the clinician at the time of the initial phone call.

- For Sheffield Children Hospital (SCH); Doncaster / Bassettlaw, Chesterfield and Derby patients -Request the clinician to arrange the VZIG delivery directly with RIgS and arrange for it to go to the respective pharmacies (SCH; Doncaster/Bassettlaw or Derby pharmacy).

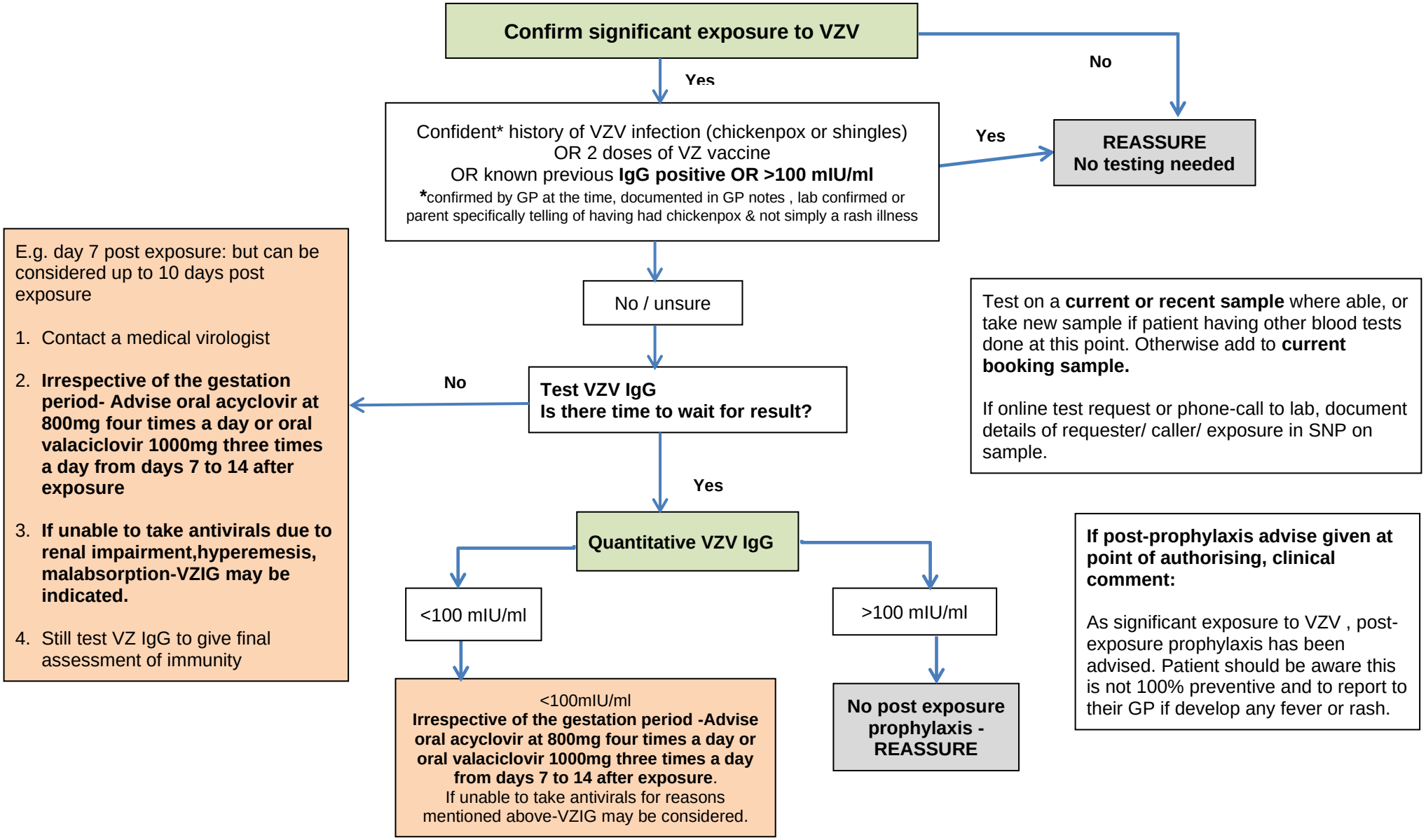
Barnsley /Rotherham to make their own arrangements with RIgS for VZIG

Management of Specific risk groups-

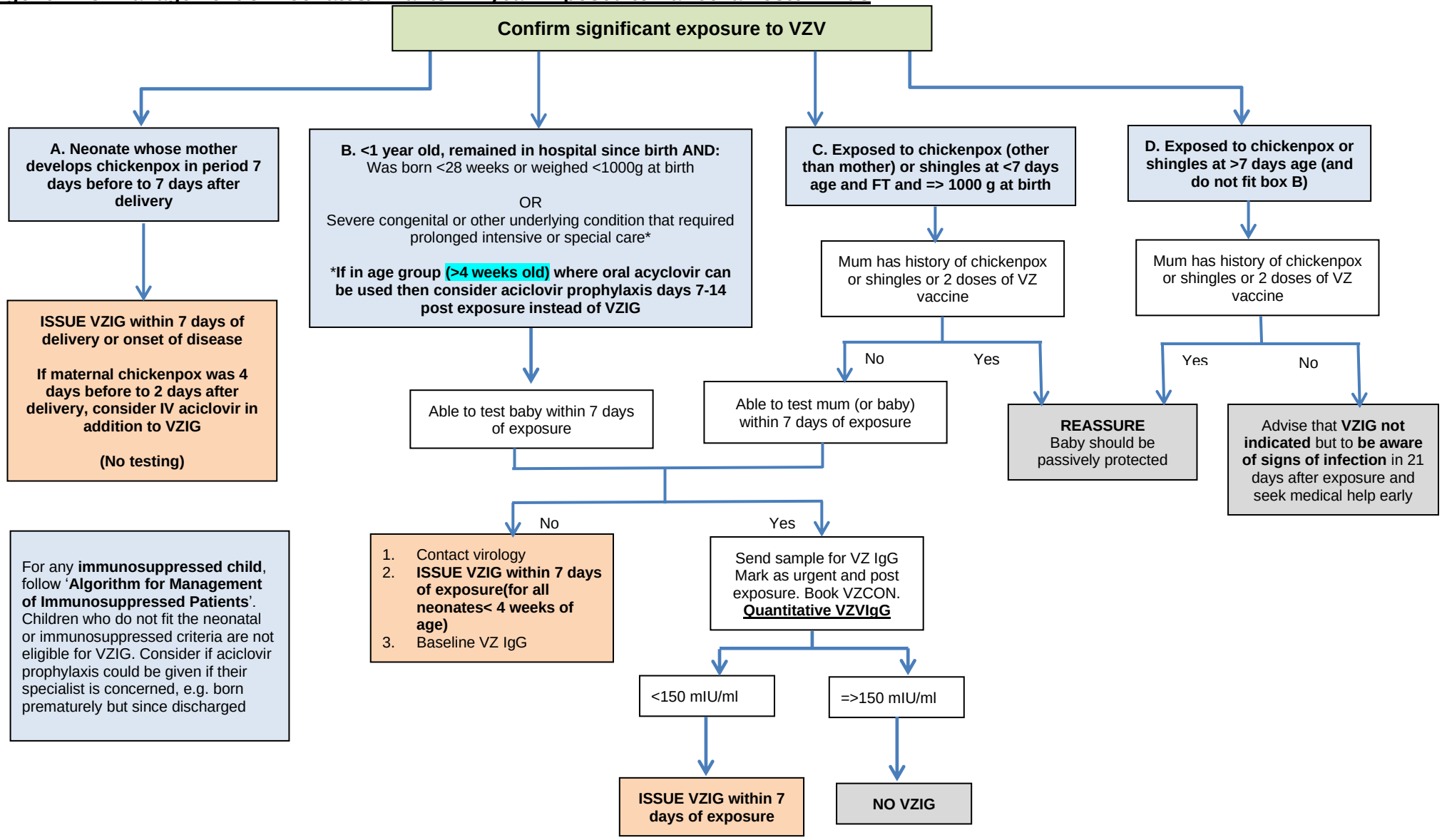
Algorithm 1: Management of Immunosuppressed patients Exposed to Varicella Zoster Virus



Algorithm 2: Management of Pregnant Patients Exposed to Varicella Zoster Virus

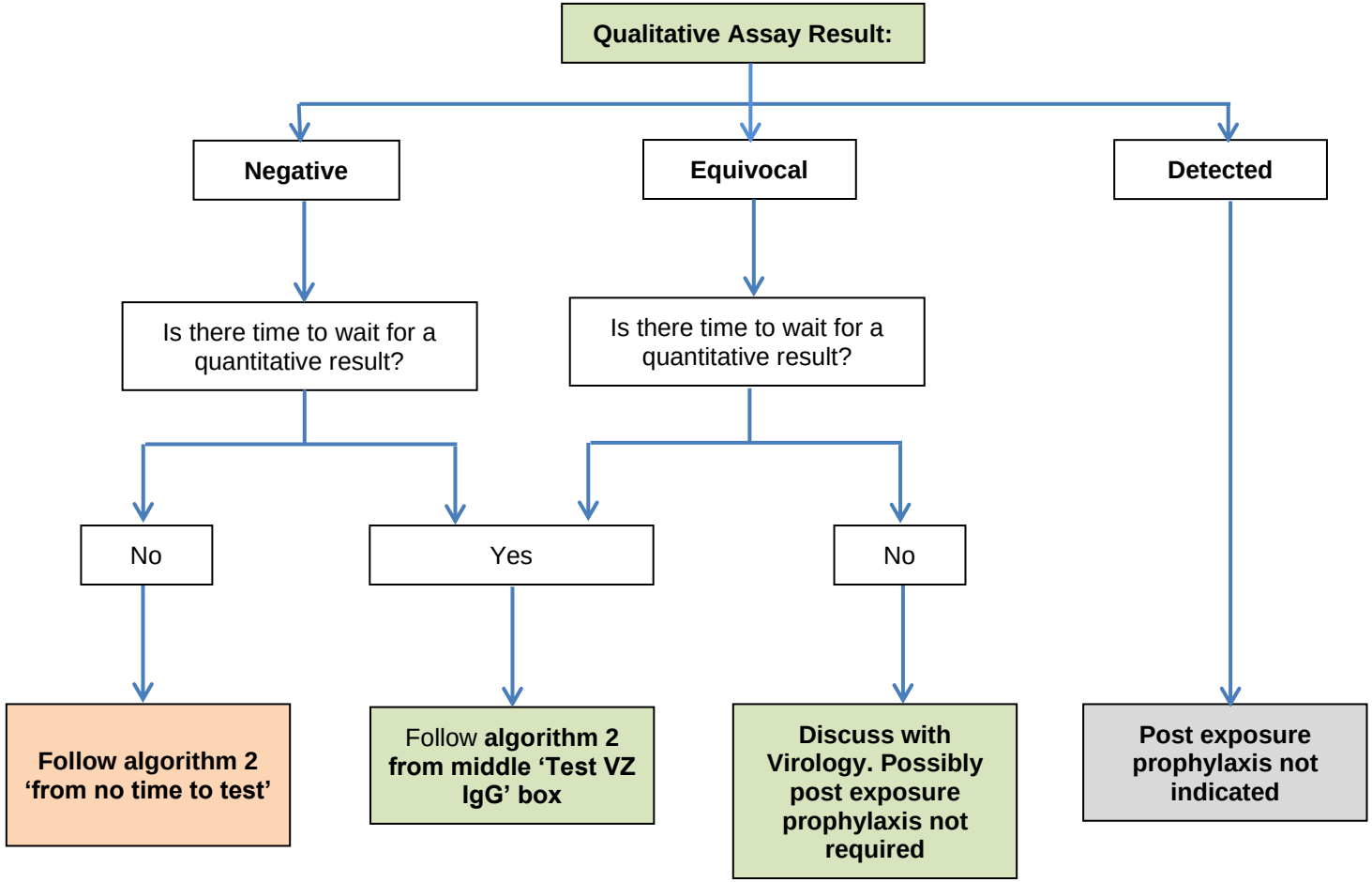


Algorithm 3: Management of Neonates/ Infants < 1 year Exposed to Varicella Zoster Virus

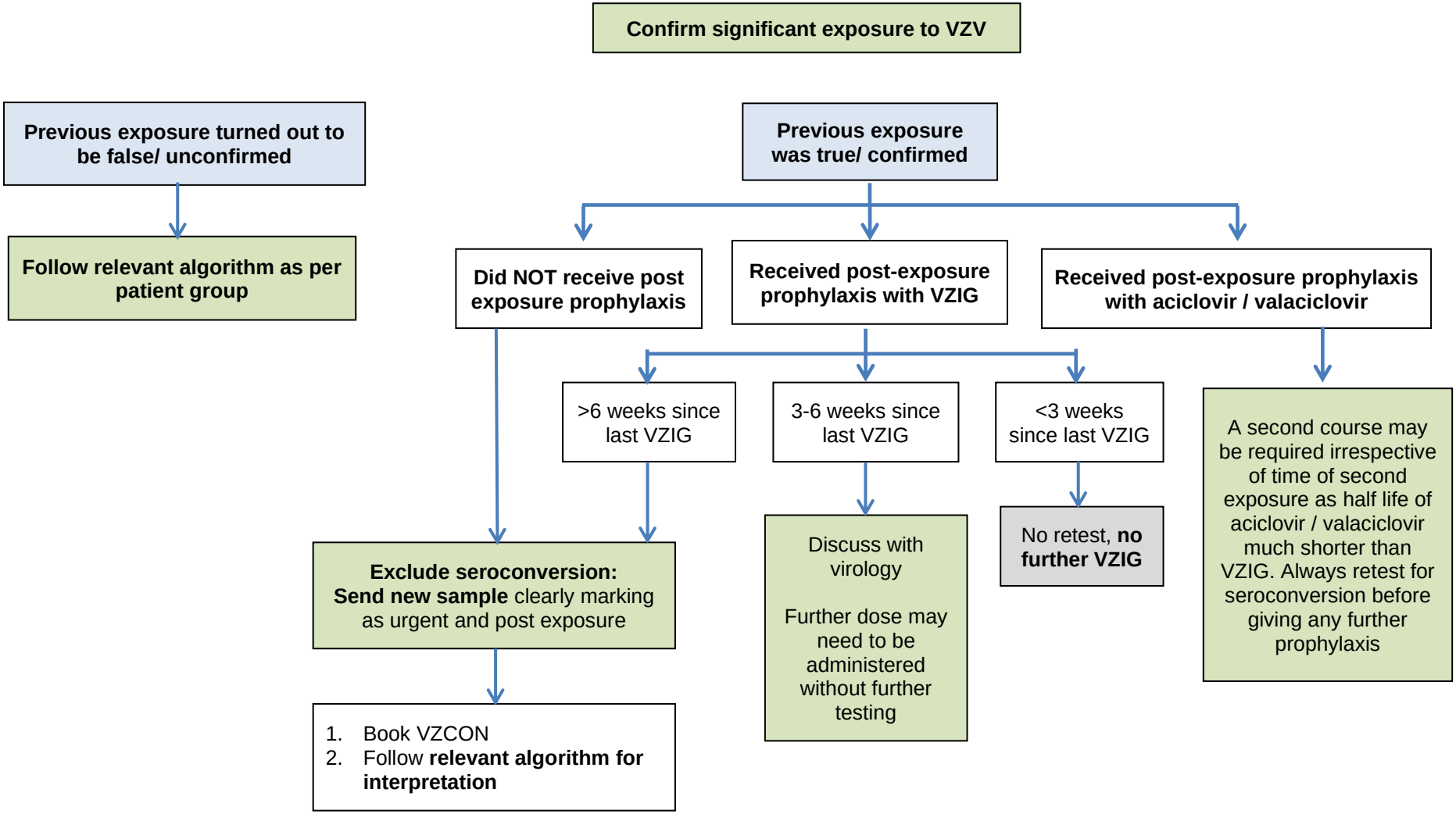


Algorithm 4: DGH Management of Pregnant Individuals Exposed to Varicella Zoster Virus

Following updated guidance from PHE, a 'quantitative' assay should be used to confirm results in some situations. In STH and Doncaster we use this type for our screening test, as well as our 2nd line assay. Barnsley, Rotherham, Chesterfield and Derby use 'qualitative' assays for VZV IgG, and so will need to send some samples to Sheffield to 'quantify' the result and make a decision about whether or not VZIG is needed, as below:



Algorithm 5: Management of Second Exposure to Varicella Zoster Virus*



F) References and Related Documents

N/A

G) Appendices

Appendix 1- Doses of post exposure prophylaxis

Table 1. Recommended doses of oral antivirals

	Oral Aciclovir	Oral Valaciclovir
Infants over 4 weeks to children under 2 years age	10mg/kg 4 times daily, days 7 to 14 after exposure	Not recommended
Children 2 to 17 years of age	10mg/kg (up to a maximum of 800mg), 4 times daily, from days 7 to 14 after exposure	20 mg/kg (up to a maximum 1,000mg) 3 times daily, from days 7 to 14 after exposure
Adults	800mg 4 times daily, from days 7 to 14 after exposure	1,000mg 3 times daily, from days 7 to 14 after exposure

Individuals on long term aciclovir or valaciclovir prophylaxis, for example post-haematopoietic stem cell transplant, may require their dose of aciclovir to be temporarily increased to the dosage as given in Table 1 above.
Further doses of PEP following second exposure-
If there is a second or subsequent exposure to chickenpox further courses of antivirals can be initiated starting 7 days after the date of onset or exposure.

Human varicella-zoster immunoglobulin (VZIG)

VZIG is issued by the Rabies and Immunoglobulin Service, UK Health Guidelines on post exposure prophylaxis (PEP) for varicella/shingles (April 2022) 10 Security Agency, Colindale (tel: 0330 128 1020), and some local UK HSA laboratories, following a risk assessment(when required) VZIG is prepared by Bio Products Limited (BPL) from the pooled plasma from non-UK blood donors and is dispensed in vials of 250 mg (minimum 100 IU/ml).

Table 2: VZIG dosage-Given by slow intramuscular injection

0 to 5 years	250mg
6 to 10 years	500mg
11 to 14 years	750mg
15 years and older	1000mg

When a large-volume injection such as VZIG is to be given, it should be administered deep into a large muscle mass. If more than 3ml is to be given to young children and infants, or more than 5ml to older children and adults, the immunoglobulin should be divided into smaller amounts and given into different sites. The upper outer quadrant of the buttock can be used to administer VZIG injection in neonates and infants.
Individuals receiving regular IVIG replacement therapy do not require VZIG if the most recent dose was administered <= 3 weeks before exposure.

Intravenous immunoglobulin (IVIG)

Contacts with bleeding disorders who cannot receive antivirals or be given an intramuscular injection should be given intravenous human normal immunoglobulin (IVIG) at a dose of 0.2g per kg body weight (4ml/kg for a 5% solution) instead. This will produce serum VZV antibody levels equivalent to those achieved with VZIG. IVIG should ideally be administered within 10 days (preferably 7 days for neonates and immunosuppressed contacts), of the first contact, but can be given later if necessary. Supplies of intravenous immunoglobulin (IVIG), if indicated, should be available from the local hospital pharmacy or from the manufacturer

Appendix 2. Immunosuppression definitions

Individuals with primary or acquired immunodeficiency states due to conditions including:

• acute and chronic leukaemias, and clinically aggressive lymphomas (including Hodgkin's lymphoma) who are less than 12 months since achieving cure

• individuals under follow up for a chronic lymphoproliferative disorders including haematological malignancies such as indolent lymphoma, chronic lymphoid leukaemia, myeloma, Waldenstrom's macroglobulinemia and other plasma cell dyscrasias (note: this list not exhaustive)

• immunosuppression due to HIV/AIDS with a current CD4 count of below 200 cells/µl (aged 5 years or less, with a CD4 count below 500 cells/µl.)

• primary or acquired cellular and combined immune deficiencies – those with lymphopaenia (< 3g/L) due to primary immunodeficiency (for example common variable immunodeficiency) or secondary to disease or therapy

• those who have received an allogeneic (cells from a donor) or an autologous (using their own cells) stem cell transplant in the previous 24 months

• those who have received a stem cell transplant more than 24 months ago but have ongoing immunosuppression or graft versus host disease (GVHD)

• persistent agammaglobulinaemia (IgG < 3g/L) due to primary immunodeficiency (for example common variable immunodeficiency) or secondary to disease or therapy

Individuals on immunosuppressive or immunomodulating therapy including:

• those who are receiving or have received in the previous 6 months immunosuppressive therapy for a solid organ transplant

• those who are receiving or have received in the previous 3 months targeted therapy for autoimmune disease, such as JAK inhibitors or biologic immune modulators including B-cell targeted therapies (including rituximab but for which a 6 month period should be considered immunosuppressive), monoclonal tumour necrosis factor inhibitors (TNFi), T-cell co-stimulation modulators, soluble TNF receptors, interleukin (IL)-6 receptor inhibitors, IL-17 inhibitors, IL 12/23 inhibitors, IL 23 inhibitors (note: this list is not exhaustive)

• those who are receiving or have received in the past 6 months immunosuppressive chemotherapy or radiotherapy for any indication

Individuals with chronic immune mediated inflammatory disease who are receiving or have received immunosuppressive therapy:

• moderate to high dose corticosteroids (equivalent ≥20mg prednisolone per day; children 1 mg/kg/day) for more than 10 days in the previous month

• long term moderate dose corticosteroids (equivalent to ≥10mg prednisolone per day or children 0.5 mg/kg/day for more than 4 weeks) in the previous 3 months

• adults on non-biological oral immune modulating drugs for example methotrexate >20mg per week (oral and subcutaneous), azathioprine >3.0mg/kg/day; 6- mercaptopurine >1.5mg/kg/day, mycophenolate >1g/day, in the previous 3 months

• children on any dose of non-biological oral immune modulating drugs

• certain combination therapies at individual doses lower than stated above, including those on ≥7.5mg prednisolone per day in combination with other immunosuppressants (other than hydroxychloroquine or sulfasalazine) and those receiving methotrexate (any dose) with leflunomide in the previous 3 months

Note-

- Individuals who have received a short course of high dose steroids (equivalent >40mg prednisolone per day or children 2 mg/kg/day for more than a week) for any reason in the previous month.

- Individuals who had received brief immunosuppression (≤40mg prednisolone per day) for an acute episode (for example asthma / chronic obstructive pulmonary disease (COPD) / coronavirus (COVID-19)) and individuals on replacement corticosteroids for adrenal insufficiency

  -are not considered severely immunosuppressed and can be treated with the standard post exposure treatment