Clinical Guideline
Herpes Simplex Virus (HSV) Infection in Pregnancy

Policy developed by: SA Maternal, Neonatal & Gynaecology Community of Practice
Approved SA Health Safety & Quality Strategic Governance Committee on: 01 March 2017
Next review due: 31 March 2020

Summary
The purpose of the Herpes Simplex Virus (HSV) Infection in Pregnancy Perinatal Practice Guideline is to give clinicians information on the causes of maternal collapse and subsequent management, including resuscitation algorithms, perimortem caesarean section and post resuscitation care.

Keywords
Perinatal practice guideline, clinical guideline, Herpes Simplex Virus (HSV) Infection in Pregnancy, herpes simplex virus, genital herpes, vesicles, HSV, aciclovir, herpes lesions, neonatal signs of HSV disease, Neonatal HSV CNS disease, HSV transmission

Policy history
Is this a new policy?  N
Does this policy amend or update an existing policy?  Y v4.0
Does this policy replace an existing policy?  Y

Applies to
All Health Networks
CALHN, SALHN, NALHN, CHSALHN, WCHN, SAAS

Staff impact
All Staff

PDS reference
CG234

Version control and change history

<table>
<thead>
<tr>
<th>Version</th>
<th>Date from</th>
<th>Date to</th>
<th>Amendment</th>
</tr>
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<td>Current</td>
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South Australian Perinatal Practice Guidelines

Genital Herpes Simplex (HSV) Infection in Pregnancy

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Note

This guideline provides advice of a general nature. This statewide guideline has been prepared to promote and facilitate standardisation and consistency of practice, using a multidisciplinary approach. The guideline is based on a review of published evidence and expert opinion.

Information in this statewide guideline is current at the time of publication.

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Health practitioners in the South Australian public health sector are expected to review specific details of each patient and professionally assess the applicability of the relevant guideline to that clinical situation.

If for good clinical reasons, a decision is made to depart from the guideline, the responsible clinician must document in the patient’s medical record, the decision made, by whom, and detailed reasons for the departure from the guideline.

This statewide guideline does not address all the elements of clinical practice and assumes that the individual clinicians are responsible for discussing care with consumers in an environment that is culturally appropriate and which enables respectful confidential discussion. This includes:

- The use of interpreter services where necessary,
- Advising consumers of their choice and ensuring informed consent is obtained,
- Providing care within scope of practice, meeting all legislative requirements and maintaining standards of professional conduct, and
- Documenting all care in accordance with mandatory and local requirements

Explanation of the Aboriginal artwork:

The Aboriginal artwork used symbolises the connection to country and the circle shape shows the strong relationships amongst families and the Aboriginal culture. The horse shoe shape design shown in front of the generic statement symbolises a woman and those enclosing a smaller horse shoe shape depicts a pregnant woman. The smaller horse shoe shape in this instance represents the unborn child. The artwork shown before the specific statements within the document symbolises a footprint and demonstrates the need to move forward together in unison.

Australian Aboriginal Culture is the oldest living culture in the world yet Aboriginal people continue to experience the poorest health outcomes when compared to non-Aboriginal Australians. In South Australia, Aboriginal women are 2-5 times more likely to die in childbirth and their babies are 2-3 times more likely to be of low birth weight. The accumulative effects of stress, low socio economic status, exposure to violence, historical trauma, culturally unsafe and discriminatory health services and health systems are all major contributors to the disparities in Aboriginal maternal and birthing outcomes. Despite these unacceptable statistics the birth of an Aboriginal baby is a celebration of life and an important cultural event bringing family together in celebration, obligation and responsibility. The diversity between Aboriginal cultures, language and practices differ greatly and so it is imperative that perinatal services prepare to respectively manage Aboriginal protocol and provide a culturally positive health care experience for Aboriginal people to ensure the best maternal, neonatal and child health outcomes.

Purpose and Scope of the PPG

The purpose of this guideline is to give clinicians information on the diagnosis and management of women with genital herpes simplex virus (HSV) infection during pregnancy, labour and birth. It includes subsequent care of their neonate(s).
Flowchart 1: HSV in Pregnancy: Risk of Vertical Transmission

**Past History of Genital Herpes**

- Recurrent herpes (HSV IgG same as HSV type in genital area)
  - If HSV detected in genital tract at delivery: risk of transmission is 1-3%; risk greater for recurrent HSV1 (15%) compared to recurrent genital HSV2 infection (<0.01%)

**No Past History of Genital Herpes**

- First episode of genital herpes during pregnancy / labour
  - Type specific PCR +/- culture (genital swab) and HSV type specific serology (blood sample)

**Primary First Episode Infection**

- Overall risk of transmission <1.0%
  - If HSV detected in genital tract at delivery: risks same as for recurrent herpes

**Non Primary First Episode Infection**

- Primary first episode infection i.e. HSV detected in genital swab but the same serotype antibody is not detected in blood e.g. HSV1 +ve genital swab and HSV1 IgG -ve and HSV2 IgG +ve in blood or HSV2 +ve genital swab and HSV2 IgG -ve and HSV1 IgG +ve in blood
  - Seroconversion well before delivery (i.e. prior to 30-34 weeks)

- **YES**
  - Risks same as for recurrent herpes
- **NO** (or unknown)
  - High risk of transmission 25-50%
Flowchart 2: Management of Genital HSV in Pregnancy

HISTORY OF GENITAL HSV (laboratory confirmed)

- Serial genital cultures not predictive of shedding during labour, so are not recommended
  
  Consider use of suppressive antiviral therapy from 36 weeks in women with multiple recurrent overt lesions or prior if frequent symptomatic recurrences

  In labour: Careful speculum examination

  - No active lesion seen
    - Proceed to vaginal birth. Fetal scalp electrode, forceps and vacuum delivery may increase risk of transmission to newborn
  
  - Active lesions seen
    - Management of newborn as per PPG or Neonatal Team

NO PRIOR HISTORY OF GENITAL HSV

- First genital HSV infection diagnosed during pregnancy

  Obtain HSV serology (type specific) and type specific PCR +/- culture (genital swab)

  Recurrent infection (HSV AB +ve to same HSV from genital swab)

  Diagnosis made early in pregnancy (first or second trimester): Counsel as for Flowchart 1

  Diagnosis made late in pregnancy (i.e. third trimester)

  - Consider suppressive antiviral from 36 weeks until birth

  - New infection (HSV AB -ve to same HSV from genital swab)

  Deliver by caesarean section. Perform HSV type specific PCR on genital swab. If vaginal birth unavoidable: fetal scalp electrode, forceps and vacuum delivery may increase risk of transmission to newborn

  Management of newborn as per PPG or Neonatal Team
Table of Contents

Flowchart 1: HSV in Pregnancy: Risk of Vertical Transmission
Flowchart 2: Management of Genital HSV in Pregnancy
Summary of Practice Recommendations
Abbreviations
Definitions

Literature Review

Antenatal Management
Infection precautions
Past history of genital herpes
First episode of genital herpes during pregnancy
  First and second trimester acquisition of HSV (types 1 or 2)
  Third trimester acquisition
Recurrent genital herpes during pregnancy
Recommended treatment options for herpes simplex virus

Genital herpes in preterm prelabour rupture of the membranes (PPROM)
First episode (primary) of genital herpes with PPROM
  Immediate birth
  Initial conservative management
  Recurrent genital herpes with PPROM

Intrapartum management
Recurrent genital HSV infection
  No active lesions seen
  Active lesions seen
Primary genital HSV lesions at onset of labour
  Caesarean birth
  Vaginal birth

Postpartum care of the neonate
Asymptomatic infant and low risk of infection
  24 hours after birth
Asymptomatic infant and high risk of infection
  At birth
  Treatment
  24 hours after birth
Symptomatic infant with clinical signs of HSV disease
  Treatment
  Management
  Follow up
  Oral Aciclovir Prophylaxis to prevent CNS Sequelae
  Neonatal HSV CNS disease +/- disseminated infection
  Skin, eye, mouth or disseminated infection without CNS involvement

References
Acknowledgements
Summary of Practice Recommendations

> Most genital HSV infections (primary, non-primary, recurrent) are asymptomatic
> Obtain serology for HSV-1 and HSV-2 and also HSV PCR typing from the genital tract for diagnosis
> Consider use of suppressive antiviral treatment from 36 weeks onwards for women with recurrent lesions\(^2\)
> Women with HSV acquisition in the first or second trimester should have treatment as per ‘first episode’ followed by suppressive antiviral treatment from 36 weeks until birth. If no active lesions at the time of birth, vaginal birth should be anticipated
> Women with recurrent HSV infection should have vaginal birth as an option even in the presence of active lesions (1-3% transmission to neonate)
> Caesarean section reduces risk of HSV transmission in women shedding HSV at the time of birth
> Caesarean section should be the recommended mode of birth for all women developing first episode genital herpes in the third trimester
> Avoid fetal scalp electrode and fetal blood sampling during labour
> Neonatal management is dependent on risk of transmission and whether symptoms are present or not

Abbreviations

<table>
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<tr>
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<th>Description</th>
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<tr>
<td>ASID</td>
<td>Australasian society for infectious diseases</td>
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<tr>
<td>CNS</td>
<td>Central nervous system</td>
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<tr>
<td>CSF</td>
<td>Cerebro-spinal fluid</td>
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<tr>
<td>DNA</td>
<td>Deoxyribonucleic acid</td>
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<td>e.g.</td>
<td>For example</td>
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<td>et al.</td>
<td>And others</td>
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<td>&gt;</td>
<td>Greater than</td>
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<tr>
<td>HSV</td>
<td>Herpes simplex virus</td>
</tr>
<tr>
<td>HSV - 1</td>
<td>Herpes simplex virus type 1</td>
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<tr>
<td>HSV - 2</td>
<td>Herpes simplex virus type 2</td>
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<tr>
<td>kg</td>
<td>Kilogram/s</td>
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<tr>
<td>&lt;</td>
<td>Less than</td>
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<tr>
<td>≤</td>
<td>Less than or equal to</td>
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<tr>
<td>mg</td>
<td>Milligram/s</td>
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<tr>
<td>%</td>
<td>Percent</td>
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<tr>
<td>PCR</td>
<td>Polymerase chain reaction</td>
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<td>PPROM</td>
<td>Preterm prelabour rupture of the membranes</td>
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<td>SA</td>
<td>South Australia</td>
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<tr>
<td>SOGC</td>
<td>The Society of Obstetricians and Gynaecologists of Canada</td>
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Definitions

| Genital Herpes Simplex Virus | Genital herpes is caused by the herpes simplex virus either type 1 or 2 (HSV-1 or HSV-2)\(^1\) After infection, the herpes simplex virus (HSV) travels along the nerves connected to the affected area and lies dormant within nerve ganglia. The virus can reactivate later and travel along the nerve to the skin surface on or near the genitals causing a recurrence of tender fluid filled vesicles containing numerous virus |
| Past history of genital herpes | Confirmed from HSV IgG serology (may be HSV-1 or HSV-2) and is consistent with the HSV type (either HSV-1 or HSV-2) by polymerase chain reaction (PCR) isolated from the genital tract |
| Primary first episode | Seronegative for both HSV-1 IgG and HSV-2 IgG with positive HSV (either type 1 or 2) PCR isolated from the genital tract. This provides evidence of first exposure to HSV (either type 1 or 2) |
| Non-primary first episode | Previous confirmed exposure to one type of HSV (by either HSV-1 IgG or HSV-2 IgG) and this is not consistent with HSV PCR type isolated from the genital tract in the peripartum period (e.g. confirmed HSV-1 IgG positive by serology with a first presentation of HSV-2 on PCR from the genital tract) |

Literature review

HSV may be prominent during pregnancy due to relative maternal immunosuppression in pregnancy\(^1\)
Most genital HSV infections (primary, non-primary, recurrent) are asymptomatic, i.e. most mothers of infants with neonatal HSV disease were previously unaware of their own infection\(^2\)
Primary infection in the first trimester is associated with an increased risk of early miscarriage. Continuation of the pregnancy does not lead to congenital abnormalities\(^1\)
85% of neonatal HSV infections are acquired perinatally. Maternal HSV infection at the time of a vaginal birth may lead to severe neonatal disease due to ascending infection after rupture of membranes\(^2\)
Intrauterine infection accounts for less than 5% of reported cases\(^2\)
Caesarean section reduces risk of HSV transmission in women shedding HSV at the time of birth, particularly in women with primary infections who are HSV type specific antibody negative\(^2\)
HSV-1 genital infection is less likely to recur than genital HSV-2

Antenatal management

Aboriginal women should be consulted about any decisions in the first instance if requested an Aboriginal Health Professional should be consulted
Women who identify as Aboriginal have a recognised increased risk

Infection precautions
Standard precautions
Past history of genital herpes
Serial genital cultures are not predictive of shedding during labour, so are not recommended
If not already done, obtain serology for HSV-1 and HSV-2 and also HSV PCR typing from the genital tract
Consider use of suppressive antiviral treatment (see Table 1 below) from 36 weeks onwards for women with recurrent lesions

First episode of genital herpes during pregnancy
If not already done, obtain serology for HSV-1 and HSV-2 and also HSV PCR typing from the genital tract
Both primary (HSV IgG negative for both HSV types 1 and 2) and non-primary first episodes diagnosed in the first or second trimester are treated as per ‘First episode’ in Table 1 below

First and second trimester acquisition of HSV (types 1 or 2)
RCOG recommend that following first or second trimester acquisition of HSV, suppression from 36 weeks of gestation as per Table 1 below should be commenced
Providing that labour and/or birth does not ensue within the next 6 weeks, the pregnancy should be managed expectantly and vaginal birth (at viability) anticipated

Third trimester acquisition
If a late diagnosis is made (in the third trimester) treat as per ‘First episode’ in Table 1 below, followed by ‘Suppressive treatment’ as per Table 1 below until birth
Seroconversion may take between 4 to 12 weeks with HSV-1 or HSV-2
If seroconversion has not occurred or is unknown and the woman proceeds to Preterm birth or Preterm prelabour rupture of the membranes (PPROM), assume a high risk of HSV transmission to the newborn of 25 to 50%
Caesarean section should be the recommended mode of birth for all women developing first episode genital herpes in the third trimester, particularly those developing symptoms within 6 weeks of expected delivery. The risk of neonatal transmission of HSV is very high
Advise the woman with active genital herpes that, if spontaneous rupture of the membranes occurs, caesarean section should be performed as soon as possible, preferably within 4 hours

Recurrent genital herpes during pregnancy
Treat recurrent episode(s) (refer to Table 1 for antiviral agents and dosing)
Commence suppressive treatment from 36 weeks until birth for women who have multiple recurrent lesions
Vaginal delivery should be anticipated in the absence of other obstetric indications for caesarean section

Table 1: Recommended treatment options for herpes simplex virus

<table>
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<tr>
<th>Indication</th>
<th>Aciclovir</th>
<th>OR valaciclovir</th>
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<tr>
<td>Treatment of first episode</td>
<td>400 mg orally three times a day for 5 days</td>
<td>500 mg orally twice a day for 5 days</td>
</tr>
<tr>
<td>Treatment of recurrent episode(s)</td>
<td>400 mg orally three times a day for 5 days</td>
<td>500 mg orally twice a day for 3 days</td>
</tr>
<tr>
<td>Suppression treatment</td>
<td>400 mg orally three times a day until birth</td>
<td>500 mg orally twice a day until birth</td>
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Genital herpes in preterm prelabour rupture of the membranes (PPROM)

First episode (primary) of genital herpes with PPROM

There is limited evidence to inform best obstetric practice when PPROM is complicated by primary HSV infection

Management should be guided by multidisciplinary team discussion involving the obstetricians, neonatologists and infectious diseases consultants and will depend on the gestation when PPROM occurred

Immediate birth

Anticipated benefits of caesarean section remain

Initial conservative management

Recommend initial intravenous aciclovir 5 mg/kg every 8 hours in the initial assessment period (24 to 48 hours), then review regarding intravenous versus oral treatment as per ‘First episode’ in Table 1

Prophylactic corticosteroids should be considered to reduce the implications of preterm delivery (see ‘Preterm prelabour rupture of the membranes’ in the A to Z index at www.sahealth.sa.gov.au/perinatal)

If birth is indicated within 6 weeks of the primary infection, caesarean section birth may still offer some benefit despite the prolonged rupture of membranes

Recurrent genital herpes with PPROM

When PPROM is encountered in the presence of recurrent genital herpes lesions, the risk of neonatal transmission is very small and may be outweighed by the morbidity and mortality associated with preterm birth

In the case of PPROM before 34 weeks there is evidence to suggest that expectant management is appropriate, with initial oral antiviral treatment as per ‘treatment of recurrent episodes in Table 1’. Consider further treatment with oral antiviral treatment as per ‘suppression treatment in Table 1’.

After 34 weeks gestation, manage according to SA Perinatal Practice Guideline ‘Preterm prelabour rupture of the membranes’ in the A to Z index at www.sahealth.sa.gov.au/perinatal

Intrapartum management

Ensure the hospital of choice is equipped with facilities for caesarean section

Management of a woman with genital herpes at the onset of labour will be based on clinical assessment as time will not permit confirmatory laboratory testing

Avoid fetal scalp electrode, fetal blood sampling

If there is an obstetric indication to expedite birth in second stage, an operative birth (instrumental or vacuum extraction) may be the safest mode; however, there is a small risk of transmission of HSV to the baby

Recurrent genital HSV infection

The overall risk of transmission is < 1%

If HSV is detected in the genital tract at birth, risk of transmission is 1-3%

Risk is greater for recurrent HSV type 1 (15%) compared to recurrent HSV type 2 (0.01%)

Careful speculum examination in early labour
No active lesions seen
Suitable for vaginal birth

Active lesions seen
ASID state “Caesarean section reduces risk of HSV transmission in women shedding HSV at the time of birth, but does not provide complete protection against neonatal HSV disease”
RCOG state “vaginal delivery should be offered to women with recurrent genital herpes lesions at the onset of labour. A caesarean section delivery can be considered but the risk to mother and future pregnancies should be balanced against the small risk of neonatal transmission of HSV with recurrent disease (1-3% for vaginal delivery)”

Primary genital HSV lesions at onset of labour

Caesarean birth
Caesarean section should be recommended to all women presenting with a primary episode of genital herpes lesions either at the start of labour OR if they have had a primary lesion within 6 weeks of the expected date of delivery
There is some evidence to suggest that the benefit of caesarean section reduces if the membranes have been ruptured for more than 4 hours\textsuperscript{3,7}. However, there may be some benefit in performing a caesarean section beyond 4 hours of rupture of the membranes

Vaginal birth
Where caesarean section is not feasible, give intravenous aciclovir (5 mg per kg every 8 hours) until delivery. However it is unknown whether this will reduce the risk of neonatal HSV infection (risk of perinatal transmission 25-50%)

Postpartum care of the neonate

Asymptomatic infant and low risk of infection
Recurrent antenatal maternal infection or primary infection with seroconversion before labour and birth (6 or more weeks before birth)
Normal postnatal care of the baby

24 hours after birth
Collect surface swabs – eye, throat, umbilicus and rectum. Send for HSV 1 and 2 PCR
Collect urine for HSV 1 and 2 PCR
Observe for any clinical signs of infection as described below in ‘clinical signs of HSV disease’

Asymptomatic infant and high risk of infection
Primary maternal HSV infection close to birth or baby born through birth canal with active maternal HSV disease and no previous history of genital HSV
Care of the infant at high risk of contracting neonatal HSV disease should ideally take place in a hospital with at least Level 5 facilities. Where this does not occur (e.g. either undiagnosed HSV infection or unplanned birth in rural area), direct consultation with the Neonatal team in a Level 6 facility or the Infectious Diseases Department at either the Women’s and Children’s Hospital or Flinders Medical Centre is required.
Standard and contact precautions and nurse in a single room
At birth
Paediatrician at delivery
Complete examination of the baby for clinical signs of HSV (see “Symptomatic Infant” below)
Transfer to neonatal care
Collect urine for HSV 1 and 2 polymerase chain reaction (PCR)
Complete blood picture (low platelets)
Liver function test
Coagulation profile
HSV polymerase chain reaction (PCR) on blood
Lumbar puncture (CSF biochemical, cell count, HSV PCR and bacteria culture)

Treatment
Pre-emptive treatment (high risk asymptomatic infant without laboratory confirmed infection)
  • 10 days IV aciclovir is recommended

24 hours after birth
Collect surface swabs – eye, throat, umbilicus and rectum. Send for HSV 1 and 2 PCR

Symptomatic infant with clinical signs of HSV disease
Vesicular skin lesions or atypical pustular or bullous lesions, especially on the presenting fetal part. An ulcer or ulcers involving the buccal mucosa. Corneal ulcer / conjunctivitis/ keratitis
Seizures
Unexplained fever or sepsis with negative blood cultures and not responding to antibiotics
Low platelets
Elevated liver enzymes
Disseminated intravascular coagulation
Respiratory distress (24 hours after birth)

Treatment
HSV infection confined to skin, eye and mouth:
  • Continue IV aciclovir for 14 days
Encephalitis or disseminated disease:
  • Continue IV aciclovir for 21 days

Management if clinical signs of HSV evident
Repeat lumbar puncture (cerebrospinal fluid analysis, viral culture, HSV polymerase chain reaction (PCR)
  • May need to be repeated after 72 hours in circumstances of clinical signs of central nervous system disease with initial negative HSV PCR result
  • Repeat near completion of treatment to confirm clearance of viral DNA. If HSV PCR remains positive, extend treatment duration or consider alternative antiviral agent e.g. Foscarnet
Follow up

Monitor baby for signs of recurrence, eye disease, hearing impairment or central nervous system sequelae

There is little data to guide management of recurrences after neonatal HSV disease. CSF examination including HSV PCR and empiric IV aciclovir (see Neonatal Medication Guideline ‘aciclovir’ at www.sahealth.sa.gov.au/neonatal) is recommended for:

- cutaneous recurrences in infants < 3 months of age, OR
- recurrences after previous neonatal encephalitis at any age, OR
- re-presentation with neurological signs +/- fever at any age

*Aboriginal women should be referred to the Aboriginal Health Professional*

Oral Aciclovir Prophylaxis to Prevent CNS Sequelae

Oral treatment should not be recommended for therapeutic or pre-emptive treatment of HSV in the neonate. The role of oral valaciclovir has not been evaluated in this context

**Neonatal HSV CNS disease +/- disseminated infection**


**Skin eye mouth or disseminated infection without CNS involvement**

Some experts also use oral aciclovir to suppress troublesome cutaneous recurrences after skin, eye, mouth disease or to reduce early reactivation after all forms of disease in any infant; or in very preterm infants, but not routinely recommended as not shown to alter neurological outcome
References


Useful website
Acknowledgements

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**Write Group Members**
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