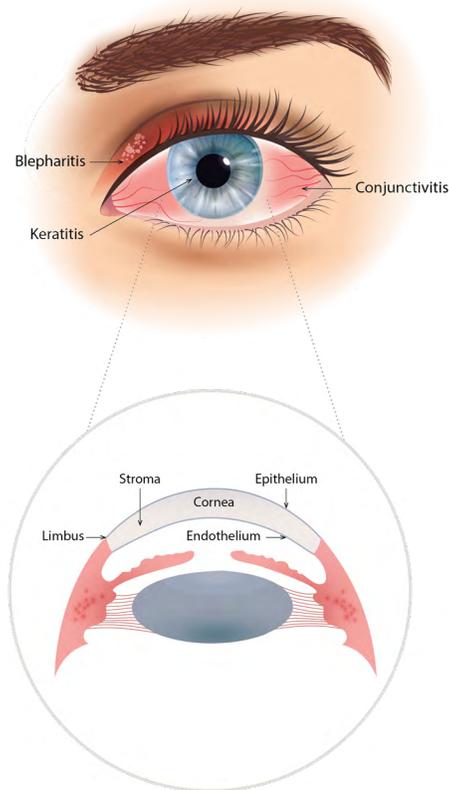


This optimal use guide is intended primarily for health professionals, including optometrists. It is provided for information purposes only and should not replace the judgement of the clinician who performs reserved activities by an act or a regulation. The recommendations were developed using a systematic process and are supported by the scientific literature and by the knowledge and experience of Québec clinicians and experts. For further details, go to iness.qc.ca.

GENERAL INFORMATION

THIS GUIDE DEALS WITH THE FOLLOWING FORMS OF HERPES SIMPLEX EYE DISEASE:

- ▶ **Blepharitis**
- ▶ **Blepharoconjunctivitis**
- ▶ **Epithelial keratitis (with dendritic ulcers)**



- ▶ **Herpes simplex virus (HSV)** types 1 and 2 belong to the family *Herpesviridae* and the subfamily *Alphaherpesvirinae*.
- ▶ HSV-1 and 2 are common causes of mucocutaneous and eye infections.
- ▶ Most adults have antibodies against HSV-1 (previous infection).
 - 20 to 40% of children and adolescents have anti-HSV-1.
- ▶ The primary infection is usually asymptomatic and is followed by a period of latency, whose reactivation can lead to a symptomatic infection.
- ▶ HSVs can infect the eyelids and all the layers of the eye.
 - **Blepharitis** is an inflammation of the eyelid with vesicular involvement.
 - When the conjunctiva is infected as well, one speaks of **blepharoconjunctivitis**.
 - **HSV keratitis** occurs when the cornea becomes infected.
 - Epithelial keratitis accounts for 67% of cases of HSV keratitis. The recurrence rate is approximately 12 to 15% and increases with each episode.
 - Keratitis can become complicated, affect the stromal and endothelial layers, and leave permanent scars on the cornea.
 - HSV keratitis is one of the leading causes of corneal blindness worldwide.
 - The first episode may involve the eyelid only, but recurrences will usually be characterized by corneal involvement.

CLINICAL PRESENTATION

- ▶ Herpes simplex eye disease is usually characterized by a history of HSV or HSV exposure/contact, the type of cutaneous lesions (on the eyelid), if present, and the presence of one to several small epithelial dendrites with end bulbs on the surface of the cornea, which are evaluated using a slit lamp. The clinician should check that there are no manifestations that could orient the diagnosis towards another clinical condition.

IMPORTANT PEDIATRIC CONSIDERATIONS WHEN SYMPTOMS AND SIGNS SUGGEST HSV EYE DISEASE

- ▶ Infants aged 8 weeks or less, that is, neonates, are at greater risk for dissemination affecting multiple organs during HSV disease.
- ▶ Compared to adults, children with HSV keratitis appear to be more susceptible to:
 - Developing a bilateral infection;
 - Having both epithelial and stromal keratitis;
 - Experiencing a recurrence during the first year following the first episode; and
 - Developing amblyopia, if they are under 8 years of age.
- ▶ **Have children with suspected HSV keratitis evaluated by an ophthalmologist urgently.**
- ▶ **Refer infants aged 3 months or less with HSV disease immediately to an emergency department for management by a pediatrician.**

- ▶ In general, no microbiological testing is necessary.

SYMPTOMS AND SIGNS		 Photo available
ACTIVE PHASE	Main symptoms and signs (order of appearance in time varies)	<ul style="list-style-type: none"> • General <ul style="list-style-type: none"> - Recurring - Pain that is not always severe or present - Mainly unilateral • Skin, eyelids (blepharitis) <ul style="list-style-type: none"> - Clusters of vesicles a few millimetres in size on an erythematous base that do not follow a dermatome and that can cross the median line (unlike herpes zoster lesions) - Usually preceded by tingling • Eye, conjunctiva (conjunctivitis) <ul style="list-style-type: none"> - Conjunctival redness - Tearing
	WARNING SYMPTOMS AND SIGNS	<ul style="list-style-type: none"> • Eye, epithelium (keratitis) and other layers of the eye <ul style="list-style-type: none"> - Decreased visual acuity - Photophobia - Pupillary constriction - Redness due to ciliary congestion - Painful eye <p>If present, a slit lamp examination¹ is required.</p>

1. A slit lamp examination is performed by a qualified professional, usually an optometrist or an ophthalmologist.

OTHER EYELID LESIONS TO CONSIDER



Photos available

Atopic dermatitis (acute eczema): Is characterized by often edematous erythema interspersed with very tight formations of superficial micropapules and/or microvesicles.

Contact dermatitis: Is characterized by often pruriginous and nonpainful edema. Presence of scaling or microvesicles that can merge to form bullae. The shape of the affected area is very well defined and matches that of the point of contact.

Herpes zoster ophthalmicus: Is characterized by the appearance of erythematous spots along a dermatome supplied by the ophthalmic branch of the fifth cranial nerve that are preceded by severe pain a few days earlier. Clusters of 2- to 3-mm vesicles develop over these spots and quickly progress to pustules and crusts. These lesions are of different ages, usually do not cross the median line, do not occur on the lower eyelid and take several weeks to heal completely.

Impetigo: Is usually characterized by honey-coloured crusts. The bullous form is characterized by flaccid vesicles and/or bullae that quickly become purulent and rupture almost immediately, leaving a collarette around the periphery of the lesion.

Infectious periorbital cellulitis: Is characterized by edema and erythema, the absence of vesicles and the presence of periorbital pain.

EYE EXAMINATION

- ▶ Evaluate visual acuity, the eyelid, the conjunctiva and corneal integrity.
 - **Corneal involvement** can be checked using **fluorescein** (slit lamp, if available).
 - HSV epithelial dendrites are characterized by the presence of end bulbs, unlike the pseudodendrites of herpes zoster ophthalmicus. Dendrites can open and become geographic ulcers.
- ▶ The eye examination should include an intraocular pressure measurement, if clinically necessary.

IMPORTANT CONSIDERATIONS REGARDING HSV EYE DISEASE

- ▶ **Caution:** The non-uptake of fluorescein does not rule out corneal involvement, especially without a slit lamp.
- ▶ If in doubt, if there are **warning symptoms and signs**, a slit lamp examination is required.

SLIT LAMP EXAMINATION

Symptoms and signs suggesting HSV eye disease	Acceptable amount of time before referring the patient to a qualified professional ¹
In adults	
<ul style="list-style-type: none"> • Isolated blepharitis: <ul style="list-style-type: none"> - Vesicles/lesions on the eyelid margins - No eye redness 	If necessary, solely according the clinician's judgement
<ul style="list-style-type: none"> • Blepharoconjunctivitis: <ul style="list-style-type: none"> - Vesicles/lesions on the eyelid margins - Conjunctival redness 	1 to 3 days To assess corneal involvement and its severity
Warning symptoms and signs present	As soon as possible; < 24 hrs
In patients with an immunocompromised state	
No warning signs or symptoms	24 to 48 hrs: discussion with ophthalmologist
In infants/children	
Infants < 8 weeks	To an emergency department at once (management by a pediatrician) and < 24 hrs: discussion with ophthalmologist
Infants between 8 weeks and 3 months or > 3 months with warning symptoms and signs	To an emergency department at once and < 24 hrs: discussion with ophthalmologist
Upon the appearance of symptoms and signs, but with no warning symptoms or signs	< 24 hrs: discussion with ophthalmologist directly or via an emergency department

1. A slit lamp examination is performed by a qualified professional, usually an optometrist or an ophthalmologist.

TREATMENT PRINCIPLES

- ▶ A first episode of HSV eye disease may resolve spontaneously within 2 weeks. However, treatment with an antiviral reduces viral replication, controls inflammation and reduces the risk of complications.

IMPORTANT CONSIDERATIONS WHEN SYMPTOMS AND SIGNS SUGGEST HSV EYE DISEASE

- ▶ Initiate antiviral therapy as soon as possible after the appearance of symptoms and signs to reduce the risk of complications. **Antiviral therapy should be started immediately by the treating clinician, even if a specialist consultation request has been made.**
- ▶ **In adults, HSV epithelial keratitis whose presentation is unequivocal can be treated by an optometrist.**
- ▶ **The use of topical corticosteroids is CONTRAINDICATED in HSV epithelial keratitis.**

- ▶ Suggest artificial tears or eye lubricants to ease the eye discomfort.
- ▶ The patient should be:
 - Informed of the recurrent nature of HSV keratitis (which requires a consultation, even if there are no warning signs or symptoms);
 - Informed of the warning symptoms and signs to be on the lookout for and that require a new consultation;
 - Advised to maintain local hygiene of the lesions, to wash his/her hands and to avoid further contact with the lesions to prevent autoinoculation at other sites;
 - Advised not to wear contact lenses;
 - Advised to avoid direct contact of the lesions with infants and with immunocompromised patients with no previous exposure to the virus;
 - Advised to take an over-the-counter oral analgesic if there is any pain.

TREATMENTS

ANTIVIRALS IN ADULTS		
Antiviral	Daily Dosage	Duration
Valacyclovir ¹ , 500 and 1000 mg tablets ²	500 mg to 1000 mg PO BID	7 days
Famciclovir ¹ , 125, 250 and 500 mg tablets	250 mg PO BID	
Acyclovir ¹ , 200, 400 and 800 mg tablets	400 mg PO 5 times per day	

1. Adjust according to renal function.

2. The 1000 mg tablets are not covered by the public prescription drug insurance plan (RPAM).

IMPORTANT PEDIATRIC CONSIDERATIONS

- ▶ **If a child** is suspected of having HSV eye disease, refer this child, if possible, directly to an **ophthalmologist** or to an emergency department for a consultation.
- ▶ **Pending the ophthalmologist’s opinion, an oral antiviral must be initiated immediately.**

ANTIVIRALS IN INFANTS AND CHILDREN			
Antiviral	Daily Dosage	Maximum Dosage	Duration
Valacyclovir ¹ , compounded 50 mg/ml, 500 and 1000 mg tablets ²	≥ 3 months: 20 mg/kg per dose PO BID ³ as a magistral preparation up to 10 kg or tablets according to weight:	1000 mg PO BID	While waiting for the consultation
	10 to 13.9 kg: 250 mg (half of a 500 mg tablet) PO BID		
	14 to 19.9 kg: 375 mg (3/4 of a 500 mg tablet) PO BID		
	20 to 27.9 kg: 500 mg (one 500 mg tablet) PO BID		
	28 to 39.9 kg: 750 mg (1½ 500 mg tablets) PO BID		
	> 40 kg: 1000 mg (two 500 mg tablets) PO BID		
Acyclovir ¹ , 200 mg/5 ml suspension	20 mg/kg per dose PO TID	800 mg TID	

1. Adjust according to renal function.
2. The 1000 mg tablets are not covered by the RPAM.
3. The 500 mg tablets can be cut and then crushed according to the calculated dose, or a 50 mg/ml suspension of valacyclovir can be compounded, in particular, for infants weighing less than 10 kg.

ANTIVIRALS			
Form	The Most Common Adverse Effects	Main Drug Interactions	Contraindications and Special Precautions
Oral (acyclovir, valacyclovir, famciclovir)	Headache, dizziness, nausea, vomiting, diarrhea and abdominal pain.	Famciclovir: probenecid, raloxifene Valacyclovir and acyclovir do not have any interactions with a clinically significant impact.	Adjust according to renal function. Recommend to the patient that he/she maintain good hydration. Acyclovir and valacyclovir are compatible with breastfeeding . Acyclovir is the first-line treatment during pregnancy.

FOLLOW-UP

- ▶ Whenever treatment is initiated, the patient’s condition should be monitored.
- ▶ If the expected change in the patient’s condition does not occur within 4 days after the start of treatment, refer the patient to an ophthalmologist.
- ▶ If corneal dendrites and lesions persist after 2 weeks of using drops, another cause should be suspected.

MAIN REFERENCES

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It should be noted that other references were consulted as well.