

DRUG ANTIBIOTICS

BLEPHARITIS

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. These recommendations do not apply to viral or parasitic blepharitis. For further details, go to inesss.qc.ca.

GENERAL INFORMATION



- ▶ Blepharitis is an inflammation of the eyelids:
 - Acute: Can be localized (hordeolum (stye) or chalazion) or generalized (affecting the entire eyelid)

or

- Chronic: Is characterized by fluctuating signs and symptoms that persist over time.
- ➤ A hordeolum (stye) is an acute inflammatory lesion of infectious origin of the sebaceous glands in the eyelid (Zeis glands), while a chalazion is a sterile inflammation of the Meibomian glands.
- ▶ In chronic blepharitis, there can be anterior and posterior involvement at the same time.
- ▶ Blepharitis is said to be anterior when the outer margin near the eyelashes is affected.
 - **Staphylococcal blepharitis:** An inflammatory response to *Staphylococcus aureus* that can cause an obstruction of the glands attached to the eyelash follicles.
 - **Seborrheic blepharitis:** A dysfunction of the Zeis glands, which are attached to the eyelash follicles. The dysfunction can become complicated by a secondary infection.
 - A combination of the two
 - Forms of infectious blepharitis not covered in this guide:
 - Viral (e.g., due to herpes simplex).
 - Parasitic (e.g., due to *Demodex folliculorum or Phthiriasis palpebrarum*).
- ▶ Blepharitis is said to be posterior when the inner margin of the eyelid is affected.
 - The main form is a Meibomian gland dysfunction that causes tear film instability and eventually leads to chronic inflammation of the eyelid margin.
- ▶ Chronic blepharitis predisposes to hordeola (styes) and chalazia.

Blepharitis Chalazion Hordeolum (Stye) Zeis glands Skin — Conjunctiva Meibomian gland Eyelashes Outer margin Anterior location Posterior location

RISK FACTORS

▶ Rosacea, seborrheic dermatitis and atopic dermatitis (eczema).



CLINICAL PRESENTATION

- ▶ Suspicion of blepharitis is based on the patient's history, the examination of the eyes and surrounding skin, and the absence of manifestations that could point to another condition.
- ▶ Chronic blepharitis is usually bilateral, despite the unilateral symptoms sometimes reported by the patient.

SYMPTOMS AND SIGNS		
In the history, look for:	 Eye and/or skin problems and eye surgery; Symptoms: eyelids stuck together in the morning waking up, eye discomfort (discomfort or pain, especially in the morning), burning sensation, pruritus, tearing, foreign-object sensation, intolerance to contact lenses, temporarily blurred vision. 	
During the examination, look for:	 Signs on the eyelids and adnexa: redness, swelling or thickening of the eyelid, crust at the base of the eyelashes, inflammation of the orifices of the glands along the eyelid margin, nodule or bump in the anterior (hordeolum (stye) or posterior (chalazion) region of the eyelids; Signs in both eyes, especially the conjunctiva and cornea: conjunctival redness; Other skin lesions on the face associated with the risk factors; Absence of herpetic vesicles on the face. 	
WARNING SYMPTOMS AND SIGNS TO LOOK FOR If present, a slit lamp examination¹ should be considered:	 Photophobia (new or exacerbated); Loss of vision or visual acuity; Severe pain in the eye or eyelid; Severe redness with diffuse conjunctival hyperemia; Keratitis with fluorescein uptake: inferior punctate uptake or ulceration. 	

^{1.} The slit lamp examination is performed by a qualified professional, usually an optometrist or an ophthalmologist.

OTHER CLINICAL CONDITIONS TO CONSIDER²



Photos available

Conjunctivitis: Is characterized by diffuse conjunctival redness (palpebral and bulbar). When viral, it often occurs in the context of a respiratory tract infection. It causes clear tearing. Preauricular adenopathy is often present. When bacterial, it is accompanied by purulent secretions.

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.

Dacryocystitis: Is characterized by localized edema and erythema in the internal angle (between the eye and the nose) and is often accompanied by tearing.

Drug-induced dermatitis caused by the use of ophthalmic drops: Is characterized by eczema of the eyelids with cardboard-like skin and scaling. Concurrently, there is often diffuse conjunctival redness.

<u>Herpes simplex eye disease:</u> Is characterized by clusters of vesicles, papules and pustules a few millimetres in size on an erythematous base that are identical to those of an individual herpes zoster lesion and usually preceded by tingling instead of pain. The clustering of vesicles, papules and pustules that do not follow a dermatome and that can cross the median line, and the recurring nature favour a diagnosis.

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.

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

Seasonal allergies: Are characterized by conjunctival redness (palpebral and bulbar) accompanied by tearing. The main symptom is itching. Often accompanied by other allergy symptoms, such as rhinorrhea.

Sebaceous carcinoma: Is characterized by redness of only one eyelid and is often accompanied by a loss of eyelashes and a distortion of the normal anatomy.

TREATMENT PRINCIPLES

- ▶ In children, nonpharmacological measures are used. However, chronic blepharitis not controlled by such measures should be managed by an ophthalmologist.
- ▶ Hordeolum (stye) and chalazion are usually treated by nonpharmacological measures, unless associated infectious periorbital cellulitis is suspected. Consider referring the patient to an ophthalmologist, who excise the hordeolum (stye) or chalazion if there is no result after using nonpharmacological measures for 3 months.
- ▶ Chronic anterior and posterior blepharitis are treated in the same manner. Nonpharmacological measures should be continued over the long term, often for life, and on a regular basis in order to control the recurrence of the symptoms.

FIRST-LINE TREATMENT

NONPHARMACOLOGICAL MEASURES IN ADULTS AND CHILDREN		
	Apply warm compresses¹ (about 40 to 45°C) or a heating mask over the eye continuously for at least 5 to 10 minutes :	
	Acute blepharitis: 2 to 4 times a day	
COMPRESSES	- With or without a hordeolum (stye): for 3 or 4 days or until the symptoms disappear.	
COMI NESSES	 With a chalazion: for several weeks to several months or until the chalazion completely disappears. 	
	Chronic blepharitis: once a day every day, with preference given to dry heat (heating mask) rather than moist heat, except in children.	
HYGIENE	Clean the eyelids with an ophthalmic wipe or a mild2, dilute soap solution:	
	Acute blepharitis:	
	- With or without a hordeolum (stye): for 3 or 4 days or until the symptoms disappear.	
	 With a chalazion: for several weeks to several months or until the chalazion completely disappears. 	
	Chronic blepharitis: every day.	
MASSAGE	Mainly for chronic posterior blepharitis: After using warm compresses, it is advisable to massage the eyelids once a day (moving the fingers towards the free margin of the eyelid to force out the secretions from the Meibomian glands or a lateral back-and-forth motion on the margins of the closed eyelids to remove the crust).	
LOCAL HYDRATATION	Acute blepharitis and chronic blepharitis: Consider using artificial tears ³ if the patient is experiencing discomfort.	

- 1. For children, a temperature close to that of bath water can be used, but do not use dry heat (heating mask), this to avoid burns.
- 2. For example, baby shampoo (diluted 1 part soap to 10 parts water, e.g., adding 10 mL of soap to 90 mL of water).
- 3. If artificial tears are to be used on a regular basis several (> 4) times a day, a preservative-free formulation should be used to avoid the toxicity due to preservatives.

SECOND-LINE TREATMENT

▶ It is important to treat the associated skin condition when managing chronic blepharitis (e.g., rosacea or seborrheic dermatitis).

IMPORTANT CONSIDERATIONS BEFORE CONSIDERING THE USE OF A TOPICAL ANTIBIOTIC

- ▶ Topical antibiotics are generally used only upon failure of nonpharmacological measures that have been used regularly and optimally.
- ▶ If required, reconsider the clinical condition.

TOPICAL ANTIBIOTICS IN ADULTS			
Condition	Topical Treatment	Dosage	Duration
Acute or chronic blepharitis not controlled by nonpharmacological measures	Erythromycin (ointment, 0.5%)	One strip in the affected eye (or on the eyelid margin) DIE at bedtime³	4 weeks
	ALTERNATIVE¹ IF ALLERGY OR INTOLERANCE		
	Fusidic acid (drops, 1%) or Polymyxin B (sulfate) - gramicidin² (drops, 10,000 units/0.025 mg)	One drop or one strip in the affected eye (or on the eyelid margin) DIE at bedtime ³	4 weeks

- 1. According to the experts consulted, because of the availability of better solutions in terms of the bacterial spectrum and the risk of resistance, ciprofloxacin (drops and ointment, 0.3%) and ofloxacin (drops, 0.3%) are not preferred options.
- 2. Available over the counter in pharmacies.
- 3. The dosage is different from that stated in the product monographs. It reflects the recommendations of the experts consulted about the indication of blepharitis.

THIRD-LINE TREATMENT

IMPORTANT CONSIDERATIONS BEFORE CONSIDERING THE USE OF A TOPICAL CORTICOSTEROID

- ▶ Reconsider the clinical condition if there is no response to first- and second-line treatment. If there are atypical symptoms or signs that could suggest another condition, refer the patient to Ophthalmology.
- ▶ Before treating chronic blepharitis in which there is a risk of complications, it is important to check that the patient does not have (or never had a history of) herpetic keratitis, as the use of a topical corticosteroid can reactivate the infection. In such circumstances, a more thorough investigation by an ophthalmologist is required.
- ➤ Treatment with a topical corticosteroid, in combination with a topical antibiotic, should be prescribed only **after a slit lamp examination by a qualified professional** aimed at detecting any warning symptoms or signs (e.g., keratitis).

IMPORTANT CONSIDERATIONS AFTER USING A TOPICAL CORTICOSTEROID

▶ Because of the adverse effects of corticosteroids (increased intraocular pressure and cataract), it is important that the patient be reevaluated within a few weeks after the start of treatment.

TOPICAL ANTIBIOTIC WITH THE ADDITION OF A TOPICAL CORTICOSTEROID IN ADULTS			
Condition	Topical Corticosteroid	Dosage	Duration
Chronic blepharitis not controlled with the use of a topical antibiotic alone and in which there is a risk of complications, based on a slit lamp examination	Fluorometholone (0.1%) or Loteprednol¹ (0.5%) ALTERNATIVE² Prednisolone (0.12% or 1%)	1 drop TID or QID⁴	1 or 2 weeks, with a regular follow-up to check improvement in the condition and for the occurrence of associated adverse effects
	COMBINATIONS Dexamethasone/tobramycin ^{1,3} (drops and ointment, 0.1%/0.3%) or Prednisolone/sulfacetamide ¹ (ointment and suspension, 0.2%/10%)		

- 1. Not covered by the public prescription drug insurance plan (RPAM).
- 2. According to the experts consulted, because of its unfavourable safety profile and the availability of a better treatment option, dexamethasone (0.1%) as monotherapy is not recommended.
- 3. According to the experts consulted, tobramycin is usually not prescribed as monotherapy in blepharitis, since it irritates the eyes.
- 4. The dosage is different from that stated in the product monographs. It reflects the recommendations of the experts consulted about the indication of blepharitis.

FOURTH-LINE TREATMENT

IMPORTANT CONSIDERATIONS BEFORE USING AN ORAL ANTIBIOTIC TO TREAT UNCONTROLLED CHRONIC POSTERIOR BLEPHARITIS

- ▶ If the course is not the one expected despite the pharmacological treatments, reconsider the clinical condition.
- ▶ If there are atypical symptoms and signs that could suggest another condition, refer the patient to Ophthalmology.
- ▶ To limit the adverse effects of long term antibiotic use, including the development of bacterial resistance, prescribing an oral antibiotic should be reserved for **rare cases** of uncontrolled chronic posterior blepharitis when:
 - The proper use of nonpharmacological measures on a regular basis for more than 4 to 6 months has been verified and the use of a topical antibiotic has not controlled the condition despite the addition of a topical corticosteroid; or
 - Secondary punctate keratitis is noted.
- ▶ Before prescribing an oral antibiotic, check the adverse effects, drug interactions, contraindications and special precautions.

ORAL ANTIBIOTICS IN ADULTS			
Condition	Oral Antibiotic ^{1,2}	Dosage	Duration
Uncontrolled chronic posterior blepharitis	Doxycycline or Minocycline	100 mg PO DIE. Can be reduced to 20 mg PO BID or 40 mg PO DIE after documented clinical improvement ^{3,4} or 100 mg PO DIE. Can be reduced to 50 mg PO QD after documented clinical improvement ⁴	2 or 3 months

- 1. Neither of the antibiotics mentioned here have received an official Health Canada indication for the treatment of blepharitis.
- 2. Because of its unfavourable safety profile for use beyond 3 weeks, azithromycin is not a preferred option.
- 3. The 20- and 40-mg doxycycline tablets are not covered by the RPAM.
- 4. According to the literature and the experts consulted, small doses can be administered upon the initiation of treatment to limit the adverse effects associated with several weeks of use.

TETRACYCLINE ANTIBIOTICS			
The Most Common Adverse Effects	Main Drug Interactions	Contraindications and Special Precautions	
Photosensitivity; dizziness or vertigo; drowsiness; fatigue; ataxia; gastrointestinal	Antacids; oral coumarin anticoagulants; antidiarrheals containing kaolin and pectin or bismuth subsalicylate; antiepileptics; oral	A history of allergic reaction to these drugs or to any of their components; severe renal or hepatic dysfunction; pregnancy or breastfeeding; children under 8 years of age; myasthenia gravis; use of retinoids .	
disturbances.	contraceptives; digoxin; hepatotoxic drugs; penicillin and retinoids .	To reduce the risk of esophagitis and esophageal ulcers, the patient should not lie down for 30 minutes after taking doxycycline.	

REFERRAL/CONSULTATION CRITERIA

- ▶ The presence of warning symptoms and/or signs.
- No response after several weeks of optimal use of nonpharmacological measures on a regular basis together with at least 1 month's treatment with a topical antibiotic.
- ▶ The presence of keratitis.

REFER THE PATIENT TO OPHTHALMOLOGY:

- ▶ If there are atypical symptoms and signs that could suggest another condition.
- ▶ If a hordeolum (stye) or chalazion persists, despite the regular and long term optimal use of nonpharmacological measures, and needs to be surgically removed.
- ▶ In a child with chronic blepharitis not controlled with nonpharmacological measures.

MAIN REFERENCES

AAO. Preferred Practice Pattern Guidelines Blepharitis. PPP. San Francisco, CA,: American Academy of Ophthalmology; 2013. Disponible à: https://www.aao.org/preferred-practice-pattern/blepharitis-ppp—2013.

AOA. Care of the Patient with Ocular Surface Disorders. OPTOMETRIC CLINICAL PRACTICE GUIDELINE. St-Louis: 2011. Disponible à: https://www.aoa.org/documents/CPG-10.pdf.

Lindsley K, Matsumura S, Hatef E, Akpek EK. Interventions for chronic blepharitis. Cochrane Database Syst Rev 2012;

The College of Optometrists. Blepharitis (Lid Margin Disease). London: The College of Optometrists; 2016. Disponible à:

https://www.college-optometrists.org/guidance/clinical-management-guidelines/blepharitis-lid-margin-disease.html (consulté le mai 2017).

Wladis EJ, Bradley EA, Bilyk JR, Yen MT, Mawn LA. Oral Antibiotics for Meibomian Gland-Related Ocular Surface Disease: A Report by the American Academy of Ophthalmology. Ophthalmology 2016; 123(3): 492-6.

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

