VIRAL EYE INFECTIONS

CHI Formulary Development Project

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Council of Health Insurance

INDICATION UPDATE

ADDENDUM- November 2023

To the CHI Original Viral Eye Infections Clinical Guidance- Issued April 2020

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Related Documents

Related SOPs

- IDF-FR-P-02-01-IndicationsReview&IDFUpdates
- IDF-FR-P-05-01-UpdatedIndicationReview&IDFUpdates

Related WI:

- IDF-FR-WI-01-01SearchMethodologyGuideForNewIndications

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Abbreviations

AIDS	Acquired Immunodeficiency Syndrome
AOA	American Optometric Assocation
AU	Anterior Uveitis
BD	Twice Daily
CAI	Carbonic Anhydrase Inhibitors
CHI	Council of Health Insurance
CMV	Cytomegalovirus
COVID	Coronavirus Disease
CPG	Clinical Practice Guideline
CrCl	Creatinine Clearance
FDA	Food and Drug Administration
HIV	Human Immunodeficiency Virus
HSCT	Hematopoietic Stem Cell Transplant
HSK	Herpes Simplex Keratitis
HSV	Herpes Simplex Virus
IDF	CHI Drug Formulary
IM	Intramuscular
IOP	Intraocular Pressure
IV	Intravenous
N/A	Not Applicable/Not Available
PCR	Polymerase Chain Reaction
PPE	Personal Protective Equipment
RD	Retinal Detachment
SEI	Subepithelial Infiltrates
SFDA	Saudi Food and Drug Authority
TDS	Three Times Per Day
VZV	Varicella Zoster Virus

Executive Summary

Eye infections can manifest as discomfort, redness, and itchiness, potentially leading to vision loss. Seeking medical attention is crucial to determine the cause and receive appropriate treatment. Common causes of viral eye infections include Herpes simplex type 1, Varicella zoster virus, and adenovirus. Symptoms of eye infections encompass redness, itching, pain, discharge, and sensitivity to light. Diagnosis involves a medical history review, symptom assessment, and eye examination. Treatment varies depending on the infection's cause and may involve anti-infective medications like eye drops, ointments, or tablets. Prevention measures include proper contact lens care, protective eyewear, allergy management, hand hygiene, and avoiding the sharing of eye-related items[1].

The prevalence of these viral eye infections can vary depending on geographic location, population demographics, and the specific virus in question. At a global level, it is estimated that approximately 4.85 billion individuals of all age groups carry a prevalent HSV-1 infection[2]. Worldwide, approximately 34 million individuals are HIV-infected, and it is evident that zoster rates are influenced by this, even though there is a lack of data regarding the HIV/AIDS pandemic's specific impact on the incidence of zoster[3].

CHI issued Viral Eye Infections clinical guidelines after thorough review of renowned international and national clinical guidelines in April 2020. Updating clinical practice guidelines (CPGs) is a crucial process for maintaining the validity of recommendations.

This report functions as an addendum to the prior CHI Viral Eye Infections clinical guidance and seeks to offer guidance for the effective management of Viral Eye Infections. It provides an **update on the Viral Eye Infections Guidelines** for CHI Formulary with the ultimate objective of updating the IDF (CHI Drug Formulary) while addressing **the most updated best available clinical and economic evidence related to drug therapies.**

Main triggers for the update were summarized, being the **addition** of the Cytomegalovirus Uveitis: **Taiwan** expert consensus (**2023**)[4], the Viral Conjunctivitis Clinical Practice Guideline from the **Royal Victorian Eye and Ear Hospital** (**2021**)[5], and the Herpes Simplex Keratitis (HSK) Prescribing Protocol and Treatment Guideline by the **Royal Australian and New Zealand College of Ophthalmologists**[6] (**2020**).

After carefully examining clinical guidelines and reviewing the SFDA drug list, Foscarnet is to be added to the CHI formulary, and there are no new drugs approved by the FDA. The following drugs are no longer SFDA-registered, and it is advisable to delist them from CHI formulary: dexpanthenol and sodium hyaluronate, ectoin and

sodium hyaluronate, glycerin and sodium carboxymethylcellulose, polymyxin b, bacitracin, and neomycin sulfate, polymyxin b, neomycin sulfate and gramicidin, and vidarabine.

All recommendations are well supported by reference guidelines, Grade of Recommendation (GoR), Level of Evidence (LoE) and Strength of Agreement (SoA) in all tables reflecting specific drug classes' role in **Viral Eye Infections** therapeutic management.

Below is a table summarizing the major changes based on the different Viral Eye Infections guidelines used to issue this report:

Table 1. General Recommendations for the Management of Viral Eye Infections

Management of Viral Eye Infections		
General Recommendations	**Level of Evidence/ Grade of Recommendation**	**Reference**
No evidence exists demonstrating the superiority of any topical antibiotic agent in conjunctivitis.	I+, Good, Strong	American Academy of Ophthalmology, 2018[7]
Topical antibiotics are not routinely used to treat viral conjunctivitis unless there is evidence of secondary bacterial infection.	N/A	Optometric Clinical Practice Guideline, 2002[8]
Artificial tears, topical antihistamines, topical steroids, oral analgesics, or cold compresses may be used to mitigate symptoms of adenoviral conjunctivitis.	N/A	American Academy of Ophthalmology, 2018[7]
Povidone-iodine 0.4% alone or in combination with dexamethasone 0.1% has demonstrated reductions in Adenoviral Conjunctivitis viral titers, virus spread, shortening of the clinical course, and preservation of visual function	N/A	American Academy of Ophthalmology, 2018[7]
Herpes simplex virus conjunctivitis is a self-limited acute condition.	N/A	American Academy of Ophthalmology, 2018[7]
Herpes Simplex Virus (HSV) Conjunctivitis: oral treatments include acyclovir (200 to 400 mg five times per day), valacyclovir (500 mg two or three times per day), or famciclovir (250 mg twice a day).	N/A	American Academy of Ophthalmology, 2018[7]

Possible topical options for Herpes Simplex Virus Conjunctivitis include ganciclovir 0.15% gel used three to five times per day or trifluridine 1% solution five to eight times per day.	N/A	American Academy of Ophthalmology, 2018[7]
Varicella (Herpes) Zoster Virus (VZV) Conjunctivitis: oral antivirals may be beneficial at a dose of 800 mg five times daily for 7 days for acyclovir, 1000 mg every 8 hours for 7 days for valacyclovir, or 500 mg three times daily for 7 days for famciclovir.	N/A	American Academy of Ophthalmology, 2018[7]
Topical antivirals alone have not been shown to be helpful in treating VZV conjunctivitis but may be used as additive treatment in unresponsive patients.	N/A	American Academy of Ophthalmology, 2018[7]
Molluscum Contagiosum treatment options include incision and curettage (aggressive enough to cause bleeding), simple excision, excision and cautery, and cryotherapy.	N/A	American Academy of Ophthalmology, 2018[7]
Neonatal Conjunctivitis: Acyclovir (30–60 mg/kg/day). Inadequate if used IV or IM q.8h. For 10–14 days alone; unnecessary with systemic treatment.	N/A	Optometric Clinical Practice Guideline, 2002[8]
There are two FDA approved topical antiviral agents with similar efficacy (ganciclovir and trifluridine) in the treatment of HSV epithelial keratitis.	N/A	Herpes Simplex Virus Keratitis, 2014[9]
Oral antiviral agents appear to be as effective as topical antiviral agents (ganciclovir, trifluridine) in the treatment of HSV epithelial keratitis.	N/A	Herpes Simplex Virus Keratitis, 2014[9]
A topical corticosteroid agent in conjunction with an oral antiviral agent for at least ten weeks is the preferred treatment for HSV stromal keratitis. The balance between antiviral and corticosteroid therapy should be adjusted	Strong Recommendation, Good Quality	Herpes Simplex Virus Keratitis, 2014[9]

depending on the presence or absence of epithelial ulceration.		
A topical corticosteroid agent in conjunction with an oral antiviral agent is the preferred treatment for HSV endothelial keratitis.	Strong Recommendation, Good Quality	Herpes Simplex Virus Keratitis, 2014[9]
A topical corticosteroid agent in conjunction with an oral antiviral agent is the preferred treatment for HSV endothelial keratitis.	Strong Recommendation, Good Quality	Herpes Simplex Virus Keratitis, 2014[9]
Consider using anti-glaucoma agents for cytomegalovirus (CMV) anterior uveitis (AU) cases with poorly controlled intraocular pressure (IOP) and disc damage.	N/A	Cytomegalovirus Uveitis, 2023[4]
To prevent CMV AU recurrence, antiviral agents are favored over steroids.	N/A	Cytomegalovirus Uveitis, 2023[4]
Systemic ganciclovir or valganciclovir is recommended for vision-threatening cases, but myelosuppression is a concern. Foscarnet is an alternative when ganciclovir/valganciclovir treatment fails.	N/A	Cytomegalovirus Uveitis, 2023[4]
Indications for Topical Steroids include pseudomembrane/membrane formation or subepithelial infiltrates (SEI) decreasing vision (<6/12). Options for topical steroids: Fluorometholone acetate eye drops, Fluorometholone eye drops, Prednisolone acetate 1%, or Dexamethasone 0.1% eye drops for moderately severe pseudomembranes.	N/A	The Royal Victorian Eye and Ear Hospital (2021)[5]
Aciclovir or valaciclovir is the first-line therapy for herpes simplex keratitis.	N/A	The Royal Australian and New Zealand College of Ophthalmologists[6]

At the end of the report, a key recommendation synthesis section is added highlighting the latest updates in **Viral Eye Infections clinical and therapeutic management**.

Section 1.0 Summary of Reviewed Clinical Guidelines and Evidence

This section is divided into two parts: the first includes recommendations from **updated versions of guidelines** mentioned in the previous CHI Viral Eye Infections report, and the second includes **newly added guidelines** that have helped generate this report.

1.1 Revised Guidelines

This part contains the updated versions of the guidelines mentioned in the April 2020 CHI Viral Eye Infections Report and the corresponding recommendations:

Table 2. Clinical Guidelines Requiring Revision

Guidelines Requiring Revision	
Old Versions	**Updated Versions**
Section 1.1 **American Academy of Ophthalmology**: Conjunctivitis Preferred Practice Pattern (**2018**)[7]	N/A*
Section 1.2 OPTOMETRIC CLINICAL PRACTICE GUIDELINE: Care of the Patient with Conjunctivitis- **AMERICAN OPTOMETRIC ASSOCIATION** (Approved by the AOA Board of Trustees June 22, 1995 (1st Edition) and November 8, **2002** (2nd Edition))[8]	N/A*
Section 1.3 Herpes Simplex Virus Keratitis: A treatment guideline by the **Department of Ophthalmology- Harvard Medical School** (approved by the Ocular Microbiology and immunology group and the Hoskins Center for Quality Eye Care, American Academy of Ophthalmology) (**2014**)[9]	N/A*

*: No updated versions available

1.1.1 American Academy of Ophthalmology: Conjunctivitis Preferred Practice Pattern (2018)

*Please refer to **Section 1.1** of CHI Viral Eye Infections Report.*

There are no new updates. The recommendations of this guideline remain unchanged[7].

1.1.2 American Optometric Association – Optometric Clinical Practice Guideline: Care of the Patient with Conjunctivitis (Approved by the AOA Board of Trustees June 22, 1995 (1st Edition) and November 8, 2002 (2nd Edition))

*Please refer to **Section 1.2** of CHI Viral Eye Infections Report.*

There are no new updates. The recommendations of this guideline remain unchanged[8].

1.1.3 Herpes Simplex Virus Keratitis: A Treatment Guideline by the Department of Ophthalmology – Harvard Medical School (Approved by the Ocular Microbiology and Immunology Group and the Hoskins Center for Quality Eye Care, American Academy of Ophthalmology) (2014)

*Please refer to **Section 1.3** of CHI Viral Eye Infections Report.*

There are no new updates. The recommendations of this guideline remain unchanged[9].

1.2 New Guidelines

This part includes the added guidelines to the previous CHI Viral Eye Infections report, along with their recommendations.

Table 3. List of Additional Guidelines

Additional Guidelines
Cytomegalovirus Uveitis: Taiwan Expert Consensus (2023)[4]
The Viral Conjunctivitis Clinical Practice Guideline from the Royal Victorian Eye and Ear Hospital (2021)[5]
The Herpes Simplex Keratitis (HSK) Prescribing Protocol and Treatment Guideline by the Royal Australian and New Zealand College of Ophthalmologists (2020)[6]

1.2.1 Cytomegalovirus Uveitis: Taiwan Expert Consensus (2023)

The consensus recommendations are outlined below[4]:

"The consensus was reached when 3/4 panelists agreed, while others did not reach a consensus that required evaluation of voting results to present different opinions."

The following recommendations are provided by the Taiwan expert consensus on the management of Cytomegalovirus Uveitis:

1. How should we diagnose patients presenting with typical cytomegalovirus (CMV) anterior uveitis (AU) symptoms but negative PCR results?
    - Diagnosis can be supported by clinical course and therapeutic response.
    - In cases with a high clinical suspicion, it is advisable to repeat PCR tests to confirm the diagnosis.
2. What is the preferred treatment approach in terms of loading and maintenance doses for CMV AU?
    - To prevent CMV AU recurrence, antiviral agents are favored over steroids.
    - In Taiwan, topical ganciclovir (20 mg/cc) is the preferred medication due to its effectiveness, safety, and convenience.
    - Consider using anti-glaucoma agents for cases with poorly controlled intraocular pressure (IOP) and disc damage.
3. How long should CMV AU treatment be continued?
    - Currently, there are no randomized controlled trials providing optimal treatment duration for CMV AU.
    - The panel recommends a 6-month antiviral treatment for initial attacks without vision-threatening complications.
    - Cases with recurrent attacks or vision-threatening complications may require extended treatment (12 months or longer).
    - Treatment duration should be individualized, considering factors such as patient age, visual acuity, corneal endothelial density, disc nerve fiber thickness, and more.
4. What are the roles of topical and systemic steroids in CMV AU treatment?
    - Steroids may lead to CMV AU becoming latent or resistant to treatment.
    - The use of steroids in the acute stage of CMV AU remains controversial, with some advocating their combined use and others opposing it.
5. How should ocular hypertension induced by CMV AU be managed?
    - Aggressively control ocular hypertension with topical and systemic IOP-lowering agents.
    - Prostaglandin analogs are acceptable for CMV AU due to their low inflammatory status.

- Topical carbonic anhydrase inhibitors (CAI) are traditionally not recommended for patients with poor corneal conditions but can be considered in refractory cases.

Note: for an in-depth review of the management of intraocular pressure and ocular hypertension, please refer to the Open Angle Glaucoma report. Examples of Prostaglandin analogs include: latanoprost, travaprost, and tafluprost. Examples of topical carbonic anhydrase inhibitors include Dorzolamide and brinzolamide.

6. What are the preferred antiviral agents for CMV retinitis in clinical practice?
    - Systemic ganciclovir or valganciclovir is recommended for vision-threatening cases, but myelosuppression is a concern.
    - Intravitreal ganciclovir is supplemental in severe cases with AIDS and bone marrow transplantation but not for mild cases.
    - Foscarnet is an alternative when ganciclovir/valganciclovir treatment fails due to resistance.
7. How should treatment efficacy be evaluated during CMV retinitis treatment, and when should treatment be discontinued?
    - Monitor intraocular and systemic conditions to assess efficacy.
    - Inactive uveitis and regressed retinitis indicate successful intraocular signs.
    - Improved systemic immune status (e.g., rising CD4+ count in HIV) is the key indicator for treatment cessation.
    - Typically, CMV treatment is continued for at least 3-6 months with inactive lesions and CD4+ count > 100 cells/mm3 in HIV patients.
8. What is the strategy for prophylaxis of retinal detachment (RD) associated with CMV retinitis?
    - There is a unanimous agreement among panelists that there is currently no recommended prophylaxis for RD associated with CMV retinitis.

1.2.2 Viral Conjunctivitis Clinical Practice Guideline from the Royal Victorian Eye and Ear Hospital (2021)

Evidence levels are outlined in the table below[5]:

Table 4. Royal Victorian Eye and Ear Hospital Hierarchy of Evidence

Level	Definition
I	Evidence obtained from a systematic review of all relevant randomized control trials.
II	Evidence obtained from at least one well designed randomized control trial.
III	Evidence obtained from well-designed controlled trials without randomization.
IV	Evidence obtained from well-designed cohort studies, case control studies, interrupted time series with a control group, historically controlled studies, interrupted time series without a control group or with case series.
V	Evidence obtained from systematic reviews of descriptive and qualitative studies.
VI	Evidence obtained from single descriptive and qualitative studies.
VII	Expert opinion from clinician, authorities and/or reports of expert committees or based on physiology.

The following recommendations were provided by the Royal Victorian Eye and Ear Hospital on the management of Viral Conjunctivitis[5]:

Red Flags:

- **Highly Contagious:**
    - Segregate patient
    - Disinfect all triage equipment and workspace.
    - Virus survives well on fomites.
- **Symptoms Lasting >3 Weeks:**
    - Consider polymerase chain reaction (PCR) for chlamydia.
- **Possible COVID-19 Presentation with Conjunctivitis:**
    - Query risk factors
    - Isolate patient
    - Use full personal protective equipment (PPE)
    - Perform COVID swab if indicated.

How to Assess:

History:

- Redness, tearing, burning, itching, photophobia, blurred vision.
- Recent contact with a person with red eye (incubation period 3-5 days)
- The second eye is usually involved 2-3 days after the first eye.
- Symptoms may be preceded by upper respiratory tract symptoms.

Examination:

- Wear gloves
- Use a cotton bud to examine/touch lids.
- Avoid checking intraocular pressure (IOP) unless suspect high intraocular pressure or considering steroid treatment.
- If IOP checked, use tonometer.
- Lid edema
- Conjunctiva: injection, chemosis, follicles, subconjunctival hemorrhages
- Punctate keratitis (use fluorescein), subepithelial infiltrates (1-2 weeks after onset)
- Pre-auricular lymphadenopathy
- Severe cases: pseudo membrane/membrane, symblepharon formation

Investigations:

- Nil if typical presentation
- Point of care test (Adenoplus®) available if helpful
- PCR swab for adenovirus if the diagnosis is in question and will alter your treatment plan.

Acute Management:

- Cool compresses
- Lubricant eye drops as required
- Pseudomembrane/membrane formation: peel membrane using topical anesthesia, cotton bud, or fine forceps
- Disinfect room/equipment immediately on discharge of the patient.

Indications for Topical Steroids:

- Pseudomembrane/membrane formation
- Subepithelial infiltrates (SEI) decreasing vision (< 6/12)
- Options for topical steroids: Fluorometholone acetate eye drops, Fluorometholone eye drops, Prednisolone acetate 1%, or Dexamethasone 0.1% eye drops for moderately severe pseudomembranes

Follow-up:

- Limit follow-up appointments, if possible, to decrease the spread of the disease
- Pseudomembrane/membrane formation: follow every 2-3 days until membrane formation ceases, then increase intervals.
- Monitor IOP if steroids prescribed.
- Subepithelial infiltrates on topical steroids: follow at 2-3 weekly intervals until improvement, then increase intervals.
- Consider Chlamydia PCR for symptoms lasting >3 weeks.

Discharge Instructions:

- Instructions on symptomatic relief of symptoms: lubricant eye drops, cool compresses
- Natural history of the condition: self-limited, can worsen in the first few days, usually resolves in 2-3 weeks
- Highly contagious, spread by contact, strict hand-washing, no sharing of linen, minimize contact with others
- Avoid work/school while contagious, especially for childcare providers/teachers/health care workers
- Medical Certificate as required
- Contact lens wearer: discard the previous lens and resume contact lens wear with a fresh contact lens only once the eye has been asymptomatic for 1 week.

1.2.3 Herpes Simplex Keratitis (HSK) Prescribing Protocol and Treatment Guideline by the Royal Australian and New Zealand College of Ophthalmologists (2020)

Evidence levels and grades of recommendations were not outlined. The following recommendations are provided by the Royal Australian and New Zealand College of Ophthalmologists on the management of Herpes Simplex Keratitis (HSK)[6]:

Clinical Criteria:

- Herpes Simplex Keratitis is diagnosed based on clinical criteria:
    - Epithelial keratitis (dendritic ulcer)
    - Stromal keratitis: vascularization, scarring, lipid keratopathy, ulceration
    - Endothelial keratitis: Stromal edema and keratic precipitates
    - Keratouveitis: Corneal epithelial and/or stromal edema, stromal keratitis, keratic precipitates, and anterior chamber cells
- Required investigations include HSV PCR.

Contraindications and Precautions:

- Contraindication: Identified allergy to aciclovir and valaciclovir
- Precautions to consider when prescribing:
    - Renal conditions
        - Increased risk of neurological adverse effects in renal impairment
        - Dose adjustment is necessary.
    - Pregnancy
        - Valaciclovir is rapidly metabolized to aciclovir; limited data do not indicate an increased risk of congenital malformations.
        - Aciclovir is preferred, especially after 36 weeks of pregnancy.
    - Breastfeeding: Safe to use

Proposed Place in Therapy:

- Medical practitioners must specify whether the drug is to be used as first, second-, or third-line treatment.
- Aciclovir or valaciclovir is the first-line therapy for herpes simplex keratitis.

Dosage and Duration of therapy

It is recommended that the Ophthalmologist adjust dosage for specific patient groups, as shown in the tables below:

Table 5. Dosage and Duration of Therapy Adapted from the 2020 Herpes Simplex Keratitis (HSK) Guideline by the Royal Australian and New Zealand College of Ophthalmologists

Epithelial HSK	Local treatment dosage: Topical acyclovir 5 times/day for 1-2 weeks	Systemic treatment dosage: Immunocompromised patients Non-compliance, inability to use or tolerate, or ocular toxicity from topical acyclovir **Oral Valaciclovir 500 mg BD for 7 days**
Stromal HSK	Without epithelial ulcer: **ORAL Valaciclovir 500 mg ONCE a day** during topical steroid use PLUS **Prednisolone 1% eye drops 4-6 times a day tapered over > 10 weeks**	With epithelial ulcer: **Oral Valaciclovir 1 g TDS for 7-10 days* PLUS** Prednisolone 1% eye drops BD tapered slowly as disease comes under control
Endothelial HSK	**ORAL Valaciclovir 500 mg to 1 g ONCE a day to TDS for 7-10 days***† PLUS **Prednisolone 1% eye drops 4-6 times a day tapered over > 10 weeks**	
Keratouveitis	**ORAL Valaciclovir 1 g TDS for 7-10 days*** PLUS **Prednisolone 1% eye drops 4-6 times a day** tapered over > 10 weeks Refer patient to cornea/uveitis clinic, respectively depending on degree of cornea or uveal involvement	

Prophylaxis	Indications:
	• Multiple recurrences of any type of HSK, especially stromal HSK
	• Patients with a history of ocular HSV:
	  ○ following any ocular surgery, including penetrating keratoplasty
	  ○ during immunosuppressive treatment
	Oral Aciclovir 400 mg BD
	OR
	Oral Valaciclovir 500 mg ONCE a day	

* Reduce Valaciclovir to prophylactic dose after 7-10 days and maintain for as long as frequent topical steroids are in use

† There is a lack of clinical evidence to guide dosage in this situation

Table 6. Adult Renal Dosing for Oral Antivirals. Adapted from the 2020 Herpes Simplex Keratitis (HSK) Guideline by the Royal Australian and New Zealand College of Ophthalmologists

CrCl (mL/min)	Dose	Frequency
Normal dose valaciclovir 500 mg ONCE per day		
< 30	500 mg	Every 48 hours
Normal dosage valaciclovir 500 mg BD		
< 30	500 mg	Every 24 hours
Normal dosage valaciclovir 1 g TDS		
30-49	1 g	Every 12 hours
10-29	1 g	Every 24 hours
< 10	500 mg	Every 24 hours
Normal dosage acyclovir 400 mg BD		
0-10	200 mg	Every 12 hours

In Pregnancy:

- Acyclovir is preferred due to more clinical experience (Category B3).
- Valacyclovir has limited data that does not suggest increased risk of congenital malformations. It may be used from 36 weeks of pregnancy (Category B3).

In Pediatric Dosing:

- Aciclovir is the drug of choice.
- Valaciclovir must only be used in children older than 12 years old.
- For local treatment, in ages 3 months to 18 years, in epithelial HSK, topical acyclovir is recommended 5 times a day for 14 days or for at least 3 days after healing, whichever is shorter.

Systemic Treatment Dosage

- Indications:
    - Stromal HSK
    - Skin involvement
    - Coexistent systemic disease

- Non-compliance, inability to use or tolerate, or ocular toxicity from topical acyclovir.
- Immunocompromised patients – seek advice from a Pediatric Infection Diseases Physician.

The following table provides systemic therapy recommendations in pediatrics:

Table 7. Systemic Therapy Recommendations in Pediatrics. Adapted from the 2020 Herpes Simplex Keratitis (HSK) Guideline by the Royal Australian and New Zealand College of Ophthalmologists

Age	Recommendation
Birth (at term) to 3 months	Seek advice from Pediatric Infection Diseases Physician
3 months to 12 years	**Oral aciclovir 10 mg/kg (max 400 mg) 5 times a day for 5-7 days** or until there are no new lesions PLUS **Prednisolone 1% eye drops BD-QID a day**. (For severe inflammation, consider hourly dosing for 1-2 days)
12 years to 18 years	**Oral aciclovir 10 mg/kg (max 400 mg) 5 times a day for 5-7 days** or until there are no new lesions OR **Oral Valaciclovir 500 mg BD for 5 days** if first episode (longer if new lesions appear during treatment or healing is incomplete) **Oral Valaciclovir 500 mg BD for 3-5 days** if recurrent episode PLUS **Prednisolone 1% eye drops BD-QID a day**. (For severe inflammation, consider hourly dosing for 1-2 days)

Important Drug Interactions:

- **Mycophenolate:**
  - Mycophenolate can potentially raise the concentration of aciclovir/valaciclovir.
  - In cases of renal impairment, both drugs may be excreted more slowly, increasing the risk of adverse effects like neutropenia.
  - Dosage adjustment is generally not required.

- **Theophylline:**
    - Aciclovir/valaciclovir may lead to an increase in the concentration of theophylline, elevating the risk of adverse effects.
    - It is advisable to monitor the theophylline concentration and watch for adverse effects.
    - Adjust the theophylline dose as necessary to manage these effects.

Administration Instructions:

- For systemic treatment, ensure the patient stays adequately hydrated, especially with high doses, to reduce the risk of renal adverse effects.
- Instruct patients to take tablets with a full glass of water.
- Ensure that patients are proficient in the proper technique for administering eye drops or ointment.

Monitoring Requirements:

- Patients should be reviewed by an ophthalmologist once the therapy has commenced, following the guidelines.
- Monitoring is necessary to confirm the safety of use and should include assessing for the following:
    - Blood and lymphatic system disorders (very rare: anaemia, leukopenia, thrombocytopenia).
    - Immune system disorders (rare: anaphylaxis).
    - Psychiatric and nervous system disorders (common: headache, dizziness, confusion, hallucinations, somnolence, convulsions; very rare: agitation, tremor, ataxia, dysarthria, psychotic symptoms, encephalopathy, coma - these events are reversible and usually reported in patients with renal impairment or excessive dosages).
    - Respiratory, thoracic, and mediastinal disorders (rare: dyspnoea).
    - Gastrointestinal disorders (common: nausea, vomiting, diarrhea, abdominal pains).
    - Hepatobiliary disorders (rare: reversible increases in bilirubin and liver-related enzymes; very rare: hepatitis, jaundice).
    - Skin and subcutaneous tissue disorders (common: pruritus, rashes, including photosensitivity; uncommon: urticaria, accelerated diffuse hair loss; rare: angioedema).

    - Renal and urinary disorders (rare: increases in blood urea and creatinine; very rare: acute renal failure, renal pain, possibly associated with renal failure).
    - General disorders (common: fatigue, fever).

Evaluating Effectiveness:

- The effectiveness of drug treatment is indicated by improved visual acuity and clinical signs, including:
    - Resolution of epithelial defect or punctate corneal staining.
    - Reduction in inflammation of corneal stromal or anterior chamber.
    - Resolution of stromal infiltrates.

Management of Complications:

- If complications such as changes in renal function occur during systemic treatment, best practices involve the following approaches: Rehydration, Dosage reduction, Stopping the drug.

Section 2.0 Drug Therapy in Viral Eye Infections

This section comprises three subsections: the first contains the newly recommended drugs, the second covers drug modifications, and the third outlines the drugs that have been withdrawn from the market.

2.1 Additions

2.1.1 Foscarnet

Table 8. Foscarnet Drug Information

SCIENTIFIC NAME **Foscarnet**[10]	
SFDA Classification	Prescription
SFDA Approval	Yes
US FDA	Yes
EMA	Yes
MHRA	Yes
PMDA	Yes
Indication (ICD-10)	B02.3, B00.5, H19.1, H19.3
Drug Class	Antiviral Agent
Drug Sub-class	
ATC Code	**J05AD01**
Pharmacological Class (ASHP)	N/A
DRUG INFORMATION	
Dosage Form	**Solution for infusion**
Route of Administration	Intravenous use
Dose (Adult) [DDD]*	**Ophthalmic disease (retinitis):** **IV (alternative agent):** Induction treatment: 60 mg/kg/dose every 8 hours or 90 mg/kg/dose every 12 hours for 14 to 21 days; for immediate sight-threatening lesions, administer in combination with intravitreal therapy. Maintenance therapy: 90 to 120 mg/kg/dose once daily; due to lower toxicity, begin with 90 mg/kg/dose once daily, may escalate to 120 mg/kg/dose

<table>
<tr><td></td><td>once daily if lower dose tolerated or for retinitis progression. Duration of maintenance therapy is ≥ 3 to 6 months and until lesions are inactive and until CD4 count is > 100 cells/mm3 for 3 to 6 months in response to antiretroviral therapy in patients with HIV.</td></tr>
<tr><td>Maximum Daily Dose Adults*</td><td>180 mg/kg/day</td></tr>
<tr><td>Dose (pediatrics)</td><td>Retinitis: Use as a component of initial therapy if immediate, sight-threatening lesions are present.
Infants and Children: IV: 180 mg/kg/day in divided doses every 8 or 12 hours; continue for 14 to 21 days. Use in combination with ganciclovir if monotherapy fails or in sight-threatening illnesses. Follow treatment with chronic suppression.
Adolescents: Combination therapy with intravitreal and intravenous antiviral therapy recommended; follow treatment/induction with chronic suppression.
IV: 180 mg/kg/day in divided doses every 8 or 12 hours for 14 to 21 days
Intravitreal: 2.4 mg/dose for 1 to 4 doses administered over 7 to 10 days in combination with valganciclovir (oral), ganciclovir (IV), foscarnet (IV), or cidofovir (IV)</td></tr>
<tr><td>Maximum Daily Dose Pediatrics*</td><td>180 mg/kg/day</td></tr>
<tr><td>Adjustment</td><td>Hepatic Impairment: There are no dosage adjustments recommended.
Renal impairment: Induction Dosing of Foscarnet in Patients with Abnormal Renal Function
<table>
<tr><th>CrCl (mL/min/kg)</th><th>Equivalent to 60 mg/kg every 8</th><th>Equivalent to 90 mg/kg every</th></tr>
</table></td></tr>
</table>

	hours	12hours
<0.4	Not recomm-ended	Not recomm-ended
≥0.4-0.5	50 mg/kg every 24 hours	50 mg/kg every 24 hours
>0.5-0.6	60 mg/kg every 24 hours	60 mg/kg every 24 hours
>0.6-0.8	40 mg/kg every 12 hours	80 mg/kg every 24 hours
>0.8-1	50 mg/kg every 12 hours	50 mg/kg every 12 hours
>1-1.4	45 mg/kg every 8 hours	70 mg/kg every 12 hours
>1.4	60 mg/kg every 8 hours	90 mg/kg every 12 hours

Maintenance Dosing of Foscarnet in Patients with Abnormal Renal Function

CrCl (mL/ min/kg)	Equivalent to 90 mg/kg every 24 hours	Equivalent to 120 mg/kg every 24 hours
<0.4	Not recomm-ended	Not recomm-ended
≥0.4-0.5	50 mg/kg every 48 hours	65 mg/kg every 48 hours
>0.5-0.6	60 mg/kg every 48 hours	80 mg/kg every 48 hours
>0.6-0.8	80 mg/kg every 48 hours	105 mg/kg every 48 hours
>0.8-1	50 mg/kg every 24 hours	65 mg/kg every 24 hours

	>1-1.4	70 mg/kg every 24 hours	90 mg/kg every 24 hours
	>1.4	90 mg/kg every 24 hours	120 mg/kg every 24 hours
Prescribing edits*	MD, PA, ST		
AGE (Age Edit): N/A			
CU (Concurrent Use Edit): N/A			
G (Gender Edit): N/A			
MD (Physician Specialty Edit): should be prescribed by an infectious diseases specialist			
PA (Prior Authorization): needs positive CMV PCR prior to therapy initiation			
QL (Quantity Limit): N/A			
ST (Step Therapy): an alternative when ganciclovir/valganciclovir treatment fails.			
EU (Emergency Use Only): N/A			
PE (Protocol Edit): N/A			
SAFETY			
Main Adverse Drug Reactions (most common and most serious)	**Most common:** headache, hypokalemia, hypophosphatemia, hypocalcemia, hypomagnesemia, nausea, diarrhea, anemia **Most serious**: granulocytopenia, renal insufficiency, first degree atrioventricular block, amnesia, dermal ulcer, aggressive behavior, nephrotoxicity		
Drug Interactions*	X Acyclovir (Systemic) X Amikacin (Systemic) X Amphotericin B (Lipid Complex) X Amphotericin B (Liposomal) X Amphotericin B Deoxycholate X Arbekacin X CycloSPORINE (Systemic) X Gentamicin (Systemic) X Isepamicin X Kanamycin X Methotrexate X Neomycin (Systemic) X Netilmicin (Systemic)		

	XParomomycin X Plazomicin X Ribostamycin X Sisomicin X Streptomycin X Tacrolimus (Systemic) X Tobramycin (Systemic) X ValACYclovir D Azosemide D Bumetanide D Ethacrynic Acid D Furosemide D Pentamidine (Systemic) D Torsemide
Special Population	Information on the use of foscarnet is lacking in the elderly. Dose adjustments and proper monitoring must be performed because of the decreased renal function common in older patients.
Pregnancy	Information related to the use of foscarnet in pregnancy is limited. Foscarnet is not the preferred treatment of cytomegalovirus infection in pregnant patients. Monitoring of amniotic fluid volumes by ultrasound is recommended weekly after 20 weeks of gestation to detect oligohydramnios if foscarnet is used. In general, intravitreous injections for local therapy are preferred for retinal disease to limit systemic exposure.
Lactation	It is not known if foscarnet is present in breast milk. Due to the potential for serious adverse reactions in the breastfeeding infant, the manufacturer recommends a decision be made whether to discontinue breastfeeding or to discontinue the drug, taking into

	account the importance of treatment to the mother.
Contraindications	Clinically significant hypersensitivity to foscarnet or any component of the formulation.
Monitoring Requirements	24-hour creatinine clearance, ECG, and electrolytes at baseline and periodically thereafter (when clinically appropriate). During induction therapy: Obtain complete blood counts, and electrolytes (including serum creatinine, calcium, magnesium, potassium, and phosphorus) twice weekly and then one weekly during maintenance therapy. More frequent monitoring may be required in some patients. Check hydration status before and after infusion.
Precautions	**Concerns related to adverse effects:** • Dental effects: Foscarnet is deposited in teeth and bone of young, growing animals; it has adversely affected tooth enamel development in rats. • Electrolyte imbalance: Imbalance of serum electrolytes or minerals occurs in at least 15% of patients (hypocalcemia, low ionized calcium, hyper/hypophosphatemia, hypomagnesemia, or hypokalemia); reducing infusion rate may decrease/prevent symptoms. Patients with low ionized calcium may experience perioral tingling, numbness, paresthesias, tetany, and seizures. Correct electrolytes before initiating therapy; use caution in patients who have any underlying electrolyte imbalances, those with neurologic or cardiac abnormalities, and those receiving medications

	that are influenced by calcium levels. Use caution when administering other medications that cause electrolyte imbalances. Patients who experience signs or symptoms of an electrolyte imbalance should be assessed immediately. • Hematologic effects: May cause anemia and granulocytopenia. • Hypersensitivity: Serious hypersensitivity reactions, including anaphylactic shock and angioedema, have been reported. Discontinue immediately and institute appropriate medical therapy if an acute reaction occurs. • Renal impairment: [US Boxed Warning]: Renal impairment occurs to some degree in the majority of patients treated with foscarnet; renal impairment may occur at any time (though typically during second week of induction therapy) and is usually reversible within 1 week following dose adjustment or discontinuation of therapy, however, several patients have died with renal failure within 4 weeks of stopping foscarnet; therefore, renal function should be closely monitored during both induction and maintenance therapy. To reduce the risk of nephrotoxicity and the potential to administer a relative overdose, always calculate the CrCl even if serum creatinine is within the normal range. Dosage adjustments are recommended for renal dysfunction; safety and efficacy in patients with a baseline Scr >2.8 mg/dL or CrCl <50 mL/minute are

	limited. Use in patients with CrCl <0.4 mL/kg/minute is not recommended. Adequate hydration may reduce the risk of nephrotoxicity; the manufacturer makes specific recommendations regarding this (see Administration). • QT prolongation: QT prolongation, including torsades de pointes, has been reported; some reports occurred in patients with confounding risk factors (eg, underlying cardiac disease, electrolyte abnormalities, concomitant medications). Use with caution in patients with a history of QT prolongation or those at increased risk for QT prolongation. • Seizures: [US Boxed Warning]: Seizures related to plasma electrolyte/mineral imbalance may occur; incidence has been reported in up to 10% of HIV patients. Risk factors for seizures include impaired baseline renal function, low total serum calcium, and underlying CNS condition. Some patients who have experienced seizures have been able to continue or resume foscarnet treatment after their mineral or electrolyte abnormality has been corrected, their underlying disease state treated, or their dose decreased. • Vascular irritant: Administer only into vein with adequate blood flow to prevent tissue irritation/ulceration. Genital vascular tissue damage has been reported; adequate hydration recommended. **Disease related concerns:**

	• Heart failure: Due to sodium content, use with caution in patients with heart failure. **Other warnings/precautions:** • Appropriate use: [US Boxed Warning]: Indicated only for immunocompromised patients with CMV retinitis and mucocutaneous acyclovir resistant HSV infection.
Black Box Warning	• Renal impairment • Seizures • Appropriate use
REMS*	N/A

HEALTH TECHNOLOGY ASSESSMENT (HTA)

The table below lists the HTA reviews and recommendations of viral eye infections treatment options by the following agencies/institutes/authorities: National Institute for Health and Care Excellence (NICE), Canadian Agency for Drugs and Technologies in Health (CADTH), Haute Autorité de Santé (HAS), Institute for Quality and Efficiency in Health Care (IQWIG), and Pharmaceutical Benefits Advisory Committee (PBAC) as applicable. **The recommendations are for Foscarnet.**

Table 9. Foscarnet HTA Analysis

MEDICATION	AGENCY	DATE – HTA RECOMMENDATION
Foscarnet	NICE	No recommendations for this medication.
	CADTH	No recommendations for this medication.
	HAS[11]	November 2019: A positive assessment for reimbursement is recommended for the treatment of cytomegalovirus (CMV) infection in recipients of hematopoietic stem cell transplants (HSCT) when the use of ganciclovir is not feasible. Additionally, a favorable recommendation for reimbursement is suggested for the treatment of disseminated CMV infections in AIDS patients and the initial treatment of mucocutaneous Herpes Simplex Virus (HSV) infections that are resistant or unresponsive to acyclovir in individuals with weakened immune systems. The therapeutic advantages of Foscarnet

		in these mentioned indications are substantial. The clinical value added by Foscarnet is significant.
	IQWIG	No recommendations for this medication.
	PBAC	No results retrieved.

CONCLUSION STATEMENT – FOSCARNET

Foscarnet is an alternative when ganciclovir/valganciclovir treatment fails. Most HTA bodies do not provide recommendations for the use of Foscarnet in Cytomegalovirus Uveitis. The HAS body provides a positive recommendation for the use of Foscarnet in CMV infection in HSCT recipients when the use of ganciclovir is not feasible, and in disseminated CMV infections in AIDs and HSV patients that are resistant/unresponsive to acyclovir.

2.2 Modifications

Topical Ganciclovir is now registered in SFDA and has been added to the drug summary spreadsheet.

2.3 Delisting

The medications below are no longer SFDA registered[12], therefore, it is advisable to delist the following drugs from CHI formulary.

In addition, antibiotics (and their combination with steroids) will be delisted since there is no high-level evidence on their role in viral eye infections for prevention of superimposed bacterial infections.

*Please refer to **Drug Therapy in Viral eye infections- Section 2** of CHI Viral Eye Infections original clinical guidance:*

- DEXPANTHENOL, SODIUM HYALURONATE
- ECTOIN, SODIUM HYALURONATE
- GLYCERIN, SODIUM CARBOXYMETHYLCELLULOSE
- POLYMYXIN B, BACITRACIN, NEOMYCIN SULFATE
- POLYMYXIN B, NEOMYCIN SULFATE, GRAMICIDIN
- VIDARABINE
- CHLORAMPHENICOL
- CIPROFLOXACIN
- DEXAMETHASONE, NEOMYCIN SULFATE
- FUSIDIC ACID
- GATIFLOXACIN
- GENTAMICIN
- MOXIFLOXACIN HYDROCHLORIDE

- NORFLOXACIN
- OFLOXACIN
- OFLOXACIN, DEXAMETHASONE
- OFLOXACIN, PREDNISOLONE, TETRAHYDROZOLINE
- POLYMYXIN B, NEOMYCIN SULFATE, DEXAMETHASONE
- POLYMYXIN B, PREDNISOLONE, NEOMYCIN SULFATE
- TETRACYCLINE
- TOBRAMYCIN
- TOBRAMYCIN,DEXAMETHASONE

Section 3.0 Key Recommendations Synthesis

American Academy of Ophthalmology, 2018

- **Conjunctivitis:**
    - No evidence exists demonstrating the superiority of any topical antibiotic agent. (I+, Good, Strong)
- **Adenoviral Conjunctivitis**
    - The patient should be educated about measures that will help reduce the spread of this infection and encouraged to make every attempt to minimize contact with other people for 10 to 14 days from the onset of symptoms in the last eye affected. [I+, Good, Strong]
    - There is no proven effective treatment for eradication of adenovirus infection; however, artificial tears, topical antihistamines, topical steroids, oral analgesics, or cold compresses may be used to mitigate symptoms.
    - Topical corticosteroids are helpful to reduce symptoms and may reduce scarring in severe cases of adenoviral keratoconjunctivitis with marked chemosis or lid swelling, epithelial sloughing, or membranous conjunctivitis. Topical corticosteroids should be tapered once inflammation is controlled.
    - Povidone-iodine 0.4% alone or in combination with dexamethasone 0.1% has demonstrated reductions in viral titers, virus spread, shortening of the clinical course, and preservation of visual function.
    - Off-label use of topical ganciclovir 0.15% ophthalmic gel has been investigated for the treatment of epidemic keratoconjunctivits (EKC) and has shown potential benefit against specific adenovirus serotypes, but further efficacy on a larger scale needs to be demonstrated before definitive recommendations can be made.
- **Herpes Simplex Virus Conjunctivitis**
    - Herpes simplex virus conjunctivitis is a self-limited acute condition.
    - Possible topical options include ganciclovir 0.15% gel used three to five times per day or trifluridine 1% solution five to eight times per day.
    - Oral treatments for HSV keratitis include acyclovir (200 to 400 mg five times per day), valacyclovir (500 mg two or three times per day), or famciclovir (250 mg twice a day).

    - Lower doses of oral antivirals are considered for long-term prophylaxis against recurrent HSV keratitis.
    - Topical corticosteroids potentiate HSV infection and should be avoided.
- **Varicella (Herpes) Zoster Virus Conjunctivitis**
    - Many clinicians treat such patients with topical antibiotics to prevent secondary infection because the vesicles will undergo necrosis before healing.
    - Topical antivirals alone have not been shown to be helpful in treating VZV conjunctivitis but may be used as additive treatment in unresponsive patients.
    - With persistent or recalcitrant acute/subacute disease in immunocompetent patients, oral antivirals may be beneficial at a dose of 800 mg five times daily for 7 days for acyclovir, 1000 mg every 8 hours for 7 days for valacyclovir, or 500 mg three times daily for 7 days for famciclovir.
    - Immunocompromised patients may need to be treated more aggressively.
- **Molluscum Contagiosum**
    - Treatment options include incision and curettage (aggressive enough to cause bleeding), simple excision, excision and cautery, and cryotherapy.

Optometric Clinical Practice Guideline, 2002

- Supportive therapy includes time honored treatment options: cold compresses, lubricants, and ocular decongestants.
- Topical antibiotics are not routinely used to treat viral conjunctivitis, unless there is evidence of secondary bacterial infection. The risk of toxic and allergic reactions may outweigh the potential benefit of antibiotic use.
- Because of the potential side effects of topical ophthalmic corticosteroids, practitioners may wish to limit the use of these agents to patients who are significantly symptomatic or who develop visual loss from inflammatory keratitis.
- Herpes zoster conjunctivitis treatment includes the use of topical antibiotic/steroid combinations to reduce the risk of secondary bacterial infection and decrease the inflammatory response.
- In contrast with their effect on herpes simplex infections, topical steroids do not exacerbate herpes zoster infections. In addition to topical therapy,

systemic antiviral treatment reduces the duration of both viral shedding and post-herpetic neuralgia.

- To be most effective in reducing the duration of post-herpetic neuralgia, systemic antiviral therapy should be started within 72 hours of the first signs of herpes zoster infection.
- Neonatal Conjunctivitis
    - Acyclovir (30–60 mg/kg/day) Inadequate if used IV or IM q.8h. for 10–14 days alone; unnecessary with systemic treatment.

Herpes Simplex Virus Keratitis, 2014

- **HSV Epithelial keratitis**
    - There are two FDA approved topical antiviral agents with similar efficacy (ganciclovir and trifluridine). There are three oral antiviral agents (acyclovir, valacyclovir, and famciclovir) available in the U.S.
    - Oral antiviral agents appear to be as effective as topical antiviral agents (ganciclovir, trifluridine) in the treatment of HSV epithelial keratitis. In spite of their similar efficacy, there are differences and there may be advantages to choosing one over the other in individual cases.
    - There is no evidence that simultaneous use of two antiviral agents, whether topical or oral, accelerates healing of HSV epithelial keratitis.
- **HSV Stromal Keratitis**
    - A topical corticosteroid agent in conjunction with an oral antiviral agent for at least ten weeks is the preferred treatment for HSV stromal keratitis. The balance between antiviral and corticosteroid therapy should be adjusted depending on the presence or absence of epithelial ulceration. (Strong Recommendation, Good Quality)
    - A treatment period greater than ten weeks has been recommended since both double blind, placebo controlled randomized clinical trials by the HEDS group found excessively high treatment failure rates six weeks after a ten-week prednisolone taper (50% and 75%), indicating the length of treatment may have been inadequate.
    - The treatment course should be titrated empirically depending on the clinical response.
    - Oral antiviral agents are recommended over topical antiviral agents for their safety profile and superior corneal penetration. The best treatment for HSV keratitis with epithelial ulceration has not been studied adequately in randomized clinical trials, but available evidence

suggests a role for therapeutic doses of oral antiviral combined with judicious use of topical corticosteroids.

- **HSV Endothelial Keratitis**
    - A topical corticosteroid agent in conjunction with an oral antiviral agent is the preferred treatment for HSV endothelial keratitis. (Strong Recommendation, Good Quality)
    - A topical corticosteroid agent in conjunction with an oral antiviral agent is the preferred treatment for HSV endothelial keratitis. (Strong Recommendation, Good Quality)
    - The mean healing time for the patients requiring treatment with combination antiviral and corticosteroid therapy ranged from 21 days to 25 days in these studies. Compared to patients with HSV stromal keratitis, those with HSV endothelial keratitis appear to respond more rapidly to treatment and may not require prolonged therapy.

Cytomegalovirus Uveitis (2023)

- To prevent CMV AU recurrence, antiviral agents are favored over steroids.
- In Taiwan, topical ganciclovir (20 mg/cc) is the preferred medication due to its effectiveness, safety, and convenience.
- Consider using anti-glaucoma agents for cases with poorly controlled intraocular pressure (IOP) and disc damage.
- Steroids may lead to CMV AU becoming latent or resistant to treatment.
- The use of steroids in the acute stage of CMV AU remains controversial, with some advocating their combined use and others opposing it.
- Systemic ganciclovir or valganciclovir is recommended for vision-threatening cases of CMV retinitis, but myelosuppression is a concern.
- Intravitreal ganciclovir is supplemental in severe cases with AIDS and bone marrow transplantation but not for mild cases.
- Foscarnet is an alternative when ganciclovir/valganciclovir treatment fails.

The Royal Victorian Eye and Ear Hospital (2021)

- **Indications for Topical Steroids include** Pseudomembrane/membrane formation or Subepithelial infiltrates (SEI) decreasing vision (<6/12). Options for topical steroids: Fluorometholone acetate eye drops, Fluorometholone eye drops, Prednisolone acetate 1%, or Dexamethasone 0.1% eye drops for moderately severe pseudomembranes.

The Royal Australian and New Zealand College of Ophthalmologists (2020)

- Aciclovir or valaciclovir is the first-line therapy for herpes simplex keratitis.

Section 4.0 Conclusion

This report serves as an annex to the previous CHI Viral Eye Infections report and aims to provide recommendations to aid in the management of Viral Eye Infections. It is important to note that these recommendations should be utilized to support clinical decision-making and not replace it in the management of individual patients with Viral Eye Infections. Health professionals are expected to consider this guidance alongside the specific needs, preferences, and values of their patients when exercising their judgment.

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Section 6.0 Appendices

Appendix A. Prescribing Edits Definition

I. Prescribing Edits (ensure consistent use of abbreviations, e.g., CU, ST)

Some covered drugs may have additional requirements, rules, or limits on coverage. These requirements and limits may include:

Prescribing edits Tools	Description
AGE (Age):	Coverage may depend on patient age
CU (Concurrent Use):	Coverage may depend upon concurrent use of another drug
G (Gender):	Coverage may depend on patient gender
MD (Physician Specialty):	Coverage may depend on prescribing physician's specialty or board certification
PA (Prior Authorization):	Requires specific physician request process
QL (Quantity Limits):	Coverage may be limited to specific quantities per prescription and/or time period
ST (Step Therapy):	Coverage may depend on previous use of another drug
EU (Emergency Use only):	This drug status on Formulary is only for emergency use
PE (Protocol Edit):	Use of drug is dependent on protocol combination, doses and sequence of therapy

II. Adult and Pediatric Quantity Limit?

This is either the adult or pediatric maximum amount of a drug that can be administered per day based on a maximum daily dose. If there is no clinical evidence supporting the quantity limit for that relevant indication, this column will be left as Blank.

III. What information is available in the notes?

“Notes” section provides details of the prescribing edits, extra important drug information and special warning and precautions.

IV. Drug interactions

- A: No known interaction
- B: No action needed
- C: Monitor therapy
- D: Consider therapy modification
- X: Avoid combination

V. Defined Daily Dose

The Defined Daily Dose (DDD) is to be set based on the WHO recommendations https://www.whocc.no/ddd/definition_and_general_considera/

VI. REMS

A Risk Evaluation and Mitigation Strategy (REMS) is a drug safety program that the U.S. Food and Drug Administration (FDA) can require for certain medications with serious safety concerns to help ensure the benefits of the medication outweigh its risks.

Appendix B. Viral Eye Infections Scope

Comparison of the 2020 and the 2023 Report

2020	Changes Performed	2023	Rationale
Section 1.0 Viral Eye Infections Clinical Guidelines			
American Academy of Ophthalmology: Conjunctivitis Preferred Practice Pattern (2018)[7]	N/A	N/A	
OPTOMETRIC CLINICAL RACTICE GUIDELINE: Care of the Patient with Conjunctivitis- AMERICAN OPTOMETRIC ASSOCIATION (Approved by the AOA Board of Trustees June 22, 1995 (1st Edition) and November 8, 2002 (2nd Edition))[8]	N/A	N/A	
Herpes Simplex Virus Keratitis: A treatment guideline by the Department of Ophthalmology- Harvard Medical School (approved by the	N/A	N/A	

Ocular Microbiology and immunology group and the Hoskins Center for Quality Eye Care, American Academy of Ophthalmology) (2014)[9]			
	Missing	Cytomegalovirus Uveitis: Taiwan expert consensus (2023)[4]	9. How should we diagnose patients presenting with typical CMV AU symptoms but negative PCR results? o Diagnosis can be supported by clinical course and therapeutic response. o In cases with a high clinical suspicion, it is advisable to repeat PCR tests to confirm the diagnosis. 10. What is the preferred treatment approach in terms of loading and maintenance doses for CMV AU? o To prevent CMV AU recurrence, antiviral agents are favored over steroids. o In Taiwan, topical ganciclovir (20 mg/cc) is the preferred medication due to its effectiveness, safety, and convenience. o Consider using anti-glaucoma agents for

			cases with poorly controlled intraocular pressure (IOP) and disc damage. 11. How long should CMV AU treatment be continued? o Currently, there are no randomized controlled trials providing optimal treatment duration for CMV AU. o The panel recommends a 6-month antiviral treatment for initial attacks without vision-threatening complications. o Cases with recurrent attacks or vision-threatening complications may require extended treatment (12 months or longer). o Treatment duration should be individualized, considering factors such as patient age, visual acuity, corneal endothelial density, disc nerve fiber thickness, and more. 12. What are the roles of topical and systemic steroids in CMV AU treatment? o Steroids may lead to CMV AU becoming latent or resistant to treatment. o The use of steroids in the

			acute stage of CMV AU remains controversial, with some advocating their combined use and others opposing it. 13. How should ocular hypertension induced by CMV AU be managed? o Aggressively control ocular hypertension with topical and systemic IOP-lowering agents. o Prostaglandin analogs are acceptable for CMV AU due to their low inflammatory status. o Topical carbonic anhydrase inhibitors (CAI) are traditionally not recommended for patients with poor corneal conditions but can be considered in refractory cases. 14. What are the preferred antiviral agents for CMV retinitis in clinical practice? o Systemic ganciclovir or valganciclovir is recommended for vision-threatening cases, but myelosuppression is a concern. o Intravitreal ganciclovir is supplemental in severe cases with AIDS and bone marrow transplantation but not for mild cases. o Foscarnet is an

			alternative when ganciclovir/valganciclovir treatment fails. 15. How should treatment efficacy be evaluated during CMV retinitis treatment, and when should treatment be discontinued? o Monitor intraocular and systemic conditions to assess efficacy. o Inactive uveitis and regressed retinitis indicate successful intraocular signs. o Improved systemic immune status (e.g., rising CD4+ count in HIV) is the key indicator for treatment cessation. o Typically, CMV treatment is continued for at least 3-6 months with inactive lesions and CD4+ count >100 cells/mm3 in HIV patients. 16. What is the strategy for prophylaxis of RD associated with CMV retinitis? o There is a unanimous agreement among panelists that there is currently no recommended prophylaxis for RD associated with CMV retinitis. <u>SFDA-registered drugs:</u> - Foscarnet

Appendix C. MeSH Terms PubMed

The following is the result of the PubMed search conducted for guideline search:

Query	Filters	Search Details	Results
((((((((((Eye Infections, Viral[MeSH Terms])) OR (Ocular Infections, Viral[Title/Abstract])) OR (Infection, Viral Ocular[Title/Abstract])) OR (Infections, Viral Ocular[Title/Abstract])) OR (Ocular Infection, Viral[Title/Abstract])) OR (Viral Ocular Infection[Title/Abstract])) OR (Viral Ocular Infections[Title/Abstract])) OR (Viral Eye Infections[Title/Abstract])) OR (Eye Infection, Viral[Title/Abstract])) OR (Infection, Viral Eye[Title/Abstract])) OR (Infections, Viral Eye[Title/Abstract])) OR (Viral Eye Infection[Title/Abstract])	Guideline, in the last 5 years, English	("eye infections, viral"[MeSH Terms] OR (("Ocular"[All Fields] OR "oculars"[All Fields]) AND "infections viral"[Title/Abstract]) OR (("infect"[All Fields] OR "infectability"[All Fields] OR "infectable"[All Fields] OR "infectant"[All Fields] OR "infectants"[All Fields] OR "infected"[All Fields] OR "infecteds"[All Fields] OR "infectibility"[All Fields] OR "infectible"[All Fields] OR "infecting"[All Fields] OR "infection s"[All Fields] OR "Infections"[MeSH Terms] OR "Infections"[All Fields] OR "Infection"[All Fields] OR "infective"[All Fields] OR "infectiveness"[All Fields] OR "infectives"[All Fields] OR "infectivities"[All Fields] OR "infects"[All Fields] OR "pathogenicity"[MeSH Subheading] OR "pathogenicity"[All Fields] OR "infectivity"[All Fields]) AND "viral ocular"[Title/Abstract]) OR (("infect"[All Fields] OR "infectability"[All Fields] OR "infectable"[All Fields] OR "infectant"[All Fields] OR "infectants"[All Fields] OR "infected"[All Fields] OR "infecteds"[All Fields] OR "infectibility"[All Fields] OR	2

		"infectible"[All Fields] OR "infecting"[All Fields] OR "infection s"[All Fields] OR "Infections"[MeSH Terms] OR "Infections"[All Fields] OR "Infection"[All Fields] OR "infective"[All Fields] OR "infectiveness"[All Fields] OR "infectives"[All Fields] OR "infectivities"[All Fields] OR "infects"[All Fields] OR "pathogenicity"[MeSH Subheading] OR "pathogenicity"[All Fields] OR "infectivity"[All Fields]) AND "viral ocular"[Title/Abstract]) OR (("Ocular"[All Fields] OR "oculars"[All Fields]) AND "infection viral"[Title/Abstract]) OR "viral ocular infection"[Title/Abstract] OR "viral ocular infections"[Title/Abstract] OR "viral eye infections"[Title/Abstract] OR (("Eye"[MeSH Terms] OR "Eye"[All Fields]) AND "infection viral"[Title/Abstract]) OR (("infect"[All Fields] OR "infectability"[All Fields] OR "infectable"[All Fields] OR "infectant"[All Fields] OR "infectants"[All Fields] OR "infected"[All Fields] OR "infecteds"[All Fields] OR "infectibility"[All Fields] OR "infectible"[All Fields] OR "infecting"[All Fields] OR "infection s"[All Fields] OR "Infections"[MeSH Terms] OR "Infections"[All Fields] OR	

		"Infection"[All Fields] OR "infective"[All Fields] OR "infectiveness"[All Fields] OR "infectives"[All Fields] OR "infectivities"[All Fields] OR "infects"[All Fields] OR "pathogenicity"[MeSH Subheading] OR "pathogenicity"[All Fields] OR "infectivity"[All Fields]) AND "viral eye"[Title/Abstract]) OR (("infect"[All Fields] OR "infectability"[All Fields] OR "infectable"[All Fields] OR "infectant"[All Fields] OR "infectants"[All Fields] OR "infected"[All Fields] OR "infecteds"[All Fields] OR "infectibility"[All Fields] OR "infectible"[All Fields] OR "infecting"[All Fields] OR "infection s"[All Fields] OR "Infections"[MeSH Terms] OR "Infections"[All Fields] OR "Infection"[All Fields] OR "infective"[All Fields] OR "infectiveness"[All Fields] OR "infectives"[All Fields] OR "infectivities"[All Fields] OR "infects"[All Fields] OR "pathogenicity"[MeSH Subheading] OR "pathogenicity"[All Fields] OR "infectivity"[All Fields]) AND "viral eye"[Title/Abstract]) OR "viral eye infection"[Title/Abstract]) AND ((y_5[Filter]) AND (guideline[Filter]) AND (english[Filter]))	

Appendix D. Treatment Algorithm

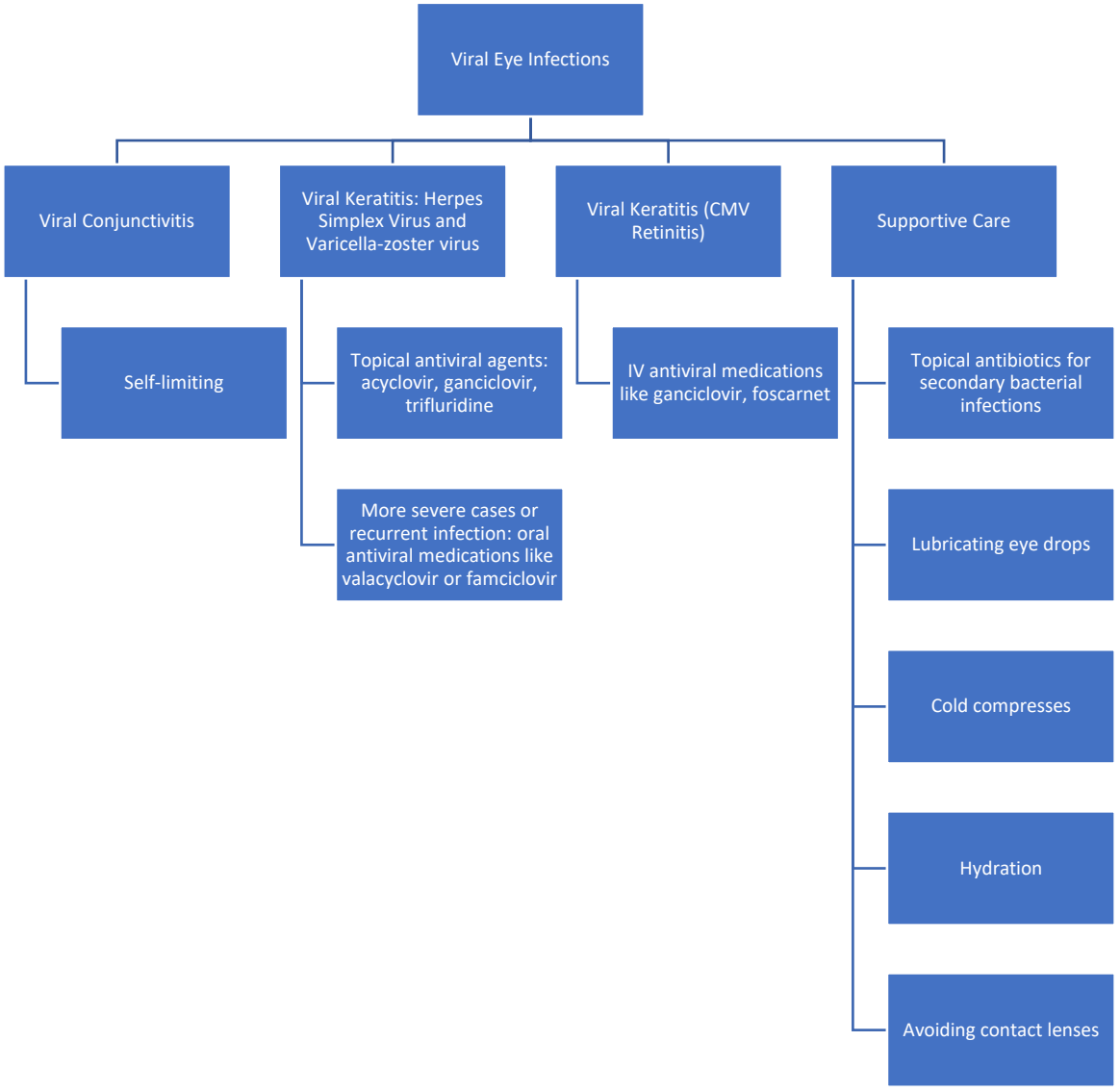

Figure 1. *Treatment Algorithm for the Management of Viral Eye Infections*