

APPENDIX VI: Summary of Treatment Recommendations

1. Epithelial Keratitis

a. Dendritic

(Therapeutic dose of topical or oral antiviral agent)

Acyclovir (Zovirax®): 400 mg 3–5 times daily for 7–10 days **or**

Valacyclovir (Valtrex®): 500 mg twice daily for 7–10 days **or**

Famciclovir (Famvir®): 250 mg twice daily for 7–10 days **or**

Trifluridine ophthalmic solution 1% (Viroptic): instillation of 1 drop into affected eye(s) 9 times daily for 7 days; may decrease dose to 5 times daily after 7 days if ulcer is healed. Treatment should not extend beyond 21 days because of potential ocular toxicity.

or

Ganciclovir ophthalmic gel 0.15% (Zirgan®): instillation of 1 drop into affected eye(s) 5 times daily while awake until healing of corneal ulcer, followed by 1 drop 3 times a day for 7 days.

b. Geographic

(Therapeutic dose of topical or oral antiviral agent)

Acyclovir (Zovirax®): 800 mg 5 times daily for 14–21 days **or**

Valacyclovir (Valtrex®): 1 g 3 times daily for 14–21 days **or**

Famciclovir (Famvir®): 500 mg twice daily for 14–21 days **or**

Trifluridine ophthalmic solution 1% (Viroptic®): instillation of 1 drop into affected eye(s) 9 times daily for 7 days; may decrease dose to 5 times daily after 7 days if ulcer is healed. Treatment should not extend beyond 21 days because of potential ocular toxicity.

or

Ganciclovir ophthalmic gel 0.15% (Zirgan®): instillation of 1 drop into affected eye(s) 5 times daily while awake until healing of corneal ulcer, followed by 1 drop 3 times daily for 7 days.

2. Stromal Keratitis

a. Without epithelial ulceration

(Therapeutic dose of topical corticosteroid PLUS prophylactic dose of oral antiviral agent)

Prednisolone 1%: 6–8 times daily tapered over greater than 10 weeks **plus**

Acyclovir (Zovirax®): 400 mg twice daily **or**

Valacyclovir (Valtrex®): 500 mg once daily **or**

Famciclovir (Famvir®): 250 mg twice daily

As disease comes under control, prednisolone can be tapered slowly to the lowest possible dose and frequency as determined by the patient's clinical condition. The lower the dose and frequency of topical corticosteroid, the longer the interval between subsequent dose reduction. Oral antiviral agents in **prophylactic** doses (above) should be maintained during corticosteroid treatment.

b. With epithelial ulceration

(Limited dose of topical corticosteroid PLUS therapeutic dose of oral antiviral agent)

Prednisolone 1%: twice daily **plus**

Acyclovir (Zovirax®): 800 mg 3–5 times daily for 7–10 days **or**

Valacyclovir (Valtrex®): 1 g 3 times daily for 7–10 days **or**

Famciclovir (Famvir®): 500 mg twice daily for 7–10 days

The oral antiviral agent is reduced to prophylactic dose and maintained as long as topical corticosteroids are in use. As disease comes under control prednisolone can be tapered slowly. Note: there is no clinical trial data to support a specific recommendation for length of treatment.

3. Endothelial Keratitis

(Therapeutic dose of topical corticosteroid PLUS therapeutic dose of oral antiviral)

Prednisolone 1%: 6–8 times daily **plus**

Acyclovir (Zovirax®): 400 mg 3–5 times daily **or**

Valacyclovir (Valtrex®): 500 mg twice daily **or**

Famciclovir (Famvir®): 250 mg twice daily

The oral antiviral agent is reduced to prophylactic dose after 7–10 days and maintained as long as topical corticosteroids are in use. As disease comes under control, the topical corticosteroid can be tapered slowly. Note: there is no clinical trial data to support a specific recommendation for length of treatment.

Topical corticosteroid options

1. Fluorometholone 0.1% ophthalmic suspension
2. Rimexolone 1% ophthalmic suspension
3. Prednisolone Sodium Phosphate 1% ophthalmic solution
4. Prednisolone Acetate 1% ophthalmic suspension
5. Difluprednate 0.05% ophthalmic emulsion

Special circumstances

Low doses of acyclovir, valacyclovir, and famciclovir are safe for long-term prophylaxis against HSV keratitis in HIV-infected patients. Atopic patients with HSV keratitis may require prolonged treatment with oral antiviral agents.

Prophylaxis of recurrent HSV keratitis

Potential indications:

1. Multiple recurrences of any type of HSV keratitis, especially HSV stromal keratitis.
2. Recurrent inflammation with scar/vascularization approaching visual axis.
3. More than one episode of HSV keratitis with ulceration: strong stimulus for corneal vascularization and lipid deposition.
4. Post-keratoplasty performed for HSV-related scarring/astigmatism.
5. Postoperatively in patients with a history of HSV ocular disease undergoing any type of ocular surgery or laser procedure.
6. In patients with a history of ocular HSV during immunosuppressive treatment.

Prophylaxis options:

1. Acyclovir (Zovirax®): 400 mg twice daily for one year **or**
2. Valacyclovir (Valtrex®): 500 mg once daily **or**
3. Famciclovir (Famvir®): 250 mg twice daily

The optimal duration of prophylaxis is not fully established, but at least one year is recommended.

RENAL DOSING

The following tables are intended as general guidelines for renal dosing of oral antivirals. However, renal dosing is best determined in conjunction with a nephrologist.

Renal Dosing: HSV Epithelial Keratitis (Dendritic)

Oral Antiviral	Creatinine Clearance (ml/min)	Dose	Frequency
Acyclovir	Normal Dosage	400 mg	3–5 times daily
	> 25	400 mg	3–5 times daily
	10–25	400 mg	Every 8 hours
	0–10	400 mg	Every 12 hours
Famciclovir	Normal Dosage	250 mg	2–3 times daily
	≥ 40–59	250 mg	Every 12 hours
	20–39	125 mg	Every 12 hours
	< 20	125 mg	Every 24 hours
	HD	125 mg	Following each dialysis
Valacyclovir	Normal Dosage	500 mg	Twice daily
	30–49	500 mg	Every 12 hours
	10–29	500 mg	Every 24 hours
	< 10	500 mg	Every 24 hours

Renal Dosing: HSV Epithelial Keratitis (Geographic)

Oral Antiviral	Creatinine Clearance (ml/min)	Dose	Frequency
Acyclovir	Normal Dosage	800 mg	5 times daily
	> 25	800 mg	3–5 times daily
	10–25	800 mg	Every 8 hours
	0–10	800 mg	Every 12 hours
Famciclovir	Normal Dosage	500 mg	Every 8–12 hours
	≥ 40	500 mg	Every 12 hours
	20–39	500 mg	Every 24 hours
	< 20	250 mg	Every 24 hours
	HD	250 mg	Following each dialysis

Renal Dosing: HSV Epithelial Keratitis (Geographic) cont...			
Oral Antiviral	Creatinine Clearance (ml/min)	Dose	Frequency
Valacyclovir	Normal Dosage	1 g	3 times daily
	30–49	1 g	Every 12 hours
	10–29	1 g	Every 24 hours
	< 10	500 mg	Every 24 hours

Renal Dosing: HSV Stromal Keratitis (without epithelial ulceration)

Oral Antiviral	Creatinine Clearance (ml/min)	Dose	Frequency
Acyclovir	Normal Dosage	400 mg	2 times daily
	> 10	400 mg	Every 12 hours
	0–10	200 mg	Every 12 hours
	Famciclovir	Normal Dosage	125 mg
≥ 40		125 mg	Every 12 hours
20–39		125 mg	Every 12 hours
< 20		125 mg	Every 24 hours
	HD	125 mg	Following each dialysis
Valacyclovir	Normal Dosage	500 mg	Once daily
	30–49	500 mg	Every 24 hours
	10–29	500 mg	Every 48 hours
	< 10	500 mg	Every 48 hours

Renal Dosing: HSV Stromal Keratitis (with epithelial ulceration)

Oral Antiviral	Creatinine Clearance (ml/min)	Dose	Frequency
Acyclovir	Normal Dosage	800 mg	3–5 times daily
	> 25	800 mg	3–5 times daily
	10–25	800 mg	Every 8 hours
	0–10	800 mg	Every 12 hours
Famciclovir	Normal Dosage	500 mg	2 times daily
	≥ 40	500 mg	Every 12 hours
	20–39	500 mg	Every 24 hours
	< 20	250 mg	Every 24 hours
	HD	250 mg	Following each dialysis
Valacyclovir	Normal Dosage	1 g	3 times daily
	30–49	1 g	Every 12 hours
	10–29	1 g	Every 24 hours
	< 10	500 mg	Every 24 hours

Renal Dosing: HSV Endothelial Keratitis

Oral Antiviral	Creatinine Clearance (ml/min)	Dose	Frequency
Acyclovir	Normal Dosage	400 mg	3–5 times daily
	> 25	400 mg	3–5 times daily
	10–25	400 mg	Every 8 hours
	0–10	400 mg	Every 12 hours
Famciclovir	Normal Dosage	250 mg	2–3 times daily
	≥ 40	250 mg	Every 12 hours
	20–39	125 mg	Every 12 hours
	< 20	125 mg	Every 24 hours
	HD	125 mg	Following each dialysis
Valacyclovir	Normal Dosage	500 mg	2 times daily
	30–49	500 mg	Every 12 hours
	10–29	500 mg	Every 24 hours
	< 10	500 mg	Every 24 hours

Renal Dosing: HSV Keratitis Prophylaxis

Oral Antiviral	Creatinine Clearance (ml/min)	Dose	Frequency
Acyclovir	Normal Dosage	400 mg	2 times daily
	> 10	400 mg	Every 12 hours
	0–10	200 mg	Every 12 hours
Famciclovir	Normal Dosage	250 mg	2 times daily
	≥ 40	250 mg	Every 12 hours
	20–39	125 mg	Every 12 hours
	< 20	125 mg	Every 24 hours
	HD	125 mg	Following each dialysis
Valacyclovir	Normal Dosage	500 mg	Once daily
	30–49	500 mg	Every 24 hours
	10–29	500 mg	Every 48 hours
	< 10	500 mg	Every 48 hours