RXADVANCE
2 Park Central Drive
Southborough, MA 01772

Clinical Policy Title:	acyclovir
Policy Number:	RxA.282
Drug(s) Applied:	Sitavig®, Avaclyr™
Original Policy Date:	02/07/2020
Last Review Date:	09/14/2020
Line of Business Policy Applies to:	All lines of business

Background

Acyclovir buccal tablet (Sitavig®), and acyclovir ophthalmic ointment (Avaclyr™) 3%, are herpes simplex virus nucleoside analog DNA polymerase inhibitors.
Sitavig® is indicated for the treatment of recurrent herpes labialis (cold sores) in immunocompetent adults.
Avaclyr™ 3% is indicated for the treatment of acute herpetic keratitis (dendritic ulcers) in patients with herpes simplex (HSV-1 and HSV-2) virus.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Acyclovir buccal tablet (Sitavig®)	Treatment of recurrent herpes labialis (cold sores)	One 50 mg buccal tablet applied as a single dose to the upper gum region (canine fossa)	50 mg
Acyclovir ophthalmic ointment (Avaclyr™) 3%	Treatment of acute herpetic keratitis (dendritic ulcers)	Apply 1 cm of ointment in the lower cul-de-sac of the affected eye 5 times per day until corneal ulcer heals. Afterwards, apply 1 cm of ointment in the affected eye 3 times per day for 7 days.	5 cm/day

Dosage Forms

- Buccal Tablet: 50 mg

- Ophthalmic ointment, 3%: 3.5 g tube

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. Initial Approval Criteria

A. Herpes Labialis (must meet all):

1. Diagnosis of recurrent herpes labialis (cold sores);
2. Request is for Sitavig®;
3. Age ≥ 18 years;
4. Member meets one of the following (a or b):
    a. Failure of two of the following generic drugs (tablets or capsules) unless contraindicated or clinically significant adverse effects are experienced;
        1. Acyclovir
        2. Valacyclovir
        3. Famciclovir
    b. Documentation supports inability to use (i.e., inability to swallow) generic acyclovir, valacyclovir, or famciclovir tablets or capsules;
5. Dose does not exceed 50 mg (single dose).

Approval Duration
Commercial: 1 month (2 doses)
Medicaid: 1 month (2 doses)

B. Herpetic Keratitis (must meet all):

1. Diagnosis of acute herpes keratitis (dendritic ulcers);
2. Request is for Avaclyr™;
3. Age ≥ 2 years;
4. Member meets one of the following (a or b):
    a. Failure of generic acyclovir tablets or capsules, unless contraindicated or clinically significant adverse effects are experienced;
    b. Documentation supports inability to use (i.e., inability to swallow) generic acyclovir tablets or capsules;
5. Dose does not exceed 3.5 grams (1 tube every 14 days).

Approval duration
Commercial: 1 month
Medicaid: 1 month

II. Continued Therapy Approval

A. Herpes Labialis (must meet all)**:**

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Request is for Sitavig®;
3. Member previously responded positively to therapy;
4. Dose does not exceed 50 mg (single dose).

Approval Duration
Commercial: 6 months

Medicaid: 6 months

B. Herpetic Keratitis (must meet all):
1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Request is for Avaclyr™;
3. Member previously responded positively to therapy;
4. Dose does not exceed 3.5 grams (1 tube every 14 days).

Approval Duration
Commercial: 6 months
Medicaid: 6 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration

APPENDIX B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
acyclovir (Zovirax®) off-label	Herpes Labialis **Initial episode:** 200 mg PO 5 times daily for 7-10 days OR 400 mg PO TID for 7-10 days **Recurrence:** 400 mg PO TID for 5 days OR 800 mg PO BID for 5 days OR 800 mg TID for 2 days **Chronic suppression:** 400 mg PO BID Herpes Keratitis 400 mg PO 5 times daily for 7-10 days	4,000 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic

APPENDIX C: Contraindications/Boxed Warnings
- Contraindication(s):
  - Hypersensitivity to acyclovir, valacyclovir, milk protein concentrate, or any other component of the product.

- Boxed Warning(s):

- None reported

APPENDIX D: General Information

- Sitavig® pivotal trial inclusion criteria for recurrent herpes labialis required at least 4 herpes episodes in the previous year.

References

1. Sitavig® Prescribing Information. Charleston, SC: EPI Health, LLC; December 2019. Available at: www.sitavig.com. Accessed August 1, 2020.
2. Avaclyr™ Prescribing Information. Locust Valley, NY: Fera Pharmaceuticals LLC; December 2018. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/0202408s000lbl.pdf. Accessed: August 1, 2020.
3. Clinical Pharmacology [database online] powered by ClinicalKey. Tampa, FL: Elsevier, 2020. Accessed with subscription at: http://www.clinicalkey.com. Updated January 14, 2020. Accessed August 1, 2020.
4. Acyclovir (Topical), Lexi-Drug. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed with subscription at: http://online.lexi.com. Accessed August 1, 2020.
5. White ML, Chodosh J, et al. Herpes simplex virus keratitis: a treatment guideline – 2014. American Academic of Ophthalmology. 2014; 1-68. August 1, 2020
6. Porter SM, Patterson A, Kho P. A comparison of local and systemic acyclovir in the management of herpetic disciform keratitis. Br J Ophthalmol. May 1990;74(5):283-5. August 1, 2020
7. Balderson DE, Cai G, Fries MA, et al. A systematic review and meta-analysis to compare the efficacy of acyclovir 3% ophthalmic ointment to idoxuridine in curing herpetic keratitis by Day 7 of treatment. BMC Ophthalmol. 2015 Apr;15:42. August 1, 2020

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Policy title table was updated: Clinical Policy Title was updated to "acyclovir"; Drug(s) Applied was updated to "Sitavig®, Avaclyr™"; Line of Business Policy Applies to was updated to "All". 2. Clinical policy was updated: Approval duration was updated for both Initial and Continued Approval Criteria; Continued Approval was rephrased to "Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy".; Included failure of 2 generic drugs for initial approval. 3. Contraindication (appendix C) was	08/01/2020	09/14/2020

updated: “Hypersensitivity to acyclovir, valacyclovir, milk protein concentrate, or any other component of the product”. 4. References were updated.		