Clinical Policy: Acyclovir Buccal Tablet (Sitavig), Ophthalmic Ointment (Avaclyr)

Reference Number: CP.PMN.210
Effective Date: 11.16.16
Last Review Date: 11.19 Revision Log
Line of Business: Commercial, Medicaid

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Acyclovir buccal tablet (Sitavig®), and acyclovir ophthalmic ointment (Avaclyr™) 3%, are herpes simplex virus nucleoside analog DNA polymerase inhibitors.

FDA Approved Indication(s)
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.

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

It is the policy of health plans affiliated with Centene Corporation® that Sitavig and Avaclyr are **medically necessary** when the following criteria are met:

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 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 50 mg (single dose).

Approval duration: 1 month (up to 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: 1 month

C. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid

II. Continued Therapy

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

1. Member meets initial approval criteria;
2. Request is for Sitavig;
3. Member previously responded positively to therapy;
4. Dose does not exceed 50 mg (single dose).

Approval duration: 1 month (up to 2 doses)

B. Herpes Keratitis (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
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: 1 month

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.CPA.09 for commercial and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

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 or acyclovir or valacyclovir
- 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.

V. Dosage and Administration

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

VI. Product Availability

- Buccal tablet: 50 mg
- Ophthalmic ointment, 3%: 3.5 g tube

VII. References

1. Sitavig Prescribing Information. Charleston, SC: EPI Health, LLC; December 2017. Available at: http://sitavig.com/prescribing-information/. Accessed May 17, 2019.
2. Avaclyr Prescribing Information. Locust Valley, NT: Fera Pharmaceuticals LLC; December 2018. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/0202408s000lbl.pdf. Accessed: April 9, 2019.
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: http://www.clinicalpharmacology-ip.com/. Sitavig Drug Monograph. Clinical Pharmacology. Accessed July 11, 2018.
4. White ML, Chodosh J, et al. Herpes simplex virus keratitis: a treatment guidelines – 2014. *American Academic of Ophthalmology*. 2014; 1-68
5. Porter SM, Patterson A, Kho P. A comparison of local and systemic acyclovir in the management of herpetic disciform keratitis. Br J Ophthalmol. 1990 May;74(5):283-5.
6. 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 17;15:42.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created: adopted from CP.CPA.153 acyclovir buccal tab (Sitavig). Added new acyclovir dosage form, ophthalmic ointment (Avaclyr), to policy along with relevant indication, dosage forms, dosing, and contraindications; created criteria for herpes keratitis; Changed Sitavig approval from One time to One month (up to 2 doses) since the package comes with two buccal tablets with one back-up in the event of a failed administration.	04.30.19	08.19
Q4 2019 annual review: no significant changes; references reviewed and updated.	08.24.19	11.19

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that

has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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