

MEDICATION COVERAGE POLICY

PHARMACY AND THERAPEUTICS ADVISORY COMMITTEE

POLICY	Viral Infections	P&T DATE	12/11/2018
THERAPEUTIC CLASS	Infectious Disease	REVIEW HISTORY	5/17, 5/16
LOB AFFECTED	Medi-Cal	(MONTH/YEAR)	

This policy has been developed through review of medical literature, consideration of medical necessity, generally accepted medical practice standards, and approved by the HPSJ Pharmacy and Therapeutic Advisory Committee.

OVERVIEW

Antiviral medications are used to treat viral infections. Examples of infections caused by viruses include: influenza (flu), cytomegalovirus, herpes, cold sores, shingles, and HIV. The purpose of this coverage policy is to review the coverage criteria of HPSJ's formulary antiviral agents (*Table 1*).

Table 1: Available Antivirals (Current as of 12/2018)

Generic (Brand)	Available Strengths	Formulary Limits	Cost per Rx	Notes
Flu				
Amantadine	100 mg capsule	NF	---	
	100mg tablet			
	50mg/5mL solution			
Rimantadine (Flumadine)	100 mg tablet	NF	---	
Oseltamivir (Tamiflu)	6mg/mL suspension	QL, FL	\$177.01	Limit 120 ml per fill. Limit 2 fills per 6 months.
	30 mg capsule	QL, FL	\$105.77	Limit 20 capsules per fill. Limit 2 fills per 6 months.
	45 mg capsule	QL, FL	\$77.50	Limit 10 capsules per fill. Limit 2 fills per 6 months.
	75 mg capsule	QL, FL	\$103.18	
Zanamivir (Relenza)	5 mg diskhaler	FL	---	Limit 2 fills per 6 months.
Peramivir (Rapivab)	200 mg/20 ml vial	NF	---	
Baloxavir marboxil (Xofluza)	20mg tablet	PA, QL	\$180.00	Limited to two tablets per strength.
	40 mg tablet	PA, QL	\$180.00	
Cytomegalovirus				
Valganciclovir (Valcyte)	450 mg tablet	PA, SP	\$1,690.33	Approval is determined by medical necessity criteria.
	50 mg/ml oral solution	NF	\$4,105.33	
Herpes Simplex Virus, Herpetic Keratitis, Cold Sores, & Shingles				
Acyclovir (Zovirax)	5% ointment	NF	\$290.09	
	5% cream	NF	---	
	200 mg capsule	-	\$6.03	
	400 mg tablet	-	\$3.43	
	800 mg tablet	-	\$7.20	
	200 mg/5 ml suspension	-	\$110.79	
Famciclovir	500 mg tablet	NF	\$24.53	
Penciclovir (Denavir)	1% cream	NF	---	
Valacyclovir (Valtrex)	500 mg tablet	NF	\$5.65	
	1 gram tablet	NF	\$23.46	
HIV/AIDS				
Didanosine (Videx EC)	DR 125 mg capsule	-	---	
	DR 200 mg capsule	-	---	
	DR 250 mg capsule	-	---	
	DR 400 mg capsule	-	---	
	EC 400 mg capsule	NF	---	
	2 gram 10 mg/ml oral solution	-	---	
	4 gram 10 mg/ml oral solution	-	---	
Zidovudine (Retrovir)	100 mg capsule	-	---	
	300 mg tablet	-	\$9.37	
	10 mg/ml intravenous solution	-	---	
	50 mg/5 ml syrup	-	---	

PA = Prior Authorization; SP = Specialty Pharmacy; QL = Quantity Limit; FL = Fill Limit; NF = Non-formulary

✚ EVALUATION CRITERIA FOR APPROVAL/EXCEPTION CONSIDERATION

Below are the coverage criteria and required information for each agent. These coverage criteria have been reviewed & approved by the HPSJ Pharmacy & Therapeutics (P&T) Advisory Committee. For conditions not covered under this Coverage Policy, HPSJ will make the determination based on Medical Necessity as described in HPSJ Medical Review Guidelines (UM06).

Flu

Amantadine, Rimantadine (Flumadine), Oseltamivir (Tamiflu), Zanamivir (Relenza), Peramivir (Rapivab), Baloxavir marboxil (Xofluza)

Oseltamivir (Tamiflu), Zanamivir (Relenza)

- Coverage Criteria:** None
- Limits:** Restricted to 2 fills per 6 months for both Oseltamivir and Zanamivir.
 - **6mg/mL suspension:** Limit 120 ml per fill.
 - **30mg capsule:** Limited to 20 capsules per fill.
 - **45 mg capsule, 75 mg capsule:** Limited to 10 capsules per fill.
- Required Information for Approval:** N/A
- Other Notes:** None
- Non-Formulary:** Amantadine, Rimantadine (Flumadine), Peramivir (Rapivab)

Baloxavir marboxil (Xofluza)

- Coverage Criteria:** Reserved for patients who meet all of the following criteria:
 - 12 years of age or older;
 - Treatment of acute, uncomplicated influenza (defined as patient's with influenza who can be treated outpatient and do not require hospitalization);
 - Documented intolerance to both Oseltamivir and Zanamivir;
 - Is not currently pregnant; AND
 - Limited to FDA approved dosing based on weight with a quantity limit of two tablets per strength.
- Limits:** Both 20 mg and 40 mg tablet are limited to two tablets per fill.
- Required Information for Approval:** Patient's age, indication for use, prescription fill history, and pregnancy status if female.
- Other Notes:** None

Cytomegalovirus

Valganciclovir (Valcyte)

- Coverage Criteria:** Approval is determined by medical necessity criteria.
- Limits:** None
- Required Information for Approval:** Relevant clinical documentation
- Other Notes:** Medication is to be dispensed by HPSJ's designated specialty pharmacy.

Herpes Simplex Virus, Herpetic Keratitis, Cold Sores, & Shingles

Acyclovir (Zovirax), Famciclovir, Penciclovir (Denavir), Valacyclovir (Valtrex)

Acyclovir (Zovirax) capsules, tablets, and suspension

- Coverage Criteria:** None
- Limits:** None
- Required Information for Approval:** N/A
- Other Notes:** None
- Non-Formulary:** Acyclovir 5% ointment & cream, Famciclovir, Penciclovir (Denavir), Valacyclovir (Valtrex)

HIV/AIDS
<i>Didanosine (Videx EC), Zidovudine (Retrovir)</i>

Didanosine, Videx oral solution, Zidovudine (Retrovir)

- Coverage Criteria:** None
- Limits:** None
- Required Information for Approval:** N/A
- Other Notes:** None
- Non-Formulary:** Videx EC

⊞ CLINICAL JUSTIFICATION

HPSJ’s viral infections management policy is based on recommendations by the *Centers for Disease Control and Prevention (CDC), Infectious Diseases Society of America (IDSA), and Advisory Committee on Immunization Practices (ACIP)*. In general, viral infections can be effectively managed with oral therapies. According to the CDC 2015 Sexually Transmitted Diseases Treatment Guidelines and the IDSA 2007 Recommendations for the Management of Herpes Zoster, use of topical antiviral therapy is discouraged due to lack of efficacy.^{1,2} Valacyclovir hydrochloride (a prodrug of acyclovir) is rapidly converted to acyclovir in the body. Acyclovir, famciclovir, and valacyclovir are equally effective for episodic genital herpes. However, famciclovir appears less effective for suppression of viral shedding and acyclovir has the most evidence of safety and efficacy for suppression of recurrent genital herpes.¹ Given the similar efficacy and cross-resistance among these three agents, oral acyclovir is the only antiviral agent on HPSJ’s formulary for herpetic infections. According to the ACIP 2011 Recommendations for Antiviral Agents for the Treatment and Chemoprophylaxis of Influenza, amantadine and rimantadine should not be used due to high levels of resistance, while oseltamivir and zanamivir are recommended for the prevention and treatment of influenza. Oseltamivir is indicated for treatment of influenza for patients of all ages. Zanamivir is indicated for treatment of influenza for patients age 6 and older.³ Most recent recommendations from the CDC include the options of Baloxavir (newly approved treatment for acute, uncomplicated influenza) and Peramivir (infusion option for influenza treatment).⁷ A summary of the recommendations by the CDC for influenza treatment is available (Table 2). Valganciclovir is the current standard oral antiviral agent for treatment of cytomegalovirus (CMV) according to the Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents 2018 Guidelines.⁴

Table 2. Summary of Recommendations and Adverse Events of Each Influenza Treatment Agent per CDC⁷

	Oseltamivir	Zanamivir	Peramivir	Baloxavir
Acute, uncomplicated influenza	X	X	X	X
Severe, complicated, or progressive influenza illness who are not hospitalized	X			
Hospitalized influenza	X			
Pregnancy	X			
Chemoprophylaxis	X	X		
Renal impairment	X		X	
Adverse Events	-Nausea -Vomiting -Headache -Serious skin reactions -Sporadic, transient neuropsychiatric events	-Risk of bronchospasm -Serious skin reactions -Sporadic, transient neuropsychiatric events	-Diarrhea -Serious skin reactions -Sporadic, transient neuropsychiatric events	-None

Oseltamivir is the primary recommended drug by the CDC. Baloxavir has no noted adverse events that differed from placebo.

☒ REFERENCES

- Centers for Disease Control and Prevention. Sexually Transmitted Diseases Treatment Guidelines, 2015. *Morbidity and Mortality Weekly Report*. 2015;64(3):1-137.
- Infectious Diseases Society of America. Recommendations for the Management of Herpes Zoster. *Clinical Infectious Diseases*. 2007;44:S1-26.
- Advisory Committee on Immunization Practices. Antiviral Agents for the Treatment and Chemoprophylaxis of Influenza. *Morbidity and Mortality Weekly Report*. 2011;66(RR01):1–24.
- Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi.pdf. Accessed December 7, 2018.
- Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV. Department of Health and Human Services. Available at <http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf>. Accessed December 7, 2018.
- Xofluza™ (baloxavir marboxil) [package insert]. San Francisco, CA: Genentech USA, Inc.; 2018.
- Centers for Disease Control and Prevention. Influenza Antiviral Medications: Summary for Clinicians. November 28, 2018; <https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm>. Accessed December 7, 2018.

☒ REVIEW & EDIT HISTORY

Document Changes	Reference	Date	P&T Chairman
Creation of Policy	HPS Coverage Policy – Infections Disease – Viral Infections 2016-02.docx	2/2016	Johnathan Yeh, PharmD
Update to Policy	HPS Coverage Policy – Infections Disease – Viral Infections 2016-02-revised in may.docx	5/2016	Johnathan Yeh, PharmD
Update to Policy	HPS Coverage Policy – Infections Disease – Viral Infections 2017-05.docx	5/2017	Johnathan Yeh, PharmD
Update to Policy	HPS Coverage Policy – Infections Disease – Viral Infections 2018-12.docx	12/2018	Matthew Garrett, PharmD

Note: All changes are approved by the HPSJ P&T Committee before incorporation into the utilization policy

- ☒ Please refer to **Hepatitis C and Liver Diseases Coverage Policies** for coverage criteria of Hepatitis C and Hepatitis B medications, respectively.
- ☒ Please refer to **Immunizations Coverage Policy** for coverage criteria of vaccines.
- ☒ Please refer to **Eye & Ear Inflammatory Disorders Coverage Policy** for coverage criteria of ophthalmic antiviral medications.
- ☒ All HIV and flu medications not mentioned in this coverage policy are specifically carved out from Medi-Cal Managed Care Plans, and should be billed directly to Medi-Cal Fee-For-Service. The **Managed Medi-Cal Prescription Drug Carve-Out** list can be found at www.hpsj.com/medication-coverage-policies/ or www.hpsj.com/pharmacy. Please note that Medi-Cal FFS may require submission of a Treatment Authorization Request (TAR) to determine appropriateness of the treatment prior to coverage.