BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 2/17/2022
LAST REVIEW DATE:
LAST CRITERIA REVISION DATE:
ARCHIVE DATE:

LIVTENCITY™ (maribavir) oral

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.
Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

LIVTENCITY™ (maribavir) oral

Criteria:

- **Criteria for initial therapy:** Livtencity (maribavir) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Infectious Disease Specialist or Transplant Specialist

2. Individual is 12 years of age or older and weigh at least 35 kg

3. A confirmed diagnosis of post-transplant (hematopoietic stem cell or solid organ recipient) cytomegalovirus (CMV) infection or disease that is refractory to treatment (with or without genotypic resistance) with ganciclovir, valganciclovir, cidofovir or foscarnet

4. **ALL** of the following **baseline tests** have been completed before initiation of treatment with continued monitoring as clinically appropriate:
    a. Prior to CMV treatment, a plasma or whole blood CMV DNA result that shows CMV infection
    b. After 14-days CMV treatment, a plasma or whole blood CMV DNA result that shows CMV is refractory

5. Documented failure (after at least 14-days), contraindication per FDA label, intolerance, or not a candidate to **ONE** the following:
    a. Valganciclovir or ganciclovir
    b. Foscarnet
    c. Cidofovir
    d. Foscarnet plus valganciclovir or ganciclovir

6. Individual does not have CMV disease involving the central nervous system including CMV retinitis

7. Individual is not undergoing treatment for active or chronic hepatitis C

8. Individual does not have other significant viral illness co-infection

9. Individual does not have an active malignancy (exception of nonmelanoma skin cancer)

10. Individual does not require mechanical ventilation or vasopressors for hemodynamic support

11. Individual does not have end-stage renal disease, including those on dialysis

12. Individual does not have severe hepatic impairment (Child-Pugh Class C)

13. There are no significant interacting drugs

Initial approval duration: 6 months

LIVTENCITY™ (maribavir) oral

- **Criteria for continuation of coverage (renewal request):** Livtencity (maribavir) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Infectious Disease Specialist or Transplant Specialist

  2. Individual's condition has responded while on therapy
     a. Response is defined as **THREE** of the following:
        i. No evidence of disease progression
        ii. Documented evidence of efficacy, disease stability and/or improvement
        iii. Achieved and maintains CMV viremia clearance define by plasma CMV DNA concentration less than the lower limit of quantification (LLOQ)
        iv. Confirmed CMV viremia clearance define by plasma CMV DNA concentration less than the LLOQ) **and** CMV infection symptom control

  3. Individual has been adherent with the medication

  4. Individual does not have CMV disease involving the central nervous system including CMV retinitis

  5. Individual is not undergoing treatment for active or chronic hepatitis C

  6. Individual does not have other significant viral illness co-infection

  7. Individual does not have an active malignancy (exception of nonmelanoma skin cancer)

  8. Individual does not require mechanical ventilation or vasopressors for hemodynamic support

  9. Individual does not have end-stage renal disease, including those on dialysis

  10. Individual does not have severe hepatic impairment (Child-Pugh Class C)

  11. There are no significant interacting drugs

  Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

  1. **Off-Label Use of Non-cancer Medications**

  2. **Off-Label Use of Cancer Medications**

LIVTENCITY™ (maribavir) oral

Description:

Livtencity (maribavir) is a cytomegalovirus (CMV) pUL97 kinase inhibitor indicated for the treatment of adults and pediatric patients (12 years of age and older and weighing at least 35 kg) with post-transplant CMV infection/disease that is refractory to treatment (with or without genotypic resistance) with ganciclovir, valganciclovir, cidofovir or foscarnet.

The antiviral activity of maribavir is mediated by competitive inhibition of the protein kinase activity of human CMV enzyme pUL97 kinase, which is required for activation/phosphorylation of ganciclovir and valganciclovir. Coadministration of Livtencity (maribavir) with ganciclovir or valganciclovir is not recommended. Some Livtencity (maribavir) pUL97 resistance-associated substitutions confer cross-resistance to ganciclovir and valganciclovir.

Definitions:

CMV infection:
- Isolation of virus or detection of viral proteins (antigens) or nucleic acid in any body fluid or tissue
  - Evidence of CMV replication regardless of symptoms

CMV disease:
- Evidence of end organ disease and CMV syndrome
  - Evidence of end organ disease is by the presence of appropriate clinical &/or signs together with documentation of CMV in tissue from the relevant organ
- Evidence of CMV infection with attributable symptoms
  - CMV disease can be further categorized as:
    - Viral syndrome (i.e., fever, malaise, leukopenia, and/or thrombocytopenia)
    - Tissue invasive ("end organ") disease

Factors associated with increased risk for CMV reactivation (high-risk stratum):

Patient meets **one** or more of the following criteria
- Human Leukocyte Antigen (HLA)-related donor with at least one mismatch at one of the following three HLA-gene loci: HLA-A, -B or –DR
- Unrelated donor with at least one mismatch at one of the following four HLA-gene loci: HLA-A, -B, -C and -DRB1
- Haploidentical donor
- Use of umbilical cord blood as stem cell source
- Use of *ex vivo* T-cell-depleted grafts (including *ex vivo* use of alemtuzamab [Campath])
- Grade 2 or greater Graft-Versus-Host Disease (GVHD) requiring systemic corticosteroids (defined as the use of ≥ 1 mg/kg/day of prednisone or equivalent dose of another corticosteroid)

Clinically significant CMV infection (prophylaxis failure) defined as:
- The occurrence of either:
  - CMV end-organ disease

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- Initiation of anti-CMV pre-emptive therapy (PET) based on documented CMV viremia (using the Roche COBAS® AmpliPrep/COBAS TaqMan® assay, LLoQ is 137 IU/mL, which is approximately 150 copies/mL)
  - CMV viremia for high risk stratum: a CMV DNA ≥ 150 copies/mL
  - CMV viremia for low risk stratum: a CMV DNA > 300 copies/mL
- The clinical condition of the individual

Resources:

Livtencity (maribavir) product information, revised by Takeda Pharmaceuticals America, Inc. 11-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 07, 2022.

Wingard JR. Prevention of viral infections in hematopoietic cell transplant recipients. In: UpToDate, Bow E, Bond S (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated November 29, 2021. Accessed February 08, 2022.

Kotton CN, Kumar D, Caliendo AM, et al.: The Third International Consensus Guidelines on the Management of CMV in Solid-organ Transplantation (SOT). Transplantation 2018; 102:900-931.

Ljungman P, Boeckh M, Hirsch HH, et al.: Definitions of cytomegalovirus infection and disease in transplant patients for use in clinical trials. CID 2017; 64 (1): 87-91.

ClinicalTrials.gov Identifier NCT02931539. A phase 3, multicenter, randomized, open-label, active-controlled study to assess the efficacy and safety of maribavir treatment compared to investigator-assigned treatment in transplant recipients with cytomegalovirus (CMV) infections that are refractory or resistant to treatment with ganciclovir, valganciclovir, foscarnet, or cidofovir. Last Updated November 03, 2021. Available from: http://clinicaltrials.gov. Accessed February 07, 2022.