PHARMACY COVERAGE GUIDELINE

LIVTENCITY™ (maribavir)
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Livtencity (maribavir) and/or generic equivalent (if available) are 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 weighing at least 35 kg

3. Individual has 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. Individual has received and completed **ALL** the following **baseline tests** before initiation of treatment and with continued monitoring of the individual 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. Individual has documented failure (after at least 14-days), contraindication per FDA label, intolerance, or is not a candidate for **ONE** the following:
    a. Valganciclovir or ganciclovir
    b. Foscarnet
    c. Cidofovir

6. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

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

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

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

10. There are no significant interacting drugs such as:
    a. Concurrent use with ganciclovir or valganciclovir
    b. Strong CYP3A4 inducers (e.g., rifampin, rifabutin, rifabutin, and St. John's wort) [Note: carbamazepine, phenobarbital and phenytoin may be used with dose adjustment and monitoring]

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Livtencity (maribavir) and/or generic equivalent (if available) are considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met **(samples are not considered for continuation of therapy)**:

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 with response defined as **THREE** of the following:
    a. No evidence of disease progression
    b. Documented evidence of efficacy, disease stability and/or improvement
    c. Achieved and maintains CMV viremia clearance define by plasma CMV DNA concentration less than the lower limit of quantification (LLOQ)
    d. 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 does not have end-stage renal disease, including those on dialysis

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

7. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

8. There are no significant interacting drugs such as:
    a. Concurrent use with ganciclovir or valganciclovir
    b. Strong CYP3A4 inducers (e.g., rifampin, rifabutin, rifabutin, and St. John's wort) [Note: carbamazepine, phenobarbital and phenytoin may be used with dose adjustment and monitoring]

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**

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:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

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

PHARMACY COVERAGE GUIDELINE

LIVTENCITY™ (maribavir)
Generic Equivalent (if available)

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
  - 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. 03-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed November 26, 2024.

Wingard JR. Prevention of viral infections in hematopoietic cell transplant recipients. In: UpToDate, Bow E, White N (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through December 2024. Topic last updated September 11, 2024. Accessed January 03, 2025.

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. Accessed February 09, 2022. Re-evaluated January 03, 2025.

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. Access May 21, 2019. Re-evaluated January 03, 2025.

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. Re-evaluated January 03, 2025.