Pharmacy Policy Bulletin: J-1171 Livtencity (maribavir) – Commercial and Healthcare Reform	
Number: J-1171	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Drugs Oral = Yes w/ Prior Authorization **Quantity Limits (1., 2., 3., or 4.):** **1.** Rx Mgmt Quantity Limits = Safety/Specialty **2.** Rx Mgmt Quantity Limits = Safety/Specialty + Dose Opt **3.** Rx Mgmt Quantity Limits = Safety/Specialty + Dose Opt + Watchful **4.** Rx Mgmt Performance = MRxC = Yes **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-1171-005	**Original Date:** 01/26/2022
Effective Date: 02/14/2025	**Review Date:** 01/29/2025

Drugs Product(s):	• Livtencity (maribavir)
FDA-Approved Indication(s):	• Treatment of adults and pediatric patients (12 years of age and older and weighing at least 35 kg) with post-transplant cytomegalovirus (CMV) infection/disease that is refractory to treatment (with or without genotypic resistance) with ganciclovir, valganciclovir, cidofovir or foscarnet.

Background:	• Livtencity is an antiviral drug against human CMV and is mediated by competitive inhibition of the protein kinase activity of human CMV enzyme pUL97 and inhibits viral replication. • CMV is a prevalent β-herpesvirus that infects the majority of humans, and the predicted overall CMV seroprevalence rate in the United States (U.S.) is 50%. For people with healthy immune systems, CMV is a quiet invader that causes no symptoms. 20-60% of solid organ transplant (SOT) recipients and 30-70% of hematopoietic stem cell transplant (HSCT) recipients develop symptomatic CMV infection. This infection occurs due to transmission from the transplanted organ, reactivation of latent infection, or after a primary infection in seronegative patients.

	• CMV infection is defined as virus isolation or detection of viral proteins (antigens) or nucleic acid regardless of symptoms. Refractory CMV infection is defined as CMV DNAemia or antigenemia increases after at least two weeks of appropriately dosed antiviral therapy. • CMV disease is characterized by CMV infection with attributable symptoms, such as viral syndrome (i.e., fever, malaise, leukopenia, and/or thrombocytopenia), or as end organ disease. Refractory CMV disease is defined as worsening in signs and symptoms or progression into end-organ disease after at least two weeks of appropriately dosed antiviral therapy. • Risk factors for drug resistance are prolonged subtherapeutic dose of antivirals, seropositive donor (D+/R-), intense immunosuppression, and lung transplantation. • Virologic relapse occurred in 50% of patients receiving Livtencity. Most of the relapses occurred within 4 weeks after drug discontinuation, with a 15-day median time to relapse. • New onset symptomatic CMV infection occurred in 6% of patients receiving Livtencity. Livtencity has been administered in clinical trials for up to 24 weeks. • Discontinuation of CMV treatment should be guided by clinical resolution of symptoms and achievement of undetectable CMV viremia on at least 2 consecutive assays. • ICD-10 Code Information: o ICD-10: B25.8 “Other cytomegaloviral diseases” B25.9 “Cytomegaloviral disease, unspecified” may apply to Livtencity; however, the prescriber must confirm that the member has a specific diagnosis of refractory disease post-transplant. • Prescribing Considerations: o Livtencity should be prescribed by or in consultation with a hematologist, oncologist, infectious disease, or transplant specialist. o Livtencity may antagonize the antiviral activity of ganciclovir and valganciclovir. Coadministration is not recommended. o Frequently monitor immunosuppressant drug levels throughout treatment with Livtencity, especially following initiation and after discontinuation of Livtencity and adjust the dose, as needed. o Coadministration with strong CYP3A4 inducers is not recommended. o Monitor CMV DNA levels and check for resistance if the patient does not respond to treatment. Some Livtencity pUL97 resistance-associated substitutions confer cross-resistance to ganciclovir and valganciclovir. o Livtencity can be taken as whole, dispersed, or crushed tablets by mouth, or as dispersed tablets through a nasogastric or orogastric tube. o If Livtencity is administered with carbamazepine, increase the dosage to 800 mg twice daily; if administered with phenytoin or phenobarbital, increase the dosage to 1,200 mg twice daily. o If approved for an additional total quantity corresponding to up to 24 weeks of therapy, a patient level authorization (PLA) up to the quantity as followed may be entered: ▪ Livtencity without concurrent anticonvulsant: 672 tablets per 365 days ▪ Livtencity co-administered with carbamazepine: 1,344 tablets per 365 days ▪ Livtencity co-administered with phenytoin or phenobarbital: 2,016 tablets per 365 days

Approval Criteria

I. Initial Authorization

When a benefit, coverage of Livtencity may be approved when all of the following criteria are met **(A. through E.)**:

A. The member is 12 years of age or older.
B. The member weighs at least 35 kg.
C. The prescriber submits documentation that the member has a diagnosis of refractory CMV infection or disease as evidenced by an antigenemia or polymerase chain reaction (PCR) test.
D. The member is a recipient of one (1) of the following **(1. or 2.)**:
  1. Hematopoietic stem cell transplant (HSCT)
  2. Solid organ transplant (SOT)
E. The member has experienced therapeutic failure to one (1) of the following agents **(1. through 4.)**:
  1. ganciclovir
  2. valganciclovir
  3. cidofovir
  4. foscarnet

II. Reauthorization*

When a benefit, reauthorization of Livtencity may be approved when all of the following criteria are met **(A. and B.)**:

A. The prescriber attests that the member has previously experienced a reduction in CMV deoxyribonucleic acid (DNA) level.
B. The member is experiencing one (1) of the following **(1., 2., or 3.)**:
  1. New onset symptomatic CMV infection
  2. Virologic relapse without treatment-emergent maribavir resistance.
  3. Requiring continued antiviral treatment to achieve virologic clearance.

***** See additional Quantity Level Limits Criteria C.

III. Quantity Level Limits

When a benefit, coverage of additional quantities of Livtencity may be approved when one (1) of the following criteria are met **(A., B., or C.)**:

A. If Livtencity is co-administered with carbamazepine, a quantity of 448 tablets per 365 days may be approved.
B. If Livtencity is co-administered with phenytoin or phenobarbital, a quantity of 672 tablets per 365 days may be approved.
C. If reauthorization criteria are met, an additional total quantity corresponding to up to 24 weeks of therapy per 365 days may be approved based on FDA-approved dosing in the prescribing information.

IV. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Livtencity has not been studied in patients with a diagnosis of CMV disease involving the central nervous system (CNS), including the retina.
II. Livtencity is not indicated for prophylaxis of CMV.
III. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
IV. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

Initial Authorization -

- Commercial and HCR Plans: If approved, up to an 8 week authorization may be granted.

Reauthorization –

- Commercial and HCR Plans: If approved, up to a 16 week authorization may be granted.
  - Total cumulative authorizations do not exceed 24 weeks

Automatic Approval Criteria

None

References:

1. Livtencity [package insert]. Lexington, MA: Takeda; March 2024.
2. Razonable RR, Humar A. Cytomegalovirus in solid organ transplant recipients—guidelines of the American Society of Transplantation Infectious Diseases Community of Practice. *Clinical Transplantation*. 2019;33(9).
3. Hibberd, PL, Tolkoff-Rubin NE, Cosimi AB, Schooley RT, Isaacson D, Doran M, et al. Symptomatic cytomegalovirus disease in the cytomegalovirus antibody seropositive renal transplant recipient treated with OKT3. *Transplantation* 1992; 53:68-72.
4. Azevedo L, Pierrotti L, Abdala E, et al. Cytomegalovirus infection in transplant recipients. *Clinics*. 2015;70(7):515-523.
5. Styczynski J. Who Is the Patient at Risk of CMV Recurrence: A Review of the Current Scientific Evidence with a Focus on Hematopoietic Cell Transplantation. *Infect Ther*. 2018;7:1-16
6. Kotton CN, Kumar D, Caliendo AM, et al. The Third International Consensus Guidelines on the management of cytomegalovirus in solid-organ transplantation. *Transplantation*. 2018;102(6):900-931.
7. National Comprehensive Cancer Network. NCCN Guidelines Version 3.2024. Prevention and Treatment of Cancer-Related Infections. Available at: https://www.nccn.org/professionals/physician_gls/pdf/infections.pdf. Accessed December 09, 2024.