09-J4000-12

Original Effective Date: 04/01/22

Reviewed: 01/10/24

Revised: 02/15/24

Subject: Maribavir (Livtencity)

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Cytomegalovirus (CMV) infection is the most common infectious complication in transplant recipients and significantly contributes to morbidity and mortality. Treatment consists of antiviral therapy with first-line agents valganciclovir or ganciclovir for a minimum of two weeks until disease resolves clinically and the virus is eradicated (as evidenced by negative DNA testing). Viral resistance may occur and should be suspected in those with treatment failure. Treatment options for those with resistance infections include increased doses of ganciclovir, foscarnet, maribavir, or combination therapy.

Maribavir (Livtencity), a CMV pUL97 kinase inhibitor, was approved by the U.S. Food and Drug Administration (FDA) in November 2021 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 safety and efficacy of maribavir were evaluated in solid organ or hematopoietic stem cell transplant recipients with treatment-refractory CMV infection. Subjects received maribavir 400 mg twice daily or investigator-assigned therapy (ganciclovir, valganciclovir, foscarnet, or cidofovir) as dosed by the investigator for up to 8 weeks. After completion of the treatment period, subjects entered a 12-week follow-up phase. The most common treatment used in the comparator arm was foscarnet which was administered in 41% of subjects followed by ganciclovir or valganciclovir, each administered in 24% of subjects.

The primary efficacy endpoint was confirmed CMV DNA level less than 137 international units/mL at the end of week 8; this outcome was observed in 56% of patients in the maribavir group (n=235) compared with 24% of those in the comparator group (n=117), for an adjusted treatment difference of 33% (95%

CI, 23% to 43%). The treatment effect was consistent across transplant type, age group, and the presence of CMV syndrome/disease at baseline, but maribavir was less effective in subjects with increased CMV DNA levels (50,000 international units/mL or greater) and in subjects without genotypic resistance.

Of those who did not respond to treatment, 34% (maribavir) and 36% (comparator) were due to virologic failure, and 9% (maribavir) and 38% (comparator) were due to drug/study discontinuation; adverse events contributed to 3% and 22% of non-response due to discontinuation in the maribavir group the comparator group, respectively.

The key secondary endpoint was CMV DNA level less than 137 international units/mL and CMV infection symptom control at the end of week 8 with maintenance of this treatment effect through week 16. This outcome was observed in 19% of those in the maribavir group and 10% of those in the comparator group, for an adjusted treatment difference of 9% (95% CI, 2% to 17%).

Virologic relapse during the follow-up period occurred in 50% of those in the maribavir group (n=131) and in 39% of those in the comparator group (n=28) who achieved virologic response during the treatment period. Most of the relapses (89%) in the maribavir group and all relapses in the comparator group occurred within 4 weeks after study drug discontinuation; the median time to relapse was 15 days (range, 7 to 71 days) in the maribavir group and 15 days (range, 7 to 29 days) in the comparator group.

POSITION STATEMENT:

Comparative Effectiveness

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Maribavir (Livtencity) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Member is post-transplant and diagnosed with cytomegalovirus (CMV) infection – laboratory documentation must be provided
2. Member's disease is refractory to treatment with ganciclovir, valganciclovir, cidofovir, or foscarnet – documentation from the medical record (or pharmacy claims system) must be provided
3. Maribavir will not be used in combination with another CMV antiviral
4. Maribavir dose does not exceed:
    a. 400 mg twice daily
    b. 800 mg twice daily **AND** is co-administered with carbamazepine
    c. 1200 mg twice daily **AND** is co-administered with phenytoin or phenobarbital

Approval duration: 3 months

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- 400 mg (two 200 mg tablets) orally twice daily with or without food

Dose Adjustments

- If co-administered with carbamazepine, increase the dosage to 800 mg twice daily
- If co-administered with phenytoin or phenobarbital, increase the dosage to 1,200 mg twice daily

Drug Availability

- Tablets: 200 mg of maribavir

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- None

Precautions/Warnings

- May antagonize the antiviral activity of ganciclovir and valganciclovir. Coadministration is not recommended.
- Virologic failure can occur during and after treatment. Monitor CMV DNA levels and check for resistance if patient does not respond to treatment. Some maribavir pUL97 resistance-associated substitutions confer cross-resistance to ganciclovir and valganciclovir.
- Concomitant use with certain drugs may result in potentially significant drug interactions, some of which may lead to reduced therapeutic effect or adverse reactions of concomitant drugs.
- Maribavir has the potential to increase the drug concentrations of immunosuppressant drugs that are CYP3A4 and/or P-gp substrates where minimal concentration changes may lead to serious adverse events (including tacrolimus, cyclosporine, sirolimus and everolimus). Frequently monitor immunosuppressant drug levels.

BILLING/CODING INFORMATION:

HCPCS Coding

J8499	Prescription drug, oral, non-chemotherapeutic, Not Otherwise Specified

ICD-10 Diagnosis Codes That Support Medical Necessity

B25.0-B25.9	Cytomegaloviral disease

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: BCBSF has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

None

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

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4. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2024 [cited 1/1/24]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.
5. Razonable RR, et al. Cytomegalovirus in solid organ transplant recipients—Guidelines of the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant. 2019;33(9):e13512.

6. Takeda Pharmaceuticals. Livtencity (maribavir) tablet. 2022 [cited 2/2/22]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=c94fc2c5-e840-4f18-b7d8-d5eacb26d3a0
7. Winston DJ, et al. Efficacy and safety of maribavir dosed at 100 mg orally twice daily for the prevention of cytomegalovirus disease in liver transplant recipients: a randomized, double-blind, multicenter controlled trial. Am J Transplant. 2012;12(11):3021-3030.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 01/10/24.

GUIDELINE UPDATE INFORMATION:

04/01/22	New Medical Coverage Guideline.
02/15/24	Review and revision to guideline consisting of updating references.