

Livtency™ (maribavir)

Policy # 00784

Original Effective Date: 05/09/2022

Current Effective Date: 05/01/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the “Company”), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member’s contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider Livtency™[‡] (maribavir) to be **eligible for coverage**** when the patient selection criteria are met.

Patient Selection Criteria

Coverage eligibility for Livtency (maribavir) will be considered when the following criteria are met:

- Requested drug is used for the treatment of cytomegalovirus (CMV) infection; AND
- Patient has undergone a hematopoietic stem cell transplant (HSCT) or solid organ transplant (SOT); AND
- Presence of post-transplant CMV infection is evidenced by CMV DNA of greater than or equal to 2,730 IU/mL in whole blood or greater than or equal to 910 IU/mL in plasma; AND
- Patient is 12 years of age or older; AND
- Patient weighs at least 35 kilograms; AND
- Patient's CMV disease is refractory to previous treatment with ganciclovir, valganciclovir, foscarnet, or cidofovir. Refractory is defined as a documented failure to achieve greater than 1 log₁₀ decrease in CMV DNA levels in whole blood or plasma after a 14 day or longer treatment period with ganciclovir, valganciclovir, foscarnet, or cidofovir; AND
- Requested drug is NOT given in combination with ganciclovir and/or valganciclovir.

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of Livtency (maribavir) when the patient selection criteria are not met to be **investigational.***

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When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider a quantity override for more than 112 tablets per 28 days of Livtencity (maribavir) to be **eligible for coverage****

Patient Selection Criteria

A quantity override for more than 112 tablets per 28 days of Livtencity (maribavir) will be considered when the criteria are met for the requested quantity:

- 224 tablets per 28 days: Patient is taking the requested drug concomitantly with carbamazepine; OR
- 336 tablets per 28 days: Patient is taking the requested drug concomitantly with phenytoin or phenobarbital.

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of Livtencity (maribavir) for a quantity greater than 112 tablets per 28 days when the patient selection criteria are not met to be **investigational.***

Background/Overview

Livtencity 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. Livtencity is dosed 400 mg (two 200 mg tablets) taken twice daily with or without food. If Livtencity is co-administered with carbamazepine, the dosage should be increased to 800 mg twice daily. If Livtencity is co-administered with phenytoin or phenobarbital, the dose should be increased to 1,200 mg twice daily. Clinical trials used an 8 week treatment duration for Livtencity. The Livtencity package insert notes that due to antagonistic drug activity, coadministration of Livtencity with ganciclovir and/or valganciclovir is not recommended.

CMV affects nearly 50% of the population in the United States. In individuals that have a properly functioning immune system, the viral infection is typically asymptomatic or there is a self-limiting febrile illness. This is followed by viral latency. In immunocompromised patients, CMV infection

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is associated with severe morbidity and mortality, including opportunistic infections and graft versus host disease. The use of prophylactic therapy (given to all “at risk” patients) and preemptive therapy (given to only to symptomatic patients with evidence of CMV replication) for CMV has decreased infections substantially. However, there is still the chance of resistance or refractory response to common first line anti-viral options, which include ganciclovir, valganciclovir, foscarnet, or cidofovir. Resistant and/or refractory infections carry a higher incidence of morbidity and mortality. Livtencity is currently the only agent approved for the treatment of post-transplant patients with treatment refractory CMV infection/disease.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Livtencity was approved in late 2021 for the 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.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Livtencity was evaluated in a Phase 3, multicenter, randomized, open-label, active-controlled superiority trial to assess the efficacy and safety of Livtencity compared to Investigator-Assigned Treatment (IAT) (ganciclovir, valganciclovir, foscarnet, or cidofovir) in 352 hematopoietic stem cell transplant (HSCT) or solid organ transplant (SOT) recipients with cytomegalovirus (CMV) infections (CMV DNA of greater than or equal to 2,730 IU/mL in whole blood or greater than or equal to 910 IU/mL in plasma) that were refractory to treatment with ganciclovir, valganciclovir, foscarnet, or cidofovir, including CMV infections with or without confirmed resistance to 1 or more of the IATs. Refractory was defined as a documented failure to achieve greater than 1 log₁₀ decrease in CMV DNA level in whole blood or plasma after a 14 day or longer treatment period with ganciclovir, valganciclovir, foscarnet, or cidofovir. Subjects were stratified by transplant type (HSCT or SOT) and screening CMV DNA levels and then randomized in a 2:1 allocation ratio to receive either Livtencity 400 mg twice daily or IAT 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 IAT arm was foscarnet which was administered in 47 (41%) subjects followed by ganciclovir or valganciclovir, each administered in 28 (24%) subjects. Cidofovir was administered in 6 subjects, the combination of foscarnet and valganciclovir in 4 subjects and the combination of foscarnet and ganciclovir in 3 subjects. The primary efficacy endpoint was confirmed

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CMV DNA level less than the lower level of quantitation, LLOQ (i.e. < 137 IU/mL), as assessed at the end of week 8. For the primary endpoint, Livtencity was statistically superior to IAT (56% vs. 24%, respectively). The treatment effect of Livtencity was consistent across transplant type, age group, and the presence of CMV syndrome/disease at baseline.

References

1. Livtencity [package insert]. Takeda Pharmaceuticals. Lexington, Massachusetts. Updated November 2021.
2. www.clinicaltrials.gov. NCT02931539. Accessed March 2022.
3. Livtencity Drug Evaluation. Express Scripts. Updated December 2021.

Policy History

Original Effective Date: 05/09/2022

Current Effective Date: 05/01/2025

04/07/2022 Medical Policy Committee review

04/13/2022 Medical Policy Implementation Committee approval. New policy.

04/06/2023 Medical Policy Committee review

04/12/2023 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

04/04/2024 Medical Policy Committee review

04/10/2024 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

04/03/2025 Medical Policy Committee review

04/09/2025 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 04/2026

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:

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1. Consultation with technology evaluation center(s);
2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

****Medically Necessary (or “Medical Necessity”)** - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient’s health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.