09-J3000-24

Original Effective Date: 04/01/19

Reviewed: 08/13/25

Revised: 09/15/25

Subject: Emapalumab-lzsg (Gamifant) IV

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.

Dosage/ Administration	Position Statement	Billing/Coding	Reimbursement	Program Exceptions	Definitions
Related Guidelines	Other	References	Updates		

DESCRIPTION:

Hemophagocytic lymphohistiocytosis (HLH) is a rare, life-threatening hyperinflammatory syndrome of intense immune activation caused by defects in cytotoxic pathways which leads to an increase in cytokines and accumulation of activated macrophages in organs and tissues. Symptoms may include fever, enlarged liver or spleen, cytopenias, neurologic abnormalities, and progression to multiorgan failure. HLH can be inherited (primary) or acquired (secondary). Primary HLH typically develops during the first months or years of life, although it may also develop later in life. Diagnostic criteria for HLH were developed by the Histiocyte Society and consist of either molecular confirmation of HLH or at least 5 of 8 specific clinical features. Treatment includes chemotherapy or immunotherapy until allogeneic hematopoietic stem cell transplant can occur.

Interferon gamma is a proinflammatory cytokine that is secreted in HLH. Emapalumab-lzsg (Gamifant) is a monoclonal antibody that binds to and neutralizes interferon gamma. It is Food and Drug Administration (FDA) approved for the treatment of adult and pediatric (newborn and older) patients with primary HLH with refractory, recurrent or progressive disease, or intolerance with conventional HLH therapy. It has also been approved for adult and pediatric patients with HLH/macrophage activation syndrome (MAS) in known or suspected Still's disease, including systemic Juvenile Idiopathic Arthritis (sJIA), with an inadequate response of intolerance to glucocorticoids, or with recurrent MAS. The NCCN guideline for the management of immune-checkpoint inhibitor-related toxicities recommends consideration of adding tocilizumab, anakinra, ruxolitinib, cyclosporine, or emapalumab for the treatment of HLH-like syndrome if no response to steroids after 5 days.

Emapalumab was evaluated in a open-label, single-arm trial in 27 pediatric patients with suspected or confirmed primary HLH with either refractory, recurrent, or progressive disease during conventional HLH therapy or who were intolerant of conventional HLH therapy. Patients were included if there was evidence of active disease by physician assessment and were 18 years of age or younger at diagnosis of

Primary HLH. Patients were included with primary HLH if based on molecular diagnosis, family history consistent with the disease, or five out of 8 of the following were fulfilled: fever, splenomegaly, cytopenia affecting 2 of 3 lineages in the peripheral blood (hemoglobin < 9 g/dL, platelets < 100 x 10^9/L, neutrophils < 1 x 10^9/L), hypertriglyceridemia (fasting triglycerides > 3 mmol/L or ≥ 265 mg/dL) and/or hypofibrinogenemia (≤ 1.5 g/L), hemophagocytosis in bone marrow, spleen, or lymph nodes with no evidence of malignancy, low or absent NK-cell activity, ferritin ≥ 500 mcg/L, soluble CD25 ≥ 2400 U/mL. Patients also were included if they did not respond or maintain a response to conventional HLH treatment, or had intolerance to conventional treatment. Prior HLH treatments included combinations of the following: dexamethasone, etoposide, cyclosporine A, and anti-thymocyte globulin. All patients received dexamethasone in the trial and could continue cyclosporine A or intrathecal methotrexate or glucocorticoids if receiving prior to treatment. Patients were excluded if malignancy was present or if there was secondary HLH due to rheumatic or malignant disease. Patients were excluded for active infections caused by pathogens favored by interferon gamma neutralization (e.g., mycobacteria and Histoplasma capsulatum) but were allowed to enroll for other active infections. All patients received prophylaxis for Herpes Zoster, Pneumocystis jirovecii and fungal infections.

There were 27 patients enrolled and the median patient age was 1 year (0.2 – 13). Eighty-two percent of patients had a genetic mutation known to cause primary HLH. Twenty patients completed the study at 8 weeks and 22 enrolled in the 1 year extension study. All patients received an initial dose of 1 mg/kg every 3 days. There were 30% of patients who increased the dose to 3-4 mg/kg and 26% who increased to 6-10 mg/kg. Efficacy was assessed by overall response rate (ORR) at the end of treatment using clinical and lab parameters and was defined as achievement of either a complete or partial response or HLH improvement. Complete response was defined as normalization of all HLH abnormalities (no fever, no splenomegaly, neutrophils > 1 x 10^9/L, platelets >100 x 10^9/L, ferritin < 2,000 mcg/L, fibrinogen > 1.5 g/L, D-dimer <500 mcg/L, normal CNS symptoms, no worsening of sCD25 > 2-fold baseline). Partial response was defined as normalization of ≥ 3 HLH abnormalities. HLH improvement was defined as ≥ 3 HLH abnormalities improved by at least 50% from baseline. The ORR was achieved by 17/27 patients (63%, p=0.013) with 7 (26%), 8 (30%), and 2 (7.4%) patients achieving a complete response, partial response or HLH improvement, respectively. Seventy percent (19/27) of patients proceeded to HSCT. The most common adverse reactions (≥ 20%) included infections, hypertension, infusion-related reactions, and pyrexia. The most common serious adverse reactions (≥ 3%) included infections, gastrointestinal hemorrhage, and multiple organ dysfunction. Fatal adverse reaction occurred in two patients and included septic shock and gastrointestinal hemorrhage. Disseminated histoplasmosis led to drug discontinuation in one patient.

POSITION STATEMENT:

Initiation of emapalumab-lzsg (Gamifant) **meets the definition of medical necessity** for the treatment of the following indications when all of the specific criteria are met:

1. Primary hemophagocytic lymphohistiocytosis (HLH)

A. **ONE** of the following – lab documentation must be submitted:

i. Presence of a primary HLH genetic mutation (e.g., PRF1, UNC13D, STX11, STXBP2 (UNC18B), RAB27A, LYST, SH2D1A, BIRC4, AP3B1)

ii. At least 5 of the following 8 clinical signs of primary HLH:

1. Fever
2. Splenomegaly
3. Cytopenia affecting at least 2 of 3 lineages in the peripheral blood (hemoglobin < 9 g/dL, platelets < 100 x 10^9/L, neutrophils < 1 x 10^9/L)
4. Hypertriglyceridemia (fasting triglycerides ≥ 3 mmol/L or ≥ 265 mg/dL) and/or hypofibrinogenemia (≤ 1.5 g/L)
5. Hemophagocytosis in bone marrow, spleen, or lymph nodes with no evidence of malignancy
6. Low or absent NK-cell activity
7. Ferritin ≥ 500 mcg/L
8. Soluble CD25 ≥ 2400 U/mL

B. Member has evidence of active disease – documentation must be submitted

C. Member has an inadequate response, intolerance, or contraindication to conventional HLH therapy (e.g., combined use of dexamethasone, etoposide, and cyclosporine A) – documentation must be submitted

D. Member does not have secondary HLH (e.g., HLH associated with rheumatic or neoplastic disease) – documentation must be submitted

E. Member will receive prophylaxis for Herpes Zoster, Pneumocystis jirovecii, fungal infections, and tuberculosis (if PPD positive)

F. Member will receive dexamethasone in combination with emapalumab-lzsg

G. Emapalumab-lzsg will be discontinued when the member receives a hematopoietic stem cell transplant

H. The member's labs will be monitored at baseline and regular intervals to assess clinical response prior to dose escalation of emapalumab-lzsg

I. The dose does not exceed the following with lab documentation submitted to support use of the minimum effective dose (Table 1):

   i. 1 mg/kg intravenously every 3 to 4 days initially

   ii. 3 mg/kg every 3 to 4 days beginning on day 4 if there is unsatisfactory improvement in clinical condition

   iii. 6 mg/kg every 3 to 4 days beginning on day 7 if there is unsatisfactory improvement in clinical condition

   iv. 10 mg/kg every 3 to 4 days beginning on day 10 if there is unsatisfactory improvement in clinical condition

   v. After stabilization of the member's clinical condition, the dose will be decreased to the minimum effective dose

2. HLH/Macrophage Activation Syndrome (MAS) in Still's disease or Systemic Juvenile idiopathic Arthritis (sJIA)

   A. Member has HLH/MAS associated with a diagnosis of Adult Onset Still's disease or sJIA (e.g.,not associated with infection or malignancy) – documentation must be submitted

B. Member has evidence of active HLH/MAS including ALL of the following – lab documentation must be submitted:
    i. Fever
    ii. Ferritin ≥ 684 ng/L
    iii. At least 2 of the following 4 clinical signs of HLH/MAS:
        1. Platelets less than or equal to 181 x 10^9/L
        2. AST greater than 48 U/L
        3. Triglycerides greater than 156 mg/dL
        4. Fibrinogen less than or equal to 360 mg/dL
C. Member does not have evidence of an infection caused by active mycobacteria, *Histoplasma capsulatum, Shigella, Salmonella, Campylobacter or Leishmania*
D. Member has an inadequate response, intolerance, or contraindication to high dose intravenous glucocorticoid treatment (e.g. methylprednisolone 30 mg/kg/day or 1 g/day) administered for greater than or equal to 3 consecutive days– documentation must be submitted
E. Member has an inadequate response, intolerance or contraindication to anakinra, calcineurin inhibitor (cyclosporine A or tacrolimus), etoposide, AND IVIG– documentation must be submitted
F. Member will receive prophylaxis for Herpes Zoster, Pneumocystis jirovecii, fungal infections, and tuberculosis (if PPD positive)
G. The member's labs will be monitored at baseline and regular intervals to assess clinical response prior to dose escalation of emapalumab-lzsg
H. The dose does not exceed the following with lab documentation submitted to support use of the minimum effective dose (Table 2):
    i. 6 mg/kg beginning on day 1
    ii. 3 mg/kg every 3 days for 5 doses on days 4 to 16
    iii. 3 mg/kg twice per week (every 3 to 4 days) from day 19 onwarda
    iv. After stabilization of the member's clinical condition, the dose will be decreased to the minimum effective dose

3. HLH-like syndrome following the use of an immune checkpoint inhibitor
    A. Member has HLH-like syndrome that developed following the use of a checkpoint inhibitor (e.g., atezolizumab, avelumab, durvalumab, ipilimumab, nivolumab, pembrolizumab)– documentation must be submitted
    B. The checkpoint inhibitor has been discontinued
    C. Member does not have non-immune checkpoint inhibitor etiologies of HLH (e.g., HLH associated with infection or lymphoma) – documentation must be submitted
    D. Member has evidence of active HLH-like syndrome including at least 5 of the following 8 clinical signs – lab documentation must be submitted:
        i. Fever
        ii. Splenomegaly
        iii. Cytopenia affecting at least 2 of 3 lineages in the peripheral blood (hemoglobin < 9 g/dL, platelets < 100 x 10^9/L, neutrophils < 1 x 10^9/L)

iv. Hypertriglyceridemia (fasting triglycerides ≥ 3 mmol/L or ≥ 265 mg/dL) and/or hypofibrinogenemia (≤ 1.5 g/L)

v. Hemophagocytosis in bone marrow, spleen, or lymph nodes with no evidence of malignancy

vi. Low or absent NK-cell activity

vii. Ferritin ≥ 500 mcg/L

viii. Soluble CD25 ≥ 2400 U/mL

E. Member does not have evidence of an infection caused by active mycobacteria, *Histoplasma capsulatum, Shigella, Salmonella, Campylobacter or Leishmania*

F. Member has an inadequate response, intolerance, or contraindication to intravenous glucocorticoid treatment (e.g. methylprednisolone 0.5 – 1 mg/kg/day) administered for greater than or equal to 5 consecutive days– documentation must be submitted

G. Member has an inadequate response, intolerance, or a contraindication to ALL of the following – documentation must be submitted:

i. Tocilizumab

ii. Anakinra

iii. Ruxolitinib

iv. Cyclosporine

H. Member will receive prophylaxis for Herpes Zoster, Pneumocystis jirovecii, fungal infections, and tuberculosis (if PPD positive)

I. Emapalumab-lzsg will be discontinued when the member no longer requires therapy for the treatment of HLH-like syndrome

J. The member's labs will be monitored at baseline and regular intervals to assess clinical response prior to dose escalation of emapalumab-lzsg

K. The dose does not exceed the following with lab documentation submitted to support use of the minimum effective dose (Table 1):

i. 1 mg/kg intravenously every 3 to 4 days initially

ii. 3 mg/kg every 3 to 4 days beginning on day 4 if there is unsatisfactory improvement in clinical condition

iii. 6 mg/kg every 3 to 4 days beginning on day 7 if there is unsatisfactory improvement in clinical condition

iv. 10 mg/kg every 3 to 4 days beginning on day 10 if there is unsatisfactory improvement in clinical condition

v. After stabilization of the member's clinical condition, the dose will be decreased to the minimum effective dose

Approval duration: 4 weeks

Continuation of emapalumab-lzsg (Gamifant) **meets the definition of medical necessity** for the treatment of primary HLH, HLH/MAS in Still's disease/sJIA, or HLH-like syndrome following the use of an immune checkpoint inhibitor when **ALL** of the following criteria are met:

1. An authorization or reauthorization for emapalumab-lzsg (Gamifant) has been previously approved by Florida Blue or another health plan in the past 2 years for the treatment of primary

HLH (if another health plan, documentation of a health plan-paid claim during the 90 days immediately before the authorization request must be provided), **OR** the member has previously met **ALL** indication-specific criteria.

2. Member has a beneficial response to treatment (e.g., improvement in at least 3 or more signs of HLH abnormalities present at baseline from Table 3 below) AND the member continues to have signs of residual active disease– documentation must be submitted
3. Treatment will be used for **ONE** of the following:
    a. For the treatment of Primary HLH when the diagnosis has been confirmed by the presence of a primary HLH genetic mutation (e.g., PRF1, UNC13D, STX11, STXBP2 (UNC18B), RAB27A, LYST, SH2D1A, BIRC4, AP3B1) – lab documentation must be submitted
    b. For the treatment of HLH/MAS in Still's disease or Systemic Juvenile idiopathic Arthritis (e.g.,not associated with infection or malignancy) and the member has recurrence of HLH/MAS while receiving treatment for Still's disease/sJIA (e.g., canakinumab, anakinra, glucocorticoids) – documentation must be submitted
    c. HLH-like syndrome following the use of an immune checkpoint inhibitor and the checkpoint inhibitor has been discontinued
4. Member will receive prophylaxis for Herpes Zoster, Pneumocystis jirovecii, fungal infections, and tuberculosis (if PPD positive)
5. **ONE** of the following:
    a. Primary HLH: The member is a candidate for stem cell transplant and emapalumab-lzsg will be discontinued when the member receives a hematopoietic stem cell transplant
    b. HLH/MAS associated with Still's disease/sJIA: Emapalumab-lzsg will be discontinued when the member no longer has signs of active HLH/MAS
    c. HLH-like syndrome following the use of a checkpoint inhibitor: Emapalumab-lzsg will be discontinued when the member no longer has signs of active HLH-like syndrome
6. The dose does not exceed the following **AND** the dose will be decreased to the minimum effective dose after stabilization of the member's clinical condition- documentation must be submitted:
    a. Primary HLH: 1 mg/kg to 10 mg/kg every 3 to 4 days with lab documentation submitted to support use of the minimum effective dose (Table 1)
    b. HLH/MAS associated with Still's disease/sJIA: 3 mg/kg twice per week with lab documentation submitted to support use of use of the minimum effective dose and frequency[a] (Table 2)
    c. HLH-like syndrome following the use of a checkpoint inhibitor: 1 mg/kg to 10 mg/kg every 3 to 4 days with lab documentation submitted to support use of use of the minimum effective dose (Table 1)

Approval duration: 4 weeks

[a] If the members clinical condition does not improve, the dose may be increased to a maximum cumulative dose of 10 mg/kg over 3 days and the frequency does not exceed every 2 days or once daily with lab documentation to support higher dose or frequency

Table 1 - HLH and ICI-induced HLH-like syndrome Dose Adjustment

Day 1	Starting dose of 1 mg/kg	N/A

From Day 4 onwards	Increase to 3 mg/kg	Unsatisfactory improvement in clinical condition, as assessed by a healthcare provider **AND** at least **ONE** of the following:
		• Fever – persistence or recurrence
		• Platelet count
		  ○ If baseline < 50,000/mm^3 and no improvement to > 50,000/ mm^3
		  ○ If baseline > 50,000/ mm^3 and less than 30% improvement
		  ○ If baseline > 100,000/ mm^3 and decrease to < 100,000/mm^3
		• Neutrophil count
		  ○ If baseline < 500/ mm^3 and no improvement to > 500/ mm^3
		  ○ If baseline > 500/ mm^3 to 1,000/ mm^3 and decrease to < 500/ mm^3
		  ○ If baseline 1,000/ mm^3 to 1,500/ mm^3 and decrease to < 1,000/ mm^3
		• Ferritin (ng/mL)
		  ○ If baseline ≥ 3,000 ng/mL and < 20% decrease
		  ○ If baseline < 3,000 ng/mL and any increase to > 3,000 ng/mL
		• Splenomegaly – any worsening
		• Coagulopathy (**BOTH** D-Dimer and Fibrinogen must apply)
		  ○ D-Dimer
		  - If abnormal at baseline and no improvement
		  - Fibrinogen (mg/dL)
		  - If baseline levels ≤ 100 mg/dL and no improvement
		  - If baseline levels > 100 mg/dL and any decrease to < 100 mg/dL

From Day 7 onwards	Increase to 6 mg/kg	
From Day 10 onwards	Increase to 10 mg/kg	Assessment by a healthcare provider that based on initial signs of response, a further increase in dose can be of benefit

Table 2. HLH/MAS Dose adjustment criteria

Day 1	Starting dose of 6 mg/kg	If unsatisfactory improvement in clinical condition, as assessed by a healthcare provider, the dose of may be increased to: • a maximum cumulative dose of 10 mg/kg over 3 days **AND** the frequency may be increased to: • every 2 days or once daily
From Day 4 to 16 onwards	3 mg/kg every 3 days for 5 doses	
From Day 19 onwards	3 mg/kg twice per week (i.e. every 3 to 4 days)	

		After the patient's clinical condition has improved, consider decreasing the dose to the previous level and assess whether clinical response is maintained. If the clinical condition is not stabilized while receiving the maximum dosage, consider discontinuing.

Table 3. Beneficial response to emapalumab-lzsg

Primary HLH	Improvement in signs of at least 3 or more of the following if present or abnormal at baseline: A. No fever B. No splenomegaly C. Neutrophils greater than 1 x 10^9/L D. Platelets greater than 100 x 10^9/L E. Ferritin less than 2000 ng/mL F. Fibrinogen greater than 1.5 g/L G. D-dimer less than 500 mcg/L H. Normal CNS symptoms I. No worsening of soluble CD25 greater than 2-fold baseline
HLH/MAS in Still's disease/sJIA	Improvement in signs of at least 3 or more of the following if present or abnormal at baseline: A. WBC and platelet greater than lower limit of normal B. LDH, AST, and ALT less than 1.5 times the upper limit of normal C. Fibrinogen greater than 100 mg/dL D. Ferritin less than or equal to 80% from baseline measure or less than 2000 ng/mL
Immune checkpoint induced HLH	Improvement in signs of at least 3 or more of the following if present or abnormal at baseline: A. No fever B. No splenomegaly C. Neutrophils greater than 1 x 10^9/L D. Platelets greater than 100 x 10^9/L E. Ferritin less than 2000 ng/mL F. Fibrinogen greater than 1.5 g/L G. D-dimer less than 500 mcg/L H. Normal CNS symptoms I. No worsening of soluble CD25 greater than 2-fold baseline

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

- **Primary hemophagocytic lymphohistiocytosis (HLH) with refractory, recurrent or progressive disease, or intolerance with conventional HLH therapy:** 1 mg/kg as an intravenous infusion over 1 hour twice per week (every 3 to 4 days). Doses subsequent to the initial dose may be increased based on clinical and lab data. . Discontinue when hematopoietic stem cell transplantation (HSCT) is performed, unacceptable toxicity, or when a patient no longer requires therapy for treatment of HLH.
- **HLH/macrophage activation syndrome (MAS) in known or suspected Still's disease, including systemic Juvenile Idiopathic Arthritis (sJIA), with an inadequate response or intolerance to glucocorticoids, or with recurrent MAS**: 6 mg/kg, followed by 3 mg/kg every 3 days for 5 doses, then 3 mg/kg twice per week as an intravenous infusion over 1 hour. Doses subsequent to the initial dose may be increased based on clinical and lab data.
- Conduct testing for latent tuberculosis infection prior to therapy. Administer tuberculosis prophylaxis to patients at risk, who test positive, or positive interferon gamma release assay. Monitor for tuberculosis, Herpes Zoster infection, adenovirus, EBV, and CMV as clinically indicated.
- Administer prophylaxis for Herpes Zoster, Pneuomocystis jirovecii, and for fungal infections prior to administration.
- For primary HLH patients not receiving dexamethasone, administer dexamethasone at a daily dose of at least 5 mg/m^2 to 10 mg/m^2 concomitantly; If dexamethasone was already being taken, the dose may be continued if at least 5 mg/m^2. Dexamethasone can be tapered at the discretion of the physician.

Dose Adjustments

- See prescribing information for dose titration for unsatisfactory improvement in clinical condition.
- For primary HLH, evaluate fever, platelet, neutrophil, ferritin, splenomegaly, coagulopathy, fibrinogen at regular intervals (Table 1). Dose is adjusted from day 1 (1 mg/kg), day 4 onwards (3 mg/kg), day 7 onwards (6 mg/kg), and day 10 onwards (up to 10 mg/kg) based on clinical condition. After the patient's clinical condition is stabilized, decrease the dose to the previous level to maintain clinical response.

Drug Availability

- 10 mg/2 mL (5 mg/mL)
- 50 mg/10 mL (5 mg/mL)

PRECAUTIONS:

Contraindications

- None

Precautions/Warnings

- Infections – may increase the risk of fatal and serious infections to include specific pathogens favored by interferon gamma neutralization, including mycobacteria, Herpes Zoster virus, and Histoplasma Capsulatum. Do not administer in patients with infections caused by these pathogens until appropriate treatment has been initiated.
- Live Vaccines: Do not administer live or live attenuated vaccines to patients receiving emapalumab and for at least 4 weeks following the last dose.
- Infusion reactions: Drug eruption, pyrexia, rash, erythema, and hyperhidrosis were reported in up to 27% of patients. Monitor for infusion related reaction and interrupt infusion to initiate appropriate medical care.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J9210	Injection, emapalumab-lzsg, 1 mg

ICD-10 Diagnosis Codes That Support Medical Necessity

D76.1	Hemophagocytic lymphohistiocytosis
M06.1	Adult-onset Still's disease
M08.09	Unspecified juvenile rheumatoid arthritis, multiple sites
M08.20	Juvenile rheumatoid arthritis with systemic onset, unspecified site

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: Florida Blue 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.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

none

RELATED GUIDELINES:

none

OTHER:

none

REFERENCES:

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 08/13/25.

GUIDELINE UPDATE INFORMATION:

04/01/19	New Medical Coverage Guideline.
07/01/19	Revision: Added HCPCS code C9050.
10/01/19	Revision: Added HCPCS J9210 and removed C9050 and J3590.
05/15/20	Review of guideline consisting of updating references.
04/15/21	Review and revision to guideline; consisting of updating the position statement and references.
04/15/22	Review and revision to guideline; consisting of updating the references.
11/15/23	Review and revision to guideline; consisting of updating the position statement and references.
01/15/24	Review and revision to guideline; consisting of updating the position statement.
04/15/24	Review and revision to guideline; consisting of updating the position statement.
09/15/25	Review and revision to guideline; consisting of updating the position statement to include HLH/MAS in Still's disease/sJIA and HLH-like syndrome following immune checkpoint inhibitor therapy.