Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Pentamidine Isethionate (Nebupent®)	MP-RX-FP-169-25	☒ MMM MA ☒ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B Drugs

Service Description

This document addresses the use of Pentamidine Isethionate (Nebupent®), an antifungal agent approved by the Food and Drug Administration (FDA) for the prevention of *Pneumocystis jiroveci* pneumonia (PJP) in high-risk, HIV-infected patients.

Background Information

Pneumocystis jirovecii pneumonia (formerly known as Pneumocystis carinii pneumonia or PCP) stands out as the predominant opportunistic respiratory infection among individuals grappling with acquired immunodeficiency syndrome (AIDS), particularly those afflicted with human immunodeficiency virus (HIV) and a CD4 count below 200 cells/microL who are not undergoing antiretroviral therapy or suitable prophylaxis.

According to current guidelines, primary PCP prophylaxis is recommended for patients meeting any of the following criteria:

- CD4 count below 200 cells/microL
- CD4 count percentage less than 14 percent
- CD4 cell count ranging between 200 and 250 cells/microL when frequent monitoring of CD4 cell counts, such as every three months, isn't feasible.

Pentamidine isethionate, an aromatic diamine compound with efficacy against Pneumocystis and various protozoal pathogens including *Leishmania* spp and *T. b. gambiense*, serves as an alternative therapy for primary and secondary prophylaxis of Pneumocystis pneumonia in both HIV-infected adults and children. However, sulfamethoxazole/trimethoprim remains the preferred choice. Despite its general tolerability, pentamidine is less effective compared to other regimens, necessitates specialized equipment, and carries the risk of transmitting other respiratory pathogens. Moreover, aerosolized pentamidine isethionate's effectiveness is confined locally, leaving untreated lung areas susceptible to PCP if not adequately dispersed.

In the case of treatment for active PCP, inhaled pentamidine is not typically the first-line therapy. Instead, systemic antibiotics such as trimethoprim-sulfamethoxazole (TMP-SMX) or alternative medications like dapsone plus trimethoprim or atovaquone are more commonly used. The duration of treatment for active PCP with these medications typically ranges from several weeks to a few months, depending on the severity of the infection and the individual's response to treatment.

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The standard dose of pentamidine isethionate is 300 mg administered monthly via a nebulizer, often accompanied by two puffs of albuterol to alleviate cough and bronchospasm. Prior to administering aerosolized pentamidine isethionate, screening for active tuberculosis, including a baseline chest x-ray, is imperative due to concerns about tuberculosis transmission via pentamidine-induced bronchospasm. Furthermore, administration should occur in a negative pressure room to contain aerosolized drug particles and potential microbe expectoration. In individual patient hospital rooms, a HEPA-filtered containment tent may be used, with airflow temporarily adjusted to negative pressure if feasible.

While aerosolized pentamidine has been utilized in various transplant settings, including renal, hematopoietic stem cell, lung, and bone marrow transplants, its safety and efficacy in these populations remain debatable. Studies have shown divergent results, with reports of high adverse reaction rates in renal transplant recipients but successful prophylaxis in lung and bone marrow transplant recipients.

Approved Indications

NebuPent® is indicated for the prevention of *Pneumocystis jiroveci* pneumonia (PJP) in high-risk, HIV-infected patients defined by one or both of the following criteria:

i. A history of one or more episodes of PJP
ii. A peripheral CD4+ (T4 helper/inducer) lymphocyte count less than or equal to 200/mm3.

Other Uses

None

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Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS	Description
J2545	Pentamidine non-comp unit (Pentamidine isethionate, inhalation solution, fda-approved final product, non-compounded, administered through dme, unit dose form, per 300 mg)
S9061	Medical supplies and equipme (Home administration of aerosolized drug therapy (e.g., pentamidine); administrative services, professional pharmacy services, care coordination, all necessary supplies and equipment (drugs and nursing visits coded separately), per diem)

Please refer to Policy Article A5266- Nebulizers for the most updated list of ICD-10 codes.

ICD-10	Description
B20	Human immunodeficiency virus [HIV] disease
B59	Pneumocystosis
T86.00	Unspecified complication of bone marrow transplant
T86.01	Bone marrow transplant rejection
T86.02	Bone marrow transplant failure
T86.03	Bone marrow transplant infection
T86.09	Other complications of bone marrow transplant
T86.10	Unspecified complication of kidney transplant
T86.11	Kidney transplant rejection
T86.12	Kidney transplant failure
T86.13	Kidney transplant infection
T86.19	Other complication of kidney transplant
T86.20	Unspecified complication of heart transplant
T86.21	Heart transplant rejection
T86.22	Heart transplant failure
T86.23	Heart transplant infection
T86.290	Cardiac allograft vasculopathy
T86.298	Other complications of heart transplant
T86.30	Unspecified complication of heart-lung transplant
T86.31	Heart-lung transplant rejection
T86.32	Heart-lung transplant failure
T86.33	Heart-lung transplant infection

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T86.39	Other complications of heart-lung transplant
T86.40	Unspecified complication of liver transplant
T86.41	Liver transplant rejection
T86.42	Liver transplant failure
T86.43	Liver transplant infection
T86.49	Other complications of liver transplant
T86.5	Complications of stem cell transplant
T86.810	Lung transplant rejection
T86.811	Lung transplant failure
T86.812	Lung transplant infection
T86.818	Other complications of lung transplant
T86.819	Unspecified complication of lung transplant
T86.830	Bone graft rejection
T86.831	Bone graft failure
T86.832	Bone graft infection
T86.838	Other complications of bone graft
T86.839	Unspecified complication of bone graft
T86.850	Intestine transplant rejection
T86.851	Intestine transplant failure
T86.852	Intestine transplant infection
T86.858	Other complications of intestine transplant
T86.859	Unspecified complication of intestine transplant
T86.890	Other transplanted tissue rejection
T86.891	Other transplanted tissue failure
T86.892	Other transplanted tissue infection
T86.898	Other complications of other transplanted tissue
T86.899	Unspecified complication of other transplanted tissue
T86.90	Unspecified complication of unspecified transplanted organ and tissue
T86.91	Unspecified transplanted organ and tissue rejection
T86.92	Unspecified transplanted organ and tissue failure
T86.93	Unspecified transplanted organ and tissue infection
T86.99	Other complications of unspecified transplanted organ and tissue

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Medical Necessity Guidelines

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Pentamidine Isethionate (Nebupent®)

A. Criteria For Initial Approval

This medical policy follows the guidelines established by CMS in LCD 33370 Nebulizers

i. The patient is HIV positive; **AND**
   A. The patient has *Pneumocystis jiroveci* pneumonia (PJP); **OR**
   B. The patient is at high risk of *Pneumocystis jiroveci* pneumonia (PJP), defined as having **ANY** of the following:
      i. A history of one or more episodes of PJP
      ii. A peripheral CD4+ (T4 helper/inducer) lymphocyte count less than or equal to 200/mm3.

OR

ii. The patient is positive for *Pneumocystis jiroveci* pneumonia

OR

iii. The patient is post-transplant and will use Pentamidine Isethionate to prevent *Pneumocystis jiroveci* pneumonia (PJP).

B. Criteria For Continuation of Therapy

i. MMM considers continuation of Pentamidine Isethionate (Nebupent®) therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) when the recommended maximum duration of therapy has not been exceeded. Progress notes, as well as CD4+ count level labs (for HIV/AIDS patients using for PJP prophylaxis) should be submitted for evaluation.

ii. Duration of therapy:
   A. According to current guidelines, primary *Pneumocystis* prophylaxis should be continued until patients respond to ART with an increase in CD4 counts from <200 cells/mm^3 to >200 cells/mm^3 for >3 months.
   B. When used for PJP prophylaxis in post-transplant patients: Indefinite use.

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C. Authorization Duration

i. Initial Approval Duration: Up to 12 months
ii. Reauthorization Approval Duration: Up to 12 months

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive).

Requests for Pentamidine Isethionate (Nebupent®) may not be approved when the above criteria (Section A: Criteria for Initial Approval) are not met and for all other indications.

Limits or Restrictions

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Drug	Recommended Dosing Schedule
Pentamidine Isethionate (Nebupent®)	300 mg once every four weeks administered via the Respirgard® II nebulizer. (quantity limit of one 300 mg lyophilized vial every 28 days)
Exceptions	
None	

Reference Information

- AIDSinfo: Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: Pneumocystis pneumonia. AIDSinfo. Rockville, MD. 2015.

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- Macesic, N., Urbancic, K.F., Ierino, F.L., & Grayson, M.L. (2016). Is Aerosolized Pentamidine for Pneumocystis Pneumonia Prophylaxis in Renal Transplant Recipients Not as Safe as We Might Think? *Antimicrobial Agents and Chemotherapy, 60*, 2502 - 2504.
- Nathan, S.D., Ross, D., Zakowski, P.C., Kass, R.M., & Koerner, S.K. (1994). Utility of inhaled pentamidine prophylaxis in lung transplant recipients. *Chest, 105 2*, 417-20 .
- Machado, C.M., Macedo, M.C., Medeiros, R.S., Massumoto, C., Silva, A., Castelli, J.B., Silva, R.L., Ostronoff, M., & Dulley, F.L. (1998). Primary Pneumocystis carinii Prophylaxis with Aerosolized Pentamidine after Bone Marrow Transplantation. *Acta Haematologica, 99*, 54 - 56.
- Clinical Info HIV.Gov. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV.
- DailyMed Package Insert.
- Thomas C. Treatment and prevention of Pneumocystis pneumonia in patients without HIV. UpToDate. Last updated 01/09/2024.
- Sax P. Treatment and prevention of Pneumocystis infection in patients with HIV. UpToDate. Last updated 09/12/2022.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

Policy History

Revision Type	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Policy Inception	New Medical Policy creation	5/20/2024	6/28/2024

Created: 04/10/2024