

arimoclomol (MiplyffaTM)

Policy # 00919

Original Effective Date: 03/01/2025

Current Effective Date: 03/01/2026

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.

Investigational or experimental services are not covered. This includes any drug, device, procedure, or service provided under the investigational arm of a clinical trial or clinical study. These services are excluded from coverage under benefits.

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 the use of arimoclomol (MiplyffaTM)[‡] for the treatment of Niemann-Pick disease type C to be **eligible for coverage**.^{**}

Patient Selection Criteria

Coverage eligibility for arimoclomol (Miplyffa) will be considered when the following criteria are met:

- **Initial**
 - Patient is greater than or equal to 2 years of age AND weighs greater than or equal to 8 kg; AND
 - Patient has a genetically confirmed diagnosis of Niemann-Pick disease type C (NPC) determined by one of the following:
 - Mutations in both alleles of *NPC1* or *NPC2*; OR
 - Mutation in one allele of *NPC1* or *NPC2* AND either a positive filipin-staining or cholestane-triol level (greater than 2 times the upper limit of normal); AND
 - Patient has one or more neurological signs of NPC. Examples of neurologic signs include loss of motor function, difficulty swallowing, speech impairment, and cognitive impairment; AND
 - Patient does NOT have adult-onset NPC (defined as the age of the first neurological symptom occurring > 15 years of age); AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
 - Patient is able to walk independently or with assistance; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
 - Patient will use Miplyffa in combination with miglustat; AND
 - Patient will NOT use Miplyffa in combination with levacetylleucine (AqneursaTM)[‡].

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- **Continuation**

- o Patient has received an initial authorization for Miplyffa; AND
- o Provider attests that the patient is experiencing a benefit from therapy as evidenced by an improvement or stabilization in a domain affected by NPC (e.g., ambulation, fine motor skills, swallowing, or speech).

*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of arimoclomol (Miplyffa) in patients with adult onset NPC or those who are unable to walk independently or with assistance to be **not medically necessary**.**

Based on review of available data, the Company considers the continued use of arimoclomol (Miplyffa) when the patient has not demonstrated improvement or stabilization in a domain affected by NPC to be **not medically necessary**.**

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 arimoclomol (Miplyffa) when the patient selection criteria are not met (except those noted to be **not medically necessary****) to be **investigational**.*

Background/Overview

Miplyffa is an oral agent indicated for the treatment of the neurological manifestations of Niemann-Pick disease type C (NPC) in patients 2 years of age and older. It is only approved by the Food and Drug Administration (FDA) for use in combination with miglustat. Miplyffa is supplied as oral capsules of varying strengths that should be administered three times daily at a dose based on the weight of the patient. Although the exact mechanism of action is unknown, it is thought that Miplyffa works to facilitate the proper folding of certain mutant NPC proteins.

NPC is an autosomal recessive lysosomal storage disorder caused by a mutation in either the *NPC1* gene or the *NPC2* gene. These genes play a role in the lysosomal transport and metabolism of lipids, including cholesterol. Mutations in these genes cause the accumulation of cellular lipids in the cell which can result in a variety of clinical manifestations. Clinical presentation is heterogenous and ranges from severe symptoms in utero to adult-onset. The early-infantile form is rapidly progressive and leads to death in early childhood due to extensive visceral involvement. The later-onset forms are primarily neurodegenerative with symptoms such as loss of previously achieved gross and fine motor skills, ataxia, seizures, cataplexy, hearing loss, and cognitive decline. Diagnosis of NPC must be confirmed through genetic testing, including sequencing of the *NPC1* and *NPC2* genes.

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Most patients have a pathogenic mutation in both alleles of either *NPC1* or *NPC2*, but some patients may only have one pathogenic mutation. In this case, a positive biomarker test (cholestane-triol) or filipin staining test can confirm the diagnosis.

Prior to the approval of Miplyffa, the standard of care for treatment of NPC was off-label miglustat (available as generic or brand Zavesca® or brand Opfolda®)†. Despite not being approved by the FDA for this indication, miglustat is widely used in the U.S. and is approved in Europe and other countries for the treatment of the neurologic complications of NPC in pediatric and adult patients. Another drug, levacetylleucine (Aqneursa), was approved 4 days after Miplyffa and is indicated for the treatment of the neurological manifestations of NPC in patients weighing at least 15 kg. Treatment guidelines have not been updated to reflect the approval of these two new agents.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Miplyffa was approved in September 2024 for use in combination with miglustat for the treatment of neurological manifestations of Niemann-Pick disease type C (NPC) in adult and pediatric patients 2 years of age and older.

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 regulations, other plan medical policies, and accredited national guidelines.

Safety and effectiveness of Miplyffa were assessed in Trial 1, a randomized, double-blind, placebo controlled, 12-month trial in patients 2 to 19 years of age who had a molecularly confirmed diagnosis of NPC. Fifty patients were randomized 2:1 to treatment with weight-adjusted Miplyffa or placebo orally three times per day. The randomization was stratified by miglustat use status at baseline.

Efficacy assessments, including the rescored 4-domain NPC Clinical Severity Scale (R4DNPCCSS) score, were performed at baseline and every 3 months until 12 months of treatment. The R4DNPCCSS is a measure of NPC disease progression that consists of the four items assessing ambulation, speech, swallow, and fine motor skills that patients with NPC and their caregivers and physicians have identified as most relevant with higher scores representing greater severity of disease.

In Trial 1, 76% and 81% of patients in the Miplyffa and placebo groups, respectively, received miglustat six months or longer prior to the time of enrollment. For the subgroup of patients who also received miglustat at enrollment, the mean age was 11.6 years, the mean time since first NPC symptom was 8.5 years, and the mean age at onset of first neurological symptom was 4.9 years. The mean baseline R4DNPCCSS score was higher in the Miplyffa group (mean = 8.9) than the placebo

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group (mean = 7) with an overall mean R4DNPCCSS score of 8.3. For the patients who also received miglustat, the change from baseline to month 12 in R4DNPCCSS score was -0.2 in the placebo group and 1.9 in the placebo group. This represented a placebo-subtracted difference of -2.2 (95% CI, -3.8, -0.6).

There were insufficient data to determine the effectiveness of the use of Miplyffa without miglustat for the treatment of neurological manifestations in patients with NPC.

References

1. Miplyffa [package insert]. Acer Therapeutics, Inc. Greenwood Village, Colorado. Updated October 2024.

Policy History

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02/06/2025 Medical Policy Committee review

02/12/2025 Medical Policy Implementation Committee approval. New policy.

02/05/2026 Medical Policy Committee review

02/11/2026 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 02/2027

*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:
 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.

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****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.

NOTICE: If an authorization for an ongoing course of treatment has been provided to a member and the member changes from one health plan to another health plan (e.g., a member moves from carrier A to Louisiana Blue), Louisiana Blue may honor the previous health plan’s authorization for the same service under the same type of in-network benefit for a 90-day transition period. Documentation of the authorization for the ongoing course of treatment from the previous health plan must be provided to us by the member or their provider and the services provided for the course of treatment must otherwise be a covered service under the Louisiana Blue health plan. This provision does not apply to medications covered under the plan’s pharmacy benefit.