MEDICAL MUTUAL®

Drug Policy

Policy:	Miplyffa™ (arimoclomol capsules – Zevra)	Annual Review Date: 08/21/2025 Last Revised Date: 08/21/2025

OVERVIEW

Miplyffa is indicated in combination with miglustat for the treatment of neurological manifestations of **Niemann-Pick disease type C (NPC)** in patients ≥ 2 years of age.[1]

The FDA concluded that data are insufficient to determine the effectiveness of Miplyffa without miglustat for the treatment of neurological manifestations in patients with NPC.[1]

POLICY STATEMENT

This policy involves the use of Miplyffa. Prior authorization is recommended for pharmacy benefit coverage of Miplyffa. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Miplyffa as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Miplyffa be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Miplyffa is recommended in those who meet the following criteria:

A) Initial Therapy: Approve if the patient meets ALL of the following (i, ii, iii, iv, v, vi, and vii):
- **i.** Patient is ≥ 2 years of age; AND
- **ii.** Patient has one or more neurological symptom(s) of Niemann-Pick disease type C; AND
  Note: Examples of neurologic symptoms of Niemann-Pick disease type C include loss of motor function, swallowing, and speech and cognitive impairment.
- **iii.** Patient can walk independently or with assistance; AND
- **iv.** The diagnosis is established by a genetic test showing biallelic pathogenic variants in either the NPC1 gene or NPC2 gene*; AND
- **v.** Patient does NOT have adult-onset Niemann-Pick disease type C; AND
  Note: Adult-onset NPC is defined as the age of the first neurological symptom occurring > 15 years of age.

vi. The patient meets ONE of the following (a or b):
  a) The medication will be taken in combination with miglustat; OR
  b) History of failure, contraindication, or intolerance to miglustat; AND

vii. The medication is prescribed by or in consultation with a geneticist, endocrinologist, metabolic disorder subspecialist, neurologist, or a physician who specializes in the treatment of Niemann-Pick disease type C or related disorders.

B) Patient is Currently Receiving Miplyffa. Approve if the patient meets ALL of the following (i, ii, iii, and iv):

i. Patient does NOT have adult-onset Niemann-Pick disease type C; AND
Note: Adult-onset Niemann-Pick disease type C is defined as the age of the first neurological symptom occurring > 15 years of age.

ii. The patient meets ONE of the following (a or b):
  a) The medication will be taken in combination with miglustat; OR
  b) History of failure, contraindication, or intolerance to miglustat; AND

iii. According to the prescriber, patient has derived benefit from treatment defined as disease stabilization, slowed progression, or improvement; AND

iv. The medication is prescribed by or in consultation with a geneticist, endocrinologist, metabolic disorder subspecialist, neurologist, or a physician who specializes in the treatment of Niemann-Pick disease type C or related disorders.

Initial Approval/ Extended Approval.
A) *Initial Approval:* *1 year*
B) *Extended Approval:* *1 year*

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Miplyffa has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **Amyotrophic Lateral Sclerosis.** Arimoclomol did not improve efficacy outcomes relative to placebo in patients with amyotrophic lateral sclerosis. A multinational, randomized, double-blind, placebo-controlled, parallel group trial assessed the efficacy of arimoclomol (400 mg three times daily) vs. placebo in adults with amyotrophic lateral sclerosis (n = 245).[10] The primary outcome was the Combined Assessment of Function and Survival (CAFS) rank score over 76 weeks of treatment. At Week 76, the CAFS score did not differ between arimoclomol and placebo groups (mean 0.51 vs 0.49, respectively; P = non-significant). Proportions of participants who died were similar between the treatment groups (18% [n = 29/160] and 23% [n = 18/79] of patients in the arimoclomol and placebo groups, respectively). Most deaths were due to disease progression.

2. **Combination use with Aqneursa (levacetylleucine granules).** Aqneursa is indicated for the treatment of neurological manifestations of Niemann-Pick disease Type C in patients ≥ 15 kg.[11] There are no data available regarding combination use of Aqneursa and Miplyffa.

3. **Gaucher Disease.** A Phase II study with arimoclomol in patients with Gaucher disease type 1 or 3 was terminated; the Coronavirus disease-19 pandemic prevented the ability to assess the trial objective.[7] Additional data are needed to determine if arimoclomol is beneficial in patients with Gaucher disease type 1 or 3.

4. **Inclusion Body Myositis.** Arimoclomol did not improve efficacy outcomes relative to placebo in patients with inclusion body myositis. A multicenter, randomized, double-blind, placebo-controlled trial assessed the efficacy of arimoclomol (400 mg three times daily) vs. placebo in adults with inclusion body myositis fulfilling the European Neuromuscular Center research diagnostic criteria 2011 (n = 152).[9] The primary endpoint was the change from baseline to Month 20 in the Inclusion Body Myositis Functional Rating Scale (IBMFRS) total score. At Month 20, the mean IBMFRS change from baseline was not significantly different between arimoclomol and placebo (-3.26; 95% confidence interval: -4.15, -2.36; P = non-significant).

5. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

***Documentation Requirements:**

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational, or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

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11. Aqneursa™ granules [prescribing information]. Austin, TX: IntraBio; September 2024.