NEW MIPLYFFA™ arimoclomol capsules

A guide for healthcare providers

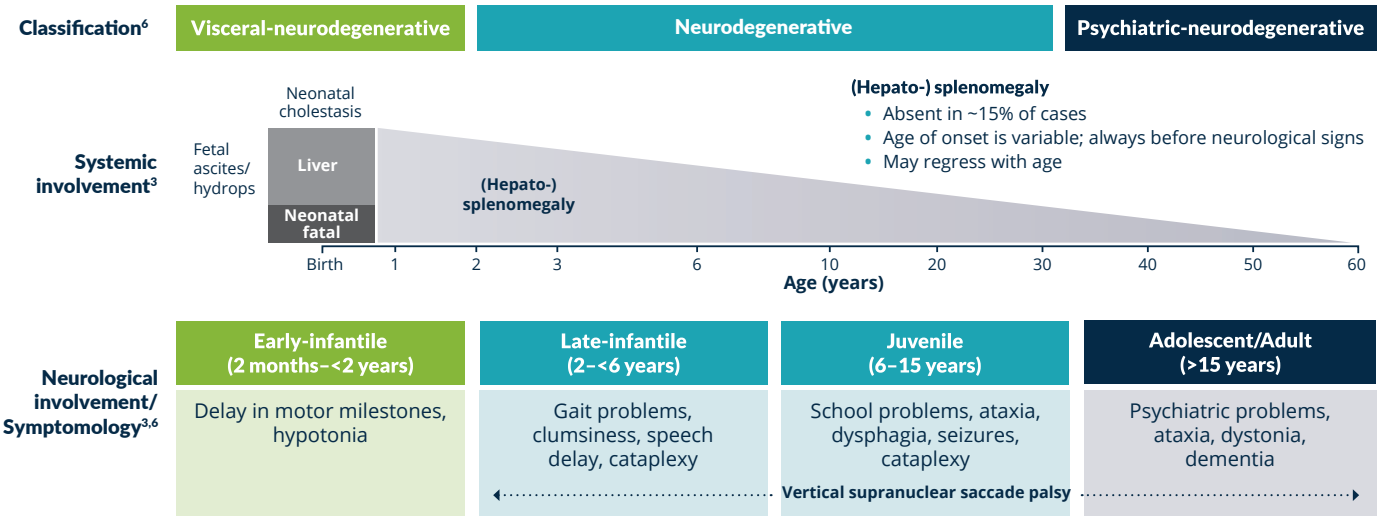
MIPLYFFA is the first FDA-approved treatment for Niemann-Pick disease type C (NPC)[1]

MIPLYFFA is indicated 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.

NPC is an ultra-rare, relentlessly progressive neurodegenerative disease[2]

- NPC is a genetic disease that leads to dysfunctional NPC proteins[2]
  - In NPC, the accumulation of unprocessed lipids leads to dysfunction in the brain, liver, and spleen[2,3]
- NPC is difficult to diagnose, and can affect patients at any age[2,4]
  - Patients aged >15 years could represent up to one-third of all patients with NPC[5]

Symptoms of NPC are progressive and may present differently depending on age[2]



IMPORTANT SAFETY INFORMATION

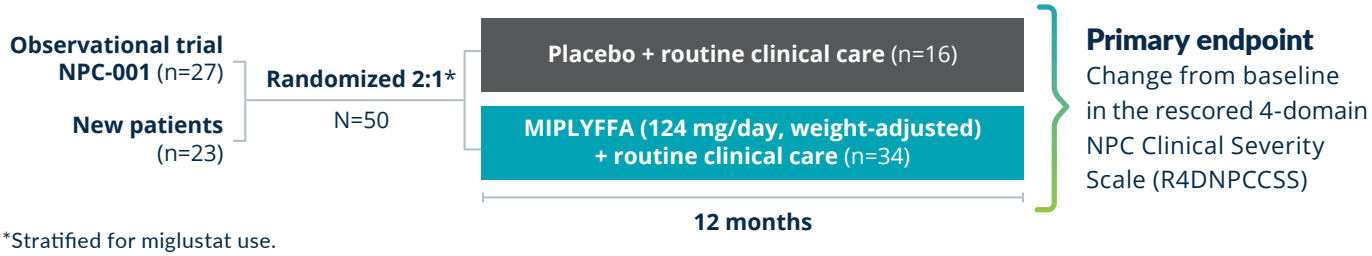
Hypersensitivity Reactions: Hypersensitivity reactions such as urticaria and angioedema have been reported in patients treated with MIPLYFFA during Trial 1: two patients reported both urticaria and angioedema (6%) and one patient (3%) experienced urticaria alone within the first two months of treatment. Discontinue MIPLYFFA in patients who develop severe hypersensitivity reactions. If a mild or moderate hypersensitivity reaction occurs, stop MIPLYFFA and treat promptly. Monitor the patient until signs and symptoms resolve.

Please see additional Important Safety Information on the following pages and the full Prescribing Information, including Instructions for Use.

Trial 1 study design

Safety and effectiveness of MIPLYFFA were studied in a 12-month multi-center, randomized, double-blind, placebo-controlled trial in patients with NPC, aged 2–19 years[1,6]

In Trial 1, 76% of patients in the MIPLYFFA group and 81% of those in the placebo group received miglustat as part of their routine clinical care.



*Stratified for miglustat use.

Baseline demographics for subgroup of patients who also received miglustat (n=39)[1]

- Mean age was 11.6 years
- Mean time since first NPC symptom was 8.5 years
- Mean age at onset of first neurological symptom was 4.9 years
- Mean baseline in the rescored 4-domain NPC Clinical Severity Scale (R4DNPCCSS) score was higher in the MIPLYFFA group (n=26; mean=8.9) than the placebo group (n=13; mean=7), with an overall mean R4DNPCCSS score of 8.3[1]

The treatment effect in Trial 1 was assessed as change from baseline on the R4DNPCCSS

The R4DNPCCSS is a measure of NPC disease progression that consists of four items assessing ambulation, speech, swallow, and fine motor skills that patients with NPC and their caregivers and physicians have identified as four of the most relevant, with higher scores representing greater severity of disease.[1]

IMPORTANT SAFETY INFORMATION

The most common adverse reactions in Trial 1 (≥15%) in MIPLYFFA-treated patients who also received miglustat were upper respiratory tract infection, diarrhea, and decreased weight.

Three (6%) of the MIPLYFFA-treated patients had the following adverse reactions that led to withdrawal from Trial 1: increased serum creatinine (one patient), and progressive urticaria and angioedema (two patients). Serious adverse reactions reported in MIPLYFFA-treated patients were hypersensitivity reactions including urticaria and angioedema.

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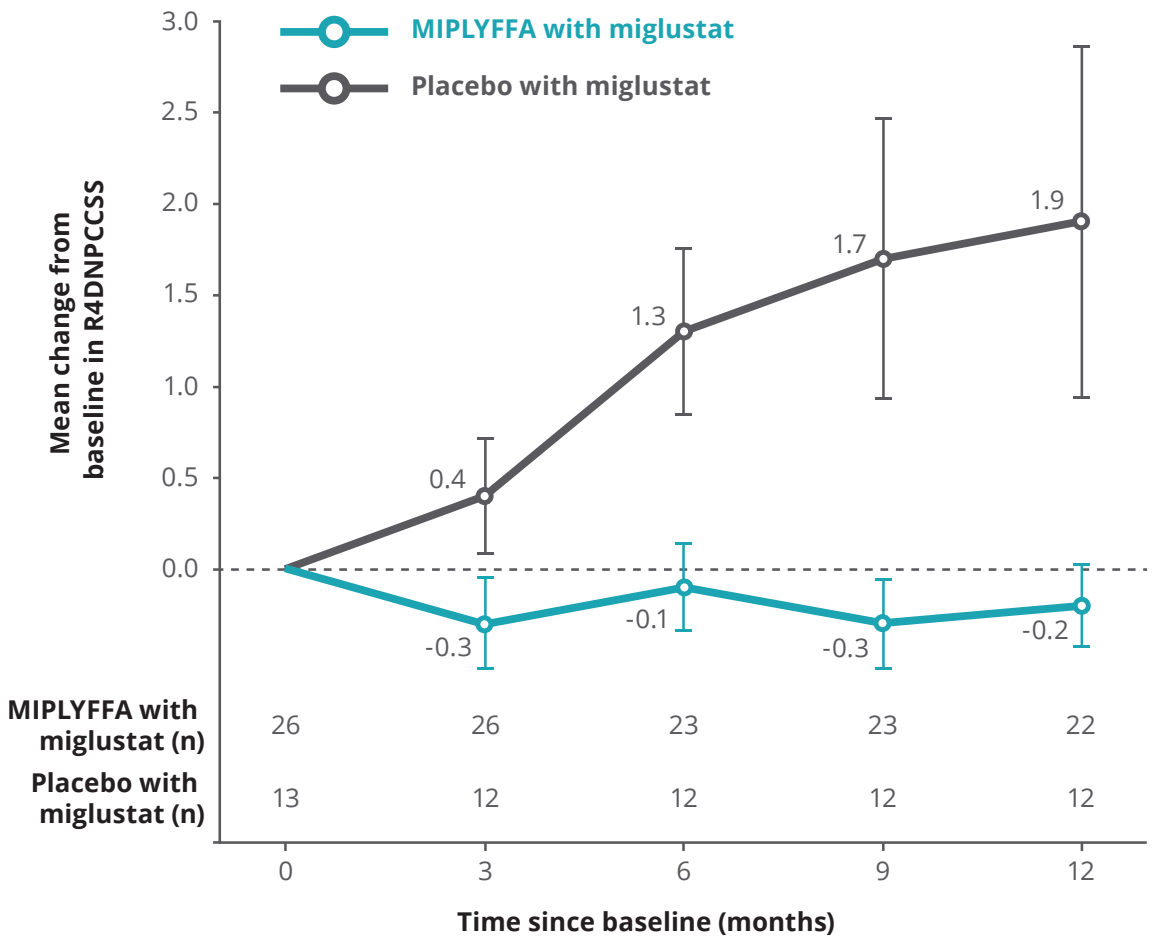
MIPLYFFA, in combination with miglustat, stopped disease progression at 12 months[1]

NPC SYMPTOM REDUCTION AT 12 MONTHS
as measured by the R4DNPCCSS score:
ambulation, speech, swallow, and fine motor skills



The estmated mean change from baseline at month 12 was
-2.2 pts.
vs miglustat alone

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.

IMPORTANT SAFETY INFORMATION

Embryofetal Toxicity: MIPLYFFA may cause embryofetal harm when administered during pregnancy based on findings from animal reproduction studies. Advise pregnant females of the potential risk to the fetus and consider pregnancy planning and prevention for females of reproductive potential.

Increased Creatinine without Affecting Glomerular Function: Across clinical trials of MIPLYFFA, mean increases in serum creatinine of 10% to 20% compared to baseline were reported. These increases occurred mostly in the first month of MIPLYFFA treatment and were not associated with changes in glomerular function.

During MIPLYFFA treatment use alternative measures that are not based on creatinine to assess renal function. Increases in creatinine reversed upon MIPLYFFA discontinuation.

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In a clinical study, MIPLYFFA was well tolerated compared to placebo[1]

Common adverse reactions ocurring in ≥8% of patients treated with MIPLYFFA and more frequently than in patients receiving placebo (subgroup who also received miglustat)

Adverse reaction[1]	MIPLYFFA with miglustat n=26 n (%)	Placebo with miglustat n=13 n (%)
Upper respiratory tract infection*	**8** (31)	**2** (15)
Diarrhea	**6** (23)	**3** (23)
Decreased weight	**4** (15)	**0**
Decreased appetite	**3** (12)	**0**
Tremor	**3** (12)	**0**
Urticaria**	**3** (12)	**0**
Headache	**3** (12)	**1** (8)
Lower respiratory tract infection	**3** (12)	**1** (8)
Seizure	**3** (12)	**1** (8)

*Upper respiratory tract infection: combined incidence of upper respiratory tract infection and rhinitis.
**Urticaria: includes one patient in which urticaria occured alone (3%) and two patients who had urticaria with angioedema (6%).

Adverse events were generally of mild to moderate severity and very few led to withdrawal of treatment[1]

- Thrombocytopenia was observed in three patients during the trial, all of whom were receiving miglustat for six months or longer at the time of enrollment. In two of these patients, the thrombocytopenia was present at baseline and persisted throughout the trial. In the other patient, the thrombocytopenia developed and resolved during the trial.
- Across the clinical trials, increases in serum creatinine (mean increase was 10%-20%) occurred mainly within the first month of dosing and were reversible upon treatment discontinuation.

INDICATIONS AND USAGE

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MIPLYFFA has convenient dosing and flexible administration options and can be taken at home

One capsule of MIPLYFFA is taken 3 times per day, with or without food, in any of 3 ways[1]:

- Capsule
- Mixed in water or soft foods
- Via feeding tube

For administration considerations, please refer to the full Prescribing Information, including Instructions for Use.

Dosing comes in 4 different strengths and is based on body weight[1]

Recommended MIPLYFFA dose for patients aged 2 years and older	18–33 lb (8–15 kg)	>33–60 lb (>15–30 kg)	>60–121 lb (>30–55 kg)	>121 lb (>55 kg)
Body weight				
Recommended dose (3 times per day)	**47 mg**	**62 mg**	**93 mg**	**124 mg**

In patients with renal impairment with an eGFR ≥15 mL/minute to <50 mL/minute, it is recommended to reduce frequency of dosing.

Getting your patients started on MIPLYFFA

MIPLYFFA is sent directly to patients through a specialty pharmacy

How to get MIPLYFFA to your patients:

- Download the **enrollment form** at **MIPLYFFA.com**
- Send the completed form to AmplifyAssist to initiate the prescription
- The prescription will be completed, and once approved, MIPLYFFA will be mailed to patients at home
- Other questions about MIPLYFFA? Call AmplifyAssist Monday through Friday at **888-668-4198** from 8:00 am to 6:00 pm (CT). You can also fax us at **888-668-2143**

Support for your patients

AmplifyAssist is available to help support your patients throughout the treatment journey, offering educational resources as well as financial and insurance assistance to eligible patients.

AmplifyAssist™
Your ally in what's ahead.

IMPORTANT SAFETY INFORMATION

MIPLYFFA capsules for oral use are available in the following strengths: 47 mg, 62 mg, 93 mg, and 124 mg.

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To report SUSPECTED ADVERSE REACTIONS, contact Zevra Therapeutics, Inc. at toll-free phone 1-844-600-2237 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Drug Interaction(s): Arimoclomol is an inhibitor of the organic cationic transporter 2 (OCT2) transporter and may increase the exposure of drugs that are OCT2 substrates. When MIPLYFFA is used concomitantly with OCT2 substrates, monitor for adverse reactions and reduce the dosage of the OCT2 substrate.

Use in Females and Males of Reproductive Potential: Based on animal findings, MIPLYFFA may impair fertility and may increase post-implantation loss and reduce maternal, placental, and fetal weights.

Renal Impairment: The recommended dosage of MIPLYFFA, in combination with miglustat, in patients with an eGFR ≥15 mL/minute to <50 mL/minute is lower than the recommended dosage (less frequent dosing) in patients with normal renal function.

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Before prescribing MIPLYFFA, please read the full Prescribing Information, including Instructions for Use.

References: 1. MIPLYFFA Full Prescribing Information. Celebration, FL, US, Zevra Therapeutics, Inc.; 09/2024. **2.** Mengel E, et al. Impacts and burden of Niemann pick type-C: a patient and caregiver perspective. *Orphanet J Rare Dis*. 2021;16(1):493. **3.** Vanier MT. Niemann-Pick disease type C. *Orphanet J Rare Dis.* 2010;5(16):1-18. **4.** Patterson MC, Clayton P, Gissen P, et al. Recommendations for the detection and diagnosis of Niemann-Pick disease type C: an update. *Neurol Clin Pract.* 2017;7(6):499-511. doi:10.1212/CPJ.0000000000000399. **5.** Geberhiwot T, Moro A, Dardis A, et al. Consensus clinical management guidelines for Niemann-Pick disease type C. *Orphanet J Rare Dis.* 2018;13(1):1-19. **6.** Patterson et al. Recommendations for the diagnosis and management of Niemann-Pick disease type C: An update. *Mol Genet Metab*. 2012;106(3):330-344.

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