Treatment Landscape

Niemann-Pick disease type C (NPC) is a rare, progressive, and fatal neurodegenerative disorder caused by impaired cholesterol trafficking.[1,2] Infantile-onset NPC (I-NPC; neurological symptom onset <6 years of age) is the most severe and rapidly progressing form of NPC.[1-3]

NPC is a rare, fatal genetic disease caused by pathogenic variants in *NPC1* or *NPC2* genes, leading to defective intracellular cholesterol transport.[4,5]

NPC is characterized by pathological lysosomal cholesterol accumulation in the brain and peripheral tissues, driving progressive neurodegeneration and premature mortality.[4,6]

Current treatment guidelines (2025) recommend managing NPC with disease-modifying therapies, combination therapies with distinct mechanisms of action, and symptomatic supportive therapies.[7]

An unmet need persists for therapies targeting the underlying pathophysiology of NPC to slow disease progression and improve survival in I-NPC.[7,8]

NO CURE EXISTS FOR NPC

Current treatment options consist of management of neurological symptoms and supportive care only, **not the underlying disease pathology**[8,9]

HEAT SHOCK PROTEIN (HSP) ACTIVATOR	GLUCOSYLCERAMIDE SYNTHASE INHIBITOR	MODIFIED AMINO ACID	INVESTIGATIONAL APPROACHES
HSP70 co-inducer is approved for neurological manifestations of NPC in adults and pediatric patients ≥2 years[10]	Substrate reduction therapy is approved in the EU to slow neurological deterioration in adult and pediatric patients with NPC[11] *Not FDA-approved for NPC; used off-label in the US*	N-acetyl amino acid derivative approved for neurological manifestations of NPC in adults and pediatric patients ≥15 kg[12]	Therapeutic approaches targeting NPC pathophysiology mechanisms are being investigated[13,14]

UNMET NEED

Despite two FDA approvals, there is no treatment available that addresses the underlying pathophysiology of NPC. Critically, neither is indicated for patients under 2 years of age, leaving earliest-onset and most severely affected patients without a treatment option.[8,10,12]

A deeper understanding of NPC pathophysiology is reshaping our approach to disease management and advancing the treatment landscape to enable intervention at earlier stages of disease.

ABBREVIATIONS: FDA, Food and Drug Administration; EU, European Union; HS70, heat shock protein 70; I-NPC, infantile-onset NPC; NPC, Niemann-Pick disease type C; NPC1, NPC intracellular cholesterol transporter 1; NPC2, NPC intracellular cholesterol transporter 2; US, United States.

REFERENCES: 1. Vanier MT. *Orphanet J Rare Dis*. 2010;5:16. **2.** Imrie J, et al. *BMC Neurol*. 2015;15:257. **3.** Bianconi SE, et al. *Mol Genet Metab*. 2019;126(4):466-469. **4.** Berry-Kravis E. *Semin Pediatr Neurol*. 2021;37:100879. **5.** Bolton SC, et al. *Orphanet J Rare Dis*. 2022;17(1):51. **6.** Winstone AM, et al. *Dev Med Child Neurol*. 2017;59(9):965-972. **7.** Hiwot T, et al. *J Inherit Metab Dis*. 2026;49(3):e70185. **8.** Bremova-Ertl T, Patterson M. Niemann-Pick Disease Type C. January 26, 2000 [Updated November 20, 2025]. Accessed September 21, 2026. https://www.ncbi.nlm.nih.gov/books/NBK1296/. **9.** Niemann Pick Disease Type C. National Organization for Rare Disorders. (NORD). [Updated September 25, 2024]. Accessed September 21, 2026. https://rarediseases.org/rare-diseases/niemann-pick-disease-type-c/. **10.** Miplyffa® (arimoclomol). Prescribing Information, October 2025. **11.** Zavesca® (miglustat). Summary of Product Characteristics, December 2012. **12.** AqneursaTM (levacetylleucine). Prescribing Information, September 2024. **13.** NCT02534844. ClinicalTrials.gov. Accessed September 21, 2026. https://clinicaltrials.gov/study/NCT02534844. **14.** NCT04860960. ClinicalTrials.gov. Accessed September 21, 2026. https://clinicaltrials.gov/study/NCT04860960.

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