NATIONAL NIEMANN-PICK DISEASE FOUNDATION, INC.

NNPDF Community Update: Xenpozyme Supply & Community Webinar Recording

Dear ASMD Community Members, Families, and Healthcare Providers,

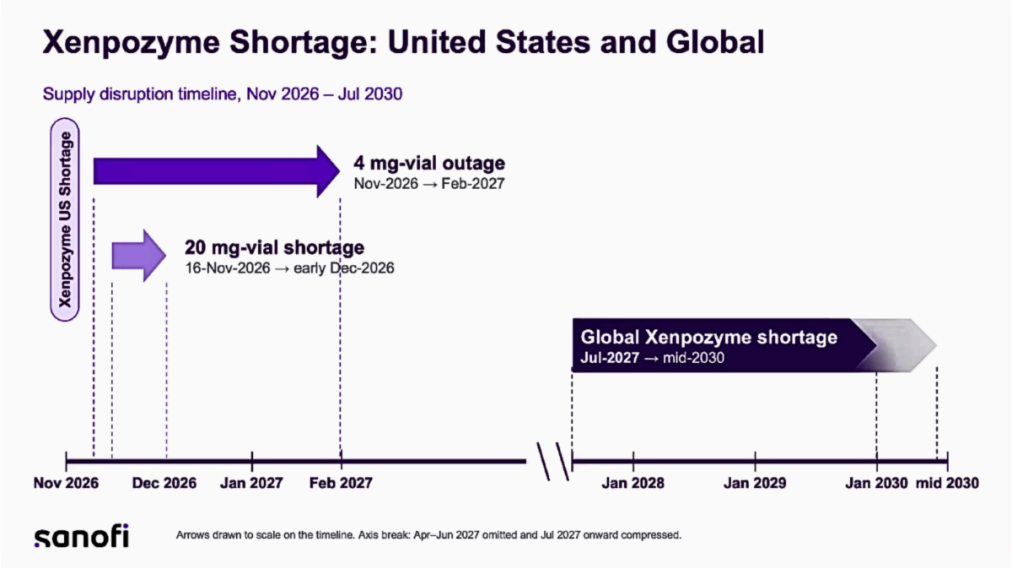
In light of this week's announcement from Sanofi regarding significant supply challenges affecting Xenpozyme (olipudase alfa), NNPDF recognizes the uncertainty, concern, and difficult decisions this news brings to individuals and families living with acid sphingomyelinase deficiency (ASMD), as well as the healthcare professionals who care for them.

As a rare disease community, we understand how critically important consistent access to treatment is and how deeply any potential interruption can affect patients and families. NNPDF's **priority remains ensuring that the patient perspective is at the forefront of every discussion, decision, and strategy moving forward.**

Immediately following the announcement, NNPDF worked alongside our global partners, including the International Niemann-Pick Disease Alliance (INPDA), our Scientific Advisory Board, and treating physicians to coordinate an urgent, collaborative response.
Olipudase alfa supply update and guidance for prescribers

This week, Sanofi informed the US community of three supply problems:

- The 4 mg vial will be unavailable until February.
- There will be an estimated 2-week window with no drug from mid-November through early December. This will not impact patients who have already received shipments of their mid-Nov to early Dec dose.
- Separately, global supply is forecast to fall short of demand from mid-2027 for about 3 years, until production can be scaled up.



NNPDF convened approximately 20 prescribing clinicians on November 10 to discuss these issues. Concerned about the long-term shortage, the clinicians discussed conserving the drug safely while monitoring for clinical progression. The clinicians compared two conservation strategies: lengthening the dosing interval from every 2 weeks to every 3 weeks vs. reducing the dose from 3 mg/kg to 2 mg/kg. Because unforeseen circumstances like acute illness or shipping delays could delay a dose beyond a 3-week interval, the clinician group endorsed 2 mg/kg every 2 weeks as the dose-conservation strategy. This strategy is most appropriate for patients who are not in dose escalation and have been stable on 3 mg/kg for an extended period. The clinicians indicate the specific dosing and conservation strategy taken in light of current supply chain problems should be decided on a case by case basis.

The immediate 4 mg vial shortage also means Sanofi will send 20 mg vials for the upcoming infusion to cover 3 mg/kg doses. This will likely result in wasted drug. Even if a clinician decides 2 mg/kg is not appropriate for a patient, lowering the next dose in suitable patients can avoid wasting part of a 20 mg vial and reduce the risk of unintentional overdose.

At a community webinar on November 11 convened by NNPDF, Sanofi presented public information regarding the three drug availability interruptions discussed above. Attendees voiced understandable frustration and anxiety and volunteered various conservation strategies, including some offering to pause therapy so patients with greater need can have access. Sanofi has submitted a mitigation strategy to the EMA and FDA. While we await a formal response from EMA and FDA, NNPDF shares this information regarding dosage guidance for prescribers considering voluntary dose reduction. NNPDF notes this is not medical advice from NNPDF and instead dosage needs to be a shared decision between the specific provider and patient.

View the complete **"ASMD Community Briefing"** recording HERE

Suggested monitoring. The monitoring domains below are derived from the 2023 ASMD Clinical Guidelines (Geberhiwot et al.); the timing is a suggested approach for this short-term situation. Lysosphingomyelin-509 (PPCS) monitoring is not guideline-directed but may be useful, especially for patients with neurologic manifestations of ASMD. If you lack a reference lab for the biomarkers, several providers have used Mayo Clinic. All other tests are standard. When possible, draw labs in the days before an infusion, with the lipid panel fasting.

Olipudase alfa monitoring plan at 2 mg/kg every 2 weeks

Proposed monitoring if patients are reduced from 3 mg/kg to 2 mg/kg every 2 weeks during the supply shortage

Domain	Before reducing (within about 1 month)	After reducing
Liver function	Liver function panel (ALT/AST, bilirubin, albumin)	3 and 6 months
Hematology	CBC with differential	3 and 6 months
Lipids	Fasting lipid panel	3 and 6 months
Biomarkers	Plasma lyso-sphingomyelin and lysosphingomyelin-509 (PPCS)	3 and 6 months
Children	Height Z-score and weight	Height and weight at every visit
Liver and spleen imaging	Abdominal ultrasound (MRI if readily available)	TBD
Lung	Pulmonary function testing, including DLco (hemoglobin-adjusted)	TBD

Geberhiwot T, et al. Consensus clinical management guidelines for acid sphingomyelinase deficiency (Niemann-Pick disease types A, B and A/B). Orphanet J Rare Dis. 2023;18:85. doi:10.1186/s13023-023-02686-6[HT1] [TH2]

Gathering this data supports patient safety. This data may also help the medical and research community evaluate and determine which dosing strategies are effective and under what circumstances. NNPDF plans to capture and report on this data through the International Niemann-Pick Disease Registry and we appreciate your help.

The general clinician guidance is a treatment option to act as a short-term bridge. Thie guidance alone does not include important information on triggers that would indicate the 2mg/kg dose is insufficient in specific cases nor does it provide guidance on management of starting new patients on olipudase alfa.

NNPDF will work with its scientific advisory board, the International Niemann-Pick Disease Alliance (INPDA), to review the regulatory response and build a comprehensive strategy. In the meantime, please don’t hesitate to reach out to us for more informatoin. Our Scientific Advisory Board members including Dr. Joshua Baker, Dr. Melissa Wasserstein and Dr. Justin Hopkin are here to support you.

Individualized Care and Clinical Support

ASMD is a rare, complex, and highly variable disease. Clinical manifestations, disease progression, treatment histories, and individual patient needs can differ significantly. As a result, no single treatment modification or monitoring strategy will be appropriate for every patient.

The guidance outlined here is intended to support general clinical discussions and information and does not replace individualized medical judgment or the established relationship between patients and their treating healthcare teams. Individual providers and patients need to engage in individualized medical and clinical evaluation to make appropriate individual medical decisions.

We strongly encourage providers who have questions about a particular patient's clinical circumstances, potential dose adjustments, monitoring results, or treatment considerations to reach out for additional consultation and support.

Sanofi Patient Support and Enrollment Resources

As patients and families navigate potential treatment interruptions and changes in medication availability, we encourage those in the United States to remain connected with their Sanofi patient support teams.

Susan King, Sanofi's Head, Rare Disease for US Patient Support Services stressed the importance in regards to treatment coordination and available support resources for U.S. patients and caregivers to contact their designated Sanofi Patient Education Liaison or Case Manager.

U.S. Patient and Caregiver Contact Information

- **Online enrollment:** www.careconnectPSS.com
- **Phone:** 1-800-745-4447, option 3
- **Direct support:** Contact your designated Sanofi Patient Education Liaison or Case Manager.

We encourage patients and caregivers to maintain open communication with both their treating healthcare providers and Sanofi support representatives as additional information about medication availability and supply management becomes available.

NNPDF will continue to serve as a resource for community questions, advocacy, and connections to clinical expertise.

Our Community Moving Forward

Our sharing of this preliminary guidance from clinicians is intended as a ***short-term bridge*** while additional information becomes available. It does not yet establish comprehensive criteria for identifying when a reduced dose may be insufficient, nor does it address the management of newly diagnosed patients or those beginning treatment.

NNPDF will continue working closely with its Scientific Advisory Board, the International Niemann-Pick Disease Alliance (INPDA), treating physicians, and our global partners to review the regulatory response and help develop a more comprehensive strategy.

We recognize that these challenges extend beyond medication supply. They affect the sense of security, stability, and hope that access to treatment provides to patients and families.

Over the coming weeks and months, NNPDF will remain actively engaged in discussions, advocate for clear and timely communication, and work to ensure that the experiences and needs of individuals living with ASMD continue to inform decisions at every level.
The response of our community over these past several days has demonstrated something especially meaningful: even in moments of uncertainty, we are stronger when we work together.

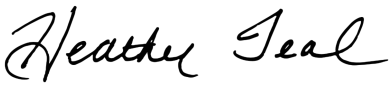
We are deeply grateful to the clinicians who have generously shared their expertise, to our international partners for their collaboration, to the families who have openly shared their concerns and experiences, and to every individual working toward solutions that protect access to care.

To our patients and families: You are not navigating this uncertainty alone. NNPDF remains committed to standing alongside you, advocating on your behalf, and helping connect you with the information, resources, and expertise you need.

We encourage anyone with questions or concerns to contact NNPDF. We will continue sharing updates as additional information becomes available.

With appreciation and continued commitment,

With regards,



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Supporting One Another. Supporting Our Community.

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