FOR HEALTHCARE PROVIDERS

Advancing care for Niemann-Pick disease type C (NPC):

The critical role of validated scales in measuring the progression and severity of NPC

Evaluating NPC is challenging[1-4]

NPC is an ultra-rare, relentlessly progressive, neurodegenerative disease that causes irreversible damage and is ultimately fatal. Diagnosis can be elusive due to its heterogeneous clinical presentation. Accurate diagnosis is critical for early intervention and effective management, with the goal of delaying progression.

Using a validated scale to measure NPC progression is important[4,5]

A predictive model and scoring system for NPC has been developed to help clinicians assess disease burden, disease progression, stabilization with therapy, and prognosis. The consistent framework of a validated clinician-reported scale, created specifically for NPC, provides a reliable and objective system that demonstrates treatment efficacy.

4 KEY DOMAINS[6]

These domains have been identified as **some of the most important** by NPC expert clinicians, caregivers, and patients, and allow for an assessment of NPC symptom progression.

AMBULATION[6]

1 Clumsiness >>> Wheelchair dependence 5

0 = Normal | **1** = Clumsiness | **2** = Ataxic gait | **4** = Assisted ambulation | **5** = Wheelchair dependence

FINE MOTOR SKILLS[6]

1 Slight dysfunction >>> Severe dystonia 5

0 = Normal | **1** = Slight dysmetria/dystonia | **2** = Mild dysmetria/dystonia | **4** = Moderate dysmetria/dystonia | **5** = Severe dysmetria/dystonia

SWALLOW[7]

1 Cough while eating >>> Tube fed 5

0 = Normal | **1** = Cough while eating | **2** = Intermittent dysphagia | **3** = Dysphagia | **4** = Some tube feeding | **5** = Tube feeding only

SPEECH[6]

1 Dysarthria >>> No communication 5

0 = Normal | **1** = Mild dysarthria | **2** = Severe dysarthria | **3** = Nonverbal/functional communication skills for needs | **5** = Minimal communication

A 1-category change in any domain, corresponding to a 1- to 2-point change in total score, in terms of decline or improvement, is **clinically meaningful**.[6]

The symptom score ranges are shown for informational purposes only and are not intended as a clinical tool. Not all domains include 5 levels of scores.

Using a validated scale for NPC in clinical practice

The NPC Clinical Severity Scale (NPCCSS) is a clinician-reported outcome measure of disease severity and progression.[6] It was **developed specifically for use in evaluating NPC**.[8] **The credibility of this scale was established through clinical trial data** to provide validity and help assess clinically meaningful change.[6]

When assessing treatment effectiveness for NPC, focus on improvement across the domains identified as **most important** by **NPC expert clinicians, patients, and caregivers**.[6]

Applying the NPCCSS domain

The validated scale originally included 17 domains to assess clinical severity. However, its complexity can be challenging to implement in everyday practice. Additionally, several domains, such as seizures, gelastic cataplexy, and psychiatric symptoms, have the potential to be confounded by symptomatic treatment interventions.[8]

The 5-domain NPCCSS is simpler, and quicker to administer and complete in a routine clinical exam while still being reliable.[5]

THE 5-DOMAIN NPCCSS

Focuses assessment on clinical severity and disease progression across the 5 domains seen as most clinically relevant, which includes cognition.[6]

- Was validated using a **wide range of disease severities**[6]
- Was demonstrated by clinical study to include the domains **most relevant to clinicians, patients, and caregivers**[6]
- Allows a **comprehensive assessment** of the symptom burden experienced by NPC patients[6]

RESCORED 4-DOMAIN NPCCSS[9]

Revised to more accurately assess a specific group of heterogeneous patients over a 12-month period.

- The **cognition domain was removed** from the 5-domain NPCCSS and the **swallow domain was rescored** to more accurately measure progressive deterioration of the swallow function[9]
- Swallow, along with ambulation and speech, was seen as a **highly salient sign of disease progression** by healthcare providers, caregivers, and patients[6]

Scan this QR code or **click here** to learn about an NPC treatment option or request a rep.

References: 1. Mengel E, Patterson MC, Chladek M, et al. Impacts and burden of Niemann pick type-C: a patient and caregiver perspective. *Orphanet J Rare Dis*. 2021;16(1):493. doi:10.1186/s13023-021-02105-8 **2.** Vanier MT. Niemann-Pick disease type C. *Orphanet J Rare Dis*. 2010;5:16. doi:10.1186/1750-1172-5-16 **3.** Mengel E, Klünemann HH, Lourenço CM, et al. Niemann-Pick disease type C symptomatology: an expert-based clinical description. *Orphanet J Rare Dis*. 2013;8:166. doi:10.1186/1750-1172-8-166 **4.** 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):50. doi:10.1186/s13023-018-0785-7 **5.** Evans W, Patterson M, Platt F, Guldberg C, Matheson T, Pacey J. International consensus on clinical severity scale use in evaluating Niemann–Pick disease Type C in paediatric and adult patients: results from a Delphi Study. *Orphanet J Rare Dis*. 2021;16(1):115. doi:10.1186/s13023-021-02115-6. **6.** Patterson MC, Lloyd-Price L, Guldberg C, et al. Validation of the 5-domain Niemann-Pick type C Clinical Severity Scale. *Orphanet J Rare Dis*. 2021;16(1):79. doi:10.1186/s13023-021-01719-2 **7.** Berry-Kravis EM, LaGorio L, Dali C, Gallo D. Qualitative assessment of the validity and standardization of the Swallow domain in the 5-domain Niemann-Pick disease type C (NPC) Clinical Severity Scale (5DNPCCSS). Poster presented at: The Child Neurology Society Annual Meeting; November 11-14, 2024; San Diego, CA. **8.** Mengel et al. Clinical disease progression and biomarkers in Niemann–Pick disease type C: a prospective cohort study. *Orphanet J Rare Dis*. 2020;15:328 Doi10.1186/s13023-020-01616-0 **9.** Mengel E. Efficacy results from a 12-month double-blind randomized trial of arimoclomol for treatment of Niemann-Pick disease type C (NPC): presenting a rescored 4-domain NPC Clinical Severity Scale. *Mol Genet Metab*. (Submitted manuscript).

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ZEVRA THERAPEUTICS