

Patient Support and Real-World Evidence Generation in Rare Disease: A Case Study in US Adult Patients with Hypophosphatasia

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INTRODUCTION

- Hypophosphatasia (HPP) is a rare, inherited metabolic disease caused by deficient alkaline phosphatase (ALP) activity leading to chronic pain and loss of physical function.^{1,2}
- Common challenges in rare diseases include limited patient-relevant real-world evidence (RWE), gaps in patient and health care professional (HCP) education, and ensuring access to medicine.
- In addition to delayed diagnosis, potential treatment access barriers include lengthy and complex prior authorization processes and requirements for genetic testing.
- Patient support programs (PSPs) can offer personalized support to patients including education, community resources, and assistance with health insurance requirements. RWE has demonstrated the potential benefits of PSPs to both patients and healthcare systems, which may include improved medication adherence and patient outcomes, and reduced healthcare resource utilization and total costs.^{3,4}

OBJECTIVES

- We describe a novel approach in which a PSP, in cooperation with an independent specialty pharmacy, may help to address evidence gaps and potentially improve access to care for patients with HPP.
- The overall objectives of this evidence generation approach are to:
 - Describe baseline lab and symptom characteristics of adult HPP patients initiating treatment;
 - Quantify time to enrollment with the PSP;
 - Quantify multisystemic symptoms across age subgroups, including those eligible for Medicare (age 65+).

CONCLUSIONS

- The clinical burden of HPP is multisystemic and includes pain, fractures, difficulty walking, and other symptoms across multiple domains.
- Not all patients present with low enzyme and/or elevated substrate levels, underscoring that HPP is a heterogeneous disease. This is in line with observations reported in the literature⁵ and may be explained by:
 - Patients having borderline ALP levels (3.6%; 40/1,109);
 - The presence of an ALP-raising condition such as inflammatory bowel disease or a recent bone fracture;^{5,6}
 - The photosensitivity of B6/PLP blood tests. Light exposure may result in falsely low results;⁶
 - The occurrence of 'normal' PEA levels in patients with less severe HPP and residual enzyme activity, and/or PEA not being a direct ALP substrate.⁶
- While many patients enroll quickly in the PSP, some delay enrollment.
- Collecting data from consenting patients through a manufacturer-sponsored PSP, combined with the centralized visibility provided by an independent specialty pharmacy focused on rare diseases, creates a scalable mechanism for generating RWE that is otherwise difficult to obtain while also supporting timely and appropriate patient access to therapy.

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METHODS

- PANTHERx Rare is a rare disease pharmacy that dispenses most of the United States (US) prescriptions for asfotase alfa, the only FDA-approved therapy for perinatal/infantile- and juvenile-onset HPP.
- PANTHERx Rare partners with Alexion's OneSource™ PSP to coordinate prior authorizations and streamline appropriate patient access to therapy.
- During intake, patients are invited to join a PSP for access to education on their condition, connections with other patients, and support in gaining access to treatment. The pharmacy reminds patients of the PSP during introduction and initial shipment calls, if not already enrolled.
- With patient consent, PANTHERx Rare's proprietary patient care management platform, SWFT™, captures genetic testing results, laboratory data, and symptom information.
- De-identified data are incorporated into a database of patients initiating treatment. Variables and outcome measures captured include patient demographics (age, sex, etc.); genetics (positive/negative/VUS); ALP and substrate levels (high, normal, low); treatment initiation vs 'never start' status; symptoms/statement of medical necessity (e.g., osteomalacia, muscle weakness, hypomineralization); childhood vs adult symptoms; prescribing physician specialty (e.g., endocrinologist, rheumatologist, geneticist); and patient education received (e.g., disease state, administration, injection site reaction management, goals of therapy).

- This retrospective, observational study analyzed data of adult patients (aged ≥18 years at time of referral) with HPP in the US who initiated treatment and opted to enroll in OneSource™ PSP.
- Data (11/1/2015 to 6/30/2025) were collected at baseline only (prior to treatment initiation, with no follow-up over the course of treatment).

RESULTS AND INTERPRETATION

Patient inclusion

- A total of 1,248 eligible adult patients (mean age 70.4±4.5 years; 80.7% female) (Figure 1) with HPP in the US contributed data from 2015-2025, reporting genetic test results (N=740), symptoms (N=477), and ALP (N=1,109), pyridoxal-5'-phosphate (PLP; N=1,066), and phosphoethanolamine (PEA; N=193) measurements.
- 99.0% of patients enrolled in the PSP.

Patient support program enrollment

- While most patients (65.1%) enrolled in the PSP immediately, nearly 1 in 10 patients enrolled more than 30 days after receiving their prescription (Table 2).

Table 2: Time to enrollment in PSP, relative to Rx date

Enrollment day relative to Rx date	N	%
Within 1 day	812	65.1%
Within 7 days	173	13.9%
Within 30 days	147	11.8%
Over 30 days	116	9.3%

PSP: Patient support program; Rx: Prescription.

Symptoms reported

- Many patients did not have symptoms documented. Among adult patients with HPP who reported symptoms (N=477), the top symptoms were muscle pain (79.7%; 380/477), bone pain (77.8%; 371/477), and fractures (70.0%; 334/477) (Figure 2).
- 40.3% (192/477) of patients reported difficulty walking.
- Patients aged 65+ years (a group not typically studied in this disease area) demonstrated similar trends in symptoms to the overall study population. Low bone density and hypomineralization were more frequently reported among patients aged 65+ years.

This large baseline dataset — not typically available for rare diseases — can enhance understanding of HPP and help reduce treatment access barriers

The top symptoms among adult patients with HPP were muscle pain, bone pain, and fractures

Figure 1: Patient Flow Diagram

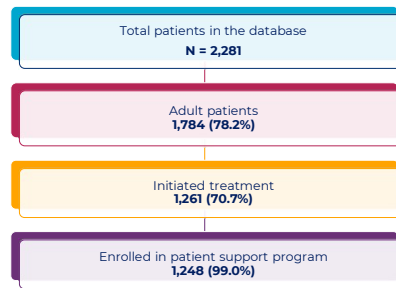
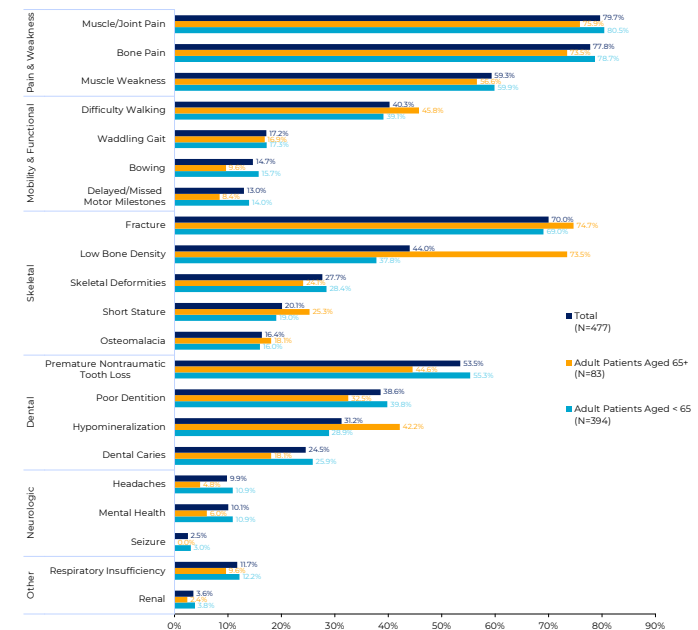


Figure 2: Symptoms among adults with HPP (N=477)



ALP and substrate levels

- Of patients with available ALP measurements, 5.9% (65/1,109) did not have low ALP levels (Table 1).*
- Of those with available substrate measurements, 16.3% (174/1,066) had normal B6/PLP and 14.5% (28/193) normal PEA.*

Table 1. ALP and substrate levels*

Total N 1,248	ALP		B6/PLP		PEA	
	n	%	n	%	n	%
N	1,109		1,066		193	
Mean (SD)	26.8 (9.8)		127.1 (30.2)		66.4 (65.5)	
Low	1,044	94.1	3	0.3	1	0.5
Borderline-Low	40	3.6	-	-	-	-
Normal	25	2.3	174	16.3	28	14.5
High	0	0	829	77.8	164	85

*Results are as reported for prior authorization purposes and are not necessarily based on repeated measurements.
ALP, alkaline phosphatase; PEA, phosphoethanolamine; PLP, pyridoxal-5'-phosphate; SD, standard deviation.

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