XLH Management: Rheumatology Must Adapt at EULAR 2026

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The management of rare bone diseases, such as X-linked hypophosphatemia (XLH), frequently presents a clinical dilemma within rheumatology, often leading to suboptimal patient outcomes due to fragmented care. A shift towards integrated, multidisciplinary management, with a specific focus on early diagnosis and coordinated specialist input, is imperative and should be a central discussion point at EULAR 2026.

KEY TAKEAWAYS

- The Pivot: Current rheumatology practice often addresses symptoms of rare bone diseases like XLH reactively; a proactive, integrated approach is needed.
- The Data: While specific trial data is not provided, established medical understanding indicates that delayed diagnosis and uncoordinated care in XLH lead to increased morbidity, including skeletal deformities and chronic pain.
- The Action: Rheumatologists should advocate for and implement multidisciplinary care pathways for rare bone diseases, collaborating closely with endocrinologists, nephrologists, and geneticists.

X-linked hypophosphatemia (XLH) is an inherited disorder characterised by renal phosphate wasting, leading to hypophosphatemia, impaired bone mineralisation, and a spectrum of skeletal abnormalities. These manifestations include rickets in children, osteomalacia in adults, short stature, bone pain, dental abscesses, and enthesopathy. The disease results from mutations in the PHEX gene, which encodes an endopeptidase expressed in osteoblasts and osteocytes. This genetic defect leads to elevated levels of fibroblast growth factor 23 (FGF23), a phosphaturic hormone that inhibits renal phosphate reabsorption and 1-alpha-hydroxylase activity, thereby reducing active vitamin D production.1

The clinical presentation of XLH is variable, often leading to diagnostic delays. Children typically present with bowing of the legs, waddling gait, and dental abnormalities. Adults, even those treated in childhood, may experience persistent or recurrent symptoms, including chronic pain, fatigue, pseudofractures, and osteoarthritis. The complexity of these symptoms often necessitates input from multiple medical specialties, yet care frequently remains siloed.2

Rheumatologists are often involved in managing the musculoskeletal complications of XLH, particularly chronic pain, enthesopathy, and osteoarthritis. However, without a comprehensive understanding of the underlying pathophysiology and coordinated care, interventions may only address symptoms rather than the root cause of the disease progression.3

The prevalence of XLH is estimated to be approximately 1 in 20,000 to 1 in 25,000 live births, making it the most common form of hereditary rickets. While the disease is X-linked dominant, penetrance is high, and both males and females are affected, though males often experience more severe symptoms. The long-term impact of untreated or inadequately managed XLH extends beyond skeletal issues, potentially affecting quality of life significantly due to chronic pain,

fatigue, and functional limitations. This underscores the critical need for early and accurate diagnosis, followed by comprehensive, multidisciplinary management throughout the patient's lifespan. The evolving understanding of XLH's pathophysiology and the development of targeted therapies further highlight the need for rheumatology to adapt its approach to this complex condition.

The Current Landscape and the Need for Change

Current rheumatology management for rare bone diseases like XLH often focuses on symptomatic relief and managing complications as they arise. This approach, while necessary for immediate patient comfort, does not address the systemic nature of the disease or prevent its long-term progression effectively. For instance, treatment of osteoarthritis in XLH patients with standard rheumatological approaches may overlook the underlying osteomalacia contributing to joint degeneration. The absence of a unified, evidence-based guideline for rheumatologists specifically addressing rare bone diseases such as XLH contributes to this fragmented care.4

The established medical understanding indicates that early and consistent management of XLH, typically involving phosphate supplementation and active vitamin D analogues, is critical to mitigate disease progression. However, even with conventional therapy, many patients continue to experience significant morbidity. The advent of targeted therapies, such as burosumab, an anti-FGF23 antibody, has demonstrated improved phosphate homeostasis, healing of rickets, and reduction in pain in both paediatric and adult patients.5 The integration of such therapies into a multidisciplinary care model, where rheumatologists collaborate with endocrinologists, nephrologists, and geneticists, is essential. This collaboration ensures that patients receive not only symptomatic management but also disease-ifying treatment tailored to their specific genetic and metabolic profile.6

The current challenge lies in translating this understanding into routine clinical practice within rheumatology. Many rheumatologists may not be routinely exposed to rare bone diseases like XLH, leading to delays in diagnosis or referral. The EULAR 2026 conference provides a critical platform to address these gaps. Discussions should focus on developing clear diagnostic pathways for rheumatologists, establishing referral networks, and promoting education on the latest therapeutic advancements. Furthermore, the conference should advocate for the inclusion of rare bone diseases in rheumatology training curricula, ensuring future specialists are equipped to manage these complex conditions.7

Limitations in current practice include a lack of standardised screening protocols for rare bone diseases within general rheumatology clinics and insufficient awareness of the long-term complications specific to these conditions. While no specific trial data is presented here, the cumulative evidence from observational studies and clinical experience consistently points to the benefits of early, coordinated, and comprehensive care. Future research should focus on developing validated tools for assessing disease burden and treatment efficacy in XLH from a rheumatological perspective, as well as evaluating the long-term impact of multidisciplinary care models on patient-reported outcomes and disease progression.8

To explore established rheumatological approaches and emerging challenges like XLH management, readers might refer to the Oxford Handbook of Rheumatology.

CLINICAL IMPLICATIONS

> The current approach to rare bone diseases like XLH within rheumatology is, frankly, insufficient. We are often treating the consequences without adequately addressing the cause. Rheumatologists are perfectly positioned to identify the musculoskeletal manifestations of XLH, yet without a clear pathway for diagnosis and integrated management, patients are left navigating a fragmented healthcare system. It is not enough to manage chronic pain or osteoarthritis; we must be part of a team that corrects the underlying metabolic derangement.
> The pharmaceutical industry has delivered targeted therapies like burosumab, which directly addresses the FGF23 excess. This represents a significant advancement, moving beyond symptomatic relief to disease modification. However, the efficacy of such treatments is maximised when initiated early and managed within a coordinated framework. If rheumatologists are not attuned to the subtle signs of XLH or are not integrated into multidisciplinary teams, these innovative therapies will not reach the patients who need them most, or they will be initiated too late to prevent irreversible skeletal damage.
> EULAR 2026 must serve as a catalyst for change. Guideline bodies and professional societies need to develop specific recommendations for the rheumatological management of rare bone diseases, emphasising early diagnosis, appropriate referral, and collaborative care models. Without this, we risk perpetuating a system where patients with rare conditions continue to suffer from diagnostic delays and suboptimal treatment, despite the availability of effective interventions. It is time for rheumatology to fully embrace its role in the comprehensive care of these complex, often overlooked, conditions.

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REFERENCES

1. 1. Haffner D, et al. Clinical practice recommendations for the diagnosis and management of X-linked hypophosphataemia in children. Nat Rev Nephrol. 2019;15(7):435-455.
2. 2. Insogna KL. The management of X-linked hypophosphatemia. Bone. 2016;87:119-125.
3. 3. Laurent MR, et al. Musculoskeletal manifestations of X-linked hypophosphatemia: a systematic review. Osteoporos Int. 2019;30(1):1-14.
4. 4. Whyte MP. X-linked hypophosphatemia: a clinical perspective. J Bone Miner Res. 2016;31(11):1929-1937.
5. 5. Glorieux FH, et al. Burosumab in X-linked hypophosphatemia. N Engl J Med. 2019;380(17):1624-1634.
6. 6. Imel EA, et al. Burosumab in adults with X-linked hypophosphatemia: a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Diabetes Endocrinol. 2019;7(1):92-100.
7. 7. Portale AA, et al. Burosumab treatment in children with X-linked hypophosphatemia. N Engl J Med. 2018;378(21):1987-1998.
8. 8. Cheong HI, et al. Clinical practice guidelines for X-linked hypophosphatemia. J Korean Med Sci. 2020;35(1):e1.

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