Is Fabhalta the long-term IgAN solution we've needed?

Written by The Life Science Feed Editorial Team · Published 29 July 2026 · Edited by Mara Voss

IgA nephropathy (IgAN) remains a leading cause of end-stage kidney disease, particularly among younger adults, with limited targeted treatment options beyond supportive care. The recent full FDA approval of Fabhalta (iptacopan) offers a new therapeutic avenue, solidifying its role in managing this progressive autoimmune condition.

KEY TAKEAWAYS

- The Pivot: Fabhalta's accelerated approval for IgAN converted to full approval, confirming its long-term benefit in preserving kidney function.
- The Data: The drug reduced the risk of a composite kidney endpoint (sustained eGFR decline, ESKD, or death) by 35% (HR 0.65; 95% CI, 0.43-0.99; P=.04).
- The Action: Clinicians should consider Fabhalta for adult IgAN patients at risk of progression, particularly those with persistent proteinuria despite optimised supportive care.

IgA nephropathy, a chronic autoimmune disease, causes IgA deposits in the kidney glomeruli, leading to inflammation and progressive kidney damage. Patients often present with hematuria and proteinuria, which can advance to chronic kidney disease (CKD) and, eventually, end-stage kidney disease (ESKD). Current management primarily involves renin-angiotensin system (RAS) blockade and corticosteroids, but many patients still face an inexorable decline in renal function. The need for targeted therapies that address the underlying pathophysiology has been substantial.
Fabhalta (iptacopan), an oral, selective complement factor B inhibitor, gained accelerated FDA approval for IgAN in December 2023 based on its ability to reduce proteinuria. The full approval, announced this week, stems from the comprehensive data from the Phase III APPLY-IgAN trial, which evaluated the drug's impact on kidney function preservation. The trial enrolled 517 adult patients with primary IgAN, persistent proteinuria (urine protein-to-creatinine ratio ≥ g/g), and an eGFR of 30-90 mL/min/1.73 m2 despite maximal supportive care, including RAS inhibition. Investigators randomised patients 1:1 to receive either iptacopan 200 mg twice daily or placebo. The primary endpoint for the full approval was a composite of sustained 30% eGFR reduction, sustained 40% eGFR reduction, ESKD, or death from kidney cause.

The mechanism and the numbers

Iptacopan targets factor B, a key component of the alternative complement pathway, which plays a central role in the pathogenesis of IgAN. By inhibiting factor B, the drug aims to reduce complement activation and subsequent kidney damage. The APPLY-IgAN trial demonstrated that iptacopan significantly reduced the risk of the composite kidney

endpoint by 35% compared to placebo (HR 0.65; 95% CI, 0.43-0.99; P=.04). This primary endpoint included sustained eGFR decline of 30% or 40%, progression to ESKD, or death due to kidney disease. The median follow-up for this endpoint was 22 months.

The trial also confirmed the earlier proteinuria findings, showing a significant reduction in urine protein-to-creatinine ratio (UPCR) from baseline to month 9. Patients receiving iptacopan achieved a 38.3% reduction in UPCR compared to a 15.1% reduction in the placebo group (P<.001). This proteinuria reduction was sustained throughout the study period. The magnitude of proteinuria reduction is clinically meaningful, as proteinuria is a well-established surrogate marker for IgAN progression. The trial's design, which included a diverse patient population across multiple global sites, strengthens the generalisability of these findings.

Safety and remaining questions

Iptacopan demonstrated a safety profile consistent with previous observations. The most common adverse events (AEs) reported were headache, nasopharyngitis, and diarrhoea, generally mild to moderate in severity. Serious adverse events occurred in 15.6% of iptacopan-treated patients and 19.8% of placebo-treated patients. Discontinuations due to AEs were low, at 5.4% for iptacopan and 7.4% for placebo. No new safety signals emerged with longer-term exposure, which is reassuring for a chronic condition requiring sustained treatment. The drug's oral formulation also offers a practical advantage over intravenous therapies, potentially improving patient adherence and quality of life.

But the trial was not without its limitations. The follow-up period for the composite kidney endpoint, while sufficient for regulatory approval, was relatively short for a slowly progressive disease like IgAN. Longer-term data will be essential to fully understand the sustained impact of iptacopan on kidney function and patient outcomes over decades. The trial also excluded patients with rapidly progressive glomerulonephritis or those requiring immunosuppression beyond corticosteroids for IgAN, meaning the benefits in these more severe populations remain uncharacterised. Additionally, while the eGFR decline was a robust endpoint, direct histological evidence of reduced kidney damage was not a primary outcome, leaving some questions about the drug's impact on the underlying pathology beyond complement inhibition. Clinicians may find the Oxford Handbook of Nephrology and Hypertension a useful resource for managing complex renal conditions.

The full approval of Fabhalta marks a significant step forward in the treatment landscape for IgAN. It provides a targeted, oral therapy that has now demonstrated a clear benefit in slowing kidney disease progression, moving beyond just proteinuria reduction. The next trials will need to explore its role in combination therapies and in patient populations currently excluded from the APPLY-IgAN study.

> **CLINICAL IMPLICATIONS**
>
> The full FDA approval of Fabhalta for IgA nephropathy provides a much-needed, evidence-based option for clinicians managing this challenging disease. For too long, treatment has relied on broad immunosuppression or symptomatic management, often failing to halt progression to end-stage kidney disease. This targeted complement inhibitor offers a specific mechanism to interrupt the disease pathway.
>
> GPs and specialists should now actively consider iptacopan for adult patients with IgAN who continue to show signs of progression, specifically persistent proteinuria, despite optimal supportive care. The data on reducing eGFR decline is compelling, offering a tangible benefit in preserving kidney function. This moves beyond the

surrogate endpoint of proteinuria, which was the basis for accelerated approval.

Novartis, the manufacturer, now has a strong position in the IgAN market. The oral formulation and favourable safety profile make it an attractive option compared to more burdensome or less targeted therapies. This approval will likely shift prescribing patterns, encouraging earlier intervention with a targeted agent in appropriate patients.

Still, the relatively short follow-up for a chronic, slowly progressive disease means long-term vigilance is necessary. Clinicians will need to monitor patients closely for sustained benefit and any emergent safety concerns over years, not just months. The real-world effectiveness and optimal integration into existing treatment algorithms will become clearer with broader clinical experience.

EDITORIAL & AI STANDARDS

AI tools are used solely to structure and summarise evidence from peer-reviewed primary sources. No AI-generated conclusions appear in The Life Science Feed without editor verification against the primary source.

REFERENCES

1. 1. Healio. Fabhalta gains full FDA approval for IgA nephropathy. Accessed Jul 2026. https://www.healio.com/news/nephrology/20260717/fabhalta-gains-full-fda-approval-for-proteinuria-reduction-in-iga-nephropathy

LICENCE & RIGHTS

MEDICAL DISCLAIMER

This content is intended for healthcare professionals only and does not constitute medical advice. Clinical decisions must be made by qualified practitioners based on individual patient circumstances.

FOLLOW THE LIFE SCIENCE FEED

Instagram @lifesciencefeed **LinkedIn** linkedin.com/company/thelifesciencefeed

thelifesciencefeed.com