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Enclosure:

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IgA Nephropathy: The Evolving Treatment Paradigm and Selective APRIL Targeting

KDIGO Emphasizes a Comprehensive Approach to IgA Nephropathy Management[1]

The 2025 KDIGO IgAN Guideline emphasizes the importance of simultaneously addressing IgA nephropathy–specific drivers of nephron loss and generic responses to IgA nephropathy–induced nephron loss[1,2]

2025 KDIGO IgA Nephropathy Treatment Algorithm[1,2]

IgA nephropathy at risk of progressive kidney function loss[a]

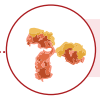
Manage the IgA nephropathy–specific drivers for nephron loss

- Stop synthesis of pathogenic forms of IgA and IgA-IC formation
- Stop IgA/IgA-IC mediated kidney injury

In all patients, these should be considered simultaneously

Manage the generic response to IgA nephropathy–induced nephron loss

- Reduce glomerular hyperfiltration, proteinuria, and the impact of proteinuria on the tubulointerstitium
- Blood pressure control
- Cardio-vascular risk reduction



Sibeprenlimab-szsi targets **an upstream immunologic driver** of IgA nephropathy[2,3]

Treatment Goals[1]



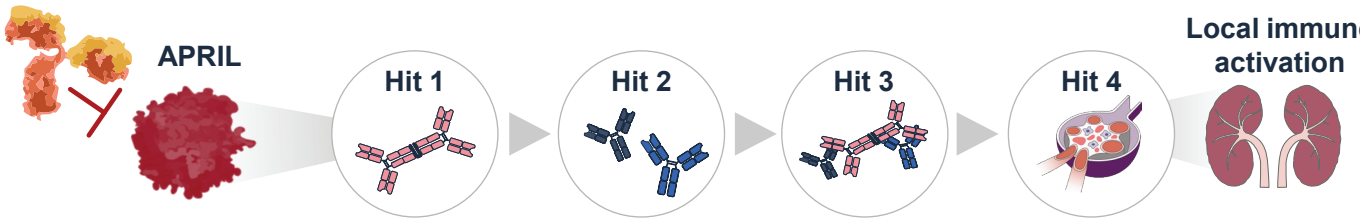
Kidney function
Slow eGFR decline to near physiologic rate
<1 mL/min/1.73 m²/y



Proteinuria
0.5 g/d, ideally 0.3 g/d

APRIL Is Implicated as a Key Driver of the 4-Hit Process of IgA Nephropathy[4,5]

Sibeprenlimab-szsi selectively binds to and blocks the biological activity of APRIL[3,6,7]

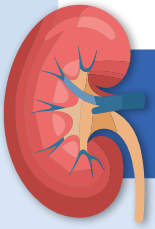


Production of pathogenic Gd-IgA1

Synthesis of autoantibodies against Gd-IgA1

Immune complex formation

Immune complex deposition in mesangium



Sibeprenlimab-szsi selectively inhibits APRIL, an upstream immunologic driver implicated in IgA nephropathy[3,7]

Scan the QR code to learn more

[a]Enrollment in a clinical trial should always be considered with all patients with IgA nephropathy.[1]

APRIL, a proliferation-inducing ligand; eGFR, estimated glomerular filtration rate; Gd-IgA1, galactose-deficient IgA1; IC, immune complex; IgA, immunoglobulin A; IgAN, IgA nephropathy; KDIGO, Kidney Disease: Improving Global Outcomes.

References: 1. KDIGO. *Kidney Int.* 2025;108(4S):S1-S71. **2.** Rovin BH, et al. *Kidney Int.* 2026;110(3):502-507. **3.** Perkovic V, et al. *Kidney Int Rep.* 2025;10(12):4207-4218. **4.** Cheung CK, et al. *Front Nephrol.* 2024;3:1346769. **5.** Mathur M, et al. *J Clin Med.* 2023;12(21):6927. **6.** VOYXACT (sibeprenlimab-szsi) [prescribing information]. Rockville, MD: Otsuka America Pharmaceutical, Inc; 2025. **7.** Perkovic V, et al. *N Engl J Med.* 2026;394(7):635-646.

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