INDIAN HEALTH SERVICE
National Pharmacy and Therapeutics Committee
Formulary Brief: *Diabetic/Hypertensive Nephropathy*
-February 2026-

Background:
The Indian Health Service (IHS) National Pharmacy and Therapeutics Committee (NPTC) conducted a pharmacotherapeutic review of hypertensive and diabetic nephropathy focusing on epidemiology, pathophysiology, diagnosis, guideline-directed management, and clinical outcomes evidence. Medication(s) currently listed on the National Core Formulary relevant to this condition include atorvastatin, empagliflozin, lisinopril, lisinopril with hydrochlorothiazide, losartan, losartan with hydrochlorothiazide, pravastatin, rosuvastatin, semaglutide, and simvastatin. Clinical guidance for this review included recommendations from major renal and diabetes organizations and outcomes from randomized clinical trials and meta-analyses evaluating disease-modifying therapies.

Finerenone, a non-steroidal mineralocorticoid receptor antagonist not listed on the National Core Formulary, was discussed in the context of guideline-directed treatment sequencing. The agent was considered during the review and may be evaluated further as additional clinical trial data and real-world evidence emerge. **No modifications** to the National Core Formulary resulted from this review.

Discussion:
Diabetic and hypertensive nephropathy remain leading contributors to chronic kidney disease (CKD) progression and end-stage kidney disease. The review summarized pathophysiologic drivers including hyperglycemia-induced glomerular hyperfiltration, RAAS activation, endothelial dysfunction, and inflammatory fibrotic signaling. Diagnosis and monitoring rely on estimated glomerular filtration rate (eGFR) and albumin-to-creatinine ratio (ACR) measurements to identify disease presence, stage severity, and track progression.[1]

Risk stratification tools were presented as clinical adjuncts for decision-making. The Kidney Failure Risk Equation (KFRE) and Chronic Kidney Disease Prognosis Consortium calculators provide validated prediction of kidney failure risk using demographic and laboratory parameters, assisting clinicians with referral timing, monitoring intensity, and patient counseling. Their use supports individualized care planning beyond categorical staging approaches.[1]

Management strategies reviewed during the NPTC meeting emphasized layered interventions including non-pharmacologic and pharmacological measures. Key non-pharmacologic components included dietary sodium restriction, exercise, weight management, smoking cessation, avoidance of nephrotoxins, and individualized nutritional modification addressing protein, phosphorus, and sodium intake based on CKD stage.[2] These interventions remain foundational for slowing disease progression and reducing cardiovascular risk.

The review further reinforced that diabetic kidney disease management extends beyond pharmacotherapy and requires coordinated multidisciplinary care. Evidence indicates improved outcomes when care integrates nephrology, primary care, pharmacy, nutrition, and other specialty services, with monitoring intensity tailored to disease risk and incorporation of routine complication surveillance.[3]

Pharmacologic management frameworks aligned with the contemporary “four pillars” approach consisting of renin–angiotensin system inhibition, sodium-glucose co-transporter 2 (SGLT2) inhibition, glucagon-like peptide-1 (GLP-1) receptor agonist therapy, and mineralocorticoid receptor antagonism. Clinical trial evidence supporting foundational therapies was reviewed. In the RENAAL study, losartan reduced the composite outcome of doubling of serum creatinine, end-stage renal disease, or death by 16% compared with placebo (Hazard Ratio [HR] 0.84, p=0.02).[4] In the 2001 IDNT study, irbesartan reduced kidney outcome risk by approximately 20% relative to placebo (p=0.02).[5]

Notably, SGLT2 inhibitors demonstrated substantial disease-modifying effects as well. The CREDENCE trial published in 2019 reported a 30% reduction in renal composite outcomes (HR 0.70, 95% CI: 0.59 to 0.82; p=0.00001).[6] The 2020 DAPA-CKD study demonstrated a 39% reduction in similar endpoints (HR 0.61, 95% CI: 0.51 to 0.72; p<0.001; Number Needed to Treat to prevent one primary outcome event, 19 [95% CI: 15 to 27]).[7] Finally, the EMPA-KIDNEY clinical trial showed a 28% reduction in kidney disease progression or cardiovascular death (HR 0.72, 95% CI: 0.64 to 0.82; p<0.001).[8] Several meta-analyses confirmed significant reductions in major kidney outcomes and heart failure hospitalization across this SGLT2 drug class.[9-10]

Evidence from GLP-1 receptor agonist therapy was also reviewed, which specifically included the FLOW clinical trial. Findings from the study showed that semaglutide reduced major kidney events by 24% (HR 0.76; 95% CI: 0.66 to 0.88; *p*=0.0003) and all-cause mortality by approximately 20% (HR 0.80, 95% CI: 0.67 to 0.95, *p*=0.01).[11]

Finerenone demonstrated reductions in kidney disease progression and cardiovascular events when added to optimized RAAS inhibition; however, guideline positioning places non-steroidal MRAs as later-line treatment for patients with persistent albuminuria despite first-line management and appropriate potassium levels.[2] This positioning, together with the availability of foundational therapies already listed on the National Core Formulary and associated monitoring considerations, informed the NPTC formulary review context.

Findings:

The review reinforced that management of hypertensive and diabetic nephropathy requires coordinated lifestyle modification, risk prediction, multidisciplinary care integration, and evidence-based pharmacotherapy. Therapies already represented within the National Core Formulary align with guideline-supported foundational treatment strategies and demonstrate robust outcome reductions across major randomized clinical trials and meta-analyses.

Finerenone demonstrated benefit in selected populations but remains positioned as an adjunctive therapy following optimization of existing first-line treatments. Based on available evidence, guideline sequencing, and therapeutic coverage already present on formulary, no changes to the National Core Formulary were warranted. Continued evaluation may occur as additional comparative effectiveness data and clinical utilization evidence become available.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov . For more information about the NPTC, please visit the NPTC website.

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