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Adjunctive nephroprotection in lupus nephritis: a scoping review of SGLT2 inhibitors, GLP-1 receptor agonists, non-steroidal mineralocorticoid receptor antagonists and endothelin receptor antagonists, with proposed practice points

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ADMINISTRATIVE INFORMATION

Support - NA.

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202690081

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 19 September 2026 and was last updated on 19 September 2026.

INTRODUCTION

Review question / Objective Immunosuppression controls immune activity in lupus nephritis (LN) but does not treat the non-immune mechanisms of nephron loss that carry patients to kidney failure. Four drug classes changed outcomes in other proteinuric kidney diseases. This review maps the evidence for each in LN and turns it into practice points clinicians can apply.

Background Immunosuppression controls immune activity in lupus nephritis (LN) but does not treat the non-immune mechanisms of nephron loss that carry patients to kidney failure. Four drug classes changed outcomes in other proteinuric kidney diseases. This review maps the evidence for each in LN and turns it into practice points clinicians can apply.

Rationale The population, adults with LN or SLE with kidney involvement; for indirect evidence, adults with proteinuric CKD of non-diabetic or glomerular cause; and for animal evidence, murine models of lupus or immune-complex glomerulonephritis. The concept, adjunctive nephroprotective drug therapy of four classes: SGLT2 inhibitors, GLP-1 receptor agonists (GLP-1 RAs), steroidal or non-steroidal mineralocorticoid receptor antagonists, and selective or dual endothelin receptor antagonists (ERAs). Immunosuppression controls immune activity in lupus nephritis (LN) but does not treat the non-immune mechanisms of nephron loss that carry patients to kidney failure. Four drug classes changed outcomes in other proteinuric kidney diseases. This review will map the evidence for each in LN and turns it into practice points clinicians can apply.

METHODS

Strategy of data synthesis PubMed, OVID, SCOPUS. Charted variables were first author, year, country, design, sample size, population, drug and

dose, comparator, follow-up, and outcomes with effect estimates. For the clinical sections, eligibility thresholds, starting doses, titration, monitoring intervals and adverse event rates will be charted separately. Each source placed in one of four tiers by directness: A, drug given to patients with SLE or LN with lupus-specific outcomes; B, animal study in a lupus or immune-complex model; C, large human trial in proteinuric CKD outside lupus; D, guideline, review, commentary or registration.

Eligibility criteria Patient with CKD and LN.

Source of evidence screening and selection Stage 1, identification and deduplication. Records returned by each prespecified search string are exported with PMID, title, journal and year, and deduplicated across strings on PMID. Records appearing in more than one string are screened once, with all source strings recorded.

Stage 2, title and abstract screening in duplicate. Two reviewers independently screen every deduplicated record against the eligibility criteria fixed before screening, recording INCLUDE, EXCLUDE or UNCLEAR and, for exclusions, one of five prespecified reason codes. Reviewers are blinded to each other's decisions until both sets are complete. Records marked UNCLEAR are carried forward to full-text assessment on the same footing as INCLUDE, so that uncertainty is resolved by reading the paper rather than by a forced call on an abstract. Before full screening, both reviewers screen the first 20 records and compare decisions to calibrate application of the criteria; any criterion found to be ambiguous is clarified in writing before screening resumes, and the 20 calibration records are then rescreened.

Stage 3, full-text assessment in duplicate. Records carried forward are retrieved in full and assessed independently by the same two reviewers against the same criteria. Reasons for exclusion at this stage are recorded individually in the retrieval log.

Stage 4, charting. Each included source is assigned a directness tier and charted on the prespecified form. Charting is performed by one reviewer and verified against the source by the second.

Resolution of disagreements. Disagreements at stages 2 and 3 are resolved by discussion between the two reviewers, working through each flagged record against the written criteria. Any disagreement not resolved by discussion is referred to the third author, whose decision is final. The number of disagreements, the number resolved by discussion, and the number requiring adjudication are recorded and reported. Inter-reviewer agreement at stage 2 is reported as raw percentage agreement and Cohen's kappa.

Scope of duplicate screening. Duplicate independent screening applies to records retrieved by the four searches that identify direct evidence in lupus. Indirect-evidence sources (large randomised trials in non-lupus proteinuric chronic kidney disease, clinical practice guidelines and background reviews) are identified purposively rather than by systematic screening, and are charted as context. This distinction is reported in the Methods.

Data management Records and formats. All retrieved records are held in a single reference ledger keyed on PMID, with DOI, full citation, and the search string that retrieved each record. Search output is exported from PubMed in CSV; the ledger is maintained in JSON and rendered to the numbered reference list used in the manuscript, so that citation numbering is generated from the ledger rather than entered by hand. Screening decisions are held in two reviewer workbooks and a reconciliation workbook (XLSX). Charted data are held in a single charting table (XLSX), one row per source, with the fields fixed before screening.

Verification. Every included record is verified against PubMed by PMID or DOI before charting. Every effect estimate entered in the charting table is checked against the source abstract or, where the abstract is unavailable or incomplete, the full text obtained from PubMed Central. Figures are transcribed exactly as reported, including confidence intervals and P values, with no rounding or recalculation. Where a study reports a value only in full text, the charting table records that fact.

Version control and provenance. Each search is logged with its string as run, the date run, the interface used, and the number of records returned (Online Resource 2). Supplementary records identified outside the prespecified searches are logged separately with their source and the verification performed. Successive drafts of the manuscript and the ledger are retained, so that any figure in the final text can be traced to the record it came from.

Confidentiality and data protection. The review uses published aggregate data and trial registrations only. No individual participant data, identifiable information or unpublished data were

obtained, so no data protection approval, data sharing agreement or de-identification procedure applies. Reviewer screening decisions are held by the reviewing authors during screening and are not personal.

Language restriction Only English.

Country(ies) involved United States.

Keywords Lupus Nephritis; Sodium-Glucose Transporter 2 Inhibitors; Glucagon-Like Peptide-1 Receptor Agonists; Mineralocorticoid Receptor Antagonists; Endothelin Receptor Antagonists; Proteinuria.

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