Lupus Nephritis

Diagnosis and biopsy, general management, therapy by ISN/RPS class, response assessment and relapse, and special situations.

2024 KDIGO Clinical Practice Guideline
Management of Lupus Nephritis
KDIGO Glomerular Diseases Work Group · Kidney Int 2024;105(1S):S1-S69

FORMAT *Condensed from recommendations + practice points, Chapter 10 (KDIGO 2021 Glomerular Diseases Guideline update).*

1 Diagnosis & Kidney Biopsy

–	GUIDANCE
Test at	SLE presentation and regular surveillance: SCr/eGFR, urinalysis (dipstick + sediment), spot PCR, serology (anti-dsDNA, complement)
Biopsy trigger	Dipstick protein ≥2+ or active sediment (acanthocytes ≥5%, RBC/WBC casts) → quantify proteinuria → consider biopsy if 24h PCR ≥500 mg/d. Or unexplained decreased/decreasing eGFR → repeat testing → consider biopsy
Biopsy report	Classify per ISN/RPS scheme; electron microscopy for podocyte injury/deposit location; report activity index (0–24) and chronicity index (0–12)

2 General Management & Risk Mitigation

–	GUIDANCE
Hydroxychloroquine	All SLE incl. LN unless contraindicated (1C) — ~5 mg/kg/d, reduce ≥25% if eGFR <30; consider G6PD testing in men before starting
Risk bundle	CV (lipids, BP, low-dose ASA in pregnancy); proteinuria/CKD (low-sodium diet, BP control, RAASi/SGLT2i if stable without AKI); infection (HBV/HCV/HIV screen + vaccination, PJP prophylaxis, zoster/TB history); bone (BMD, Ca/vitamin D, bisphosphonates); UV protection; fertility counseling (GnRH agonist, cryopreservation); limit lifetime cyclophosphamide <36g

3 Class I/II & Class V (Membranous)

–	GUIDANCE
Class I/II	Low-level proteinuria: immunosuppression guided by extrarenal SLE activity. Nephrotic syndrome: evaluate for podocytopathy (EM) — treat as MCD if confirmed; otherwise consider maintenance low-dose steroid + another agent
Class V, low proteinuria	Monitor and prevent complications (thrombosis, dyslipidemia, edema); RAS blockade + BP control
Class V, nephrotic-range	RAS blockade + BP control, plus immunosuppression (moderate/reduced-dose steroid + MPAA, cyclophosphamide, or similar) + hydroxychloroquine; escalate if proteinuria worsens or complications develop

4 Class III/IV — Initial Therapy

–	GUIDANCE
Regimen	Active Class III/IV ± membranous: glucocorticoids plus one of — MPAA (1B); low-dose IV cyclophosphamide (1B); belimumab + MPAA or cyclophosphamide (1B); MPAA + CNI if eGFR >45 (1B)
Selection factors	IV cyclophosphamide if adherence concerns; MPAA-based preferred if high infertility risk; CNI-based if preserved kidney function + nephrotic-range proteinuria or MPAA-intolerant; triple regimen (belimumab) if repeated flares/high progression risk
Steroid taper	Reduced-dose regimen after short methylprednisolone pulse course when kidney + extrarenal disease improve satisfactorily
Alternatives	Azathioprine or leflunomide if intolerance/unavailability/cost (likely inferior efficacy); rituximab for refractory or inadequate response

5 Class III/IV — Maintenance Therapy

–	GUIDANCE
Regimen	MPAA after initial therapy (1B); azathioprine alternative if MPAA intolerant/unavailable or considering pregnancy
Dosing	MMF ~750–1000mg BID early maintenance (MPA ~540–720mg BID); triple regimens (belimumab/CNI) can continue as maintenance; CNI/mizoribine/leflunomide if MPAA and azathioprine unusable
Steroids	Taper to lowest dose; consider discontinuation after ≥12mo complete renal response
Duration	Total initial + maintenance immunosuppression ≥36 months for proliferative LN

6 Response Assessment & Relapse

–	GUIDANCE
Complete response	PCR <0.5 g/g + stable/improved eGFR (±10–15%), within 6–12mo (can take longer)
Partial response	Proteinuria ↓≥50% and to < 3 g/g + stable/improved eGFR within 6–12mo
Unsatisfactory response	Verify adherence → check drug levels/infusion records → repeat biopsy if chronicity/other diagnosis suspected → switch regimen if active disease persists → refractory: add rituximab/biologic, extended IV cyclophosphamide, or clinical trial
Relapse	Treat with the same initial regimen that achieved prior response, or an alternative recommended regimen

7 Special Situations

–	GUIDANCE
TMA	Test ADAMTS13 + antiphospholipid antibodies, use PLASMIC score; start plasma exchange + glucocorticoid while awaiting results. Low ADAMTS13 (<10%): SLE-associated TTP. Normal ADAMTS13 + negative APLA: evaluate other TMA (consider eculizumab if complement-mediated). Normal ADAMTS13 + positive APLA: antiphospholipid syndrome nephropathy — anticoagulation ± plasma exchange
Pregnancy	Avoid conception during active disease/teratogenic therapy and for ≥6mo after inactive; continue hydroxychloroquine; low-dose aspirin before 16wk. Safe: glucocorticoids, hydroxychloroquine, azathioprine, tacrolimus, cyclosporine. Avoid MMF, cyclophosphamide, warfarin
Children	Similar regimens to adults, adjusted for dosing, growth, fertility, and psychosocial factors
Kidney failure	Hemodialysis, peritoneal dialysis, or transplantation — transplant preferred over long-term dialysis

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