Systemic Lupus Erythematosus — Treatment

GRADE recommendations for non-renal SLE: glucocorticoid strategy, hydroxychloroquine, immunosuppressive therapy, and organ-specific management. Lupus nephritis is addressed in a separate 2024 ACR guideline.

2025 ACR Guideline
Treatment of Systemic Lupus Erythematosus (Non-Renal)
Sammaritano et al. · Arthritis Care Res 2025

GRADE — Strong | Conditional For | Conditional Against | GPS · Good Practice

1 Treatment Goals & Monitoring

GPS	Goal of SLE treatment is optimal control of disease (**remission or low disease activity**) to improve long-term outcomes; screen/manage comorbidities — infection, cardiovascular disease, bone/joint damage, malignancy, reproductive health, antiphospholipid antibodies.
Cond. Very Low	Assess **disease activity regularly** (incl. with any change in clinical status/medications, e.g. SLEDAI or physician global assessment) and **disease damage at least annually** (e.g. SLICC/ACR-DI).

2 Glucocorticoid & Hydroxychloroquine Strategy

GPS	Prescribe glucocorticoids promptly for rapid control of acute inflammation using the **lowest dose/shortest duration** necessary; start immunosuppressive therapy **early** to minimize steroid toxicity.
Cond. Very Low	**Organ/life-threatening flares** — pulse methylprednisolone (250–1,000 mg × 1–3 days) + oral taper preferred over high-dose oral taper without pulse.
Strong Low	Stable controlled SLE on **prednisone > 5 mg/day** — taper to ≤5 mg/day (ideally zero) within **6 months**.
Cond. Very Low	Sustained remission on ≤5 mg/day — slow taper toward zero. Unable to taper ≤5 mg/day — initiate/escalate immunosuppressive therapy.
Strong V.Low–Mod	Routine treatment with **hydroxychloroquine (HCQ)** unless contraindicated; continue indefinitely, even in sustained remission (Conditional, Low).
Cond. V.Low–Low	Long-term average HCQ dose goal **≤5 mg/kg/day** over >5 mg/kg to minimize retinal toxicity; brief higher-dose (5–6.5 mg/kg/d) courses acceptable at initiation.

3 Immunosuppressive Therapy & Escalation

Cond. Low	Sustained remission/low disease activity — **taper immunosuppressive therapy after 3–5 years** toward discontinuation.
Strong V.Low–Mod	Ongoing activity in **any organ system refractory** to initial therapy — escalate therapy.
GPS	Organ/life-threatening SLE treated **urgently/emergently** with aggressive therapy (pulse/high-dose GC + immunosuppressive, combination therapy as time may not permit sequential trials).

4 Hematologic & Neuropsychiatric Manifestations

Cond. Against Very Low	**Asymptomatic leukopenia/lymphopenia** (<1,000/mcL) attributed to SLE — against initiating immunosuppression absent other disease activity.
Cond. Very Low	**Thrombocytopenia/hemolytic anemia** — chronic asymptomatic (<30,000/mcL): GC + additional agent (MPAA/AZA/CNI/anti-CD20/belimumab/IVIG) over observation/GC alone. Symptomatic (active bleeding/hemodynamic instability): initial GC + IVIG and/or anti-CD20 preferred over conventional immunosuppressants.
Cond. Very Low	**Severe NPSLE** (optic neuritis, acute confusional state, mononeuritis multiplex) — pulse/high-dose GC + IVCYC, MPAA, or anti-CD20 over GC monotherapy. **Myelitis** — GC + IVCYC preferred. **Psychosis** — antipsychotic + GC/CYC/MPAA/anti-CD20. **Seizure** — anti-seizure medication + immunosuppression.
Cond. Against Very Low	Isolated **cognitive dysfunction** (documented by neuropsych testing) — against adding immunosuppressive therapy to cognitive therapy alone.

5 Cutaneous, Musculoskeletal & Serositis

GPS	Educate on **sun protection**; initial cutaneous lupus therapy (+HCQ) is topical (glucocorticoid/calcineurin inhibitor) ± intralesional or brief oral glucocorticoid.
Cond. Very Low	Mild skin-predominant lupus despite HCQ/topicals — modify antimalarial (add quinacrine/switch to chloroquine) over adding immunosuppressive agent. Moderate–severe refractory — add MTX, MPAA, anifrolumab, and/or belimumab; further refractory — add/substitute **lenalidomide**.
Cond. Very Low	**Bullous lupus** — mild: add dapsone over initiating GC. Moderate–severe refractory: add conventional immunosuppressant (MPAA/MTX/AZA) and/or anti-CD20.
Cond. V.Low–Low	Persistent/recurrent **arthritis** on HCQ — initial MTX, MPAA, or AZA, with low threshold to add belimumab/anifrolumab for inadequate response, over initial biologic therapy.
Cond. Very Low	**Pleuropericarditis** — initial NSAID/colchicine (low threshold to escalate to GC) over GC alone; ongoing/recurrent despite HCQ/NSAID/colchicine/GC — add conventional (MPAA/AZA) or biologic immunosuppression.

6 Systemic Vasculitis & Cardiopulmonary

Cond. V.Low–Low	SLE-attributed **vasculitis** — pulse/high-dose GC + conventional/biologic immunosuppression over GC monotherapy. **Severe** — IVCYC or anti-CD20 preferred initial agent. **Life-threatening** (diffuse alveolar hemorrhage, mesenteric vasculitis) — add PLEX and/or IVIG to GC + immunosuppressive therapy.
Cond. Very Low	Acute/worsening **myocarditis** — GC + IVCYC, MPAA, anti-CD20, and/or IVIG over GC monotherapy. **Libman-Sacks endocarditis** — immunosuppressive therapy and/or anticoagulation.

Format note: "we strongly recommend" = Strong; "we conditionally recommend" = Conditional. GPS = ungraded good practice statement based on panel consensus. Condensed from Table 3, Recommendations and Good Practice Statements.

Sammaritano LR, Askanase A, Bermas BL, et al. 2025 American College of Rheumatology (ACR) Guideline for the Treatment of Systemic Lupus Erythematosus. *Arthritis Care Res (Hoboken).* 2025.
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