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2025 American College of Rheumatology (ACR) Guideline for the Treatment of Systemic Lupus Erythematosus (SLE)

Guideline Summary

In this guideline, we present treatment recommendations as well as ungraded, consensus-based good practice statements that are applicable to children and adults with Systemic Lupus Erythematosus (SLE). Goals of SLE management are to achieve and maintain remission or a low level of disease activity, to reduce morbidity and mortality, and to minimize treatment-related toxicities for those living with SLE.

For treatment of SLE, we recommend universal use of hydroxychloroquine, minimizing glucocorticoid exposure, and early introduction of conventional and/or biologic immunosuppressive therapies. We strongly emphasize the role of shared decision-making between patients and clinicians, as multiple factors will impact therapy choice.

Therapy recommendations are presented without hierarchy when evidence-based data, clinical expertise, and patient-reported experiences and preferences do not clearly support the use of one medication over another. All treatment decisions should be individualized and include shared decision-making, essential to respecting patient values and preferences. Potential limitations to implementing recommendations may arise due to limited access to testing, specialists, procedures, and medications; accordingly, if recommended therapies are unavailable, are not tolerated, or are not preferred, we encourage discussion of reasonable alternative therapies. Collaborative care between rheumatologists and other specialists is encouraged. Recommendations also aim to alleviate healthcare disparities, which are important factors impacting outcomes in people with SLE.

Recommendations and Good Practice Statements	Strength	Level of Evidence
Note: We suggest referring to the explanatory text throughout the "Results" section of the full manuscript, once it is available, for details regarding rationale, development, and implementation of the recommendations and good practice statements summarized below.		
Monitoring		
In people with SLE, we conditionally recommend: …Assessing disease activity regularly, including when there is a change in clinical status or SLE-directed medications.	Conditional	Very Low
…Assessing disease damage at least annually.	Conditional	Very Low
Comorbidities and Risk Management		
GPS: *All people with SLE should receive screening, monitoring, and management for comorbid conditions associated with SLE and its therapies (including infection, cardiovascular disease, bone and joint damage, malignancy, reproductive health complications, and presence of antiphospholipid antibodies.*		
Medication Guidance and Treatment Goals		
GPS: *The goal of SLE treatment should be optimal control of disease (e.g., remission or a low level of disease activity) to improve long-term clinical outcomes.* **GPS:** *Prescribe glucocorticoids promptly to obtain rapid control of acute inflammation using the lowest dose and shortest duration necessary and initiate immunosuppressive therapy early to minimize glucocorticoid-related toxicity.*		
Glucocorticoid therapy: In people with SLE with organ- or life-threatening SLE flares:		

...We conditionally recommend pulse methylprednisolone treatment (250-1000 mg for 1-3 days) followed by oral glucocorticoid taper over high-dose oral glucocorticoid taper without pulse treatment.	Conditional	Very Low
In people with SLE with stable controlled SLE on prednisone >5 mg/day: ...We strongly recommend tapering the prednisone to a dose of ≤5 mg daily (and ideally to zero) within 6 months.	Strong	Low
In people with SLE: With sustained remission on prednisone ≤5 mg/day: ...We conditionally recommend a slow taper toward zero. Who are unable to taper prednisone to ≤5 mg/day: ...We conditionally recommend initiating or escalating immunosuppressive therapy.	Conditional Conditional	Very Low Very Low
Hydroxychloroquine therapy: In people with SLE: …We strongly recommend routine treatment with HCQ unless contraindicated.	Strong	Very Low to Moderate
In people with SLE: …We conditionally recommend continuing HCQ therapy indefinitely, even in the setting of sustained remission. In people with SLE on HCQ therapy: …We conditionally recommend a long-term average daily HCQ dose goal of ≤5 mg/kg over a dose goal of >5 mg/kg to minimize retinal toxicity; use of short courses of higher dose (between 5 and 6.5 mg/kg/d) therapy may be necessary at initiation of treatment or to maintain disease control.	Conditional Conditional	Low Very Low to Low
Immunosuppressive therapy: In people with SLE with sustained clinical remission or low disease activity: …We conditionally recommend tapering immunosuppressive therapy after 3-5 years with the goal of discontinuation.	Conditional	Low
General treatment strategies		
GPS: *People with active SLE symptoms should be diagnosed and treated promptly, with severity of lupus activity guiding intensity and choice of therapy.* **GPS:** *When multiple organ systems are involved at onset or during a flare of SLE, therapy should be directed toward all manifestations but should prioritize areas at greatest risk for irreversible damage.* **GPS**: *Organ- or life-threatening SLE should be treated urgently/emergently with aggressive therapy (e.g., pulse/high-dose glucocorticoid and immunosuppressive therapy), including consideration of combination therapies, as time may not permit sequential therapy; the clinical situation and patient's preference should guide the specific combination therapy.* **GPS:** *When medications, procedures, and surgeries beyond the scope of rheumatology practice are considered, the decision to proceed with such therapies requires multidisciplinary discussion between the rheumatologist and the relevant specialists/proceduralists/surgeons.* ***GPS:*** *When clinical or serologic findings suggest an additional diagnosis or overlap with SLE (e.g., aquaporin-4 antibodies in setting of known SLE and new onset transverse myelitis or optic neuritis), therapy should be adjusted if necessary, depending upon which process is predominant and in consultation with the relevant specialist(s).*		
Organ-specific manifestations		
For ongoing SLE disease activity in any organ system(s) refractory to initial therapy, …We strongly recommend escalation of therapy.	Strong	Very Low - Moderate

Hematologic		
Leukopenia: For asymptomatic neutropenia and/or lymphopenia (absolute counts <1000/mcL for either) attributed to SLE …We conditionally recommend ***against*** initiating immunosuppressive treatment (glucocorticoids, conventional or biologic immunosuppressants) in the absence of other lupus disease activity.	Conditional Against	Very Low
Thrombocytopenia: For chronic asymptomatic thrombocytopenia (<30,000/mcL) attributed to SLE …We conditionally recommend initiation of glucocorticoid with an additional therapy (MPAA, AZA, CNI, anti-CD 20 agents, belimumab, and/or IVIG) over observation or glucocorticoid monotherapy.	Conditional	Very Low
Thrombocytopenia: For symptomatic thrombocytopenia (i.e., active significant bleeding) attributed to SLE: …We conditionally recommend initial glucocorticoid therapy with addition of IVIG and/or anti-CD20 therapy over the addition of conventional immunosuppressive agents.	Conditional	Very Low
***Hemolytic Anemia*:** For symptomatic autoimmune hemolytic anemia (i.e., ischemic manifestations and/or hemodynamic instability) attributed to SLE: …We conditionally recommend initial glucocorticoid therapy with addition of IVIG and/or anti-CD20 therapy over the addition of conventional immunosuppressive agents.	Conditional	Very Low
Neuropsychiatric		
Severe neuropsychiatric syndromes: For Active lupus optic neuritis -OR- Lupus acute confusional state -OR- Active lupus mononeuritis multiplex: …We conditionally recommend initial therapy with pulse/high-dose glucocorticoid taper plus immunosuppressive therapy with IV CYC, MPAA, or anti-CD20 therapy over pulse/high-dose glucocorticoid monotherapy alone.	Conditional	Very Low
For active lupus myelitis: …We conditionally recommend initial therapy with pulse/high-dose glucocorticoid and IV CYC over pulse/high-dose glucocorticoid combined with other (non-CYC) immunosuppressive agents.	Conditional	Very Low
For active lupus psychosis: …We conditionally recommend anti-psychotic therapy plus glucocorticoid, IV CYC, MPAA, or anti-CD20 therapy over anti-psychotic therapy alone.	Conditional	Very Low
***Seizure**:* For seizures attributed to active SLE: …We conditionally recommend anti-seizure medication plus glucocorticoid, CYC, MPAA, AZA, and/or anti-CD20 over anti-seizure medication alone.	Conditional	Very Low
Cognitive dysfunction**:* For cognitive dysfunction or decline attributed to active SLE and documented by neuropsychological testing: …We conditionally recommend ***against addition of immunosuppressive therapy (including glucocorticoid) to cognitive therapy over cognitive therapy alone.	Conditional Against	Very Low
Cutaneous/mucocutaneous		
GPS: *People with SLE should be educated on the use of sunscreen and other sun-protection measures to reduce risk of rash and potential disease flare.* **GPS**: *Initial therapy for cutaneous lupus rash—in addition to HCQ—should be topical, including glucocorticoid and/or calcineurin inhibitors; initial therapy may also include a course of intralesional glucocorticoid with dermatology and/or a brief, limited course of oral glucocorticoid.*		
Acute, subacute and chronic cutaneous lupus: For mild, ongoing skin-predominant lupus despite treatment with HCQ and/or topical therapies:		

…We conditionally recommend modifying antimalarial therapy (adding quinacrine or switching to chloroquine) over adding an immunosuppressive agent.	Conditional	Very Low
For ongoing moderate-severe cutaneous lupus refractory to topical and antimalarial therapies, and/or oral glucocorticoid necessitating escalation of therapy: …We conditionally recommend the addition of MTX, MPAA, anifrolumab and/or belimumab.	Conditional	Very Low - Moderate
For ongoing moderate-severe cutaneous lupus refractory to topical therapies, antimalarials, and conventional and/or biologic immunosuppressive agents necessitating escalation of therapy: …We conditionally recommend adding or substituting lenalidomide.	Conditional	Very Low
Bullous lupus erythematosus: For mild ongoing bullous lupus despite treatment with topical therapies and antimalarial therapies: …We conditionally recommend the initial addition of dapsone over initiation of glucocorticoid.	Conditional	Very Low
For moderate-severe bullous lupus refractory to topical therapies, antimalarials, and/or oral glucocorticoid necessitating escalation of therapy: …We conditionally recommend adding a conventional immunosuppressive agent (MPAA, MTX, AZA) and/or anti-CD-20 therapy.	Conditional	Very Low
Chilblain lupus: For chilblain lupus despite symptomatic, topical, and antimalarial therapies (including quinacrine): …We conditionally recommend the addition of pentoxifylline, PDE5 inhibitors (e.g., sildenafil, tadalafil), and/or calcium channel blockers (e.g., nifedipine) over initiation of immunosuppressive therapies.	Conditional	Very Low
Leukocytoclastic vasculitis: For ongoing mild cutaneous vasculitis despite topical and antimalarial therapies: …We conditionally recommend addition of dapsone or colchicine over immunosuppressive therapies including oral glucocorticoid.	Conditional	Very Low
Serositis		
Pleuropericarditis: For lupus pleuropericarditis: …We conditionally recommend initial treatment with NSAID, colchicine, or their combination, with a low threshold for escalation to glucocorticoid therapy over initiating glucocorticoid therapy alone.	Conditional	Very Low
For ongoing/recurrent episodes of lupus pleuropericarditis despite treatment with HCQ, NSAIDs, colchicine, and/or glucocorticoids necessitating escalation of therapy: …We conditionally recommend conventional (MPAA, AZA) or biologic immunosuppressive therapies.	Conditional	Very Low
Musculoskeletal		
GPS: *Initial therapy for acute or recurrent episodes of inflammatory arthritis in people with SLE may include a course of NSAID or a limited course of oral glucocorticoid while waiting for recommended long-term therapies to take effect.*		
Arthritis: For persistent or recurrent active SLE arthritis on HCQ, regardless of prior/current NSAIDs or short-term glucocorticoid therapy: …We conditionally recommend initial therapy with MTX, MPAA, or AZA, with a low threshold to add or substitute with belimumab or anifrolumab for inadequate response over initial biologic therapy.	Conditional	Very Low to Low

Systemic Vasculitis		
For vasculitis attributed to active SLE: …We conditionally recommend initial therapy with pulse/high-dose glucocorticoid taper and conventional (IV CYC, MPAA, AZA) or biologic (anti-CD 20 therapy, belimumab, anifrolumab) immunosuppressive therapy over glucocorticoid monotherapy alone;	Conditional	Very Low to Low
…We conditionally recommend IV CYC or anti-CD20 therapy as initial therapy over other immunosuppressive therapies.	Conditional	Very Low
For life-threatening vasculitis attributed to active SLE (e.g., diffuse alveolar hemorrhage or mesenteric vasculitis): …We conditionally recommend the addition of PLEX and/or IVIG to pulse/high-dose glucocorticoid taper and immunosuppressive therapy over glucocorticoid and immunosuppressive therapy alone.	Conditional	Very Low
Cardiopulmonary		
Myocarditis: For lupus myocarditis that is acute and/or worsening: …We conditionally recommend treatment with glucocorticoid and IV CYC, MPAA, anti-CD20 therapy and/or IVIG over glucocorticoid monotherapy.	Conditional	Very Low
Non-bacterial (Libman-Sacks) endocarditis: For non-bacterial (Libman-Sacks) endocarditis: …We conditionally recommend immunosuppressive therapy and/or anticoagulation.	Conditional	Very Low

This summary was approved by the ACR Board of Directors on May 7, 2025. These recommendations are included in a full manuscript, which will be submitted for publication in Arthritis & Rheumatology and Arthritis Care and Research.