# Clinical Description: Systemic Lupus Erythematosus (SLE) – Active, Moderate-to-Severe

**Synonyms:** Lupus, SLE

## 1. Clinical Case Definition

Systemic Lupus Erythematosus (SLE) is a chronic, heterogeneous autoimmune disease characterized by the production of autoantibodies directed against nuclear antigens. This process leads to immune complex formation, complement activation, and subsequent inflammation and damage across multiple organ systems. The clinical course is typically marked by periods of relapse (flares) and remission.

This clinical description specifically defines active SLE exhibiting moderate-to-severe disease activity. This state implies the involvement of major organ systems or significant, persistent activity across multiple domains. Patients frequently present with constitutional symptoms, such as profound fatigue, fever, and weight loss, alongside specific organ involvement.

Key manifestations defining moderate-to-severe activity include:

- **Renal (Lupus Nephritis):** Characterized by clinically significant proteinuria, active urinary sediment (hematuria, cellular casts), and/or impaired glomerular filtration rate. Renal biopsy is the gold standard for diagnosis and classification.
- **Neuropsychiatric:** Severe central or peripheral nervous system involvement, such as seizures, psychosis, myelitis, or mononeuritis multiplex.
- **Hematologic:** Clinically significant cytopenias, including thrombocytopenia, autoimmune hemolytic anemia, leukopenia, or lymphopenia.
- **Serosal:** Pleuritis or pericarditis, often presenting with effusions.
- **Musculoskeletal:** Significant inflammatory arthritis, myositis, or severe arthralgias.
- **Mucocutaneous:** Extensive acute cutaneous lupus (e.g., malar rash), severe subacute or chronic lesions, oral/nasal ulcerations, and alopecia.

The diagnosis is established based on recognized clinical and immunological criteria. Key laboratory findings supporting the diagnosis and indicating active disease include high titers of Antinuclear Antibodies (ANA), specific autoantibodies such as anti-dsDNA and anti-Smith (anti-Sm), hypocomplementemia (low C3 and C4 levels indicating immune complex consumption), and elevated inflammatory markers (ESR or CRP).

## 2. Phenotype Scope & Granularity

- **Temporal Context:** Prevalent. Intended to identify patients with an established diagnosis of SLE.

- **Severity:** Moderate-to-Severe only. This scope is not inclusive of mild SLE.
- **Acuity / Chronicity:** Active disease (current flare or chronic persistent activity). This scope is not inclusive of SLE in Remission or Lupus Low Disease Activity State (LLDAS). The presence of chronic organ damage without concurrent active inflammation is insufficient.
- **Etiology:** Idiopathic/Primary SLE.
- **Population Context:** Primarily the adult population (≥18 years).

## 3. Related Conditions & Scope Boundaries

The following conditions represent related clinical entities, etiologies, or disease states that are not within the scope of this specific phenotype definition:

- **Drug-Induced Lupus (DIL):** This is a distinct etiology and is not within the scope of this idiopathic phenotype.
- **Isolated Cutaneous Lupus Erythematosus (CLE):** CLE without systemic involvement is outside the scope of this systemic phenotype.
- **Mild SLE:** Cases without major organ involvement or significant systemic activity are outside the scope of this moderate-to-severe definition.
- **Undifferentiated Connective Tissue Disease (UCTD) and Overlap Syndromes:** Conditions such as Mixed Connective Tissue Disease (MCTD), where SLE is not the primary diagnosis or driver of activity, are outside this scope.
- **Other Systemic Autoimmune Diseases:** Differential diagnoses such as Sjögren's syndrome, Rheumatoid Arthritis, and Vasculitis are related but distinct conditions.

## 4. Key Complications & Common Comorbidities

The following conditions are frequent complications or comorbidities of SLE and should be distinguished from the core definition of the active disease state itself:

- **Antiphospholipid Syndrome (APS)**
- **Accelerated Cardiovascular Disease**
- **Infections**
- **Osteoporosis**
- **Irreversible Organ Damage:** Including End-Stage Renal Disease (ESRD) and Stroke.

## 5. Intended Data Sources

This clinical description is intended for building concept sets against real-world administrative claims, electronic health record (EHR) databases, and patient registries. The target data should be standardized to the OMOP Common Data Model. Examples of licensable data sources where this concept set would be applied include:

- **Optum®** (Clinformatics® Data Mart, SES, Pan-Therapeutic)

- **Merative™** (MarketScan® Commercial Claims and Encounters)
- **Veradigm** (Health Verity, Practice Fusion EHR)
- **IQVIA** (AmbEMR, PharMetrics Plus)
- **HealthVerity**