

Clinical Description: Active, Severe Non-Infectious Uveitis (Intermediate, Posterior, or Panuveitis)

Synonyms: Systemic NIU, Sight-threatening Non-Infectious Uveitis, Steroid-dependent Uveitis, Non-infectious intermediate uveitis, posterior uveitis, or panuveitis.

1. Clinical Case Definition

Non-Infectious Uveitis (NIU) is a heterogeneous group of intraocular inflammatory disorders arising from autoimmune or autoinflammatory processes. It may manifest as a purely ocular condition (idiopathic) or be associated with systemic diseases (e.g., sarcoidosis, Behçet's disease, spondyloarthritis). This phenotype specifically defines active, severe inflammation involving the intermediate, posterior, or all segments of the uveal tract (panuveitis). The severity is characterized by inflammation that is sight-threatening, chronic, recurrent, or refractory to management with local therapies alone (often characterized as steroid-dependent).

The diagnosis of NIU is contingent upon the rigorous exclusion of infectious etiologies (e.g., syphilis, tuberculosis, viral retinitis) and masquerade syndromes (e.g., intraocular lymphoma). Clinical assessment relies on comprehensive ophthalmologic examination, including slit-lamp biomicroscopy and dilated fundus examination. Disease activity is confirmed and graded using standardized criteria (e.g., Standardization of Uveitis Nomenclature (SUN) criteria), assessing anterior chamber cells/flare and vitreous haze.

The clinical presentation varies by anatomical location:

- **Intermediate Uveitis:** Characterized primarily by inflammation of the vitreous (vitritis), often presenting with floaters and blurred vision. Key signs include vitreous cells, "snowballs" (inflammatory aggregates), and "snowbanking" (exudate over the pars plana).
- **Posterior Uveitis:** Involves the retina and/or choroid, often causing significant vision loss or scotomas. Findings may include retinal vasculitis (sheathing, leakage), chorioretinitis, retinitis, and optic disc edema.
- **Panuveitis:** Concurrent inflammation involving the anterior chamber, vitreous, and retina/choroid, often presenting with severe symptoms combining features of anterior (pain, redness, photophobia) and posterior inflammation.

Supporting investigations include laboratory tests for inflammatory markers (ESR, CRP) and screening for systemic autoimmune associations (e.g., HLA-B27, ANA, ACE levels). Ocular imaging is essential; Optical Coherence Tomography (OCT) is used to detect and quantify cystoid macular edema (CME), and Fundus Fluorescein Angiography (FFA) identifies retinal vasculitis and posterior segment leakage.

2. Phenotype Scope & Granularity

- **Temporal Context:** Prevalent. Intended to identify patients with established chronic or recurrent disease experiencing active inflammation (either an incident flare or persistent activity).
- **Severity:** High severity. This scope is defined by inflammation that is sight-threatening, steroid-dependent, or refractory to local treatment. It excludes mild cases managed solely with local therapies.
- **Acuity / Chronicity:** Active disease (current flare or persistent inflammation) within a chronic or recurrent context.
- **Etiology:** Non-Infectious (autoimmune or autoinflammatory). Includes both idiopathic NIU and NIU associated with systemic autoimmune diseases.
- **Population Context:** Patients with confirmed anatomical involvement of the intermediate segment, posterior segment, or panuveitis meeting the severity criteria.

3. Related Conditions & Scope Boundaries

The following conditions represent distinct clinical entities or different states of the disease and are not within the scope of this phenotype:

- **Infectious Uveitis:** Uveitis caused by bacterial, viral, fungal, or parasitic agents is a distinct etiology and is not within the scope of this non-infectious phenotype.
- **Masquerade Syndromes:** Conditions mimicking uveitis, such as intraocular lymphoma, are distinct pathological entities and are not within scope.
- **Isolated Anterior Uveitis:** Inflammation confined solely to the anterior chamber represents a different anatomical scope and typically a different severity profile; it is not within the scope of this phenotype.
- **Inactive (Quiescent) NIU:** Disease states without active inflammation are not within the scope of this active phenotype.
- **Mild or Locally Controlled NIU:** Uveitis that is fully controlled by local therapies (topical, periocular, or intravitreal) represents a lower severity and is not within the scope of this severe phenotype.

4. Key Complications & Common Comorbidities

The following conditions are frequent complications of the disease, associated systemic conditions, or consequences of common treatments (e.g., corticosteroids). They must be differentiated from the core definition of active severe NIU itself.

- **Ocular Complications:**
 - Cystoid Macular Edema (CME)
 - Cataracts
 - Glaucoma / Ocular Hypertension
 - Optic Atrophy

- **Associated Systemic Diseases (Comorbidities):**
 - Sarcoidosis
 - Behçet's disease
 - Spondyloarthritis
- **Common Iatrogenic/Treatment-Related Conditions:**
 - Osteoporosis
 - Diabetes Mellitus
 - Systemic Hypertension

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**