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To:
Compassionate Allowances Program Office
Social Security Administration

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Proposed Condition Name

Thrombosis with Thrombocytopenia Syndrome (TTS) / Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT)

Alternate Names

- Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT)
- Thrombocytopenia with Thrombosis Syndrome (TTS)
- Heparin-Independent Heparin-Induced Thrombocytopenia–Like Syndrome
- Immune-Mediated Thrombosis with Thrombocytopenia

Summary

Thrombosis with Thrombocytopenia Syndrome (TTS), also known as Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT), is a rare but severe immune-mediated disorder characterized by the simultaneous occurrence of thrombosis (often in unusual sites such as cerebral venous sinuses or splanchnic veins) and thrombocytopenia, typically occurring 5–30 days after certain adenoviral vector COVID-19 vaccines [1,2].
The syndrome is mediated by pathogenic antibodies against platelet factor 4 (PF4) that activate platelets, leading to widespread clot formation despite low platelet counts [3].

The condition is associated with high morbidity and mortality due to life-threatening clot locations, rapid progression, and potential for hemorrhagic complications secondary to low platelets [2,4].

Description of Condition

The immunopathogenesis of TTS/VITT closely resembles autoimmune heparin-induced thrombocytopenia (aHIT) but occurs without prior heparin exposure [3].
Autoantibodies bind to PF4, forming immune complexes that activate platelets via FcγIIa receptors, triggering disseminated clot formation in arterial and venous beds [4].
Common clot sites include:

- Cerebral venous sinuses (CVST)
- Splanchnic veins
- Pulmonary arteries
- Deep veins of the legs
- Arteries of the extremities or viscera

Diagnostic Testing

Laboratory Findings:

- Platelet count <150 × 10^9/L
- Elevated D-dimer (often markedly elevated)
- Low fibrinogen in some cases
- Positive anti-PF4 ELISA (heparin-independent binding)

Imaging Studies:

- CT or MR venography for cerebral venous sinus thrombosis
- Abdominal CT with contrast for splanchnic vein thrombosis
- Doppler ultrasound for DVT
- CT pulmonary angiography for pulmonary embolism

Confirmatory Testing:

- Functional platelet activation assays (e.g., serotonin release assay) if available

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Physical Findings

- Severe headache, visual disturbances, focal neurological deficits (CVST)
- Abdominal pain, nausea, vomiting (splanchnic thrombosis)
- Dyspnea, chest pain (pulmonary embolism)
- Limb swelling, pain, pallor, or cyanosis (DVT/arterial thrombosis)
- Petechiae, purpura, mucosal bleeding (secondary to thrombocytopenia)

ICD-10 Codes

- **D69.3** — Immune thrombocytopenic purpura (for immune-mediated platelet destruction)
- **I82.0** — Budd-Chiari syndrome (for hepatic vein thrombosis)
- **I67.6** — Nonpyogenic thrombosis of intracranial venous system
- **I26.9** — Pulmonary embolism, unspecified
- **I82.90** — Embolism and thrombosis of unspecified vein

Onset

Typical onset is 5–30 days post-vaccination with adenoviral vector-based COVID-19 vaccines, though rare cases have occurred outside this window [1,2]. Symptoms often develop abruptly and progress rapidly.

Course / Progression

Without prompt recognition and treatment, TTS/VITT can progress to massive thrombosis, multi-organ failure, intracranial hemorrhage, and death. Even with treatment, survivors may experience long-term disability from stroke, organ infarction, or post-thrombotic syndrome [2,4].

Treatment

Acute Management:

- Immediate discontinuation of heparin (contraindicated due to HIT-like mechanism)
- Administration of non-heparin anticoagulants (e.g., argatroban, bivalirudin, fondaparinux, direct oral anticoagulants)
- High-dose intravenous immune globulin (IVIG) to block FcγIIa-mediated platelet activation
- Corticosteroids in some cases

Supportive Care:

- Neurosurgical intervention for severe CVST with mass effect
- Hematology and critical care consultation
- Platelet transfusions generally avoided unless life-threatening bleeding occurs

Rationale for Compassionate Allowance

- Acute, rapidly progressive, and life-threatening condition
- High rates of severe neurological or organ damage in survivors
- Documented long-term disability in many cases
- Strong objective diagnostic criteria
- Urgent treatment required to reduce mortality

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