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To:
Compassionate Allowances Program Office
Social Security Administration

From:
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Proposed Condition Name

Post-Vaccination Mast Cell Activation Syndrome (MCAS)

Alternate Names

- Mast Cell Activation Disorder (MCAD)
- Secondary Mast Cell Activation Syndrome
- Non-clonal Mast Cell Activation Syndrome
- Immune-mediated Mast Cell Hyperreactivity

Summary

Post-Vaccination Mast Cell Activation Syndrome (MCAS) is a chronic multisystem disorder characterized by episodic symptoms of mast cell mediator release—such as flushing, urticaria, hypotension, tachycardia, gastrointestinal distress, and neurocognitive dysfunction—following immune stimulation from vaccination.
In susceptible individuals, vaccination may act as a trigger for persistent mast cell hyperactivation through immune dysregulation, resulting in recurrent systemic symptoms that mimic anaphylaxis but without evidence of IgE-mediated allergy [1,2].

Description of Condition

Mast cells are tissue-resident immune cells that store and release inflammatory mediators (e.g., histamine, tryptase, prostaglandins, leukotrienes, cytokines). In MCAS, inappropriate mast cell activation occurs without the proliferation of abnormal mast cell clones (as seen in systemic mastocytosis).
The condition manifests as recurrent, unpredictable episodes of:

- Dermatologic symptoms: flushing, pruritus, urticaria, angioedema
- Cardiovascular symptoms: tachycardia, hypotension, presyncope/syncope
- Gastrointestinal symptoms: abdominal pain, diarrhea, nausea, vomiting
- Neurologic symptoms: brain fog, headache, light sensitivity

In post-vaccination cases, onset often follows within days to weeks of administration and persists chronically, with flares triggered by minor stressors, infections, heat, or chemical exposures.

Diagnostic Testing

Laboratory Markers (during or soon after flare):

- Elevated serum tryptase (> baseline by ≥20% + 2 ng/mL)
- Elevated plasma histamine or urinary histamine metabolites
- Elevated urinary prostaglandin D2 or 11β-prostaglandin F2α
- Elevated urinary leukotriene E4

Additional Workup:

- Exclusion of systemic mastocytosis (via KIT D816V mutation testing, bone marrow biopsy if indicated)
- Exclusion of IgE-mediated allergy (skin prick testing, specific IgE assays)
- Exclusion of other differential diagnoses (pheochromocytoma, carcinoid syndrome, autonomic disorders)

Physical Findings

- Flushing (episodic, diffuse)
- Dermatographism
- Tachycardia during episodes
- Hypotension or orthostatic changes
- Urticaria or angioedema during flares

ICD-10 Codes

- **D89.40** — Mast cell activation, unspecified
- **D89.41** — Mast cell activation syndrome, unspecified
- **D89.42** — Secondary mast cell activation
- **T88.1XXA** — Other complications following immunization, initial encounter

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Onset

In post-vaccination cases, onset typically occurs within days to weeks of immunization, often after a single dose, though sometimes after subsequent doses. Symptoms may become chronic with relapsing-remitting flares over months to years.

Course / Progression

MCAS can range from mild but persistent symptoms to severe, life-threatening episodes resembling anaphylaxis (mast cell activation anaphylaxis).
Post-vaccination MCAS may show:

- Chronic low-grade symptoms between flares
- Episodic exacerbations triggered by heat, exercise, stress, infection, medications, or additional immune challenges
- Potential overlap with dysautonomia (including POTS), chronic fatigue, and neuroinflammation

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Treatment

Acute Symptom Management:

- H1 antihistamines (e.g., cetirizine, loratadine)
- H2 antihistamines (e.g., famotidine)
- Leukotriene receptor antagonists (e.g., montelukast)
- Mast cell stabilizers (e.g., cromolyn sodium)
- Non-steroidal anti-inflammatory drugs (NSAIDs) if tolerated
- Epinephrine autoinjector for severe episodes

Long-term Management:

- Trigger avoidance
- Combination H1/H2 blockade
- Prophylactic mast cell stabilizers
- Low-histamine diet in select patients
- Immunomodulatory therapy in refractory immune-mediated cases

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Rationale for Compassionate Allowance

- Can cause sudden, severe, disabling multisystem episodes
- High morbidity from unpredictable flares and risk of anaphylaxis-like reactions
- Chronic disease requiring strict lifestyle modifications and daily medication
- Clear diagnostic criteria when using consensus definitions and biomarker confirmation
- Potential for secondary disability due to autonomic instability and chronic fatigue

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References

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2. Valent P, Akin C, Arock M, et al. Definitions, criteria and global classification of mast cell disorders with special reference to mast cell activation syndromes: a consensus proposal. *Int Arch Allergy Immunol*. 2012;157(3):215–225.
3. Molderings GJ, Haenisch B, Brettner S, et al. Pharmacological treatment options for mast cell activation disease. *Naunyn Schmiedebergs Arch Pharmacol*. 2016;389(7):671–694.