

## What is Mast Cell Activation Syndrome (MCAS)?

MCAS is a mast cell disorder that involves an over-activation of mast cells without an increase in their number. It differs from mastocytosis which is characterised by abnormal accumulation or proliferation of mast cells. Mastocytosis is therefore typically associated with an elevated serum mast cell tryptase level; usually normal in MCAS. MCAS presents with a wide range of allergic or inflammatory symptoms across multiple body systems. These symptoms can be quiescent for periods and then flare, with flares or exacerbations varying in duration or intensity. MCAS affects both children and adults; onset is unpredictable.

## Symptoms

Symptoms are often chronic and persistent. Treatment, drug and non-drug (e.g. acupuncture, physiotherapy, and psychology), aim to help mitigate and control but not necessarily totally alleviate symptoms. Triggers can vary widely. They need not be classical allergens, and therefore can include:

- Hormonal fluctuations and intercurrent acute infections.
- Aerosols, perfumes, odours (from for example cleaning agents)
- Medications and chemicals (such as drug colourants or excipients).
- Foods and pollens.
- Temperature changes, exercise and stress.

### Dermographic

- Flushing/redness
- Hives or wheals
- Itching with or without a rash
- Swelling

### Cardiovascular

- Chest pain
- Low blood pressure
- Fast heart rate
- Fainting or light-headedness

### Respiratory

- Sore throat
- Hoarseness
- Wheezing
- Shortness of breath
- Throat swelling

### Genital and urinary

- Genital pain or swelling
- Pain when urinating
- Vaginal pain, discharge or itching
- Bladder urgency or loss of control

### Gastrointestinal

- Bloating
- Stomach cramps or pain
- Reflux
- Feeling or being sick
- Diarrhoea
- Constipation
- Dumping syndrome
- Food allergies or intolerance

### Neurological

- Headache
- Brain fog
- Numbness, pain or tingling skin
- Anxiety
- Behavioural issues, rages

### Musculoskeletal

- Joint & muscle pain
- Osteoporosis
- Loss of bone mass

### Nasal-ocular

- Nose congestion
- Eye watering and itching

### General

- Extreme tiredness
- Anaphylaxis

## Diagnostic Criteria

Blood tests may consistently be normal. Diagnosis requires a systematic approach:

1. **Clinical Symptoms:** Episodic or persistent, involving multiple body systems.
2. **Response to Treatment:** Symptom improvement with mast cell-targeted therapies.
3. **Mediator Tests:** Elevated mast cell mediators in blood or urine during symptoms.
4. **Exclusion of Other Conditions:** Differential diagnosis is essential as some symptoms overlap.

In some cases, a definitive diagnosis may not be possible, leading to a classification of "suspected MCAS." Diagnostic frameworks include Molderings et al. (2011), Valent et al. (2019), and Giannetti et al. (2021) and Diagnosis of mast cell activation syndrome: a global "consensus-2" L Afrin et al (2021)

## Comorbidities

MCAS frequently coexists with other conditions. The exact relationship between MCAS and these conditions remains under investigation. Comorbidities include:

- Connective Tissue Disorders: Ehlers-Danlos Syndrome (EDS), Marfan Syndrome
- Dysautonomia: Postural Orthostatic Tachycardia Syndrome (PoTS)
- Long Covid and Chronic Fatigue Syndrome (CFS)

## Management and Treatment

The primary goal of treatment is symptom management through a combination of self-care and pharmacological interventions. While no medications are currently licensed specifically for MCAS, various drugs can help stabilise mast cells and alleviate symptoms. Key management strategies include identifying and avoiding triggers, implementing dietary modifications, and utilising stress management techniques alongside appropriate pharmacological support.

Treatment typically follows a stepwise approach, starting with H1 and H2 antihistamines, followed by mast cell stabilisers, leukotriene receptor antagonists, and other adjuncts as needed. Dosing is often individualised, with some patients requiring higher-than-standard doses for symptom control. NICE Evidence Summary on Chronic Urticaria advises that the standard dose of antihistamine could increase up to 4-fold where required (incremental up-dosing in poor response, off-licence use)

Excipients in medications can act as triggers, leading to variable tolerability between different brands. Any changes in medication should be made one at a time, with patients keeping a symptom diary to monitor their response. If a patient experiences issues with a specific brand, prescribing an alternative formulation may improve tolerability. Although antihistamines are available over the counter, prescribing them may be more appropriate for patients requiring higher doses to ensure consistent access and adherence to treatment.

Category	Medication	Purpose	Primary Care Prescribable?
H1 blockers	Cetirizine, Fexofenadine, Loratadine	Reduce histamine effects	Yes
H2 blockers	Famotidine	Manage gastric symptoms	Yes
Leukotriene blockers	Montelukast	Address leukotriene effects	Yes
Mast cell stabilisers	Sodium cromoglicate	Prevent mediator release	Yes
Mast cell stabilisers	Ketotifen	Prevent mediator release	Yes
Corticosteroids	Prednisolone	Reduce inflammation symptoms	Yes
Bioflavonoids	Quercetin	Natural mast cell stabilisers	OTC
Vitamins	Vitamin C, Vitamin D, Probiotics, Magnesium	Support stabilising mast cells, control histamine levels & histamine production	OTC
Emergency medication	Adrenaline	Anaphylaxis management	Yes
	Low Dose Naltrexone	Mast cell stabilisers	No *

**Onward referral:** Consider referral to secondary care if symptoms are severe, significantly impact daily life, do not respond to first-line treatments or if specialist input is needed for further diagnostic evaluation & management.

## References

Mast cell activation syndrome: Current understanding and research needs (2024)

<https://pubmed.ncbi.nlm.nih.gov/38851398/>

Dilemma of Mast Cell Activation Syndrome: Overdiagnosed or Underdiagnosed? (2024)

<https://pubmed.ncbi.nlm.nih.gov/38458701/>

Mast Cell Activation Syndrome Update-A Dermatological Perspective (2023)

<https://pubmed.ncbi.nlm.nih.gov/37511729/>

Mast Cell Activation Disorder and Postural Orthostatic Tachycardia Syndrome: A Clinical Association (2023)

<https://pubmed.ncbi.nlm.nih.gov/37511729/>

Mast Cell Activation Syndrome: A Research Update (2023)

<https://www.medcentral.com/immunology/research-update-mast-cell-activation-syndrome>

A Puzzling Mast Cell Trilogy: Anaphylaxis, MCAS, and Mastocytosis (2023)

<https://pubmed.ncbi.nlm.nih.gov/37958203/>

Idiopathic mast cell activation syndrome is more often suspected than diagnosed—A prospective real-life study (2022)

<https://onlinelibrary.wiley.com/doi/10.1111/all.15304>

Updated Diagnostic Criteria and Classification of Mast Cell Disorders: A Consensus Proposal (2021)

<https://pubmed.ncbi.nlm.nih.gov/34901755/>

Mast Cells as a Target—A Comprehensive Review of Recent Therapeutic Approaches (2023)

<https://pmc.ncbi.nlm.nih.gov/articles/PMC10136699/>

Mast Cell Diseases in Practice and Research: Issues and Perspectives Raised by Patients and Their Recommendations to the Scientific Community and Beyond (2022)

[https://www.jaci-inpractice.org/article/S2213-2198\(22\)00640-7/fulltext](https://www.jaci-inpractice.org/article/S2213-2198(22)00640-7/fulltext)

Mast Cells and Vitamin D Status: A Clinical and Biological Link in the Onset of Allergy and Bone Diseases (2022)

<https://pubmed.ncbi.nlm.nih.gov/36009422/>

Health-related quality of life and health literacy in patients with systemic mastocytosis and mast cell activation syndrome (2022)

<https://pmc.ncbi.nlm.nih.gov/articles/PMC9336039/>

Depression, psychosocial correlates, and psychosocial resources in individuals with mast cell activation syndrome (2022)

<https://pubmed.ncbi.nlm.nih.gov/34000855/>

Effect of Dietary Fiber and Metabolites on Mast Cell Activation and Mast Cell-Associated Diseases (2018)

<https://pubmed.ncbi.nlm.nih.gov/29910798/>

**Additional Information:** For further guidance and resources, including more on testing and management, see the 'Health Professionals' tab on the Mast Cell Action website ([www.mastcellaction.org](http://www.mastcellaction.org)). You can also join our professional network to receive important updates

With thanks to Dr. Johanna Theron, MBCHB, RCGPTB COE, MSC Pain Management, PGC Clin Ed, Dr. Bethan Myers MA(Cantab), MB BCh, FRCP, FRCPATH, DTM&H, Dr. Jose Costa, MD FRCPCH, and Dr. David Luyt MBCh, FCP(SA), MD, for their expert review of this document.