TABLE 7: Symptom-specific assessment and management considerations for physical fatigue in Long COVID

Assessment Element	Assessment Details
History 	• Differentiate between: o Fatigue o PEM/PESE† (i.e., exaggerated worsening of symptoms after exertion) o Exercise intolerance‡ (i.e., difficulty beginning or continuing physical activity) • If PEM/PESE present, inquire about other ME/CFS symptoms§[15,51] • If suspicious for MCAS, inquire about other symptoms of mastocytosis (e.g., episodic itching, flushing, hives, runny nose, red eyes, rapid heartrate, lightheadedness/fainting, shortness of breath, abdominal pain, nausea, diarrhea, headache)[80] • Use a validated tool to assess and trend severity (e.g., Fatigue Severity Scale)[74] • Assess for sleep, mood, diet, and/or medication considerations as modifiable contributors to fatigue
Physical exam	• Is the patient: o Seated and conversing? Lying down? o Participating in the interview independently or with assistance? o Tolerating the interview/encounter? • If concern for autonomic dysfunction, see Table 10 [Autonomic Table]
Treatment Element	**Treatment Details**
Non-pharmacologic management	• Discuss energy conservation strategies: o "The 4 P's" for essential tasks: Pacing, Planning, Prioritizing, Positioning o "The 3 D's" for non-essential tasks: Delete, Defer, Delegate • Treat coexisting orthostatic intolerance, if present (See Table 10 [Autonomic Table]) o Orthostatic stress can worsen fatigue • Begin an individualized and structured, titrated return to activity program (See Figure 1) • Consider cognitive behavioral therapy (to address cognitive and behavioral factors that can perpetuate fatigue)[75]
Pharmacologic management	• Consider weaning/de-prescribing sedating and anticholinergic medications • See Table 5 for commonly used medications for Long COVID
Referral, as needed	• To immunology, if concern for MCAS and history is suggestive of anaphylaxis

†Post-exertional malaise (PEM) / post-exertional symptom exacerbation (PESE) is "the worsening of symptoms following even minor physical or mental exertion, with symptoms typically worsening 12 to 48 hours after activity and lasting for days or even weeks." [61] It is a diagnostic criterion for ME/CFS.[19]

‡Exercise intolerance can be caused by cardiovascular, pulmonary, myopathic, motor neuron, and other conditions.

§ME/CFS is characterized by the reduced ability to "engage in pre-illness levels of activity," PEM/PESE, unrefreshing sleep, and cognitive impairment and/or orthostatic intolerance. Other symptoms may be present, as well.[19, 61, 88]

¶Fatigue can be present even if a patient appears to tolerate the encounter without difficulty, for instance due to relapsing/remitting symptoms or onset of PEM/PESE after the encounter.

Abbreviations: PEM (post-exertional malaise), PESE (post-exertional symptom exacerbation), ME/CFS (myalgic encephalomyelitis / chronic fatigue syndrome), MCAS (mast cell activation syndrome).