



Important Message from the PMSF Medical Advisory Committee

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Catatonia and Neuroleptic Malignant syndrome (NMS)

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Dear families in the Phelan-McDermid syndrome community,

The PMSF Medical Advisory Committee and the Phelan-McDermid syndrome Neuropsychiatric Consultation Group (PMS-NCG) provide support to families and to physicians caring for people with Phelan-McDermid syndrome with complex behavioral presentations. Based on our experience with more than 100 affected individuals, and knowing the difficulty that families encounter in accessing appropriate psychiatric care, we have developed this information sheet for you to share with your providers as relevant.

Phelan-McDermid syndrome is a rare genetic disorder which usually involves changes in a critical gene (*SHANK3*) on the long arm of chromosome 22. The *SHANK3* protein is a scaffolding protein in glutamatergic synapses, including among other functions the positioning of the NMDA receptor. Clinical features often include intellectual disability, autism, epilepsy, sensory-seeking behaviors, pica, chronically disrupted sleep, and severe constipation with related behavioral disturbances.

Around puberty or in early adulthood, some people with Phelan-McDermid syndrome are prone to develop bipolar disorder, associated psychotic features, and severe anxiety or obsessive-compulsive symptoms. When distressed, some may develop new aggression or self-injurious behaviors, or try to run away.

Emergency Department and Urgent Care providers must be aware that:

- People with Phelan-McDermid syndrome are extremely sensitive to antipsychotics, with high rates of extrapyramidal symptoms, medication-induced catatonia, and **neuroleptic malignant syndrome (NMS)**
- Antipsychotics should be used only when alternative medications to manage difficult symptoms have been explored, and then at only low doses.
- Intramuscular doses of medications like haloperidol have triggered NMS in some people with Phelan-McDermid syndrome, and repeated doses of antipsychotics can induce catatonia.
- The use of more than one antipsychotic medication at a time is strongly discouraged.
- Catatonia occurs in roughly 50% of Phelan-McDermid syndrome patients who develop psychiatric symptoms.
- Catatonia itself can be the first episode of psychiatric disturbance.
- When catatonia occurs, it may be stuporous, but hypermotoric catatonia with prominent, purposeless restlessness, agitation, and atypical aggression resembling manic delirium is also well described in Phelan-McDermid syndrome.
- If catatonia is suspected, Phelan-McDermid syndrome patients tend to respond well to lorazepam TID, sometimes requiring increases to high doses (see [Pharmacological Treatment Guidelines](#) - Catatonia).

Details about requesting a consult from the Phelan-McDermid syndrome Neuropsychiatric Consultation Group can be found here:
<https://pmsf.org/neuropsychiatric-consultation-group/>