



Important Message from the PMSF Medical Advisory Committee

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Sensitivity to Psychiatric Medications in Phelan-McDermid Syndrome

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Dear families in the Phelan-McDermid syndrome community,

It has come to the attention of the PMSF Medical Advisory Committee that many individuals with Phelan-McDermid syndrome have significant difficulty tolerating commonly used psychiatric medications for behavioral symptoms, mood and anxiety disorders, and sleep disturbance. For this reason, we wanted to provide the following guidance that we hope will inform discussions of appropriate interventions with your providers.

The Phelan-McDermid syndrome Neuropsychiatric Consultation Group (<https://pmsf.org/neuropsychiatric-consultation-group/>) was formed in 2018 to collect data on treating neuropsychiatric symptoms associated with Phelan-McDermid syndrome and to provide remote consultation to physicians caring for these challenging individuals. These case consultations, along with additional evidence from the published literature, have identified two patterns of concern we would like to highlight here:

1. Treatment with selective serotonin reuptake inhibitors (SSRIs) for symptoms of depression in Phelan-McDermid syndrome is associated with a high rate of emergence of manic symptoms and worsening behavioral agitation.
2. Treatment with antipsychotic medications appears to be less well tolerated in Phelan-McDermid syndrome as compared to in other neurodevelopmental disorders, with an increased risk of symptoms of catatonia as well as higher rates of other associated side effects.

Given these early clinical observations, we urge caution with the use of SSRIs in Phelan-McDermid syndrome. While some individuals with Phelan-McDermid syndrome may benefit from SSRIs, the risk of rapid conversion to mania needs to be monitored carefully.

We also urge caution with the use of antipsychotics, especially if catatonia is suspected. There is now emerging evidence to support the use of anticonvulsants or lithium for mood stabilization in Phelan-McDermid syndrome. If antipsychotics are deemed necessary for behavioral or psychotic symptoms, we encourage starting with very low doses and titrating slowly. Finally, clinicians working with individuals with Phelan-McDermid syndrome should be highly vigilant in monitoring for the emergence of mania and catatonia, including excited catatonia with psychomotor agitation, which may be hard to distinguish from mania.

It should be recognized that although we are reporting general trends in problems with medication use that have been observed in Phelan-McDermid syndrome, and which merit careful observation and monitoring, there are always exceptions to these trends, and some people with Phelan-McDermid syndrome may do well on these classes of medications. Thus, these recommendations are meant to provide guidance, but clinical observations with respect to medication benefit in each individual with Phelan-McDermid syndrome should also guide treatment.