Expert Consensus Recommendations* for the Pharmacological Management of Attention Deficit, Hyperactivity, and Impulsivity in Phelan-McDermid Syndrome

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### Diagnostic assessment

- **Medical causes (e.g., sleep, epilepsy, infectious, gastrointestinal, metabolic)?**
  - Yes: Treat/refer for treatment
  - No: Other neuropsychiatric causes (e.g., anxiety, sensory-seeking behaviors)?
    - Yes: Treat/refer to specialist/refer to specific algorithms
    - No: Improvement?
      - Yes: Follow up as needed
      - No: Consider

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### Treatment Strategies

- **Increase as tolerated; consider extended release**
  - *Response*
  - Partial or nonresponse
    - *Methylphenidate, amphetamine* (Partial response or nonresponse)
      - Response
      - Partial or nonresponse
        - Combined treatment: stimulant + alpha agonist
          - Response
          - Partial or nonresponse
            - Atomoxetine (if patient can swallow pills whole) (Partial response or nonresponse)
              - Response
              - Partial or nonresponse
                - Antipsychotics +/- stimulant, alpha agonist, atomoxetine (Partial or nonresponse)
                  - Response
                  - Nonresponse
                    - Clinical Consultation

*These recommendations are not established as “evidence-based.”
**Expert Consensus Recommendations* for the Pharmacological Management of Sleep Disturbance in Phelan-McDermid Syndrome**

1. **Diagnostic assessment**
   - Medical causes (e.g., epilepsy, infectious, gastrointestinal, metabolic, pulmonary)?
     - No
     - Yes
     - Neuropsychiatric causes?
       - Yes
         - Treat/refer to specialist/refer to specific algorithms
       - No
         - Assess and implement adequate sleep hygiene

2. **Improvement?**
   - Yes
     - Follow up as needed
   - No
     - Continue treatment

3. **Healine Medications**
   - **Melatonin**
     - Increase up to 10 mg; consider extended release
       - Partial response or nonresponse
         - Response
         - Nonresponse
       - Partial response or nonresponse
         - Response
         - Nonresponse
   - **Clonidine**
     - Increase up to 0.3 mg; consider extended release
       - Partial response or nonresponse
         - Response
         - Nonresponse
   - **Trazodone, mirtazapine, doxepine**
     - Increase as tolerated
       - Partial response or nonresponse
         - Response
         - Nonresponse
   - **Quetiapine**
     - Increase as tolerated
       - Partial response or nonresponse
         - Response
         - Nonresponse
   - **Gabapentin, benzodiazepines, antihistamines**
     - Nonresponse
     - Clinical Consultation

*These recommendations are not established as “evidence-based.”
**Expert Consensus Recommendations* for the Pharmacological Management of Irritability and Aggression in Phelan-McDermid Syndrome**

**Diagnostic assessment**

- Medical causes (e.g., epilepsy, infectious, gastrointestinal, metabolic, pulmonary)?
  - Yes → Treat/refer for treatment → Improvement?
    - Yes → Follow up as needed
    - No → Treat/refer to specialist/refer to specific algorithms

- Other neuropsychiatric causes?
  - Yes → Treat/refer to specialist/refer to specific algorithms
  - No → Continue as tolerated; consider extended release

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### Guanfacine; clonidine

- Partial response or nonresponse → Response → Continuation/Maintenance
  - Response → Continuation/Maintenance
  - Nonresponse → Divalproex sodium, lamotrigine, carbamazepine, oxcarbazepine → Continuation/Maintenance

### Divalproex sodium, lamotrigine, carbamazepine, oxcarbazepine

- Partial response or nonresponse → Response → Continuation/Maintenance
  - Response → Continuation/Maintenance
  - Nonresponse → Risperidone, aripiprazole, quetiapine (and XR), olanzapine → Continuation/Maintenance

### Risperidone, aripiprazole, quetiapine (and XR), olanzapine

- Partial response or nonresponse → Response → Continuation/Maintenance
  - Response → Continuation/Maintenance
  - Nonresponse → Benzodiazepines, gabapentin, antihistamines, baclofen, propranolol → Continuation/Maintenance

### Benzodiazepines, gabapentin, antihistamines, baclofen, propranolol

- Partial response or nonresponse → Response → Continuation/Maintenance
  - Response → Continuation/Maintenance
  - Nonresponse → Lithium, chlorpromazine, perphenazine, clozapine

### Lithium, chlorpromazine, perphenazine, clozapine

- Nonresponse → Clinical Consultation

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*These recommendations are not established as “evidence-based.”
Expert Consensus Recommendations* for the Pharmacological Management of Mood Cycling in Phelan-McDermid Syndrome

Diagnostic assessment

Medical causes (e.g., epilepsy, immunologic, metabolic)?

Yes

Treat/refer for treatment

Improvement? Yes

Follow up as needed

No

Treat/refer to specialist/refer to specific algorithms

Consider

Nonresponse

Other neuropsychiatric cause? rule out catatonia

Yes

Monotherapy with second generation antipsychotic (QUE, ARI, OLZ, RISP)

No

Treat/refer to specialist/refer to specific algorithms

Increase cautiously as tolerated

Partial response or nonresponse

Response

Partial Response

Augment with mood stabilizer (VPA, LI, LAM)

Nonresponse

Switch monotherapy agent (SGA: QUE, ARI, OLZ, RISP)

Nonresponse

Switch monotherapy to mood stabilizer (VPA, LI, LAM)

Partial response or nonresponse

Augment with second mood stabilizer monotherapy (LI, VPA, LAM, CBZ, OXC, TOP)

Nonresponse

Switch mood stabilizer monotherapy (CBZ, OXC, TOP)

Response

Nonresponse

Clinical Consultation

*These recommendations are not established as “evidence-based.”
Expert Consensus Recommendations* for the Pharmacological Management of Catatonia** in Phelan-McDermid Syndrome

Diagnostic assessment

Medical causes (e.g., neuroleptic side effects epilepsy, infectious, metabolic)?
Yes: Treat/refer for treatment
No: Other neuropsychiatric causes?
Yes: Consider
No: Increase cautiously as tolerated

Improvement?
Yes: Follow up as needed
No: Treat/refer to specialist/refer to specific algorithms

Increase frequency as tolerated

Partial response or nonresponse
Response
Continuation/Maintenance

Partial or Nonresponse
Electroconvulsive therapy (ECT) +/− benzodiazepines

Response
Continuation/Maintenance
Partial response

Increase ECT frequency and/or dose as tolerated

Partial response or nonresponse
Response
Continuation/Maintenance
Partial or nonresponse
ECT maintenance + benzodiazepines

Response
Continuation/Maintenance

Increase dose as tolerated

Partial response or nonresponse
Response
Continuation/Maintenance
Nonresponse
Clinical Consultation

Benzodiazepines (e.g., lorazepam 0.5-8mg TID)

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**Notes for the Treatment Algorithm for the Pharmacological Management of Catatonia in Phelan-McDermid Syndrome**

- Would recommend starting lorazepam 0.5-1 mg TID, and increasing by 0.5 mg TID every few days, based on response.
- Track frequency of catatonia symptoms objectively to carefully guide titration; increase lorazepam until symptom improvement plateaus, or until the point of over-sedation.
- Monitor vital signs closely and if unstable, expedite to urgent referral for ECT.
- If no response to benzodiazepines, ECT alone is the next step assuming symptom severity warrants it. If the patient is simply prompt dependent with psychomotor retardation, ECT may not be indicated.
- If only PARTIAL response to benzodiazepines, consider ECT while remaining on the benzodiazepine, and using flumazenil reversal. It is NOT necessary to taper the benzodiazepine.
- If there is PARTIAL response to benzodiazepines, and the remaining symptoms do not warrant ECT, consider adjunctive antidepressant or mood stabilizer, depending on the underlying psychopathology.
- Acute ECT needs to be delivered at least three times weekly with BILATERAL electrode placement and monitoring for seizure quality.
- If inadequate response to bilateral ECT, consult with an expert to address ECT technical parameters and associated medications to improve seizure quality.
- Every patient who responds to ECT requires medication to decrease maintenance ECT frequency while maintaining clinical stability.
- Once the patient is on twice weekly ECT, start lithium and titrate to a therapeutic serum level as you decrease ECT frequency.