Drug Use Research & Management Program
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Prospective Safety Edit Policy Proposal: Antipsychotics In Young Children

Policy Proposal:

Evidence for use of antipsychotics in children was recently evaluated by the Pharmacy and Therapeutics Committee.[1] Utilization data indicates that a small proportion of children less than 6 years of age are prescribed antipsychotics (66 patients in 2020). Because evidence regarding the use of antipsychotics in children is limited, recommendations were made by the Pharmacy and Therapeutics Committee in April 2021 to implement safety edits to ensure appropriate use of antipsychotics in children.

Antipsychotics can be associated with significant risk of long-term adverse events. Few antipsychotics have been studied in young children, and efficacy and safety has not been established for any antipsychotic in young children less than 5 years of age. Indications with the most evidence of effectiveness in children include use for irritability associated with autistic disorder (including symptoms of aggression towards others, deliberate self-injuriousness, temper tantrums, and quickly changing moods). Both risperidone and aripiprazole have an indication for irritability associated with autism for patients at least 5 and 6 years of age, respectively.[2,3] Common indications and FDA-approved ages for other antipsychotics include use for bipolar disorder or schizophrenia in adolescents, but none have an FDA-approved indication for these conditions in young children. Current guidelines recommend non-pharmacological therapy as first-line therapy for children prior to prescription of an antipsychotic.[4-6]

Due to known long-term adverse effects associated with long-term antipsychotic use and unknown benefits of use in young children, the following proposal was developed in conjunction with input from experts in child psychiatry and intends to support appropriate use of antipsychotics in children 5 years of age or less. The proposal targets children after their first prescription in order to accommodate prescribing for urgent or acute symptoms and to avoid interruptions in therapy during transitions of care for patients newly enrolled in Medicaid. Ongoing therapy will require documentation of clinical rationale, metabolic monitoring, use of first-line non-pharmacologic therapy, and specialist consult. Upon their first claim for an antipsychotic, outreach will be conducted for prescribers of the antipsychotic in order to assess appropriateness of care, provide education on evidence-based use of non-pharmacological therapy, and facilitate access to services for appropriate patients. A flowchart of the proposed process to perform provider outreach and facilitate access of antipsychotics for appropriate patients is available in **Appendix 2**.

Recommendation:

- Implement a safety edit to ensure appropriate use of antipsychotics in children 5 year of age or less (**Appendix 1**).
- Implement a retrospective provider outreach program to facilitate access to medications for appropriate children (**Appendix 2**).

References:

1. Fletcher, S. Drug Use Research and Management. OHSU Drug Effectiveness Review Project Summary Report – Second Generation Antipsychotic Medications in Children and Adolescents. April 2021. https://www.orpdl.org/durm/meetings/meetingdocs/2021_04_01/archives/2021_04_01_SGAinChildren_DERPSummary.pdf. Accessed April 29, 2021.
2. Abilify (aripiprazole) tablets [package labeling]. Tokyo, Japan: Otsuka Pharmaceuticals, LLC; February 2020.
3. Risperdal (risperidone) tablets [package labeling]. Titusville, NJ: Janssen Pharmaceuticals, Inc; February 2021.
4. National Institute for Health and Care Excellence. Psychosis and schizophrenia in children and young people: recognition and management. Clinical guideline [CG155]. October 2016. https://www.nice.org.uk/guidance/cg155. Accessed October 30, 2019.
5. National Institute for Health and Care Excellence. Bipolar Disorder: assessment and management. Clinical guideline [CG184]. April 2018. https://www.nice.org.uk/guidance/cg185. Accessed October 30, 2019.
6. National Institute for Health and Care Excellence. Autism spectrum disorder in under 19s: support and management. Clinical guideline [CG170]. August 2013. https://www.nice.org.uk/guidance/cg170. Accessed October 30, 2019.

Antipsychotic Use in Children

Goal(s):

- Ensure safe and appropriate use of antipsychotics in children
- Discourage off-label use not supported by compendia

Length of Authorization:

- Up to 12 months

Requires PA:

- Antipsychotic use beyond 30 days in children 3-5 years of age
- All antipsychotic use in children 2 years of age or younger

Note: use of olanzapine as an antiemetic for chemotherapy does not require PA

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Table 1. FDA-Approved Indications and Ages for Oral Second-generation Antipsychotics in Children

FDA-Approved Indications and Ages				
Drug	**Schizophrenia**	**Bipolar I disorder**	**Major depressive disorder (adjunct)**	**Other**
aripiprazole	≥13 yrs	≥10 yrs	≥18 yrs	Irritability associated with Autistic Disorder ≥6 yrs Tourette's Disorder ≥6 yrs
asenapine maleate	≥18 yrs	≥10 yrs		
lurasidone HCl	≥13 yrs	≥10 yrs		
olanzapine	≥13 yrs	≥13 yrs	≥18 yrs	
paliperidone	≥12 yrs			Schizoaffective disorder ≥18 yrs
quetiapine fumarate	≥13 yrs	≥10 yrs		Bipolar depression ≥18 yrs
risperidone	≥13 yrs	≥10 yrs		Irritability associated with Autistic Disorder ≥5 yrs

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 code.	
2. Is the request for use of olanzapine as an antiemetic associated with cancer or chemotherapy?	**Yes:** Approve for 12 months	**No:** Go to #3
3. Has the patient been screened for diabetes (blood glucose or A1C) within the last 12 months?	**Yes:** Go to #5	**No:** Go to #4
4. Is there documented clinical rationale for lack of metabolic monitoring (e.g. combative behaviors requiring sedation)? Note: Caregivers failing to take patients to the laboratory is not a clinical rationale for lack of monitoring.	**Yes:** Document rationale. Go to #5	**No:** Pass to RPh. Deny; medical appropriateness. Annual metabolic screening is required for chronic use of antipsychotics. Refer denied requests to the OHA for follow-up. A single 90 day continuation of therapy may be granted upon request to allow for laboratory testing.

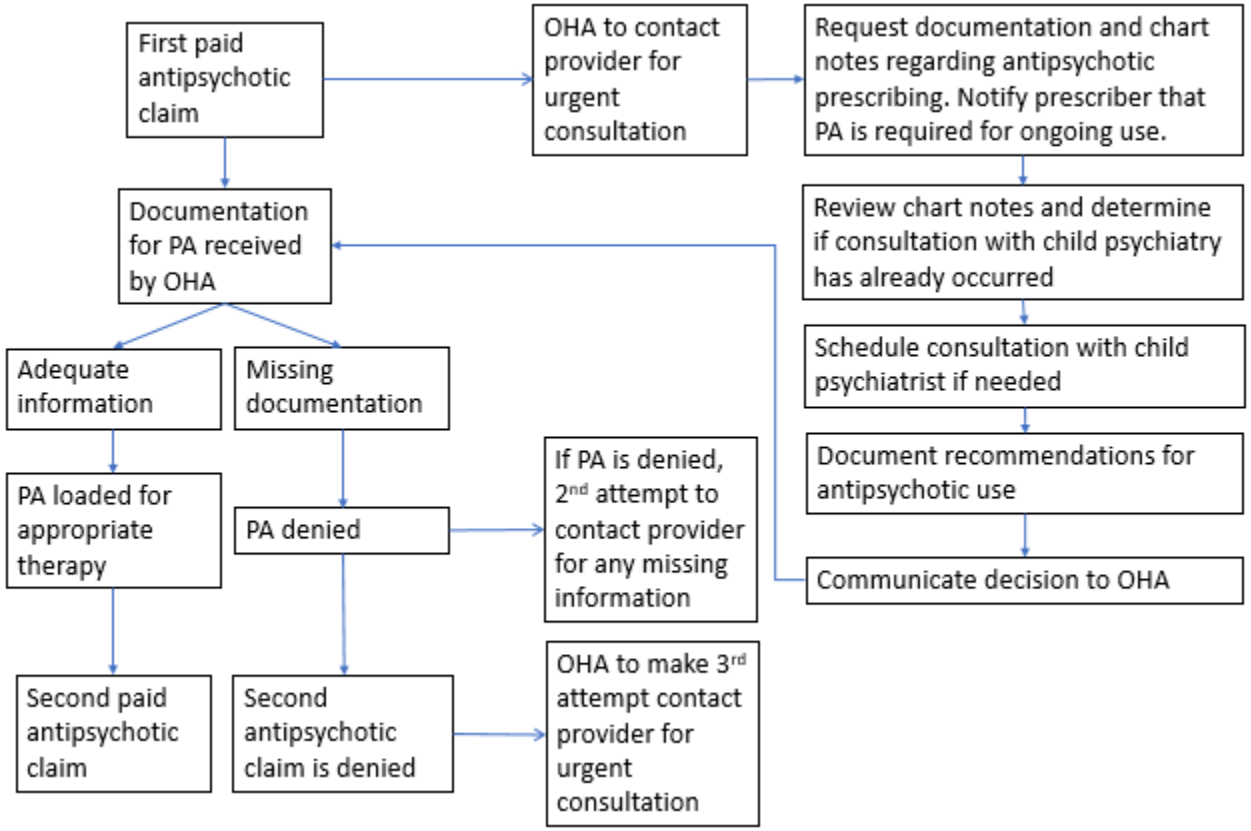
Approval Criteria		
5. Is the patient engaged in, been referred for, or have documented inability to access evidence based first-line non-pharmacological therapy (e.g., applied behavior analysis therapy for autism, parent behavioral therapy, or parent child interaction therapy)?	**Yes:** Go to #6	**No:** Pass to RPh. Deny; medical appropriateness. Refer denied requests to the OHA for follow-up. A single 90 day continuation of therapy may be granted upon request to allow time for engagement.
6. Is the drug prescribed by or in consultation with a child psychiatrist or developmental pediatrician?	**Yes:** Approve for up to 12 months or length of therapy, whichever is less	**No:** Go to #7

Approval Criteria		
7. Is there detailed documentation regarding risk/benefit assessment and the decision to prescribe antipsychotic therapy? A thorough assessment should include ALL the following: a. Multidisciplinary review including a mental health specialist b. Mental health assessment including documentation of diagnoses, symptoms, and disease severity c. Discussion and consideration of first-line non-pharmacological therapies d. Assessment of antipsychotic risks and monitoring strategies e. Specific therapeutic goals of antipsychotic therapy, and for ongoing therapy, discussion of progress toward or achievement of therapeutic goals (or reasons for lack of progress and remediation strategies) f. Anticipated duration of therapy g. Detailed follow-up plan	**Yes:** Approve for up to 12 months or length of therapy, whichever is less	**No:** Pass to RPh. Deny; medical appropriateness. Refer denied requests to the OHA for follow-up. A single 90 day continuation of therapy may be granted upon request to allow for submission of required documentation.

P&T/DUR Review: 6/21(SS)
Implementation: TBD

Appendix 2. Provider notification Retrospective safety program to facilitate review of antipsychotic use in children less than 5 years of age

Figure A1. Notification process



Provider Notification

- Inclusion criteria will target 3 basic patient populations:
    1. Patients with a soon-to-expire PA based on the following criteria OR
        - Patients <= 5 years of age AND
        - a prior authorization for an antipsychotic with an expiration date within the next 30 days (PDL classes: antipsychotics, 1st gen; antipsychotics, 2nd gen; antipsychotics, parenteral) AND
        - a recent paid FFS claim for an antipsychotic in past 45 days AND
        - no subsequent prior authorization request approved for an antipsychotic
    2. Patients with a new start of an antipsychotic in the past 2 weeks defined based on the following criteria OR
        - Patients <= 5 years of age AND
        - with a paid FFS antipsychotic claim in the past 2 weeks AND
        - no currently active prior authorization for the antipsychotic AND
        - no paid claims for the same HSN within the prior 3 months.

3. Patients with a denied claim for an antipsychotic defined based on the following criteria
    - Patients <= 5 years of age AND
    - with a denied FFS antipsychotic claim in the past 2 weeks due to the safety edit AND
    - with no currently active prior authorization for the antipsychotic AND
    - with no subsequent paid claims for the same HSN

- Exclusion criteria:
    1. Providers with notifications sent for the same patient and drug (based on HSN) in the past 3 months
    2. Patients not currently enrolled in Medicaid
    3. Patients who are deceased

HEALTH SYSTEMS DIVISION
Provider Services
500 Summer St NE
Salem, OR 97301

Oregon Health Authority

Kate Brown, Governor

Voice: 800-336-6016
Fax: 503-945-6873
TTY: 711

Date issued: <Month Day, Year>

<PROVIDER First Name><Last Name>
<1234 MAIN STREET>
<SUITE 100>
<PORTLAND, OR 97227>

For billing ID: «Billing_Provider_Medicaid_ID»

Patient Safety Notice for Antipsychotic Use in Young Children for:
Patient: Billy Smith; DOB: 10/10/2017; Medicaid#: 12345; Drug: risperidone 0.5 mg tablet

Effective XX/XX/2021, the Oregon Health Authority (OHA) has implemented safety edits for children under 6 years old prescribed off-label antipsychotics. These edits are intended to encourage appropriate evidence-based care and are focused on optimal outcomes for children prescribed antipsychotics. Your collaboration with this initiative is highly valued.

This notice was generated to support appropriate care because:

- your NPI was linked to a paid antipsychotic claim for this patient AND
- documentation of medical necessity and appropriateness will be required for ongoing use

What should you do?

- Consider consultation with a child psychiatrist and referral for evidence-based non-pharmacologic therapy.
  - For young children with autism, consider applied behavior analysis (ABA) therapy or other well-supported models shown to reduce self-injury and other symptoms of autism.
  - For other behavioral health diagnoses, consider Parent Child Interaction Therapy (PCIT).
- For any patient where benefits of antipsychotic use outweigh risks, please request a prior authorization (PA). PA requests should document all the following:
  - Laboratory monitoring for diabetes
  - Discussion of first-line, evidence-based non-pharmacological therapy
  - Consultation with a child psychiatrist or developmental pediatrician OR an assessment of risks, benefits, and decision to prescribe antipsychotics. A thorough risk/benefit assessment should include all the following:
    - a multidisciplinary review
    - a mental health evaluation (including diagnoses, symptoms and disease severity)
    - specific therapeutic goals and anticipated length of therapy
    - monitoring strategies for adverse events (e.g., tardive dyskinesia, weight gain, etc.)
    - a detailed follow-up plan
- You can submit PA requests three ways:
  - Call the Oregon Pharmacy Call Center at 888-202-2126;
  - Submit via the secure Provider Web Portal at https://www.or-medicaid.gov; or
  - Fax to 888-346-0178. Use the form at https://apps.state.or.us/Forms/Served/oe3978.pdf.

Questions?

- For questions about this message, email OHA's Pharmacy Program at DMAP.RXQUESTIONS@dhsoha.state.or.us
- For additional information and resources on alternative psychiatric options for children visit the following websites:
  - Provider consultation and support: https://www.oregon.gov/oha/HSD/BH-Child-Family/Pages/Supports.aspx
  - Evidence-based treatments: https://www.oregon.gov/oha/HSD/BH-Child-Family/Pages/Early-Childhood.aspx