

## Tetanus Prevention and Vaccination

Tetanus (also called lockjaw) is rare, but neurological complications can be permanent, and the mortality rate is up to 20%.<sup>10</sup> Wounds at risk of tetanus require tetanus toxoid vaccine and sometimes tetanus immune globulin. Antibiotic prophylaxis for tetanus is not effective for wound management.<sup>2</sup> The chart below answers common questions about the appropriate management of wounds for the prevention of tetanus.

Question	Answer/Pertinent Information		
What is tetanus?	<ul style="list-style-type: none"> <li>• Tetanus is caused by an endotoxin that is produced by <i>Clostridium tetani</i> spores, which are found in contaminated soil, and sometimes animal and human feces.<sup>3</sup></li> <li>• Symptoms of tetanus include generalized rigidity and skeletal muscle spasms, often initiating in the jaw and neck.<sup>2</sup></li> <li>• Tetanus is rare due to routine immunization from infancy through adulthood.<sup>2</sup></li> <li>• A patient's risk of tetanus is determined by the nature of the wound and their immunization status.<sup>2</sup></li> </ul>		
How long does tetanus immunity last after vaccination?	<ul style="list-style-type: none"> <li>• The routine initial three-dose tetanus toxoid vaccine series provides about 99% protection; however, immunity wanes over time.<sup>3</sup></li> <li>• Most patients have antitoxin levels close to the minimum protection level at ten years, therefore a tetanus toxoid booster is recommended <b>every ten years</b>.<sup>2</sup></li> <li>• A small percentage of people have a drop in antitoxin levels below the minimum protection level before ten years, which is why tetanus toxoid vaccine is recommended for all patients if they have a qualifying wound and if it has been more than five years since their last tetanus toxoid vaccine dose.<sup>2</sup></li> </ul>		
When is the tetanus toxoid vaccine needed for a wound?	<ul style="list-style-type: none"> <li>• All wounds should be cleaned. This can remove <i>C. tetani</i> spores, if present.<sup>2,3</sup></li> <li>• Having previously had tetanus disease does not confer immunity. Active immunization with tetanus toxoid vaccine should be given as soon as possible following a qualifying wound.<sup>2</sup></li> </ul>		
	<b>Tetanus toxoid immunization history</b>	<b>Clean, minor wound<sup>2,3</sup></b>	<b>All other wounds<sup>2,3,a</sup></b>
	Unknown or <3 doses	Tetanus toxoid vaccine needed	Tetanus toxoid vaccine needed
	3 or more doses AND <5 years since last booster dose	No vaccination	No vaccination <sup>b</sup>
	3 or more doses AND >5 years, but <10 years since last booster dose	No vaccination	Tetanus toxoid vaccine needed
	3 or more doses AND >10 years since last booster dose	Tetanus toxoid vaccine needed	Tetanus toxoid vaccine needed

Question	Answer/Pertinent Information
Which tetanus toxoid vaccine can be used for wound management?	<ul style="list-style-type: none"><li>• Any tetanus toxoid vaccine can be given for wound management, as they all contain the same dose of tetanus toxoid.</li><li>• Tetanus toxoid vaccines are only available in combination with diphtheria and are also found in combination with other vaccines (e.g., pertussis in DTaP, Tdap).<sup>2,3</sup></li><li>• Either Tdap or Td is appropriate for patients seven years and older. Use vaccines with a capital “D” for children under seven years (e.g., DTaP) to ensure the correct dose of the diphtheria component.<sup>2,3</sup></li><li>• See the chart at the end of this document for a comparison of available tetanus toxoid vaccines. Choose the vaccine based on the patient’s age, other vaccine requirements, pregnancy status, etc.</li></ul>
What are the contraindications and adverse effects of tetanus toxoid vaccine?	<ul style="list-style-type: none"><li>• Tetanus toxoid vaccine is contraindicated in patients who have had a severe allergic reaction/anaphylaxis with a previous dose.<sup>2,3,5</sup></li><li>• Tetanus toxoid vaccine should be used with caution in patients who have had a moderate or severe acute reaction to tetanus toxoid vaccine. The benefit typically outweighs the risk when tetanus toxoid vaccine is indicated for wound management.<sup>2</sup></li><li>• Local reactions (e.g., erythema, induration, pain at site) are common but are self-limiting.<sup>2,3</sup></li><li>• Arthus reactions (reaction involving severe pain, swelling, edema, etc) are not common.<sup>2,3</sup><ul style="list-style-type: none"><li>▪ Typically starts two to eight hours after the injection.<sup>2</sup></li><li>▪ More common in adults, particularly those who’ve received frequent doses of diphtheria or tetanus toxoid vaccines. Usually, patients who have Arthus reactions have high serum tetanus antitoxin levels.<sup>2</sup></li><li>▪ <b>Do NOT give tetanus toxoid vaccine to patients with a history of an Arthus reaction more than every ten years.</b><sup>2,3,7</sup> The risk of Arthus reactions does not appear to be increased with close administrations; however, it is still recommended that anyone (including pregnant women) with a history of Arthus reactions after a dose of Td or Tdap, should have an interval of at least ten years between doses.<sup>6</sup></li></ul></li></ul>
What is the role of tetanus immune globulin (TIG) in wound management?  <i>Continued...</i>	<ul style="list-style-type: none"><li>• TIG (<i>HyperTET</i>) provides antitoxin for immediate, passive, temporary immunity until the administered vaccine produces an immune response in the patient.<sup>2,3</sup> TIG only helps to remove unbound tetanus toxin, it does not affect toxin that is already bound to nerve endings.<sup>2,3</sup></li><li>• When indicated, TIG should be <b>administered as soon as possible</b>, typically in the emergency department.<sup>3,4</sup><ul style="list-style-type: none"><li>▪ The higher the risk of infection (e.g., puncture wound, wounds contaminated with soil or fecal matter AND no history of immunization), the faster TIG and tetanus toxoid vaccination should be given.<sup>4</sup></li><li>▪ There is little benefit a week or so after an injury if the patient has had some previous tetanus toxoid vaccination.<sup>4</sup></li><li>▪ For completely unvaccinated patients, TIG administration up to three weeks after injury may still be beneficial.<sup>4</sup></li></ul></li><li>• When administering both, TIG and tetanus toxoid vaccine should be given in separate syringes at different sites.<sup>3,7</sup></li><li>• Intravenous immune globulin (IVIG) is sometimes given (off-label) if TIG is not available.<sup>10</sup> Anti-tetanus antibodies vary widely from lot to lot with IVIG.<sup>10</sup></li><li>• For wound prophylaxis, TIG is given as a single 250 IU deep intramuscular dose.<sup>3,8-10</sup></li></ul>

Question	Answer/Pertinent Information		
Role for tetanus immune globulin (TIG), continued	<b>Tetanus Immunization History</b>	<b>Clean, minor wound</b> <sup>2,3,c</sup>	<b>All other wounds</b> <sup>2,3,a-c</sup>
	Unknown or <3 doses	TIG is <b>not indicated</b>	TIG is needed
	3 or more doses AND <5 years since last booster dose	TIG is <b>not indicated</b>	TIG is <b>not indicated</b>
	3 or more doses AND >5 years, but <10 years since last booster dose	TIG is <b>not indicated</b>	TIG is <b>not indicated</b>
	3 or more doses AND >10 years since last booster dose	TIG is <b>not indicated</b>	TIG is <b>not indicated</b>

- a. All other wounds: wounds such as, but not limited to, those contaminated with dirt, feces, soil, or saliva; puncture wounds; avulsions; and those resulting from missiles, crushing, burns, and frostbite.<sup>3</sup>
- b. **Per Canadian guidance:** patients with humoral immune deficiency (e.g., human immunodeficiency virus [HIV], agammaglobulinemia or hypogammaglobulinemia) may not adequately respond to tetanus toxoid vaccination. Therefore, patients with humoral immune deficiency with wounds that are not minor and clean should receive both TIG and tetanus toxoid vaccine, regardless of the time elapsed since the last booster.<sup>3</sup>
- c. **Per US guidance:** patients with HIV or severe immunodeficiency who have contaminated wounds should receive TIG, regardless of their tetanus immunization status.<sup>2</sup>

*--Continue to the next section for a Comparison of Available Tetanus Toxoid Vaccines--*

### Comparison of Available Tetanus Toxoid Vaccines

Tetanus toxoid vaccines are only available in combination with diphtheria, and can also be found in combination with other vaccines. Tetanus toxoid vaccines all have the same dose of tetanus toxoid. Pediatric tetanus-diphtheria vaccines contain a higher dose of diphtheria and pertussis, required for children under seven years (denoted by the capitals “D” and “P” in the descriptions [e.g., DT, DTaP]).<sup>12</sup> Product selection will depend on the appropriateness and dose requirement of the vaccine’s other components. This chart outlines routine tetanus immunization.

<b>ROUTINE VACCINATION</b> (Can be given at the same time as other routine vaccinations, in a different injection site. <sup>13</sup> )				
Vaccine Type	DOSE FREQUENCY			
	Children 6 weeks to less than 7 years	Children 7 years to 18 years (17 years [Canada])	Adults	Pregnancy
<b>DTaP</b> <i>(Infanrix [US only], Daptacel [US only])</i>  Combination products available in the US and Canada (See footnote a.)	<ul style="list-style-type: none"> <li>• <b>Five doses</b> of DTaP: 2, 4, and 6 months; 15 to 18 months (12 to 23 months [Canada]), and 4 to 6 years.<sup>3,5</sup></li> <li>• DTaP may be combined with other vaccinations in the same product. Product selection may depend on which other vaccinations are also needed.</li> </ul>	<ul style="list-style-type: none"> <li>• Not indicated for patients seven years and older.</li> </ul>	<ul style="list-style-type: none"> <li>• Not indicated for patients seven years and older.</li> </ul>	<ul style="list-style-type: none"> <li>• Not indicated for patients seven years and older.</li> </ul>
<b>DT</b> (US only)	<ul style="list-style-type: none"> <li>• <b>Alternative</b> to DTaP vaccines (above) when infants and children should not get a pertussis-containing vaccine.<sup>5,e</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Not indicated for patients seven years and older.</li> </ul>	<ul style="list-style-type: none"> <li>• Not indicated for patients seven years and older.</li> </ul>	<ul style="list-style-type: none"> <li>• Not indicated for patients seven years and older.</li> </ul>
<b>Td</b> <i>(Td Adsorbed, TdVax [US only], Tenivac [US only])</i>	<ul style="list-style-type: none"> <li>• Not indicated for patients less than seven years.</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Alternative</b> to Tdap (below) when a pertussis-containing vaccine should not be given.<sup>3,7</sup></li> </ul>	<ul style="list-style-type: none"> <li>• <b>Booster dose every ten years.</b><sup>5</sup> Either Td or Tdap (below) can be used.<sup>7,11,c</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Tdap (below) is preferred.<sup>7</sup></li> </ul>
<b>Tdap</b> <i>(Adacel, Boostrix)</i>  <b>Combination products</b> (Canada only): <sup>d</sup> Tdap-IPV	<ul style="list-style-type: none"> <li>• Not indicated for patients less than seven years.<sup>5</sup></li> <li>• Tdap-IPV may be used as an alternative to the DTaP dose given at 4 to 6 years of age in Canada.<sup>3</sup></li> </ul>	<ul style="list-style-type: none"> <li>• <b>US:</b> one dose at 11 or 12 years.<sup>1,5</sup></li> <li>• <b>Canada:</b> one dose at 14 to 16 years.<sup>3</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Adults should receive <b>one tetanus booster dose</b> containing pertussis.<sup>3</sup></li> <li>• Possible <b>alternative</b> to Td (above) for the every-ten-year tetanus booster.<sup>11,b,c</sup></li> <li>• <i>Boostrix</i> is preferred in the US for patients 65 years or older, but <i>Adacel</i> can also be used.<sup>5,11</sup></li> </ul>	<ul style="list-style-type: none"> <li>• <b>One dose with every pregnancy</b> to immunize against pertussis, preferably between 27 and 36 weeks gestation.<sup>3,5</sup></li> </ul>

- a. DTaP combination products: DTaP-IPV (*Kinrix* [US only], *Quadracel* [US only]), DTaP-IPV-Hib (*Pentacel* [US only], *Pediacel* [Canada only]), DTaP-IPV-HB (*Pediarix* [US only]), DTaP-IPV-Hib-HB (*Vaxelis* [US only], *Infanrix hexa* [Canada only]).
- b. New in 2020, in order to increase flexibility in product selection, Tdap can now be used in adults for indications where previously only Td was recommended (i.e., every ten-year booster, tetanus prophylaxis for wound management, and any required catch-up vaccinations). Repeated doses of Tdap do not appear to cause increased risks of adverse effects.<sup>1,11</sup>
- c. There do not appear to be serious safety concerns if there is an unknown or short interval between the administration of Tdap and a previous dose of Td or Tdap [Evidence Level C].<sup>1</sup> Observational data do suggest that there may be an increased risk of local injection site reactions (e.g., redness or swelling) when these vaccines are given at intervals of two years or less. The risk of more serious reactions (e.g., entire limb swelling, Arthus reactions [a type III hypersensitivity reaction involving severe pain, swelling, edema, etc]) does not appear to be increased with close administrations. However, it is still recommended that anyone (including pregnant women) with a history of Arthus reactions after a dose of Td or Tdap, should have an interval of at least ten years between doses.<sup>1</sup>
- d. Tdap combination products: Tdap-IPV (*Adacel-Polio* [Canada only], *Boostrix-Polio* [Canada only]).
- e. DT vaccines are no longer being manufactured in the US. Per the CDC, guidance will be coming on vaccination of patients who should not receive acellular pertussis-containing vaccines.<sup>14</sup>

**Abbreviations:** aP = high-dose acellular pertussis (for kids); ap = low-dose acellular pertussis (for adults); D = high-dose diphtheria (for kids); d = low-dose diphtheria (for adults); HB = hepatitis B; Hib = *Haemophilus influenzae* type b; IM = intramuscular; IPV = inactivated polio vaccine; T = tetanus.

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*Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.*

## Levels of Evidence

In accordance with our goal of providing Evidence-Based information, we are citing the **LEVEL OF EVIDENCE** for the clinical recommendations we publish.

Level	Definition	Study Quality
<b>A</b>	Good-quality patient-oriented evidence.*	<ol style="list-style-type: none"> <li>High-quality randomized controlled trial (RCT)</li> <li>Systematic review (SR)/Meta-analysis of RCTs with consistent findings</li> <li>All-or-none study</li> </ol>
<b>B</b>	Inconsistent or limited-quality patient-oriented evidence.*	<ol style="list-style-type: none"> <li>Lower-quality RCT</li> <li>SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings</li> <li>Cohort study</li> <li>Case control study</li> </ol>
<b>C</b>	Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening.	

\***Outcomes that matter to patients** (e.g., morbidity, mortality, symptom improvement, quality of life).

[Adapted from Ebell MH, Siwek J, Weiss BD, et al. Strength of recommendation taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. *Am Fam Physician*. 2004 Feb 1;69(3):548-56. <https://www.aafp.org/pubs/afp/issues/2004/0201/p548.html>.]

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## Potentially Harmful Drugs in Children

The chart below provides information and alternatives for potentially inappropriate drugs and excipients in pediatrics. This chart includes many drugs on the KIDS (**K**ey **P**otentially **I**nappropriate **D**rugs) List from the Pediatric Pharmacy Association, plus others with known risks not meeting inclusion criteria for the KIDS List. Think of this list as a “warning light” to think twice about using these medications in children, as with the Beers Criteria for the elderly.

Drug or Drug Class	Concern(s)	Other Considerations (e.g., alternatives)
<b>Analgesics</b>		
Aspirin	<ul style="list-style-type: none"> <li>Reye’s syndrome in children with suspected viral illness (e.g., flu, chickenpox)<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>High-dose aspirin is indicated for Kawasaki syndrome.<sup>2</sup></li> <li>For alternatives for pain, see our chart, <i>Keeping Pediatric Patients Safe</i>.</li> </ul>
Choline magnesium trisalicylate (US)	<ul style="list-style-type: none"> <li>Reye’s syndrome in children with suspected viral illness (e.g., flu, chickenpox)<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>For alternatives for pain, see our chart, <i>Keeping Pediatric Patients Safe</i>.</li> </ul>
Codeine	<ul style="list-style-type: none"> <li>Respiratory depression<sup>1,3</sup></li> </ul>	<ul style="list-style-type: none"> <li>For alternatives for pain and information on pharmacogenetic concerns, see our chart, <i>Keeping Pediatric Patients Safe</i>.</li> </ul>
Meperidine	<ul style="list-style-type: none"> <li>Respiratory depression, especially in neonates<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>See our FAQ, <i>Analgesics in Kids</i>, for alternatives.</li> </ul>
Oxycodone	<ul style="list-style-type: none"> <li>Respiratory depression<sup>3</sup></li> </ul>	<ul style="list-style-type: none"> <li>For alternatives for pain, see our chart, <i>Keeping Pediatric Patients Safe</i>.</li> </ul>
Hydrocodone	<ul style="list-style-type: none"> <li>Respiratory depression<sup>3</sup></li> </ul>	<ul style="list-style-type: none"> <li>For alternatives for pain, see our chart, <i>Keeping Pediatric Patients Safe</i>.</li> </ul>
Salsalate (US)	<ul style="list-style-type: none"> <li>Reye’s syndrome in children with suspected viral illness (e.g., flu, chickenpox)<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>For alternatives for pain, see our chart, <i>Keeping Pediatric Patients Safe</i>.</li> </ul>
Tramadol	<ul style="list-style-type: none"> <li>Respiratory depression<sup>1,3</sup></li> </ul>	<ul style="list-style-type: none"> <li>For alternatives for pain and information on pharmacogenetic concerns, see our chart, <i>Keeping Pediatric Patients Safe</i>.</li> </ul>

Drug or Drug Class	Concern(s)	Other Considerations (e.g., alternatives)
<b>Antibiotics, systemic</b>		
Azithromycin	<ul style="list-style-type: none"> <li>Hypertrophic pyloric stenosis in neonates<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>May be appropriate for <i>Bordetella pertussis</i>, <i>Chlamydia trachomatis</i> pneumonia, or <i>Ureaplasma</i>.<sup>1</sup></li> </ul>
Ceftriaxone	<ul style="list-style-type: none"> <li>Kernicterus in newborns<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>Acceptable for term infants without hyperbilirubinemia.<sup>2</sup> Cefazidime or cefepime may be appropriate alternatives (e.g., for meningitis).<sup>2</sup></li> </ul>
Chloramphenicol	<ul style="list-style-type: none"> <li>Grey baby syndrome (circulatory collapse) in neonates<sup>1,2</sup></li> </ul>	<ul style="list-style-type: none"> <li>Reserve last-line for serious infections.<sup>2</sup></li> <li>If used, monitor serum concentrations.<sup>1</sup></li> </ul>
Daptomycin	<ul style="list-style-type: none"> <li>Neuromuscular and skeletal adverse events in children &lt;1 year of age<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>Not a first-line agent.</li> <li>For skin/soft tissue infection or endocarditis, consider vancomycin.<sup>5,6</sup></li> </ul>
Demeclocycline (US)	<ul style="list-style-type: none"> <li>Tooth discoloration in children &lt;8 years of age<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>Rarely used as an antibiotic. For SIADH, consider fluid restriction, saline, diuresis, etc.<sup>47</sup></li> </ul>
Dicloxacillin	<ul style="list-style-type: none"> <li>Kernicterus in neonates<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>For methicillin-sensitive skin or soft tissue infection, consider cephalexin.<sup>5</sup></li> </ul>
Doxycycline	<ul style="list-style-type: none"> <li>Potential for tooth discoloration in children &lt;8 years of age<sup>2</sup></li> </ul>	<ul style="list-style-type: none"> <li>Controversial. Short-term use (<math>\leq 21</math> days) in children may not be associated with tooth discoloration.<sup>2</sup></li> </ul>
Erythromycin	<ul style="list-style-type: none"> <li>Hypertrophic pyloric stenosis in neonates<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>May be appropriate for <i>Chlamydia trachomatis</i> pneumonia.<sup>1</sup></li> </ul>
Fluoroquinolones	<ul style="list-style-type: none"> <li>Articular side effects.<sup>2</sup></li> </ul>	<ul style="list-style-type: none"> <li>May be appropriate for anthrax, complicated urinary tract infections, or pyelonephritis.<sup>2</sup></li> </ul>
Minocycline	<ul style="list-style-type: none"> <li>Abnormal skeletal and tooth development in children &lt;8 years of age<sup>2</sup></li> </ul>	<ul style="list-style-type: none"> <li>Do not use in children &lt;8 years of age.<sup>2</sup></li> </ul>
Nitrofurantoin	<ul style="list-style-type: none"> <li>Hemolytic anemia in neonates<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>Alternative: empiric therapy as for other febrile infants<sup>2</sup></li> </ul>



Drug or Drug Class	Concern(s)	Other Considerations (e.g., alternatives)
Sulfonamides (sulfamethoxazole, sulfadiazine [US])	<ul style="list-style-type: none"> <li>Kernicterus in neonates<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>Sulfadiazine (US) may be appropriate for congenital toxoplasmosis.<sup>1</sup></li> </ul>
Tetracycline	<ul style="list-style-type: none"> <li>Tooth discoloration and enamel hypoplasia in children, and interference with bone development in premature neonates<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>Avoid use in children &lt;8 years of age or &lt;12 years of age (Canadian labeling), unless other options are contraindicated or unlikely to be effective.<sup>9,10</sup></li> </ul>
Tigecycline	<ul style="list-style-type: none"> <li>Tooth discoloration and reversible inhibition of bone growth in children &lt;8 years of age<sup>11</sup></li> </ul>	<ul style="list-style-type: none"> <li>Use not recommended in children &lt;8 years of age (Canada: &lt;18 years of age, due to paucity of information in children).<sup>11,12</sup></li> </ul>
<b>Antidepressants</b>		
Desipramine	<ul style="list-style-type: none"> <li>Sudden cardiac death<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>For depression, escitalopram, fluoxetine, or sertraline; they have the best evidence in adolescents.<sup>4</sup> Fluoxetine is FDA-approved for depression in children ≥8 years of age.<sup>48</sup></li> </ul>
Imipramine	<ul style="list-style-type: none"> <li>Sudden cardiac death<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>For depression, escitalopram, fluoxetine, or sertraline; they have the best evidence in adolescents.<sup>4</sup> Fluoxetine is FDA-approved for depression in children ≥8 years of age.<sup>48</sup></li> <li>For ADHD, see our chart, <i>Comparison of ADHD Medications (US)(Canada)</i> for alternatives.</li> </ul>
Paroxetine	<ul style="list-style-type: none"> <li>May pose a higher suicide risk<sup>4</sup></li> </ul>	<ul style="list-style-type: none"> <li>For depression, escitalopram, fluoxetine, or sertraline; they have the best evidence in adolescents.<sup>4</sup> Fluoxetine is FDA-approved for depression in children ≥8 years of age.<sup>48</sup></li> <li>For anxiety disorders, consider sertraline, fluoxetine, fluvoxamine, or duloxetine.<sup>46</sup></li> </ul>
Venlafaxine	<ul style="list-style-type: none"> <li>May pose a higher suicide risk<sup>4</sup></li> </ul>	<ul style="list-style-type: none"> <li>For depression, escitalopram, fluoxetine, or sertraline; they have the best evidence in adolescents.<sup>4</sup> Fluoxetine is FDA-approved for depression in children ≥8 years of age.<sup>48</sup></li> <li>For anxiety disorders, consider sertraline, fluoxetine, fluvoxamine, or duloxetine.<sup>46</sup></li> </ul>

Drug or Drug Class	Concern(s)	Other Considerations (e.g., alternatives)
<b>Antiepileptics</b>		
Lamotrigine	<ul style="list-style-type: none"> <li>Serious dermatologic reaction<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>Titrate slowly.<sup>1</sup> Consult product labeling for titration schedule.</li> </ul>
Valproate, valproic acid	<ul style="list-style-type: none"> <li>Pancreatitis, hepatotoxicity, death in children &lt;6 years of age, especially &lt;2 years of age<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>Avoid in children &lt;2 years of age.<sup>1</sup> Use caution in children &lt;6 years of age.<sup>1</sup></li> <li>Symptoms may include abdominal pain, loss of appetite, vomiting, lethargy, weakness, fever, worsening seizure control, or jaundice.<sup>13,14</sup></li> <li>Parenteral valproate is a second-line option for status epilepticus.<sup>15</sup></li> </ul>
<b>Antiparasitic Agents, systemic</b>		
Ivermectin (oral)	<ul style="list-style-type: none"> <li>Encephalopathy in children &lt;1 year old<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>See our chart, <i>Management of Head Lice</i>, for alternatives.</li> <li>For scabies, if &lt;2 months of age, sulfur 5% to 10% ointment is safe.<sup>49</sup> If ≥2 months of age (Canada: ≥3 months of age), permethrin 5% cream is the drug of choice.<sup>49,50</sup></li> </ul>
<b>Antipsychotics</b>		
First-generation agents (e.g., haloperidol, chlorpromazine)	<ul style="list-style-type: none"> <li>Movement disorders, respiratory depression<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>Consider an atypical antipsychotic. Several are approved for use in children of various ages for schizophrenia (e.g., aripiprazole, paliperidone [US], quetiapine [US], quetiapine XR [US], risperidone [US]), autism irritability (aripiprazole [US], risperidone [US]), bipolar disorder (e.g., aripiprazole, asenapine [US], quetiapine [US], quetiapine XR [US], risperidone [US]), or Tourette's disorder (aripiprazole [US]).<sup>30-34,51,52</sup></li> </ul>
Olanzapine	<ul style="list-style-type: none"> <li>Higher risk of weight gain, hyperlipidemia, and hyperglycemia than other atypicals<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>Avoid use for more than 24 weeks.<sup>1</sup></li> <li>If using olanzapine or any alternative atypical antipsychotic, monitor for metabolic side effects. For a monitoring tool, see <a href="http://partnersforkids.org/wp-content/uploads/2020/04/APM-Lab-Monitoring-Tool_final.pdf">http://partnersforkids.org/wp-content/uploads/2020/04/APM-Lab-Monitoring-Tool_final.pdf</a>.</li> </ul>
<b>Antiretrovirals</b>		
Atazanavir	<ul style="list-style-type: none"> <li>Kernicterus in neonates<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>Consult guidelines for alternatives (e.g., <a href="https://clinicalinfo.hiv.gov/en/guidelines/pediatric-arv/whats-new">https://clinicalinfo.hiv.gov/en/guidelines/pediatric-arv/whats-new</a>).</li> </ul>
Darunavir	<ul style="list-style-type: none"> <li>Seizures and death in children &lt;3 years of age or &lt;10 kg<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>Consult guidelines for alternatives (e.g., <a href="https://clinicalinfo.hiv.gov/en/guidelines/pediatric-arv/whats-new">https://clinicalinfo.hiv.gov/en/guidelines/pediatric-arv/whats-new</a>).</li> </ul>
Indinavir	<ul style="list-style-type: none"> <li>Kidney stones (children) and kernicterus (neonates)<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>Consult guidelines for alternatives (e.g., <a href="https://clinicalinfo.hiv.gov/en/guidelines/pediatric-arv/whats-new">https://clinicalinfo.hiv.gov/en/guidelines/pediatric-arv/whats-new</a>).</li> </ul>

Drug or Drug Class	Concern(s)	Other Considerations (e.g., alternatives)
<b>Cardiac Drugs</b>		
Aspirin	<ul style="list-style-type: none"> <li>Reye's syndrome<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>High-dose aspirin is indicated for Kawasaki syndrome.<sup>2</sup></li> </ul>
Verapamil	<ul style="list-style-type: none"> <li>Asystole in children &lt;1 year of age<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>First-line antihypertensives in kids include ACEIs, ARBs, and long-acting dihydropyridine calcium channel blockers.<sup>53,54</sup></li> </ul>
<b>Central Nervous System Agents, misc.</b>		
Midazolam	<ul style="list-style-type: none"> <li>Intraventricular hemorrhage, periventricular leukomalacia, or death in very low birth weight (&lt;1,500 g) infants<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>Routine use of sedation/analgesia is not recommended in preterm neonates. Consider conservatively-dosed morphine, for the shortest duration necessary, if pharmacotherapy is deemed necessary for sedation in a mechanically ventilated neonate.<sup>16</sup></li> </ul>
Naloxone	<ul style="list-style-type: none"> <li>Seizures in neonates when used for postpartum resuscitation<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>Follow Neonatal Advanced Life Support algorithm.</li> </ul>
Propofol	<ul style="list-style-type: none"> <li>Doses &gt;4 mg/kg/hour for &gt;48 hours associated with propofol-related infusion syndrome<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>Watch for cardiac depression, arrhythmias, rhabdomyolysis, metabolic acidosis, hyperkalemia, lipemic plasma, or elevation of serum creatinine or transaminases.<sup>55</sup></li> </ul>
<b>Cough, Cold, and Allergy Medications</b>		
Antihistamines	<ul style="list-style-type: none"> <li>The risks of side effects or overdose of over-the-counter cough and cold medicines may outweigh benefit in children &lt;6 years of age<sup>18,22</sup></li> </ul>	<ul style="list-style-type: none"> <li>For treatment options for seasonal allergies, see our chart, <i>Managing Seasonal Allergies</i>.</li> <li>Diphenhydramine may be more commonly associated with adverse effects and toxicity than other "first generation" antihistamines.<sup>36,56</sup></li> <li>Avoid carbinoxamine (<i>Karbinal ER</i>, US) in children &lt;2 years of age due to reports of death in this age group.<sup>37</sup></li> </ul>
Cough medicines (e.g., dextromethorphan, codeine)  <i>Continued...</i>	<ul style="list-style-type: none"> <li>The risks of side effects or overdose of over-the-counter cough and cold medicines may outweigh benefit in children &lt;6 years of age<sup>18,22</sup></li> <li>Respiratory depression (codeine, hydrocodone).<sup>20,38</sup></li> </ul>	<ul style="list-style-type: none"> <li>Consider fluids to thin the mucus to make it easier to cough up.<sup>23</sup></li> <li>Consider honey for children ≥1 year of age:<sup>18</sup> <ul style="list-style-type: none"> <li>One to five years of age: 2.5 mL</li> <li>Six to 12 years of age: 5 mL</li> <li>≥12 years of age: 10 mL</li> </ul> </li> <li>Consider cough drops/lozenges for children ≥4 years of age.<sup>18</sup></li> <li>Consider benzonatate (US only) for children ≥10 years of age.<sup>20,21</sup></li> </ul>

Drug or Drug Class	Concern(s)	Other Considerations (e.g., alternatives)
Cough medicine, continued		<ul style="list-style-type: none"> <li>Consider a mentholated rub for children <math>\geq 2</math> years of age (see camphor, below).<sup>18</sup></li> <li>US: codeine- and hydrocodone-containing cough medicines are indicated for adults only.<sup>20</sup></li> <li>Canada: codeine is not recommended for any use in children <math>&lt; 12</math> years of age, and hydrocodone is not recommended in children <math>&lt; 6</math> years of age.<sup>38</sup></li> </ul>
Decongestants (e.g., pseudoephedrine, phenylephrine)	<ul style="list-style-type: none"> <li>The risks of side effects or overdose of over-the-counter cough and cold medicines may outweigh benefit in children <math>&lt; 6</math> years of age.<sup>18,22</sup></li> </ul>	<ul style="list-style-type: none"> <li>Consider saline nose drops or spray, with a rubber suction bulb for infants.<sup>18</sup></li> <li>Consider humidity from a warm shower, or vaporizer or humidifier (follow safety and cleaning instructions).<sup>18,23</sup></li> <li>For treatment options for seasonal allergies, see our chart, <i>Managing Seasonal Allergies</i>.</li> </ul>
<b>Excipients</b>		
Benzyl alcohol, sodium benzoate, benzoic acid	<ul style="list-style-type: none"> <li>Gaspings syndrome in neonates<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>Limit is <math>\leq 99</math> mg/kg/day in neonates.<sup>1</sup> Therefore, many medications that contain it may not exceed limit in small doses.</li> <li>Sodium phenylacetate/sodium benzoate (<i>Ammonul</i>) ok for treatment of urea cycle disorders.<sup>1</sup></li> </ul>
Ethanol	<ul style="list-style-type: none"> <li>CNS depression, hypoglycemia<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>Use caution in children <math>&lt; 6</math> years of age.<sup>1</sup> Max 5% vol/vol.<sup>1</sup></li> <li>Ethanol lock therapy is acceptable.<sup>1</sup> Follow institutional guidelines for age/weight.</li> </ul>
Parabens	<ul style="list-style-type: none"> <li>Kernicterus<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>Use caution in children <math>&lt; 2</math> months of age<sup>1</sup></li> </ul>
Phenylalanine	<ul style="list-style-type: none"> <li>CNS damage in children with phenylketonuria<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>Avoid if phenylketonuria test is positive or result is unknown.<sup>1</sup></li> </ul>
Polysorbate 80	<ul style="list-style-type: none"> <li>Renal and liver failure, thrombocytopenia (“E-Ferol syndrome,” named after the intravenous vitamin E supplement with which it was reported in the mid-1980s)<sup>45</sup></li> </ul>	<ul style="list-style-type: none"> <li>Avoid in children <math>&lt; 1</math> year of age.<sup>1</sup></li> </ul>

Drug or Drug Class	Concern(s)	Other Considerations (e.g., alternatives)
Propylene glycol (e.g., in lorazepam)	<ul style="list-style-type: none"> <li>Lactic acidosis, CNS effects (e.g., seizures, CNS depression), hypoglycemia, hemolysis<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>Avoid &gt;3 g/day in neonates, and use caution with doses &gt;34 mg/kg/day in neonates.<sup>1</sup></li> </ul>
<b>Gastrointestinal Drugs</b>		
Bismuth subsalicylate	<ul style="list-style-type: none"> <li>Reye's syndrome in children with suspected viral illness (e.g., flu, chickenpox)<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>Can use for travelers' diarrhea in children ≥3 years of age (Canada: or ≥2 years of age).<sup>19</sup></li> <li>See our charts, <i>Acute Infectious Diarrhea</i> for alternatives.</li> </ul>
Dicyclomine	<ul style="list-style-type: none"> <li>Apnea in children &lt;6 months of age<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>For colic, no pharmacotherapy has been shown to be safe and effective. Address parental behaviors and expectations. Consider changing feeding technique or environment.<sup>17</sup> Probiotics (<i>Limosilactobacillus .reuteri</i> DSM 17938 drops) are possibly effective<sup>17,25</sup></li> </ul>
Diphenoxylate and atropine	<ul style="list-style-type: none"> <li>Respiratory depression and death in children &lt;6 years of age<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>See our charts, <i>Acute Infectious Diarrhea</i> for alternatives.</li> </ul>
Linaclotide	<ul style="list-style-type: none"> <li>Death from dehydration in children &lt;6 years of age<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>Pharmacotherapy for IBS in children has been poorly studied. Consider parent and child education, cognitive behavioral therapy, and treatment of anxiety or depression.<sup>24</sup></li> </ul>
Loperamide	<ul style="list-style-type: none"> <li>Ileus, lethargy, and rarely death in children &lt;3 years of age with acute infectious diarrhea<sup>43</sup></li> </ul>	<ul style="list-style-type: none"> <li>See our charts, <i>Acute Infectious Diarrhea</i> for alternatives.</li> </ul>
Metoclopramide	<ul style="list-style-type: none"> <li>Movement disorders (e.g., dystonia), respiratory depression<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>Avoid in children &lt;2 years of age.<sup>1</sup></li> <li>Consider ondansetron (e.g., for gastroenteritis).<sup>26</sup></li> <li>For information on use for treatment of pediatric migraine, see our chart. <i>Drugs for Acute Migraine</i>.</li> </ul>
Mineral oil (oral)	<ul style="list-style-type: none"> <li>Lipoid pneumonia in children &lt;1 year of age<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>See our chart, <i>Management of Constipation</i>, for alternatives.</li> </ul>
Plecanatide ( <i>Trulance</i> )	<ul style="list-style-type: none"> <li>Dehydration and death in children &lt;6 years of age<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>Pharmacotherapy for IBS in children has been poorly studied. Consider parent and child education, cognitive behavioral therapy, and treatment of anxiety or depression.<sup>24</sup></li> </ul>

Drug or Drug Class	Concern(s)	Other Considerations (e.g., alternatives)
Prochlorperazine	<ul style="list-style-type: none"> <li>• Movement disorders (e.g., dystonia), respiratory depression<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Avoid in children &lt;2 years or older children &lt;9 kg.<sup>13</sup></li> <li>• Consider ondansetron (e.g., for gastroenteritis).<sup>26</sup></li> <li>• For information on use for treatment of pediatric migraine, see our chart. <i>Drugs for Acute Migraine.</i></li> </ul>
Promethazine	<ul style="list-style-type: none"> <li>• Fatal respiratory depression in children &lt;2 years of age<sup>13</sup></li> <li>• Extravasation injury<sup>13</sup></li> <li>• Movement disorders (e.g., dystonia)<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Consider rectal route over parenteral (for children ≥2 years of age, with caution), or ondansetron (e.g., for gastroenteritis).<sup>13,26</sup></li> <li>• For alternatives for treatment of pediatric migraine, see our chart. <i>Drugs for Acute Migraine.</i></li> <li>•</li> </ul>
Sodium phosphate enema	<ul style="list-style-type: none"> <li>• Electrolyte imbalance, acute kidney injury, arrhythmia, and death in children &lt;2 years of age<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>• See our chart, <i>Management of Constipation</i>, for alternatives.</li> </ul>
Sodium polystyrene sulfonate	<ul style="list-style-type: none"> <li>• Colonic perforation<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Avoid in very low birth weight neonates.<sup>1</sup> Consider insulin/glucose.<sup>27</sup></li> </ul>
<b>Topicals</b>		
Benzocaine	<ul style="list-style-type: none"> <li>• Methemoglobinemia when used for teething or pharyngitis in children &lt;2 years of age<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>• For alternatives for <b>teething</b>, see the FDA’s “Safely Soothing Teething Pain and Sensory Needs in Babies and Older Children” at <a href="https://www.fda.gov/consumers/consumer-updates/safely-soothing-teething-pain-and-sensory-needs-babies-and-older-children">https://www.fda.gov/consumers/consumer-updates/safely-soothing-teething-pain-and-sensory-needs-babies-and-older-children</a>.</li> <li>• For <b>pharyngitis</b>, consider acetaminophen or ibuprofen.<sup>28</sup></li> </ul>
Camphor (e.g., in <i>Vicks VapoRub</i> )	<ul style="list-style-type: none"> <li>• Skin, eye, and nose irritation<sup>29</sup></li> <li>• Systemic toxicity (e.g., confusion, seizures, vomiting, bradycardia), mostly with ingestion.<sup>7</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Use as directed, and only in children ≥2 years of age.<sup>23</sup> Put the product out of the child’s reach after use.<sup>23</sup></li> </ul>
Chlorhexidine	<ul style="list-style-type: none"> <li>• Chemical burns in very low birth weight neonates<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Most neonatal intensive care units use chlorhexidine, but it must be used with caution.<sup>1,42</sup> Assess and document skin condition at each use.<sup>8</sup> To reduce exposure, avoid pooling of the antiseptic under the neonate, and rinse the skin with saline after use.<sup>41,44</sup> Avoidance of alcohol-containing solutions has also been suggested.<sup>41,44</sup></li> </ul>

Drug or Drug Class	Concern(s)	Other Considerations (e.g., alternatives)
Corticosteroids, medium to very high potency	<ul style="list-style-type: none"> <li>Adrenal suppression due to high systemic absorption when used in children &lt;1 year of age<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>Low-potency corticosteroid (e.g., hydrocortisone 1% cream).<sup>35</sup></li> </ul>
Gentamicin ophthalmic ointment	<ul style="list-style-type: none"> <li>Severe ocular reactions in neonates<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>For neonatal ocular prophylaxis, erythromycin 0.5% ophthalmic ointment is recommended (US).<sup>39</sup></li> </ul>
Hexachlorophene	<ul style="list-style-type: none"> <li>Neurotoxicity in neonates<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>See chlorhexidine, above.</li> </ul>
Isopropyl alcohol	<ul style="list-style-type: none"> <li>Chemical burn in very low birth weight neonates<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>See chlorhexidine, above.</li> </ul>
Lidocaine 2%, viscous	<ul style="list-style-type: none"> <li>Seizures, arrhythmia, CNS depression, death when used for teething<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>For alternatives for teething, see the FDA’s “Safely Soothing Teething Pain and Sensory Needs in Babies and Older Children” at <a href="https://www.fda.gov/consumers/consumer-updates/safely-soothing-teething-pain-and-sensory-needs-babies-and-older-children">https://www.fda.gov/consumers/consumer-updates/safely-soothing-teething-pain-and-sensory-needs-babies-and-older-children</a>.</li> </ul>
Lindane	<ul style="list-style-type: none"> <li>Seizures and spasms in children &lt;10 years of age or &lt;50 kg<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>See our chart, <i>Management of Head Lice</i>, for alternatives.</li> </ul>
Malathion	<ul style="list-style-type: none"> <li>Organophosphate poisoning in children &lt;1 year of age<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>See our chart, <i>Management of Head Lice</i>, for alternatives.</li> </ul>
Methyl salicylate	<ul style="list-style-type: none"> <li>Reye’s syndrome in children with suspected viral illness (e.g., flu, chickenpox)<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>For alternatives for pain and information on pharmacogenetic concerns, see our chart, <i>Keeping Pediatric Patients Safe</i>.</li> </ul>
Silver sulfadiazine	<ul style="list-style-type: none"> <li>Kernicterus in neonates<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>For umbilical care, consider dry cord care.<sup>40</sup></li> </ul>

**Abbreviations:** ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; CNS = central nervous system; IBS = irritable bowel syndrome; OTC = over-the-counter; SIADH = syndrome of inappropriate antidiuretic hormone secretion

*Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.*

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