

DRUG TREATMENTS FOR CHILDREN AND ADOLESCENTS WITH COVID-19



This flowchart applies to **children and adolescents up to 16 years of age**. Depending on physical size and/or developmental status, either paediatric or adult guidance can be applied.

Where appropriate, based on age or physical size, refer to the flowchart on **DRUG TREATMENTS FOR ADULTS WITH COVID-19**

DEFINITION OF DISEASE SEVERITY*	Mild	Moderate	Severe	Critical
	<p>Not requiring oxygen</p> <p>Respiratory/vital signs</p> <ul style="list-style-type: none"> No or mild upper respiratory tract symptoms No or mild work of breathing <p>Feeding/hydration/conscious state</p> <ul style="list-style-type: none"> Normal or mildly reduced feeding 	<p>Requiring low-flow oxygen</p> <p>Respiratory/vital signs</p> <ul style="list-style-type: none"> Moderate work of breathing Abnormal vital signs for age (tachycardia, tachypnoea) but does not persistently breach Early Warning System (e.g. Medical Emergency Team) Criteria ** Brief self-resolving apnoea (infants) <p>Feeding/hydration/conscious state</p> <ul style="list-style-type: none"> Poor feeding, unable to maintain hydration without nasogastric or IV fluids, and Normal conscious state 	<p>Requiring high-flow oxygen or non-invasive ventilation</p> <p>Respiratory/vital signs</p> <ul style="list-style-type: none"> Moderate-severe work of breathing Abnormal vital signs for age (tachycardia, tachypnoea) with breaches of Early Warning System (e.g. Medical Emergency Team) Criteria Apnoea needing support/stimulation (infants) <p>Feeding/hydration/conscious state</p> <ul style="list-style-type: none"> Poor feeding, unable to maintain hydration without nasogastric or IV fluids Drowsy/tired but easily rousable 	<p>Requiring invasive mechanical ventilation</p> <p>Respiratory/vital signs</p> <ul style="list-style-type: none"> Unable to maintain breathing or prevent apnoea without advanced modes of support Abnormal vital signs for age with persistent breaches of Early Warning System (e.g. Medical Emergency Team) Criteria Haemodynamically unstable without inotropic or vasopressor support Other organ failure <p>Feeding/hydration/conscious state</p> <ul style="list-style-type: none"> Poor feeding, unable to maintain hydration without nasogastric or IV fluids Altered conscious state/unconscious

Children with common childhood illness such as croup or bronchiolitis can also be SARS-CoV-2 positive. In general, treat as for croup and bronchiolitis. Seek expert advice about COVID-specific therapy, particularly for older children, adolescents and those with severe comorbidities.

CONDITIONAL RECOMMENDATION FOR	Mild	Moderate	Severe	Critical
	<p>Consider using inhaled corticosteroids (budesonide or ciclesonide) within 14 days of symptom onset for the treatment of symptomatic COVID-19 in children and adolescents who do not require oxygen and who have one or more risk factors[^] for disease progression.[#]</p>	<p>Consider using dexamethasone daily intravenously or orally for up to 10 days (or acceptable alternative regimen) in children and adolescents with acute COVID-19 who require oxygen (including mechanically ventilated patients).</p>	<p>Consider using tocilizumab[‡] for the treatment of COVID-19 in children and adolescents who require supplemental oxygen, particularly where there is evidence of systemic inflammation.[#]</p>	

CONSENSUS RECOMMENDATION FOR	Mild	Moderate	Severe	Critical
	<p>Consider using one of the following:</p> <p>Consider using, in exceptional circumstances, nirmatrelvir plus ritonavir (Paxlovid)^{###} for the treatment of COVID-19 within 5 days of symptom onset in children and adolescents aged 12 years and over and weighing at least 40 kg who do not require oxygen and who are at high risk[^] of deterioration.[#]</p> <p>Consider using nirmatrelvir plus ritonavir in eligible children and adolescents who have not received a vaccine dose or had a SARS-CoV-2 infection in the past 6 months, those who are immunocompromised regardless of vaccination / previous infection status, or those who are not eligible for vaccination based on age but who are at high risk of disease progression. Do not routinely use nirmatrelvir plus ritonavir in children and adolescents who have received a vaccine dose or had a SARS-CoV-2 infection in the past 6 months unless immunocompromised.</p> <p>Decisions about the appropriateness of treatment with nirmatrelvir plus ritonavir should be based on the individual's risk of severe disease, including their age, presence of multiple risk factors, and whether they have received a COVID-19 vaccine dose or had a SARS-CoV-2 infection in the past 6 months.</p>		<p>Consider using, in exceptional circumstances, remdesivir for the treatment of COVID-19 in children and adolescents aged 28 days or older and weighing at least 3 kg who are hospitalised with severe COVID-19 (considered likely to progress to ventilation), who require systemic corticosteroids and oxygen but do not require non-invasive or invasive ventilation, where other treatments are not available / appropriate.^{##}</p>	<p>Consider using baricitinib[‡] for the treatment of COVID-19 in children and adolescents who require non-invasive or invasive ventilation.</p>

Not requiring oxygen	Not requiring oxygen	Requiring oxygen but not invasive mechanical ventilation	Requiring invasive mechanical ventilation
<p>Consider using, in exceptional circumstances, tixagevimab plus cilgavimab (Evusheld) for the treatment of COVID-19 within 5 days of symptom onset in children and adolescents aged 12 years and over and weighing at least 40 kg who do not require oxygen and who are at high risk[^] of deterioration.[#]</p> <p>Consider using tixagevimab plus cilgavimab in eligible children and adolescents who have not received a vaccine dose or had a SARS-CoV-2 infection in the past 6 months, or those who are immunocompromised regardless of vaccination / previous infection status. Do not routinely use tixagevimab plus cilgavimab in children and adolescents who have received a vaccine dose or had a SARS-CoV-2 infection in the past 6 months unless immunocompromised.</p> <p>Decisions about the appropriateness of treatment with tixagevimab plus cilgavimab should be based on the individual's risk of severe disease, including their age, presence of multiple risk factors, and whether they have received a COVID-19 vaccine dose or had a SARS-CoV-2 infection in the past 6 months.</p>	<p>Consider using, in exceptional circumstances, tixagevimab plus cilgavimab (Evusheld) for the treatment of COVID-19 within 12 days of symptom onset in children and adolescents aged 12 years and over and weighing at least 40 kg who require oxygen but not mechanical ventilation, and who are at high risk[^] of deterioration.[#]</p> <p>Consider using tixagevimab plus cilgavimab in children and adolescents who have not received a vaccine dose or had a SARS-CoV-2 infection in the past 6 months, or those who are immunocompromised regardless of vaccination/ previous infection status. Do not routinely use tixagevimab plus cilgavimab in children and adolescents who have received a vaccine dose or had a SARS-CoV-2 infection in the past 6 months unless immunocompromised.</p> <p>Decisions about the appropriateness of treatment with tixagevimab plus cilgavimab should be based on the individual's risk of severe disease, including their age, presence of multiple risk factors, and whether they have received a COVID-19 vaccine dose or had a SARS-CoV-2 infection in the past 6 months.</p>		
<p>Consider using, in exceptional circumstances, remdesivir for the treatment of COVID-19 within 7 days of symptom onset in children and adolescents aged 28 days and over and weighing at least 3 kg who do not require oxygen and are at high risk[^] of deterioration, where other treatments are not available/ appropriate.^{##}</p> <p>Consider using remdesivir in eligible children and adolescents who have not received a vaccine dose or had a SARS-CoV-2 infection in the past 6 months, or those who are immunosuppressed regardless of vaccination / previous infection status, or those who are not eligible for vaccination based on age but who are at high risk of disease progression. Do not routinely use remdesivir in children and adolescents who have received a vaccine dose or had a SARS-CoV-2 infection in the past 6 months unless immunocompromised.</p> <p>Decisions about the appropriateness of treatment with remdesivir should be based on the individual's risk of severe disease, including their age, presence of multiple risk factors, and whether they have received a COVID-19 vaccine dose or had a SARS-CoV-2 infection in the past 6 months.</p>			
<p>DO NOT routinely use dexamethasone (or other oral or parenteral steroids) to treat COVID-19 in children and adolescents who do not require oxygen.</p>			
<p>DO NOT use the following for the treatment of COVID-19:</p> <ul style="list-style-type: none"> • aspirin • azithromycin • colchicine • favipiravir 	<ul style="list-style-type: none"> • hydroxychloroquine • hydroxychloroquine plus azithromycin • interferon β-1a • interferon β-1a plus lopinavir-ritonavir 		<ul style="list-style-type: none"> • ivermectin • lopinavir-ritonavir
	<p>DO NOT use convalescent plasma for the treatment of COVID-19 in patients who require supplemental oxygen.</p>		<p>DO NOT start remdesivir in children or adolescents hospitalised with COVID-19 who require non-invasive or invasive ventilation.</p>

CONSENSUS RECOMMENDATION FOR (CONT.)

CONDITIONAL RECOMMENDATION AGAINST

NOT RECOMMENDED

Please refer to the bottom of page 3 of this flowchart for footnotes

	Not requiring oxygen	Not requiring oxygen	Requiring oxygen but not invasive mechanical ventilation	Requiring invasive mechanical ventilation
ONLY IN RESEARCH	DO NOT use nirmatrelvir plus ritonavir (Paxlovid) for the treatment of COVID-19 in children under 12 years of age without risk factors [^] for deterioration who do not require oxygen , outside of randomised trials with appropriate ethical approval.			
	DO NOT use tixagevimab plus cilgavimab (Evusheld) for the treatment of COVID-19 in children under 12 years of age without risk factors [^] for deterioration who do not require oxygen outside of randomised trials with appropriate ethical approval.			
	DO NOT use convalescent plasma for the treatment of COVID-19 in patients who do not require oxygen outside of randomised trials with appropriate ethical approval.			
	<p>Do not use the following for the treatment of COVID-19 outside of randomised trials with appropriate ethical approval:</p> <ul style="list-style-type: none"> • anakinra • angiotensin 2 receptor agonist C21 • aprepitant • baloxavir marboxil • bamlanivimab • bamlanivimab plus etesevimab • bebtelovimab • bromhexine hydrochloride • camostat mesilate • CD24Fc • chloroquine • combined metabolic activators (CMA) • darunavir-cobicistat • doxycycline • dutasteride • enisamium • ensovibep • fluvoxamine • human umbilical cord mesenchymal stem cells • immunoglobulin • immunoglobulin plus methylprednisone • inhaled interferon β-1a • interferon β-1b • interferon gamma • interferon kappa plus trefoil factor 2 (IFN-K plus TFF2) • ivermectin plus doxycycline • lenzilumab • metformin • molnupiravir (Lagevrio) • N-acetylcysteine • nitazoxanide • opaganib • peginterferon lambda • recombinant human granulocyte colony-stimulating factor (rhG-CSF) • regdanvimab • ruxolitinib • sabizabulin • sarilumab • sofosbuvir-daclatasvir • sulodexide • telmisartan • tofacitinib • triazavirin • umifenovir • vitamin C • vitamin D analogues (calcifediol / cholecalciferol) • zinc • other disease-modifying treatments 			
[^] RISK FACTORS FOR DISEASE PROGRESSION	<p>Risk factors for disease progression Based on international cohort studies (Children with SARS-CoV-2 in the National COVID Cohort Collaborative [N3C]), risk factors for deterioration / disease progression include:</p> <ul style="list-style-type: none"> • paediatric complex chronic conditions (PCCC): congenital and genetic, cardiovascular, gastrointestinal, malignancies, metabolic, neuromuscular, renal and respiratory conditions • severe asthma (for example, in the past 12 months ≥ 1 exacerbation requiring ICU admission or IV treatment, OR ≥ 2 hospital admissions for asthma; children requiring biologic therapy for symptoms) • obesity (above the 95th percentile on BMI for age growth chart) 			
	<p>Refer to the Decision Support Tool for specific guidance on drug treatments for at risk children and adolescents with COVID-19 who do not require oxygen.</p>			
	<p>Source National COVID-19 Clinical Evidence Taskforce – Australian guidelines for the clinical care of people with COVID-19.</p>			

Note 1: This flowchart does not apply to children and adolescents on home oxygen due to pre-existing conditions. Use clinical judgement in these cases.

Note 2: Sotrovimab or Ronapreve (casirivimab plus imdevimab) can be used in the target population but have been omitted due to reduced effectiveness against the circulating Omicron variant. The Taskforce is aware of concerns about the potential for decreased effectiveness of Evusheld (tixagevimab plus cilgavimab) against the BA.4 and BA.5 Omicron sub-variants, based on in vitro data. Recommendations will be updated when definitive evidence becomes available.

Refer to the Australian guidelines for the clinical care of people with COVID-19 for guidance on the use of **pulse oximetry** in children and adolescents.

* These disease severity definitions are intended to be a guide for clinicians and disease severity assessment should also take into account individual patient factors with appropriate assessment by trained clinicians. Cardiorespiratory and vital parameters must be considered within the normal age-appropriate ranges for neonates and children. If criteria fall across different severity classifications, use the more severe classification to manage illness. Comorbidities (e.g. preterm infants, oncology, immunosuppressed, etc.) may increase the risk of more severe disease.

** Temperature instability should be considered an abnormal vital sign in infants. Fever is common in children and does not contribute to determination of illness severity in isolation.

‡ Consider using either tocilizumab or baricitinib. There are limited safety data on concurrent use of these drugs.

Not approved for use by TGA for this indication.

Remdesivir is not TGA approved for mild disease in children <40 kg. There are potential concerns with the use of cyclodextrin in infants, so the benefits and risks should be carefully assessed.

Check for common, serious drug-drug interactions before prescribing and administering nirmatrelvir plus ritonavir (Paxlovid) with other medications.