Framework for the Management of Symptomatic COVID in Children

### Significant comorbidity (see Box 1 for specific criteria):

- **NATIONAL MEDICINES STOCKPILE (NMS) CRITERIA:**
  - Congenital heart defects
  - Congenital lung defects with significant hypoxia
  - Severe immunodeficiency
  - Respiratory failure requiring invasive ventilation

### Significant immunosuppression:

- Primary or acquired immunodeficiency
- Congenital hematopoietic stem cell disorders
- Genetic (including trisomy 21)
- Pneumonia requiring prolonged antibiotic therapy
- Hematopoietic malignancies
- Autoimmune hemolytic anemia
- Primary or acquired immunodeficiency

### Chemoprophylaxis with casirivimab-imdevimab

- Recommended for children aged ≥4 years with congenital heart defects and symptomatic COVID-19
- Dose: 1000 mg iv split over 2 days

### Chemoprophylaxis with baricitinib

- Recommended for children with symptomatic COVID-19 and severe systemic inflammation
- Dose: 2 mg po daily

### Chemoprophylaxis with tocilizumab

- Recommended for children with symptomatic COVID-19 and severe systemic inflammation
- Dose: 800 mg iv single dose

### Immunocompetent

- Fully COVID vaccinated

### Immunosuppressed

- Not hypoxic

- Hypoxic, \( \text{SaO}_2 \geq 93\% \) in room air

#### Symptom onset ≤ 5 days prior

- No Rx

#### Symptom onset > 5 days prior

- Yes

### Discuss with ID to Consider Remdesivir

- No Rx

### Symptom onset ≤ 7 days prior

- Yes

### Symptom onset > 7 days prior

- No

### Discuss with ID to Consider Casirivimab-imdevimab

- No Rx

### Discuss with ID to Consider Tocilizumab

- No (or if Tocilizumab unavailable)

### Box 1: Specific criteria for significant comorbidity:

- **1.** Chronic obstructive lung disease
  - CF (or bronchiectasis) + FEV₁ <60%
  - Congenital tracheal stenosis
  - Chronic lung disease with pulmonary hypertension Rx O₂
  - Neumuscular dis (req daytime resp support)
  - Tracheostomy req ventilation
- **2.** Heart failure
  - Cardiomyopathy (requiring diuretics)
  - Not fully vaccinated
  - Significant immunosuppression
  - Significant immunsuppression
- **3.** Severe asthma
  - In last 12m, ≥3 exacerbation requiring ICU admission or iv treatment OR
  - High-dose inhaled corticosteroid to control symptoms OR
  - Moderate-dose inhaled corticosteroid plus LABA to control symptoms
- **4.** Biologics or DMARDs
  - Select biologics or DMARDs are those where a 3rd primary dose of COVID-19 vaccine is recommended by ATAGI (see Recommendations on the use of a 3rd primary dose of COVID-19 vaccine in individuals who are severely immunocompromised [health.gov.au])

### Table: Medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remdesivir*</td>
<td>[via NMS] D1: 5 mg/kg (max 200 mg) iv load D2-D5: 2.5 mg/kg (max 100 mg) iv daily</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>0.15 mg/kg (max 6 mg) x po daily up to 10 days</td>
</tr>
<tr>
<td>Casirivimab-imdevimab</td>
<td>800 mg iv single dose</td>
</tr>
<tr>
<td>Baricitinib*</td>
<td>2.5 mg po daily</td>
</tr>
<tr>
<td>Tocilizumab</td>
<td>ONE iv stat dose&lt;br&gt;90 kg; 8 mg/kg&lt;br&gt;30–40 kg; 8 mg/kg&lt;br&gt;41–65 kg; 400 mg&lt;br&gt;66–90 kg; 600 mg&lt;br&gt;≥90 kg; 800 mg</td>
</tr>
</tbody>
</table>

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*Alternative to Budesonide:

Flixotide MDI via spacer

- <5y: 125 µg bd
- ≥5y: 250 µg bd

**Chemoprophylaxis with casirivimab-imdevimab** should be considered on a case-by-case basis in discussion with ID in children with ALL of the following criteria:

- Households or significant case exposure ≤4 days prior
- ≥12y

**Chemoprophylaxis with baricitinib**

- <60% flow rate >30 L/min and \( \text{FiO}_2 \) >40%

**Chemoprophylaxis with tocilizumab**

- ≤90 kg: 800 mg iv single dose
- >90 kg: 1600 mg iv single dose

<table>
<thead>
<tr>
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<th>Dosage</th>
</tr>
</thead>
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</tr>
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<td>Baricitinib*</td>
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<tr>
<td>Tocilizumab</td>
<td>ONE iv stat dose&lt;br&gt;90 kg; 8 mg/kg&lt;br&gt;30–40 kg; 8 mg/kg&lt;br&gt;41–65 kg; 400 mg&lt;br&gt;66–90 kg; 600 mg&lt;br&gt;≥90 kg; 800 mg</td>
</tr>
</tbody>
</table>

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Amanda Gwee, Hanna Holschier and Nigel Curtis on behalf of RCH Infectious Diseases, Version 3.6, Nov 2021

This framework provides a framework for decisions around the treatment of children with symptomatic COVID-19. This should be adapted for local use in line with institutional and governance requirements.

This is based on evidence from trials in adults and drugs that are prescribed off label should have informed parent/guardian consent (e.g., *Remdesivir* and *Baricitinib*).

To be used only in conjunction with COVID-19 medication guideline documents that detail contraindications to be considered in all cases.

Thromboprophylaxis, infection control and supportive care are important in management but not included in this framework.
Table 1.

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Admission to PICU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity (BMI &gt;95th Centile)</td>
<td>Yes</td>
</tr>
<tr>
<td>Oestrogen containing OCP</td>
<td>No</td>
</tr>
<tr>
<td>CVC</td>
<td>No</td>
</tr>
<tr>
<td>Length of stay anticipated &gt; 3 days</td>
<td>No</td>
</tr>
<tr>
<td>Immobility that is not longstanding</td>
<td>No</td>
</tr>
<tr>
<td>Personal Hx of VTE</td>
<td>No</td>
</tr>
<tr>
<td>Known thrombophilia</td>
<td>No</td>
</tr>
<tr>
<td>First degree relative with VTE</td>
<td>No</td>
</tr>
<tr>
<td>Active malignancy</td>
<td>No</td>
</tr>
<tr>
<td>Recent surgery/trauma</td>
<td>No</td>
</tr>
<tr>
<td>Severe dehydration</td>
<td>No</td>
</tr>
<tr>
<td>Underlying medical condition (Nephrotic syndrome, CF, Sickle cell disease, Cardiac disease, Chronic inflammatory disorder (e.g. JIA, IBD), post splenectomy)</td>
<td>No</td>
</tr>
</tbody>
</table>

Table 2. Contraindications to thromboprophylaxis

<table>
<thead>
<tr>
<th>Contraindications</th>
<th>Consideration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke/intracranial haemorrhage</td>
<td></td>
</tr>
<tr>
<td>Uncontrolled bleeding</td>
<td></td>
</tr>
<tr>
<td>Likely to need surgery in &lt;24/24</td>
<td></td>
</tr>
<tr>
<td>Congenital bleeding disorder</td>
<td></td>
</tr>
<tr>
<td>Platelets &lt;50x10^9/L</td>
<td></td>
</tr>
<tr>
<td>Uncontrolled hypertension</td>
<td></td>
</tr>
<tr>
<td>* Consider UFH if CrCl &lt;30ml/min</td>
<td></td>
</tr>
</tbody>
</table>

# Mechanical thromboprophylaxis

Consider mechanical thromboprophylaxis for all patients admitted for COVID-19 reasons
- TED Stockings
- And/or pneumatic calf compressors
COVID-19 (SARS-CoV-2) Quick Medication Guide

Summary of therapy course depending on symptoms during hospitalisation

Please see the RCH guideline for management of symptomatic COVID for detailed information on when therapies are indicated.

Summary of disease modifying therapies

Dexamethasone

<table>
<thead>
<tr>
<th>Eligible patients</th>
<th>As per the algorithm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>- Oxygen saturations (SaO₂) &lt; 92% on room air</td>
</tr>
<tr>
<td></td>
<td>- Oxygen saturation (SaO₂) ≥ 92% on room air and persistent tachypnoea (MET call criteria)</td>
</tr>
<tr>
<td>Dose</td>
<td>IV, oral: 0.15mg/kg (max 6mg) once daily for up to 10 days or until discharge (whichever is first)</td>
</tr>
<tr>
<td>Notes</td>
<td>Give in the morning with food</td>
</tr>
</tbody>
</table>

Inhaled Budesonide (Pulmicort)

Inhaled budesonide has been shown to improve time to recovery with the chance of reducing prolonged hospital admissions in patients with confirmed SARS-CoV-2 who are at a higher risk of further complications.

Studies have only been performed in adult patients; however, it is recommended to consider utilising inhaled budesonide for the treatment of symptomatic SARS-CoV-2 in children and adolescents who do not require oxygen and who may be at high risk for disease progression.

<table>
<thead>
<tr>
<th>Eligible patients</th>
<th>As per the algorithm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>- Patients with a significant co-morbidity (outlined in the algorithm)</td>
</tr>
<tr>
<td></td>
<td>- High-risk groups (outlined in the algorithm) who have had symptoms for ≤ 14 days and NOT on inhaled corticosteroids</td>
</tr>
<tr>
<td>Non-eligible patients</td>
<td>Patients already on inhaled corticosteroids</td>
</tr>
<tr>
<td>Dose</td>
<td>4 to 11 years old: Inh 400mcg twice daily via dry powder inhaler (DPI)²</td>
</tr>
<tr>
<td></td>
<td>≥ 12 years of age: Inh 800mcg twice daily via dry powder inhaler (DPI)²</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Patients unable to appropriately inhale from a DPI. Inhaled budesonide only comes in the DPI form in Australia and requires the ability to properly deeply inhale via the device for proper drug disposition into the lungs.</td>
</tr>
</tbody>
</table>
If patients are unable to inhale from DPI, use Fluticasone (Flixotide) metered dose inhaler (MDI):
< 5 years: 125 mcg twice daily via MDI +/- spacer
≥ 5 years: 250 mcg twice daily via MDI +/- spacer

**Notes**
Rinse mouth out after use to minimise risk of developing oral candidiasis.

### Remdesivir (Veklury)
Remdesivir is a nucleoside analogue prodrug, which has inhibitory effects on pathogenic animal and human coronaviruses, including SARS-CoV-2 (COVID-19).

<table>
<thead>
<tr>
<th>Indication for use for patients ≥ 12 years of age and for patients weighing ≥ 40kg</th>
<th>As per the algorithm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>- Patients requiring non-invasive ventilation or flow rate &gt;30L/min and FiO₂ &gt; 40% (REMAP CAP)</td>
</tr>
<tr>
<td></td>
<td>- Immunocompromised patients who have had a positive SARS-CoV-2 PCR ≤ 3-4 days prior and are considered VERY high risk (initiation of remdesivir in this population will occur in consultation with the ID team)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Indication for use for patients &lt; 12 years of age and/or for patients weighing &lt; 40kg</th>
<th>Use of remdesivir for children or adolescents with COVID-19 outside of a trial setting should not be considered routine treatment. However, if treatment is considered in exceptional circumstances, it should be in direct consultation with the relevant stake-holders³</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>As of today, there is no clear route to access remdesivir for patients in this age group. Once access is confirmed, this will be updated accordingly.</td>
</tr>
</tbody>
</table>

### Inclusion Criteria for patients ≥ 12 years of age and ≥ 40kg
Current inclusion criteria as per the NMS include (all MUST apply):
- Informed consent has been provided by the patient, or patients legal guardian
- Age ≥ 18 years of age, or aged ≥ 12 and ≤ 18 years of age and weighing ≥ 40 kg.
- Hospitalised with confirmed SARS-CoV2 or known contact with a confirmed case with syndrome consistent with COVID-19 awaiting confirmation by diagnostic testing
- Oxygen saturation (SaO₂) ≤ 92% on room air and requiring supplemental oxygen
- Alanine aminotransferase (ALT) < 5 x upper limit of normal (ULN) by local laboratory measure and/or ALT < 3 x ULN and bilirubin < 2 x ULN
- EGFR > 30ml/min and not on dialysis or continuous veno-venous haemo-filtration

### Exclusion Criteria
Current exclusion criteria include:
- Evidence of multi-organ failure including but not limited to coagulopathy (significant thrombocytopenia), hepatic failure (elevated bilirubin) or renal failure (low urine output or estimated glomerular filtration rate (eGFR) <30ml/min) or significant cardiomyopathy (low cardiac output)
- Renal failure requiring dialysis or continuous veno-venous haemo-filtration
- Mechanical ventilation for longer than 48 hours at time of application
- Receiving extracorporeal membrane oxygenation (ECMO)
- Known hypersensitivity to the study drug, the metabolites, or formulation excipient

<table>
<thead>
<tr>
<th>Precautions/Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-marketing reports;</td>
</tr>
<tr>
<td>- Bradycardia; including</td>
</tr>
<tr>
<td>severe bradycardia which</td>
</tr>
<tr>
<td>can be fatal has been</td>
</tr>
<tr>
<td>reported in patients</td>
</tr>
<tr>
<td>receiving remdesivir for</td>
</tr>
<tr>
<td>SARS-CoV2</td>
</tr>
<tr>
<td>- Mild-moderate increase of</td>
</tr>
<tr>
<td>serum alanine aminotransferase and increased aspartate aminotransferase has been reported in patients receiving remdesivir for SARS-CoV2</td>
</tr>
</tbody>
</table>

### Dose for patients ≥ 12 years of age and ≥ 40kg

| Dose | 200mg loading dose on day 1, followed by 100mg daily for a further 4 days |

### Dose for patients < 12 years of age and/or < 40kg

<table>
<thead>
<tr>
<th>Dose</th>
<th>3.5kg to &lt;40kg: IV: 5mg/kg loading dose on day 1, followed by 2.5mg/kg/dose once daily for a further 4 days.</th>
</tr>
</thead>
<tbody>
<tr>
<td>As of today, there is no clear route to access remdesivir for patients in this age group. Once access is confirmed, this will be updated accordingly.</td>
<td></td>
</tr>
</tbody>
</table>

### Dose adjustment for renal impairment (based on eGFR)

<table>
<thead>
<tr>
<th>eGFR</th>
<th>Dose adjustment</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 30ml/min/1.73m²</td>
<td>No dose adjustment required</td>
<td></td>
</tr>
<tr>
<td>&lt; 30ml/min/1.73m²</td>
<td>Remdesivir is not indicated in patients with renal impairment. Patient will be excluded for accessing remdesivir.</td>
<td></td>
</tr>
</tbody>
</table>

### Dose adjustment for hepatic impairment

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not recommended in patients with hepatic impairment (criteria above outlined). Patient will be excluded from accessing remdesivir.</td>
<td></td>
</tr>
<tr>
<td>If hepatic impairment develops in patients treated with remdesivir (elevation of ALT and/or signs of liver inflammation), discontinue remdesivir treatment.</td>
<td></td>
</tr>
</tbody>
</table>

### Administration

**Drug access (patients ≥ 12 years of age and ≥ 40kg)**

Access to remdesivir is through the National Medicines Stockpile. Please refer to the “Request to Access Remdesivir” form for further information.

**Drug access (patients < 12 years of age and/or < 40kg)**

As of now, there is no clear route to access remdesivir for patients in this age group. Once access is confirmed, this will be updated accordingly.

**RCH Approval**

DUC Approval required

**Notes**

- Initial supply of remdesivir from the NMS will be for 5 days only. If a 10-day course is required, a subsequent application to the NMS for remdesivir will be required. A 10-day course MUST be approved by the appropriate clinicians (initial DUC member included).
- The remdesivir formulation contains the excipient SBECO which accumulates in patients with kidney dysfunction, so patients with known kidney dysfunction will be excluded from remdesivir therapy.

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**Tocilizumab**

Tocilizumab (Actemra) binds to and inhibits the activity of interleukin-6 (IL-6). In critically ill patients with SARS-CoV-2, tocilizumab may decrease the hyper-inflammation associated with SARS-CoV-2 and possibly improve overall outcomes.

As of the 17th August 2021, there is a significant shortage of tocilizumab within Australia and as a result its use is significantly restricted to ensure appropriate supply for its TGA-approved indications. As a result, in patients who are receiving supplemental oxygen but are not mechanically ventilated, baricitinib should be considered instead of tocilizumab, unless contraindicated.

<table>
<thead>
<tr>
<th><strong>Indication for use</strong></th>
<th>Consider tocilizumab in addition to dexamethasone in patients who are hospitalised with COVID-19 who require supplemental oxygen and where there is evidence of systemic inflammation.</th>
</tr>
</thead>
</table>
| **Inclusion Criteria** | As per the algorithm:  
  - Deteriorating hospitalised patients on dexamethasone with confirmed SARS-CoV-2 infection who have signs of systemic inflammation (CRP ≥ 75 or rapidly rising) |
| **Exclusion Criteria** | Current exclusion criteria include:  
  - Known hypersensitivity to tocilizumab.  
  - Severe hepatic impairment (ALT/AST > 10 x ULN)  
  - Patients with active, severe infections (excluding SARS-CoV2).  
    - Tocilizumab has a significant warning for the risk of serious infections due to its immune suppressing effects, this includes tuberculosis and other opportunistic infections. Extreme care should be |
taken when utilising tocilizumab in patients with active infections (viral, bacterial or fungal).

<table>
<thead>
<tr>
<th>Precautions</th>
<th>Tocilizumab causes immune system suppression so should be used in caution in immunocompromised patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose</td>
<td>For patients &gt; 2 years of age</td>
</tr>
<tr>
<td></td>
<td>- Patients &lt; 30kg: 12mg/kg IV stat for ONE dose</td>
</tr>
<tr>
<td></td>
<td>- Patients 30-40kg: 8mg/kg IV stat for ONE dose</td>
</tr>
<tr>
<td></td>
<td>- Patients 40 to 65kg: 400mg IV stat for ONE dose</td>
</tr>
<tr>
<td></td>
<td>- Patients 65 to 90kg: 600mg IV stat for ONE dose</td>
</tr>
<tr>
<td></td>
<td>- Patients &gt; 90kg: 800mg IV stat for ONE dose</td>
</tr>
<tr>
<td>Dose adjustments in renal impairment (based on eGFR)</td>
<td>No dosage adjustment required in renal impairment.</td>
</tr>
<tr>
<td>Dose adjustments in hepatic impairment</td>
<td>Not recommended in patients with active hepatic disease or hepatic impairment, described as ALT/AST &gt; 10 x ULN.</td>
</tr>
<tr>
<td>Administration</td>
<td>Please refer to the Paediatric Injectable Guideline (PIG) or Australian Injectable Drug Handbook (AIDH) on appropriate dilution and administration information</td>
</tr>
<tr>
<td>Drug Access</td>
<td>Access to tocilizumab is through the National Medicines Stockpile. Please refer to the “Request to Access Tocilizumab” form for further information.</td>
</tr>
<tr>
<td>RCH Approval</td>
<td>DUC Approval</td>
</tr>
<tr>
<td>Notes</td>
<td>Though the literature does support a second dose of tocilizumab &gt; 8 hours post the initial dose if no shown improvement, due to the significant shortage in tocilizumab a secondary dose may not be able to be sourced.</td>
</tr>
</tbody>
</table>

**Baricitinib (Olumiant)**

Baricitinib (Olumiant) is a Janus kinases 1 and 2 inhibitor. Baricitinib, through its inhibitory mechanism, may decrease hyper-inflammation associated with SARS-CoV-2 and may improve overall outcomes.

Due to the significant shortage of tocilizumab (Actemra), baricitinib has received conditional approval from the Australian National COVID-19 Taskforce and the TGA to be utilised for hospitalised patients with COVID-19 who require supplemental oxygen.

<table>
<thead>
<tr>
<th>Indication for Use</th>
<th>Consider baricitinib in addition to dexamethasone₆ in patients who are hospitalised with COVID-19 who require supplemental oxygen and are deteriorating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inclusion Criteria</td>
<td>As per the algorithm</td>
</tr>
<tr>
<td></td>
<td>- Deteriorating hospitalised patients on dexamethasone with confirmed SARS-CoV-2 infection</td>
</tr>
</tbody>
</table>
Deteriorating hospitalised patients on dexamethasone with confirmed SARS-CoV-2 infection who have signs of systemic inflammation and unable to access tocilizumab

### Exclusion Criteria

Current **exclusion** criteria include:
- Known hypersensitivity to baricitinib
- < 2 years of age
- Patients with active, severe infections (excluding SARS-CoV2)
  - Baricitinib has a significant warning for the risk of serious infections due to its immune supressing effects, this includes tuberculosis and other opportunistic infections. Extreme care should be taken when initiating baricitinib in patients with active infections (viral, bacterial or fungal)

### Precautions

Baricitinib causes immune system suppression so should be used in caution in immunocompromised patients.

Cytopenia may occur during treatment with baricitinib, recommended to avoid or cease treatment in patients who have:
- Lymphocyte count < 0.5 x 10⁹ cell/L
- Haemoglobin < 80g/L
- Absolute neutrophil count < 1 x 10⁹ cells/L

Care should be given when initiating in patients with renal impairment, dose adjustment will be required (see below).

### Dose

<table>
<thead>
<tr>
<th>Age Range</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 2 years of age</td>
<td>Not recommended and no dosage information available.</td>
</tr>
<tr>
<td>2 to &lt; 9 years</td>
<td>PO 2mg daily for 14 days or until hospital discharge, whichever is first</td>
</tr>
<tr>
<td>9 years to adult</td>
<td>PO 4mg daily for 14 days or until hospital discharge, whichever is first</td>
</tr>
</tbody>
</table>

### Dose adjustments for renal impairment (based on eGFR)

<table>
<thead>
<tr>
<th>eGFR (mL/min/1.73m²)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 60</td>
<td>2 to &lt; 9 years: PO 2mg daily</td>
</tr>
<tr>
<td>30 to 60</td>
<td>2 to &lt; 9 years: PO 1mg daily</td>
</tr>
<tr>
<td>15 to &lt;30</td>
<td>2 to &lt; 9 years: Not recommended.</td>
</tr>
<tr>
<td>&lt; 15</td>
<td>Not recommended.</td>
</tr>
</tbody>
</table>

### Dose adjustments for hepatic impairment

No dosage adjustment recommended. However, if baricitinib induced liver injury is suspected, cease treatment immediately.

### Administration

- **HAZARDOUS** medication, appropriate PPE required when handling.
- Gloves when handling intact tablets and patients can swallow whole.
- Gloves, gown, N95 and eye protection when dispersing tablets.
- For patients unable to swallow whole tablets; disperse tablets in 10ml of sterile water for injection (WFI). Tablet should disperse in less than 5 minutes. Give immediately. Medication may be administered by gastrostomy feeding tubes and nasogastric feeding tubes. There is no evidence for jejunal administration, so do not administer by naso-jejunal or jejustomy feeding tubes.

### Drug Access
Medication accessed via RCH pharmacy department. Patients must satisfactorily meet the above inclusion criteria and have approval before supply will be granted.

### RCH Approval
**DUC Approval**

### Notes
Medication is under constrained supply. All doses supplied that are not utilised (blister pack intact) should be returned to pharmacy.

### Sotrovimab
Sotrovimab is a monoclonal antibody therapy that has been given provisional approval for the use in mild-to-moderate SARS-CoV2 infected patients who may be at a higher risk of progressing to severe complications from the infection.

Sotrovimab is currently still an investigational product, so long term safety and efficacy in patients with COVID-19 continues to be evaluated.

<table>
<thead>
<tr>
<th>Indication for use</th>
<th>Consider sotrovimab in high-risk patients (outlined in the algorithm) or patients with a significant comorbidity (outlined in the algorithm) who have had symptoms for &lt; 5 days.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inclusion criteria</td>
<td><strong>Patient must be ≥ 12 years of age AND ≥ 40kg</strong></td>
</tr>
</tbody>
</table>
| **Vaccination status (MUST meet one)** | - Unvaccinated OR  
- Partially vaccinated OR  
- Immunosuppressed regardless of vaccine status (please see sotrovimab request form & algorithm for definition of high-risk immunosuppressed patient cohorts) |

**Must meet ALL of the following criteria:**
- Confirmed SARS-CoV2 AND;
- < 5 days from symptom onset (must clarify date of onset) AND;
Sotrovimab can only be accessed via the NMS at this time. Additional NMS criteria must be met before medication can be supplied.

Please refer to the following documents for the most up to date additional criteria:
1. Current sotrovimab requisition form
2. Algorithm for specific paediatric criteria

At least ONE of the additional criteria must be met before access can be granted.

<table>
<thead>
<tr>
<th>Exclusion criteria</th>
<th>Patients &lt; 12 years of age OR &lt; 40kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Precautions</td>
<td>No known current contraindications for sotrovimab.</td>
</tr>
<tr>
<td>Dose</td>
<td>IV: 500mg as a single dose (administered within 5 days of symptom onset)</td>
</tr>
<tr>
<td>Dose adjustment for renal impairment (based on eGFR)</td>
<td>No dosage adjustment required</td>
</tr>
<tr>
<td>Dose adjustments for hepatic impairment</td>
<td>No dosage adjustment required (has not been studied)</td>
</tr>
<tr>
<td>Administration</td>
<td>Please refer to the Paediatric Injectable Guideline (PIG) or Australian Injectable Drug Handbook (AIDH) on appropriate dilution and administration information</td>
</tr>
<tr>
<td>Drug Access</td>
<td>Access to sotrovimab is through the National Medicines Stockpile. Please refer to the “Request to Access Sotrovimab” form for further information.</td>
</tr>
<tr>
<td>RCH Approval</td>
<td>DUC Approval</td>
</tr>
<tr>
<td>Monitoring</td>
<td>Monitor for possible anaphylactic and infusion reactions during the infusion and for ONE hour after the infusion. Infusion reactions include: fever, dizziness, dyspnoea, pruritus and rash. For mild to moderate infusion reactions, slow or stop the infusion and treat accordingly. Anaphylactic reactions are rare, but are a medical emergency. Stop the infusion and commence treatment immediately.</td>
</tr>
</tbody>
</table>

Casirivimab and Imdevimab (Ronapreve)
Casirivimab and imdevimab are two recombinant monoclonal antibodies formulated together to target the spike protein of SARS-CoV-2 to inhibit infection of host cells. It has been provisionally approved in Australia for both treatment and post-exposure prophylaxis of COVID-19.
<table>
<thead>
<tr>
<th>Indication for use</th>
<th>Consider casirivimab-imdevimab in high-risk patients (outlined in the algorithm) or patients with a significant comorbidity (outlined in the algorithm) for treatment or post-exposure prophylaxis of COVID-19</th>
</tr>
</thead>
</table>
| Inclusion criteria – TREATMENT – mild disease (no O₂ requirement) | **Patient must be ≥ 12 years of age AND ≥ 40kg**  
**Vaccination status (MUST meet one)**  
- Unvaccinated OR  
- Partially vaccinated OR  
- Immunosuppressed regardless of vaccine status (please see Ronapreve request forms & algorithm for definition of high-risk immunosuppressed patient cohorts)  
**Must meet ALL of the following criteria:**  
- Confirmed SARS-CoV2 AND;  
- No oxygen requirements  
- 6 – 7 days since onset of symptoms  
Casirivimab-imdevimab can only be accessed via the NMS at this time. Additional NMS criteria must be met before medication can be supplied.  
Please refer to the following documents for the most up to date additional criteria:  
1. Current Ronapreve requisition form for TREATMENT of mild disease  
2. Algorithm for specific paediatric criteria  
At least ONE of the additional criteria must be met before access can be granted. |
| Inclusion criteria – TREATMENT – moderate to critical disease | **Patient must be ≥ 12 years of age AND ≥ 40kg**  
**Must meet ALL of the following criteria:**  
- Confirmed SARS-CoV2 AND;  
- Seronegative for antibodies to SARS-CoV-2  
- Moderate, severe, or critical disease as defined in Section 4.2 of the Australian Guidelines for the Clinical Care of People with COVID-19  
Casirivimab-imdevimab can only be accessed via the NMS at this time.  
Please refer to the following documents for the most up to date additional criteria: |
<table>
<thead>
<tr>
<th>Inclusion criteria – Post Exposure PROPHYLAXIS</th>
<th>Patient must be ≥ 12 years of age AND ≥ 40kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccination status (MUST meet one)</td>
<td>- Unvaccinated OR</td>
</tr>
<tr>
<td></td>
<td>- Partially vaccinated OR</td>
</tr>
<tr>
<td></td>
<td>- Immunosuppressed regardless of vaccine status (please see Ronapreve request form &amp; algorithm for definition of high-risk immunosuppressed patient cohorts)</td>
</tr>
<tr>
<td>Must meet ALL of the following criteria:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Contact of individual with confirmed SARS-CoV-2</td>
</tr>
<tr>
<td></td>
<td>- Household contact OR</td>
</tr>
<tr>
<td></td>
<td>- Care setting contact of significant exposure</td>
</tr>
<tr>
<td></td>
<td>- Asymptomatic (NOTE: symptomatic patients awaiting PCR results are not eligible)</td>
</tr>
<tr>
<td></td>
<td>- ≤ 4 days from exposure (day of first exposure is day 0)</td>
</tr>
<tr>
<td></td>
<td>- Significant immunosuppression</td>
</tr>
<tr>
<td>Casirivimab-imdevimab can only be accessed via the NMS at this time. Additional NMS criteria must be met before medication can be supplied.</td>
<td></td>
</tr>
<tr>
<td>Please refer to the following documents for the most up to date additional criteria:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1. Current Ronapreve requisition form for Post exposure PROPHYLAXIS</td>
</tr>
<tr>
<td></td>
<td>2. Algorithm for specific paediatric criteria</td>
</tr>
<tr>
<td>At least ONE of the additional criteria must be met before access can be granted.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exclusion criteria</th>
<th>Patients &lt; 12 years of age OR &lt; 40kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Precautions</td>
<td>No known current contraindications for casirivimab-imdevimab.</td>
</tr>
<tr>
<td>Dose</td>
<td>TREATMENT (mild disease): 1200 mg once by IV infusion (preferred route) or SC injection</td>
</tr>
<tr>
<td></td>
<td>TREATMENT (moderate-critical disease): 8000 mg once by IV infusion</td>
</tr>
<tr>
<td></td>
<td>Post-Exposure PROPHYLAXIS: 1200 mg by SC injection or IV infusion</td>
</tr>
</tbody>
</table>
**Ongoing prophylaxis:** 600 mg by SC injection or IV infusion every 4 weeks until no longer required (maximum 6 doses)

<table>
<thead>
<tr>
<th><strong>Dose adjustment for renal impairment (based on eGFR)</strong></th>
<th>Mild-Moderate impairment – no adjustment needed. There is no information on dosage adjustment in severe renal impairment.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dose adjustments for hepatic impairment</strong></td>
<td>Mild-Moderate impairment – no adjustment needed. There is no information on dosage adjustment in severe hepatic impairment.</td>
</tr>
<tr>
<td><strong>Administration</strong></td>
<td>Please refer to the Paediatric Injectable Guideline (PIG) or Australian Injectable Drug Handbook (AIDH) on appropriate dilution and administration information</td>
</tr>
<tr>
<td><strong>Drug Access</strong></td>
<td>Access to Ronapreve is through the National Medicines Stockpile. Please refer to the “Request to Access Ronapreve” forms for further information.</td>
</tr>
<tr>
<td><strong>RCH Approval</strong></td>
<td>DUC Approval</td>
</tr>
<tr>
<td><strong>Monitoring</strong></td>
<td>Monitor patient for 1 hour after infusion for signs of allergy or infusion reactions</td>
</tr>
</tbody>
</table>

Version 1.1

Compiled & written by Hanna Holschier (RCH PICU Pharmacist) 25/10/21

Updated Christine Plover (Medicines Information) 19/11/2021

**References**

3. National COVID-10 Clinical Evidence Taskforce. [https://app.magicapp.org/#/guideline/L4Q5An/section/L6q73j](https://app.magicapp.org/#/guideline/L4Q5An/section/L6q73j)
5. RECOVERY collaborative group. Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. Lancet. 2021 May 1; 397 (10285): 1637-1645
7. Lexicomp.
Background:
Sotrovimab is a monoclonal antibody which targets a spike protein on the SARS CoV-2 virus. It has been reported to reduce the risk of disease progression in patients with symptomatic COVID-19 who have certain risk factors. This engineered monoclonal antibody targets a highly conserved epitope (99.6%) within the sarbecoviruses, rather than targeting the rapidly mutating angiotensin-converting enzyme 2 receptor. The mechanism of action is uncertain but appears to inhibit a step after virus attachment to the cell but before fusion of the membranes.

This therapy has been approved by the Therapeutic Goods Administration (TGA) and licenced for adults and children 12 years and above if certain risk factors are present. It has been reported to reduce the risk of hospitalisation by up to 85% in high risk patients. Once administered, patients are unable to receive the COVID-19 vaccination for 90 days.

Evidence:
This protocol is developed based upon the following resources:

**The COMET-ICE trial:**
Randomised, double blind, multicentre, placebo-controlled Phase 1, 2 and 3 trial of Sotrovimab for the prevention of mild-moderate COVID-19 in those at higher risk of disease progression (Gupta et al, Early Covid-19 treatment with SARS-CoV-2 neutralising antibody Sotrovimab, (May 2021)

**Australian Public Assessment Report for Sotrovimab:**
Evaluation of Sotrovimab submitted to the TGA for approval of a drug (Aug 2021)

**A Detailed Guide for the Use of Sotrovimab under Emergency Use Authorization:**
FDA guideline regarding emergency use guidelines for the unapproved Sotrovimab under the emergency use of drugs during the COVID-19 pandemic (July 2021)

Inclusion Criteria:
Demographics (ALL of the following):
- Patient must be ≥ 12 years old AND ≥40 kg
  - The COMET-ICE trial only studied the drug efficacy in adults 18 years plus however the drug has been licensed down to age 12 years based upon pharmacokinetic data regarding drug clearance and volume of distribution and no requirement for dose adjustment for weight 40-160kg
- Confirmed SARS-CoV2
- Within 5 days of symptom onset (must clarify date of onset)
- No oxygen requirement

Vaccination status (MUST meet one of):
- Unvaccinated OR
- Partially vaccinated OR Immunosuppressed regardless of vaccination status (please see below and Appendix 1 for further definition)

Children may be eligible if at high risk of disease progression with significant medical comorbidity and not fully vaccinated OR immunosuppressed in a high risk group (further defined below). Please refer to the RCH Guideline for Management of Symptomatic COVID algorithm for further information (available on the intranet or within RCH COVID clinical management guidelines package).

**Significant comorbidities (and not fully COVID vaccinated):**

Children should meet 1 National Medical Stockpile (NMS) criteria AND the corresponding paediatric specific criteria below (indicated by a *) if relevant

**NMS Criteria (must meet ONE of):**
- Chronic obstructive lung disease*
- Heart failure *
- Severe asthma *
- Obesity (BMI ≥95th centile CDC or ≥97th centile WHO for age)
- Diabetes (insulin dependent)
- Chronic kidney disease (GFR <15ml/min/1.73m²)
- For paediatric patients:
  - Other significant co-morbidities including sickle cell disease OR
  - Paediatric Complex Chronic conditions (PCCC): severe congenital and genetic (including Trisomy 21), cardiovascular, gastrointestinal, malignancies, metabolic, neuromuscular, renal and respiratory conditions

**Paediatric specific criteria for NMS criteria:**
- Chronic obstructive lung disease
  - Cystic fibrosis (or bronchiectasis) with FEV₁<60%
  - Congenital tracheal stenosis
  - Chronic lung disease with pulmonary hypertension requiring oxygen
  - Neuromuscular disease requiring daytime respiratory support
  - Tracheostomy requiring ventilation
- Heart failure
  - Cardiomyopathy requiring diuretics
  - Shunt dependent pulmonary blood flow
  - Pulmonary hypertension (requiring pulmonary hypertension specific therapy)
  - Single ventricle
- Severe asthma
  - ≥ 1 severe exacerbation in last 12 months (defined as requiring ICU admission or intravenous treatment)
  - OR high dose inhaled corticosteroids to control symptoms
  - OR moderate-dose inhaled corticosteroids plus long-acting beta agonist (LABA) to control symptoms

**Immunosuppressed in a high risk group:**
- Primary or acquired T cell immunodeficiency
- Haematologic neoplasms (leukaemias, lymphomas, myelodysplastic syndrome)
- Post-transplant: solid organ (on immunosuppressive therapy), haematopoietic stem cell transplant (within 24 months)
- Other significant immunocompromising conditions (after discussion with ID/immunology consultant)
- Immunosuppressive therapy (current or recent) including:
  - Chemotherapy
  - High dose corticosteroids (≥ 0.5 mg/kg/day or ≥ 20 mg/day prednisone or equivalent) for ≥ 14 days
  - All biologics and most disease modifying anti-rheumatic drugs (DMARDs)

Please refer to the RCH COVID clinical management guidelines package for further information (intranet).

**Exclusion criteria:**
- Weight < 40kg
- Day 6 or more of symptoms (AND infusion must occur by day 5)
- Symptoms of severe COVID or saturations <92%
- Previous anaphylaxis or Type I/IV hypersensitivity to a monoclonal antibody
- Allergy to ingredients in medication (L-histidine, L-histidine monohydrochloride, L-methionine, sucrose, polysorbate 80)

**Adverse Events**
- Most commonly reported side effects were mild diarrhoea and mild rash
- Infusion reactions include fever, dizziness, dyspnoea, pruritus and rash
- Anaphylaxis is rare (i.e. one case of anaphylaxis in a previous study)
- Other reported side effects include headache, chest pain, altered heartbeat, upset stomach

**Patient Identification**

There are three potential pathways for identification of eligible patients:
- Via the COVID positive pathway
- Direct referral from subspecialty clinicians
- Referral from ED

Relevant teams and groups are being contacted to notify them of this procedure.

**Referrals from Emergency Department:**
- Follow the Referral and Intake process below.
- In hours referrals should be discussed with the Sotrovimab clinician and urgent after hours referrals discussed with the ID consultant who is on call.
- The patient’s bed in Dolphin will change from ED to SSU for the infusion.

**Referral and Intake Process**

The Sotrovimab clinician (Suzanne Boyce or nominee) is available business hours (Monday – Friday 9am-5pm, excluding public holidays) to perform intake assessments, obtain informed consent from families if approved and liaise with the bed manager to arrange infusion.

The Sotrovimab clinician details:
Dr Suzanne Boyce
Pager 4005 (external referrals please go via switch and request pager 4005)
Suzanne.boyce@rch.org.au or EPIC inbox for correspondence (NOT to be used for referrals)

The Sotrovimab clinician will:
- Receive referrals from clinicians
- Liaise with the patient/family and any relevant specialist to ascertain eligibility
- Discuss infusion procedure including small risk of adverse events (e.g. small risk of infusion reaction, extremely rarely to have anaphylaxis)
- Email the Consumer Medical Information and patient handout to family (Appendix 1 and 2)
- If eligibility criteria are met, refer to ID fellow (in hours) or consultant (after hours) to obtain ID approval
  - In hours, contact DUC member
  - If approved after hours by ID, online webform to be completed next business day (ID team should notify Sotrovimab clinician during business hours)
- Follow booking procedure below
- Audit referral numbers and outcomes

If approval granted, the Sotrovimab clinician will:
- Obtain verbal informed consent of the procedure
  - Signed informed consent not required
- Obtain consent for collection of additional bloods for research purposes (to be confirmed)
- Follow booking procedure below
- Completes “Request to access Sotrovimab” form and sends to pharmacy (rch.pharmacy@rch.org.au) and Alfred pharmacy (pharmdist@alfred.org.au)
- Place orders EPIC for upcoming encounter
  - Sotrovimab (XEVUDY) 500mg in sodium chloride 0.9% 100ml IV infusion over 30 minutes
  - Emergency medications
    - Adrenaline 1:1000 (1mg/ml) 10mcg/kg MAX 500mcg
    - Cetirizine 1mg/ml solution 5-10mg BD prn for allergy
    - Sodium chloride 0.9% IV flush 1-10ml prn
  - Research bloods (to be confirmed)
  - Child life therapy or sedation if required
- Consider referral to RCH Hospital in the Home for additional monitoring if warranted
- Complete vaccine exemption form once infusion completed

Booking procedure

When booking infusions, the Sotrovimab clinician must ensure infusions will occur by day 5 of symptoms. Infusions should ideally occur Monday to Friday however urgent infusions may be able to be facilitated over the weekend (see Urgent Referrals below instead).

The Sotrovimab clinician will:
- Contact the Bed Manager on x54000
- Complete a “Medical Elective Admission Request” in EPIC
- Bed Manager will liaise with Director Clinical Operations (Access & Wards) to determine most appropriate location for infusion to occur
- Bed Manager (or team) will contact family to confirm admission time and arrival instructions for family
- Admissions to Dolphin will be under the Gen Med SSU team. Admissions to ward negative pressure rooms should be under the General Medicine team of the day.

**Pharmacy Procedure**

- Sotrovimab release form sent to pharmacy (rch.pharmacy@rch.org.au)
- Pharmacist liaises with Alfred Hospital for release of stock
- Dispense medication for release on day of infusion (ensuring that relevant approvals and release forms have been completed for each patient).

**Urgent Referrals**

Urgent (time critical) referrals should be discussed with the Sotrovimab clinician (business hours) or ID Consultant (after hours). Referrals during business hours should follow the booking procedure above. After hour referrals that must be completed on Saturday, Sunday or public holidays will be approved by the ID consultant. Once approval granted, they should liaise with General Medicine Registrar on call to facilitate the booking.

The General Medicine Registrar (or Dolphin Registrar if patient admitted to Dolphin) will:

- Contact bed manager to arrange an urgent admission +/- referral to HITH
  - Infusions should occur when pharmacist onsite to release the medication (Saturday 9-1pm and Sunday 10-12pm)
  - Infusions outside these hours would require the oncall pharmacist to return onsite
- Completes "Request to access Sotrovimab" form and sends to pharmacy (rch.pharmacy@rch.org.au) and Alfred pharmacy (pharmdist@alfred.org.au) https://www.rch.org.au/pharmacy-intranet/medicines-information/COVID-19_medications_-_access_and_prescribing/#request-forms-for-access-to-medications-from-nms
- Place orders in EPIC for the infusion
  - Sotrovimab (XEVUDY) 500mg in sodium chloride 0.9% 100ml IV infusion over 30 minutes
  - Emergency medications
    - Adrenaline 1:1000 (1mg/ml) 10mcg/kg MAX 500mcg
    - Cetirizine 1mg/ml solution 5-10mg BD prn for allergy
    - Sodium chloride 0.9% IV flush 1-10ml prn
  - Research bloods (to be confirmed)
- Consider referral to RCH Hospital in the Home for additional monitoring if warranted
- Obtain verbal informed consent from parent and document in EMR
  - Please provide parent handout (Appendix 1) and CMI (Appendix 2) to parent
- Ensure patient is not hypoxic on arrival (as will be ineligible for infusion otherwise)
- Cannulate patient if required (collect bloods if clinically relevant)
- Email Sotrovimab clinician (Suzanne.boyce@rch.org.au) once infusion complete to notify
- Inform family that the Sotrovimab clinician will send them a vaccination exemption letter and submit the relevant form to the Immunisation register
  - Sotrovimab clinician will also complete DUC webform during business hours
- Respond to any clinical issues during infusion
**Staffing:**

Initial staffing will occur within existing resources however the workload will be monitored closely.

- **Sotrovimab clinician:**
  - Receive referrals for Sotrovimab
  - Perform intake assessment to ensure eligibility
  - Obtain approval from ID and DUC (during business hours)
    - Submit online webform for after-hours infusions during business hours
  - Gain informed consent
  - Submit application for release of infusion
  - Book infusion procedure and order infusion in Day Medical encounter
  - Complete Australian Immunisation Registrar exemption form
  - Audit referral numbers and outcomes
- **General Medicine registrar or Dolphin Registrar**
  - First response for infusion reactions or clinical concern
  - Cannulate patients if required
  - May facilitate urgent (weekend) infusions under direction by ID consultant
    - See urgent procedure above
  - Refer to Hospital in the Home if patient warrants additional monitoring
- **DUC committee member/ ID consultant**
  - Provides approval for use of Sotrovimab
- **Pharmacy**
  - Apply to release of Sotrovimab
  - Dispense Sotrovimab to be supplied to Dolphin ward on arrival of patients
- **Ward RN**
  - Prepare and administer infusion
  - Monitoring of patient during and after infusion

**Medication:**

*Refer to Paediatric Injectable Guidelines*

**Storage:**

- Prior to dilution store refrigerates 2-8 degrees Celsius in original carton and protect from light

**Preparation**

- Remove Sotrovimab from refrigeration and allow to come to room temperature over 15 minutes
- Gently swirl the vial several times (do not shake)
- Withdraw 8ml from one vial and inject into prefilled saline bag (50-100ml)
- Gently rock infusion mixture back and forth 3-5 times
- Administer solution immediately or store up to 4 hours at room temperature (or refrigerated up to 24 hours)
- Infuse via a 0.2micron in-line filter

**Procedure**

**Patient arrival:**
- Bed manager will confirm arrival procedure with family

**Infusion procedure:**

- General nursing admission is completed and name band is applied
- Set of observations performed (infusion not to continue if saturations <92%)
  - If any clinical concern, RN to liaise with General medical staff
- Notify pharmacy patient is going ahead – send a MAR message to request dose to be sent
- Determine the need for Angel Cream/Emla or Nitrous for sedation and apply if necessary
- Obtain intravenous access if not already present on patient and bloods collected if clinically relevant
- Prepare Sotrovimab in medication room using appropriate PPE (as per Hazardous medications precaution policy which is met with airborne PPE for COVID):
  - Sotrovimab 500mg/8ml vial
- Sotrovimab 500mg Infusion commenced and run over 30 minutes
  - Observations (HR, RR, O2 sat, BP every 10 minutes)
- Post infusion, flush intravenous line with normal saline 10ml at a rate at the same rate as the infusion (not faster)
- Observed for 1 hour post infusion with observations every 30 minutes
- AVS and discharge paperwork provided
  - Medical staff should email Sotrovimab clinician to complete a vaccine exemption letter and AIR form
- If patient has been referred to (or is under the care of HITH), nursing staff should contact Wallaby ward to notify of transfer home
- Patient and carer transferred via yellow lifts back to their vehicle location

It is anticipated that the average length of stay will be 2-3 hours (depending upon sedation requirements).

**Adverse Events**

- General Medicine or Dolphin Medical staff will be called for any concerns regarding an infusion reaction
- MET (22 22) will be called if required
- For mild to moderate infusion reactions, slow or stop the infusion and treat accordingly
- Anaphylactic reactions are rare but are a medical emergency. STOP the infusion and commence treatment immediately
- Adverse events should be notified to the Sotrovimab Infusion service medical lead and an ADR report should be submitted to pharmacy ([https://www.rch.org.au/pharmacy-intranet/medicines-information/Adverse_Drug_Reaction_(ADR)_reporting/](https://www.rch.org.au/pharmacy-intranet/medicines-information/Adverse_Drug_Reaction_(ADR)_reporting/))

**Governance**

- Sotrovimab infusion service overseen by Department of General Medicine and Infectious Diseases
- Sotrovimab Medical Lead is Dr Suzanne Boyce
- Infectious Disease Lead is A/Prof Amanda Gwee
- Dolphin nurse lead is Alysia Alexander-Cochrane
- RCH Pharmacy lead is Christine Plover
Appendix 1:

Sotrovimab Parent Handout
Sotrovimab Parent Handout

Sotrovimab is a man-made antibody that attaches to the COVID-19 virus to prevent it entering your cells. If your child has one or more risk factors that may lead to severe COVID-19 disease, giving this drug may reduce the risk of hospitalisation by up to 85%. However, the medication needs to be given early in the illness (within the first 5 days of symptoms). This drug has been approved for children as young as 12 years old.

How do I know if my child is eligible?
Your child will be referred to the RCH Sotrovimab Infusion service if they have certain conditions that make them more susceptible to severe COVID-19 disease. The referral will be reviewed by a senior doctor who will contact you to discuss your child. If your child is eligible, they will discuss the procedure with you. If you agree to the procedure, they will organise for your child to come into RCH for a couple of hours to receive this treatment.

How is Sotrovimab given?
Sotrovimab is given into a vein (intravenous) over 30 minutes. If your child doesn’t have a long-term intravenous line, they will need to have a cannula inserted before the medication is given. The doctor or nurse may take a small amount of blood before the procedure. After the infusion, your child will need to remain in hospital for an hour to ensure they do not develop a side effect of the medication (which is rare). This medication is being given in our Dolphin ward which is where children who have COVID-19 are cared for in the hospital.

What are the side effects of Sotrovimab?
Most patients who receive Sotrovimab do not have any side effects. A small number of patients may experience the following reactions:
- Fever or chills
- Nausea
- Headache
- Shortness of breath or difficulty breathing
- Dizziness
- Fast, slow or uneven heart rate
- Chest pressure or discomfort
- Wheezing
- Swelling of face, lips or throat
- Rash or hives

You will be monitored closely for all these reactions and should tell the nurse immediately if you are feeling any of these. If you have a reaction, a doctor will assess you and you may need to stay longer and receive some treatment.

What should I tell the doctor?
Please tell the doctor if you have had an allergic reaction to any of the following:
- Monoclonal antibodies
- Other chemicals in the medication: L-histidine, L-histidine monohydrochloride, L-methionine, sucrose, polysorbate 80
The doctor should also know:

- If your child is taking any other medication (prescription, over the counter, vitamins or herbal preparations). Sotrovimab has not been shown to interact with any medications however it is important for your doctor to know
- If you child is pregnant or breastfeeding. We do not know the impact on fertility.

Please also read the Consumer Medicine Information (CMI) document we will provide to you.

**What about receiving the COVID-19 vaccination?**

After Sotrovimab, your child will not be able to be vaccinated against COVID-19 for 90 days. You will be provided with a medical exemption letter for this period and your doctor will complete an Australian Immunisation Registry vaccination exemption form. However, after having COVID-19 as well as receiving Sotrovimab, your child is likely to be protected against getting COVID-19 again during these 90 days.

**What do I need to do for my child after receiving Sotrovimab?**

After your child is discharged, you will need to return home and continue isolation as per instructions from the Department of Health. You should continue to monitor for symptoms of COVID-19.

Your child may be enrolled into our Hospital-in-the-Home (HITH) program for closer monitoring upon discharge. If so, the HITH team will speak to you about the service, and you will have daily phone calls or telehealth until improving. Otherwise, you should call your GP or the COVID-19 advice line if you have any concerns. If you develop serious symptoms of COVID-19 or feel like you are having an allergic reaction, please call 000 and say that you have COVID-19 and are in isolation and that you received this medication.


Reviewed November 2021
Appendix 2: Sotrovimab (XEVUDY) CMI

RCH PIMS-TS/MIS-C Guideline

Key Points

- Consider PIMS-TS in a febrile child with any of the following:
  - rash
  - conjunctival injection
  - abdominal symptoms (pain, vomiting, diarrhoea)
  - features of shock (tachycardia and/or hypotension for age)
- Early recognition of a child with possible PIMS-TS improves outcomes
- Children with PIMS-TS require a multidisciplinary team approach – initial referral should be made to the Infectious Diseases team
- Investigations and empiric therapy for sepsis and/or toxic shock syndrome should be commenced while MDT being arranged to discuss need for specific therapies (IVIG and/or steroids)

Background

Paediatric Inflammatory Multisystem Syndrome Temporally associated with SARS-CoV-2 (PIMS-TS), also known as Multisystem Inflammatory Syndrome in Children (MIS-C) is a novel, rare post-infectious syndrome that occurs in those with previous SARS-CoV-2 infection.

- It occurs 2-4 weeks after acute COVID-19
- The preceding acute COVID-19 illness may be mild or asymptomatic
- The median age of patients is 9 years but has been described from infancy to mid-adulthood
- It is more common in
  - non-European Caucasian race/ethnicity
  - boys
  - those who are overweight or have obesity

Diagnosis

- The diagnosis is made on clinical and laboratory criteria, which are variably present
- There is no diagnostic test
- Early recognition is key

Appropriate investigations and prompt discussion with a multi-disciplinary team (including Paediatric Infectious Diseases, Rheumatology, General Paediatrics, Immunology, Haematology, Cardiology, Intensive Care as available) is essential. The initial referral should be made to the Infectious Diseases team.

The severity of PIMS-TS varies from mild disease to fulminant life-threatening shock and organ dysfunction. The clinical phenotype of PIMS-TS varies with age and is heterogeneous. Fever and evidence of systemic inflammation are typical.
Three over-lapping clinical phenotypes have been observed and may occur at any age (adapted from Schlapback LJ et al 2021).

(i) **Kawasaki disease (KD)-like phenotype** (often fulfilling AHA diagnostic criteria for complete or incomplete KD) is more common in children aged less than 5 years. Typical features include:
- fever
- polymorphous non-blanching rash
- mucosal involvement
- non-purulent conjunctival injection
- peripheral oedema
- cervical lymphadenopathy (can present as stiff, painful neck)
- coronary artery dilatation or aneurysms may be evident on echocardiography.

(ii) **Shock-like presentation** is more common in those over 5 years and characterised by:
- GI symptoms and signs (abdominal pain, diarrhoea, vomiting)
- distributive shock (due to myocardial dysfunction)
- polymorphous rash
- headache
- altered conscious state.
- coronary artery dilatation or aneurysms may be evident on echocardiography

(iii) **Undefined inflammatory presentation** is more common in children aged over 5 years, and is characterised by:
- persistent fever
- abdominal pain
- no cardiac involvement or shock
- other signs of PIMS-TS may be variably present (rash, conjunctival injection, peripheral oedema, cervical lymphadenopathy)
- may progress to more severe disease or resolve, even without treatment.
Case Definition

Note this definition is designed principally for research and surveillance purposes and should not be used to exclude the diagnosis.

Children and adolescents (< 18 years of age) with fever ≥3 days

AND two or more of the following:

a) Rash or bilateral non-purulent conjunctivitis or muco-cutaneous inflammation signs (oral, hands or feet)
b) Age-specific hypotension or 'shock' within 24 hours of presentation
c) Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated Troponin/NT-proBNP)
d) Evidence of coagulopathy (by PT, PTT, elevated d-dimers)
e) Acute gastrointestinal problems (diarrhoea, vomiting or abdominal pain).

AND Elevated markers of inflammation such as CRP, procalcitonin.

AND Exclusion of other infectious causes of inflammation, including bacterial sepsis, toxic shock syndrome (note that treatment for PIMS-TS may need to be commenced before alternative diagnoses are definitively excluded)

AND Evidence of current or recent SARS-CoV-2 infection (RT-PCR, rapid antigen test or serology), or confirmed contact with COVID-19 case.

Note: results of testing may be delayed, particularly serology. If all other criteria are met, a diagnosis of PIMS-TS may be made with expert advice, and treatment initiated.

Assessment

History

• New symptoms can present sequentially over several days, thus history should include asking about diagnostic features that may have resolved by the time of presentation

Examination

• Findings can present sequentially over a number of days, thus careful daily examination is important
• Examine for features consistent with PIMS-TS and to exclude complications or alternative diagnoses (Table 1)
• Features of cardiovascular dysfunction – refer to sepsis guideline
• Features of toxic shock syndrome – may include fever, vomiting, diarrhoea, myalgia, conjunctival injection, confusion, collapse and a widespread erythematous rash
Table 1. Symptoms and signs suggestive of PIMS-TS

<table>
<thead>
<tr>
<th>General</th>
<th>• Fever</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal</td>
<td>• Abdominal pain</td>
</tr>
<tr>
<td></td>
<td>• Diarrhoea, vomiting (can mimic appendicitis)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>• Chest pain</td>
</tr>
<tr>
<td></td>
<td>• Tachycardia for age</td>
</tr>
<tr>
<td></td>
<td>• Hypotension, shock, oliguria</td>
</tr>
<tr>
<td>Respiratory</td>
<td>• Cough, sore throat, respiratory distress</td>
</tr>
<tr>
<td></td>
<td>• Hypoxia</td>
</tr>
<tr>
<td>Dermatologic</td>
<td>• Conjunctivitis, periorbital swelling/redness</td>
</tr>
<tr>
<td></td>
<td>• Mucous membrane changes</td>
</tr>
<tr>
<td></td>
<td>• Rash</td>
</tr>
<tr>
<td></td>
<td>• Lymphadenopathy</td>
</tr>
<tr>
<td></td>
<td>• Swollen hands/feet</td>
</tr>
<tr>
<td>Neurologic</td>
<td>• Headache, confusion, irritability</td>
</tr>
<tr>
<td></td>
<td>• Reduced level of consciousness</td>
</tr>
<tr>
<td></td>
<td>• Syncope</td>
</tr>
</tbody>
</table>

Differential Diagnoses

• Sepsis
• Toxic shock syndrome
• Acute abdomen, e.g. appendicitis
• Malignancy
• Haemophagocytic lymphohistiocytosis
• Systemic onset juvenile idiopathic arthritis

Management

Principles

All children with suspected PIMS-TS should have:

• Review by a senior clinician
• Early involvement of Multi-disciplinary Team; Infectious Diseases, Rheumatology, General Paediatrics and Immunology teams to guide initial management with Cardiology, Haematology and Intensive Care input as required. The initial referral should be made to the Infectious Diseases team.
• Blood cultures taken prior to commencing empiric broad spectrum antimicrobials as per RCH sepsis guidelines
• Regular observations and three-lead ECG monitoring
• If the child is profoundly ill or has signs of sepsis treat accordingly and involve ICU early as per sepsis guidelines
Investigations

Bloods
- Venous blood gas
- FBE, UEC, LFT, CRP, ESR
- Blood culture
- Coagulation profile, D-Dimer
- Ferritin, LDH, CK
- Troponin
- SARS-CoV-2 serology
- Serum to store (prior to any IVIG)
- Consider according to clinical presentation:
  - CMP, triglycerides, pro-BNP, procalcitonin (if in ICU)

Other investigations
- Respiratory PCR including SARS-CoV-2
- Chest X-ray – assess for cardiomegaly
- ECG – arrhythmia, heart block
- Echocardiography – urgent if clinical instability or treating for PIMS-TS/KD
  - Myocardial dysfunction, pancarditis

Consider
- Abdominal ultrasound – if concerns of acute abdomen
- Neuroimaging – if concern reading neurological status

Table 2. Investigations consistent with PIMS-TS

<table>
<thead>
<tr>
<th>Inflammatory and other biomarkers</th>
<th>Elevated CRP</th>
<th>Elevated ESR</th>
<th>Elevated ferritin</th>
<th>Elevated procalcitonin</th>
<th>Elevated creatinine kinase</th>
<th>Elevated lactate dehydrogenase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haematology</td>
<td>Lymphopaenia</td>
<td>Neutrophilia</td>
<td>Thrombocytopenia</td>
<td>Elevated D-dimer</td>
<td>Elevated fibrinogen</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Elevated troponin</td>
<td>Elevated pro-BNP</td>
<td>Myocardial dysfunction</td>
<td>Pericardial effusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Abnormal liver function tests</td>
<td>Hypoalbuminaemia</td>
<td>Colitis/ ileitis</td>
<td>Ascites</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CXR / CT scan</td>
<td>Patchy infiltrates</td>
<td>Pleural effusion</td>
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</tbody>
</table>
**Treatment**

**Supportive care**
- Fluid resuscitation if signs of shock – caution if features of myocardial dysfunction due to risk of pulmonary oedema - see sepsis guideline
- Strict fluid balance chart
- Gastric protection (eg. omeprazole) for children receiving steroids

**Antimicrobials**
- All children with suspected PIMS-TS should be covered with broad-spectrum antimicrobials (IV ceftriaxone and IV flucoxacillin) after blood cultures are collected
- See sepsis guideline

**Anti-inflammatory**
- Anti-inflammatory treatment should be initiated following discussion with a multidisciplinary team once a diagnosis of PIMS-TS is made.
- Options for initial treatment are IVIG or steroids, or both
- Treatment should be tailored depending on the age of the child, clinical features and investigations, in discussion with Infectious Diseases and Rheumatology
- General approach at RCH:
  - **PIMS-TS KD**: IVIG 2 g/kg (max 100 g), consider oral prednisolone 2 mg/kg/day (max 60 mg)
  - **PIMS-TS shock**: IVIG 2 g/kg (max 100 g), pulse IV methylprednisolone 10 mg/kg/day (max 1 g)
  - **PIMS-TS undefined**: consider IVIG, consider oral prednisolone at doses as above.
  
  *Note that IVIG is a considerable oncotic load and may precipitate cardiac failure if there is myocardial dysfunction. Consider administering more slowly.*

**Thromboprophylaxis**
- All children should receive low-dose aspirin 3-5 mg/kg oral as a daily dose
- Low-molecular weight heparin (LMWH) may also be indicated, after consultation with the Haematology team

**Ongoing Monitoring and Management**
- Close clinical observation for recurrence of fevers and signs of ongoing inflammation (e.g., conjunctival injection)
- Regular observations including blood pressure
- Daily weights

If there are signs of ongoing inflammation after initial treatment (fever, rising or persistently elevated inflammatory markers), then further treatment is indicated but should be pursued with consultation by the ID and Rheumatology Teams. Treatment options include a further dose of IVIG, steroid therapy or biologic agents (anakinra, tocilizumab, infliximab).

**The risk of coronary artery dilatation/aneurysms in PIMS-TS is 15-25%**. Echocardiography is indicated at diagnosis and at 4-6 week follow-up; additional echocardiography as indicated by clinical course in discussion with Cardiology.
Coronavirus (COVID-19)

Children with confirmed or suspected coronavirus (COVID-19) who do not require respiratory or hydration support but are at risk of deterioration can be admitted to HITH for monitoring. As with all HITH admissions, this needs a safe home environment and consent. External referrals are accepted.

HITH (Wallaby) admission criteria and referral

**HITH not appropriate**
- MORE SEVERE ILLNESS (CPG/Taskforce definition)
  - Oxygen requirement per clinical judgement
  - Persistent tachypnoea
  - Requiring NG/IV fluids
  - PIMS-TS or similar inflammatory features
- MILD ILLNESS AND LOW RISK OR ASYMPTOMATIC
  - Mild usually managed by parents +/- GP

**HITH possible**
- ASYMPTOMATIC with high-risk co-morbidities (*chronic respiratory/neurodisability/extreme obesity/immunocompromise/cyanotic heart dis) or neonate – most can be GP, case-dependent
- MILD ILLNESS and 1-3 months old
- Support for children out of usual home care
- Social complexity is not an exclusion

**HITH appropriate**
- MODERATELY UNWELL (HITH-specific definition)
  - Mild to moderate work of breathing but maintaining oxygen sats >92% in air
  - <2/3 usual intake but no NG/IV fluid needed
  - Transition to home after inpatient admission
- MILDLY UNWELL BUT HIGHER RISK
  - Mild symptoms with high-risk co-morbidities*
  - Neonates (if febrile, other causes excluded)

**Admit under appropriate team**

**Refer back to GP**

**Internal: Contact HITH fellow in hours on 52784 or consultant on call for HITH after hours via switch. Complete EMR HITH referral**

**External: For referral by clinicians call 93454770. If accepted, complete referral form at link below**

- Referrals are accepted from clinicians in RCH ED/wards/outpatients, external hospitals (including ED), GP, community health, public health, maternal child health nurses, adult HITH colleagues

Prior to family leaving please ensure:
- HITH AUM has obtained consent, current contact information, name and contact details of an alternate person and plan if parent(s) are admitted to hospital
- HITH COVID-19 handout given to family
- Family and referring team are aware that reviews are via telehealth at a specified time. Face-to-face reviews will occur only if clinically indicated. This includes the admission process.
HITH protocol – nursing and medical

Daily care requirements

Moderately unwell
Daily medical telehealth review +/- nursing telehealth review in the afternoon

Higher risk, mild symptoms
Daily nursing telehealth review – escalation as required

Telehealth review includes:
- respiratory assessment – work of breathing, activity level, respiratory rate, colour
- hydration assessment – oral intake, wet nappies, activity level

Any concerns will lead to a home visit (staff to wear personal protective equipment (PPE)) or presentation to hospital with parents or via ambulance depending on acuity.

HITH team available 24/7 for family to escalate their concerns – phone calls to come to HITH AUM in hours, ED AUM after hours and escalate to HITH consultant on call as required.

Red flags for escalation

- Inadequate oral intake (< 3 wet nappies in 24 hours, <2/3 oral intake, clinical signs of dehydration) – transfer back to hospital (see below)
- Respiratory deterioration (SaO2 <94%, apnoea, colour change, change in work of breathing) – transfer back to hospital (see below)
- Chest pain/dizziness/palpitations/fainting/breathless (consider myocarditis) – follow RCH CPG
- Fever >5 days, lymphadenopathy, rash (consider PIMS-TS) – transfer back to hospital
- Parental anxiety – increase daily support/telehealth reviews/home visits

Readmission
If clinically appropriate and a ward bed is available, Wallaby will liaise with General Medicine (or most appropriate team) and the bed manager to arrange direct admission to the ward.

If direct admission is not possible or urgent clinical review needed, they will be asked to present to ED. Wallaby will notify the ED admitting officer and General Medicine if this occurs.

Personal protective equipment (PPE)
Airborne precaution PPE prior to entering the home (N95 mask, eye protection, gown, gloves)
Advise only one carer to be in the room during the visit; remind them of physical distancing 1.5 m, no unwell family members in the room
At the end of the visit, once outside, remove PPE into a disposal bag and leave for family to discard.
Complete hand hygiene prior to returning to car.

Discharge plan
Discharge when clinical condition improving – patients may deteriorate around 5 days.
If high risk group and mild symptoms, can discharge after 7 days.
Family must continue isolation until advised otherwise by Dept of Health.