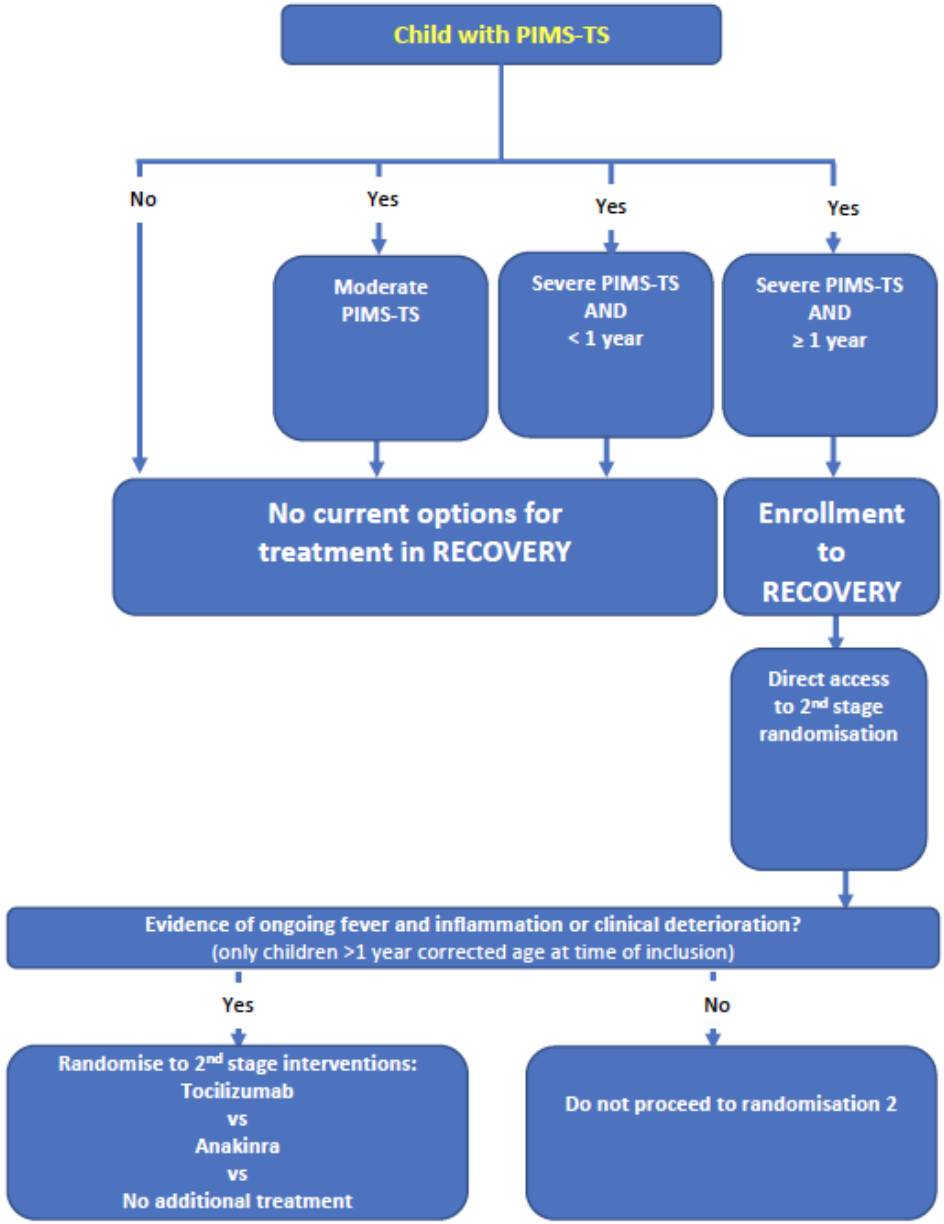
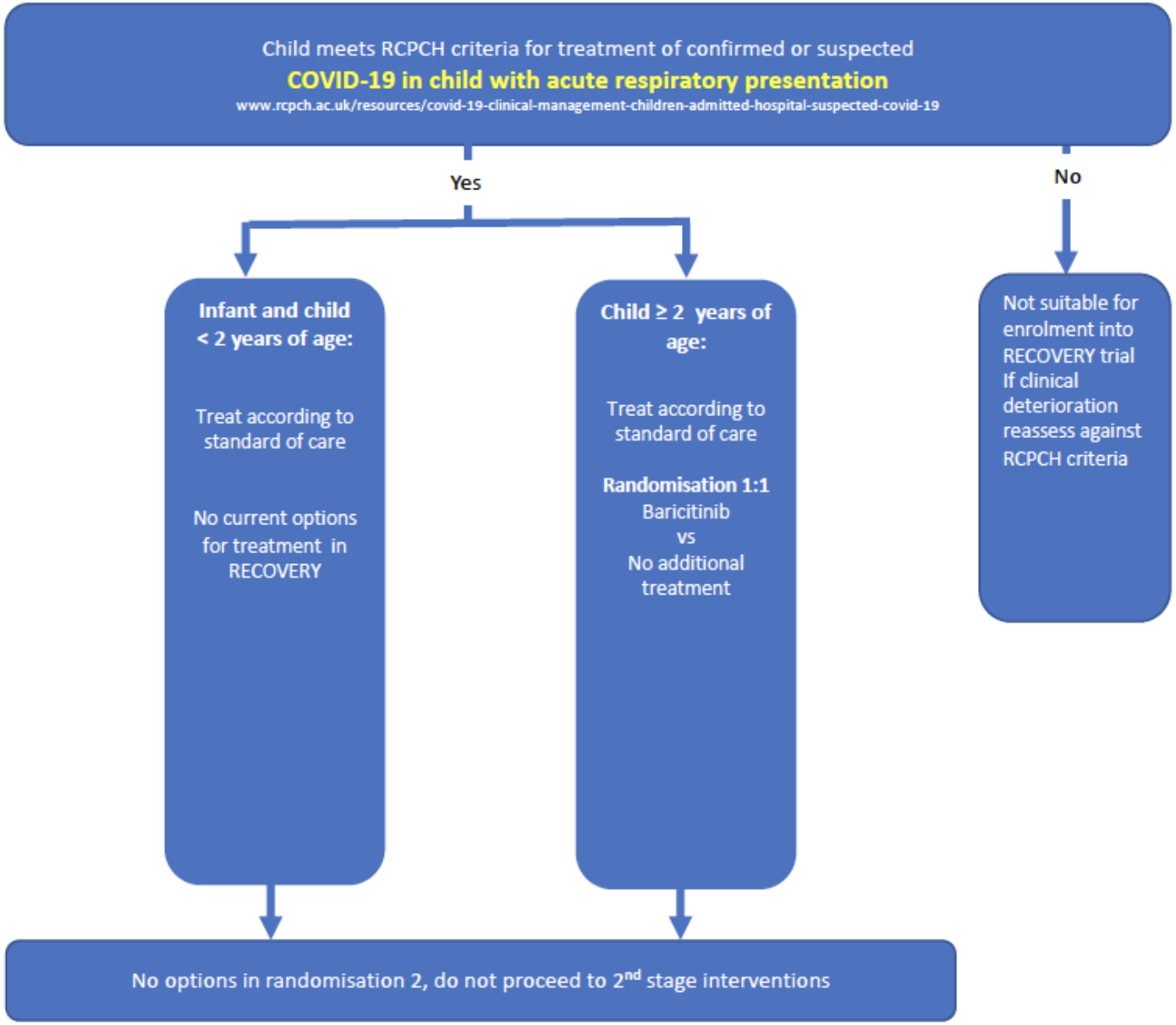
# Paediatric Patients

**Adapted for paediatric patients**

| | RECOVERY Protocol | |
|---|---|---|
| **Eligibility** | In the original protocol, patients were eligible if all they were:<br>- Aged at least 18 years<br>- Hospitalised<br>- SARS-CoV-2 infection (clinically suspected or laboratory confirmed)<br>- No medical history that might, in the opinion of the attending clinician, put the patient at significant risk if he/she were to participate in the trial | **See page 2 to 5 for details on which children should be offered participation in RECOVERY**. |
| **1st stage Interventions** | 1st stage randomisation consists of different parts to allow for the factorial design. The available arms are different between adults and children.<br><br>If one or more of the active drug treatments is not available at the hospital or is believed, by the attending clinician, to be contraindicated (or definitely indicated) for the specific patient, then this fact will be recorded via the web- based form prior to randomisation; random allocation will then be between the remaining arms. | **Children with PIMS-TS (Corrected gestational age >44 weeks):**<br>- No current options<br>Note: See 2nd stage interventions for severe PIMS-TS<br><br>**Children with respiratory COVID phenotype (≥2 years):**<br>- No additional treatment<br>- Baricitinib<br>Note: No current options for children <2 years |
| **2nd stage Interventions** | | **Children (≥1 year) with severe PIMS-TS who have not responded to therapy with intravenous immunoglobin (IVIg) and/or corticosteroids (or if IVIg or corticosteroids are not considered indicated) randomised 2:2:1 to:**<br>- Tocilizumab<br>- Anakinra<br>- No additional treatment<br>Note: see page 7 for other exclusion criteria |
| **Follow-up/outcomes** | Ascertained at the time of death or discharge or at 28 days after randomisation (whichever is sooner):<br>- Vital status (alive/ dead, with date and presumed cause of death)<br>- Hospitalisation status (inpatient/ discharged, with date of discharge)<br>- Use of ventilation (none/ previous/ ongoing, with days of use and type)<br>- Use of renal dialysis or haemofiltration (none/ previous/ ongoing) | Same outcome measures. |


Child with PIMS-TS
No
Yes
Yes
Yes
Moderate PIMS-TS
Severe PIMS-TS AND < 1 year
Severe PIMS-TS AND ≥ 1 year
No current options for treatment in RECOVERY
Enrollment to RECOVERY
Direct access to 2nd stage randomisation
Evidence of ongoing fever and inflammation or clinical deterioration?
(only children >1 year corrected age at time of inclusion)
Yes
No
Randomise to 2nd stage interventions:
Tocilizumab
vs
Anakinra
vs
No additional treatment
Do not proceed to randomisation 2


Child meets RCPCH criteria for treatment of confirmed or suspected
COVID-19 in child with acute respiratory presentation
www.rcpch.ac.uk/resources/covid-19-clinical-management-children-admitted-hospital-suspected-covid-19
Yes
No
Infant and child < 2 years of age:
Treat according to standard of care
No current options for treatment in RECOVERY
Child ≥ 2 years of age:
Treat according to standard of care
Randomisation 1:1
Baricitinib
vs
No additional treatment
Not suitable for enrolment into RECOVERY trial If clinical deterioration reassess against RCPCH criteria
No options in randomisation 2, do not proceed to 2nd stage interventions

## FAQ - General

- **Who has endorsed the trial?** The trial itself has been endorsed by all of the UK Chief Medical Officers and NHS England Medical Director. Inclusion of children has been endorsed by NHS England, the Royal College of Paediatrics and Child Health, and the NIHR CRN:Children.
- **Who should take consent for inclusion in the trial?** Any healthcare professional with appropriate training (completed online) and knowledge of the trial can take consent.
- **Who can take part?** There are no special approvals needed for including children. If the site Principal Investigator is not a paediatric healthcare professional, one will be identified, to work alongside them.

## FAQ – Recruitment and randomisation

1. **Should a child who has laboratory confirmed SARS-CoV-2 but only displaying mild symptoms of COVID-19 be recruited?** No.
2. **Which child should be considered for RECOVERY?**

   **Respiratory presentations of acute COVID-19 and ≥2 years:** The **RCPCH guidance** **(click to link to pdf**) should be used to guide the decision about thresholds for treatment and therefore consideration of enrolment into RECOVERY. These criteria include:

   - Unventilated requiring FiO2 >40% to maintain saturation 88-97%

   **or**

   - Ventilation: Oxygenation index: 4 ≤ 16 / Oxygenation saturation index: 5 ≤ 12.3

   **Paediatric multisystem inflammatory syndrome temporally associated with COVID-19 (PIMS-TS): Children can specifically be recruited to RECOVERY if they have suspected PIMS-TS.**
   Randomisation stage 1 (comparing steroids, intravenous immunoglobulin, and no additional treatment) closed on the 16th July 2021.
   Currently, only 2nd stage randomisation (tocilizumab *vs* anakinra *vs* standard of care) remains open for children who have severe PIMS-TS (those who have not responded to therapy with IVIg and/or corticosteroids or if IVIg or corticosteroids are not considered indicated).

3. **Which neonates/infants should be considered for RECOVERY?** No current treatment options in RECOVERY for neonates/infants.
4. **Can children be enrolled if they have suspected acute respiratory COVID-19 or PIMS-TS, but a negative SARS-CoV2 PCR on a respiratory sample?** Yes, children with clinically suspected or confirmed COVID-19 may be enrolled in RECOVERY. This includes children who test negative for SARS-CoV2, who are suspected of having PIMS-TS or have clinically suspected COVID-19 (typical symptoms and compatible CXR).

**The table below shows potential clinical scenarios and randomisation options within RECOVERY for each clinical scenario.**
**Potential clinical scenarios (≥1 year - 18th birthday):**

**R= recommended option**

| | | Acute respiratory presentation of COVID-19 | With evolving inflammatory phenotype | PIMS-TS | |
|---|---|---|---|---|---|
| | **Phenotypes** | **Primarily respiratory symptoms AND ≥2 years** | **Initially respiratory symptoms (dexamethasone given, any doses), now deteriorating with features of PIMS-TS** | **Moderate PIMS-TS** | **Severe PIMS-TS Children (those who have not responded to therapy with IVIg and/or corticosteroids or if IVIg or corticosteroids are not considered indicated) AND ≥1 years** |
| **1st stage interventions, randomisation** | **No additional treatment** | R | No options for randomisation | No options for randomisation | Proceed directly to 2nd stage. |
| | **Baricitinib** | R | | | |
| **2nd stage interventions** | **No additional treatment** | No option to 2nd stage randomisation. Manage as clinically indicated | No options for randomisation | No options for randomisation | **R** |
| | **Tocilizumab** | | | | |
| | **Anakinra** | | | | |

5. **Can a child be enrolled if one (or more) of the intervention arms is contra-indicated for that patient?** Yes, the child can be entered into the trial. The attending clinician would be asked to record on the web-based form which treatment(s) are unsuitable for the patient prior to randomisation. Random allocation will then be between the remaining arms. Refer to the table above and the next section on "Randomisation: additional intervention-specific considerations" for additional guidance (page 7).

6. **If the child is transferred from one centre to another, can they remain in the trial**? Yes. They can remain in the trial and the trial drugs will be provided by the receiving site.

7. **Can we randomise children (with respiratory phenotype) to the baricitinib arm if they have an absolute lymphocyte count of less than 0.5 x 10^9 cells/L?** Yes, they can be included for randomisation to the baricitinib arm. Lymphopaenia is a risk marker for severe COVID-19 so this would potentially exclude the participants who had the most to gain from baricitinib therapy.

8. **Should children be screened for tuberculosis and hepatitis before inclusion for randomisation for baricitinib, tocilizumab or anakinra?** The RECOVERY trial protocol does not require screening for tuberculosis or hepatitis given the short treatment duration. Screening can be carried out at the discretion of the attending clinician but do not delay treatment while waiting for results.

9. **The child is female of child-bearing potential, is a pregnancy test required prior to randomisation to baricitinib**? Yes, baricitinib should be marked as unsuitable if a pregnancy test has not been done or is positive in a female considered of childbearing potential.

## FAQ – Clinical management

20. **Is any dose adjustment required in a child with renal impairment?** No dosage adjustment is required for tocilizumab and anakinra. For baricitinib, please refer to dosing table.

21. **A child has been randomised and started on baricitinib. However, the patient is now presenting with evolving inflammatory phenotype. Can we proceed to 2nd stage randomisation?** The 2nd stage randomisation is only available to children with PIMS-TS diagnosis at trial enrolment**.** If the clinical decision is to start tocilizumab, we recommend that baricitinib is stopped (half-life of baricitinib in adults is 12 hours). The use of toculizumab will be considered off-protocol and should be recorded in the paediatric case report form.

22. **For children who have received baricitinib, tocilizumab or anakinra, what is the advice on live and live attenuated vaccines?** Limited data are available on the response to vaccination with live vaccines in children receiving these drugs. We recommend that live and live attenuated vaccines be avoided for at least 12 weeks.

## Randomisation: ADDITIONAL intervention-specific considerations

**In addition** to the information provided below, the attending clinician can, based on their clinical judgement, indicate on the web-based form that one or more of the interventions is deemed **unsuitable** for the specific patient.

| Drug | Additional considerations relating to randomisation |
|---|---|
| **Baricitinib** | Select "Yes" to question A14 to reflect that this drug is **unsuitable** if any of the following circumstances apply:<br>- Patient < 2 year<br>- Known hypersensitivity to baricitinib<br>- Known hepatitis B, hepatitis C or tuberculosis infection<br>- Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) > 3 x Upper Limit of Normal<br>- Received biologic immunomodulators or Janus Kinase inhibitors within the 30 days prior to randomisation.<br>- Absolute neutrophil count <0.5 x $10^9$/L<br>- On renal replacement therapy<br>- Positive pregnancy test or breast feeding |
| **Tocilizumab** | Select "Yes" to question A14 to reflect that this drug is **unsuitable** if any of the following circumstances apply:<br>- Patient < 1 year<br>- Known hypersensitivity to tocilizumab<br>- Known hepatitis B, hepatitis C or tuberculosis infection<br>- Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) > 3 x Upper Limit of Normal<br>- Received biologic immunomodulators or Janus Kinase inhibitors within the 30 days prior to randomisation. |
| **Anakinra** | Select "Yes" to question A14 to reflect that this drug is **unsuitable** if any of the following circumstances apply:<br>- Patient < 1 year<br>- Known hypersensitivity to anakinra or E. coli derived proteins<br>- Known hepatitis B, hepatitis C or tuberculosis infection<br>- Absolute neutrophil count <1.5 x $10^9$/L<br>- Received biologic immunomodulators or Janus Kinase inhibitors within the 30 days prior to randomisation. |

## Paediatric dosing information

### Children with respiratory COVID phenotype (≥2 years)

<table>
<tr><th>Arm</th><th>Route</th><th>Age/Weight</th><th>Dose</th></tr>
<tr><td>Baricitinib<br><br>- 2 and 4 mg tablets</td><td>Oral/ other enteral routes</td><td>≥ 2 years</td><td>For children ≥ 2 years with respiratory presentation of COVID-19:<br><br>Once daily for 10 days or until discharge, whichever is sooner<br><br>
<table>
<tr><th>eGFR</th><th>2 to < 9 yr</th><th>≥ 9 yr</th></tr>
<tr><td>≥ 60</td><td>2mg</td><td>4mg</td></tr>
<tr><td>30 to <60</td><td>2mg alt day</td><td>2mg</td></tr>
<tr><td>15 to <30</td><td>Excluded</td><td>2mg alt day</td></tr>
</table>
Those on renal replacement therapy are excluded</td></tr>
</table>

### Children with severe PIMS-TS who have already received high dose steroid and intravenous immunoglobulin

<table>
<tr><th>Arm</th><th>Route</th><th>Age/Weight</th><th>Dose</th></tr>
<tr><td>Tocilizumab</td><td>Intravenous</td><td colspan="2">Infants < 1 year excluded</td></tr>
<tr><td></td><td></td><td>< 30 kg</td><td>For children with PIMS-TS:<br>12 mg/kg<br><br>A second dose may be given ≥12 and ≤24 hours later if, in the opinion of the attending clinicians, the patient’s condition has not improved.</td></tr>
<tr><td></td><td></td><td>≥ 30 kg</td><td>For children with PIMS-TS:<br>8 mg/kg (max 800 mg)<br><br>A second dose may be given ≥12 and ≤24 hours later if, in the opinion of the attending clinicians, the patient’s condition has not improved.</td></tr>
<tr><td>Anakinra</td><td>Subcutaneous<br><br>(Intravenous route if clinically required)</td><td colspan="2">Infants < 1 year or <10 kg excluded</td></tr>
<tr><td></td><td></td><td>≥ 10 kg</td><td>For children with PIMS-TS:<br>2 mg/kg daily for 7 days or until discharge, whichever is sooner</td></tr>
</table>

## Second randomisation of paediatric participants

The RECOVERY protocol includes a second randomisation for participants who fulfil the following criteria:

(i) Randomised into the RECOVERY trial no more than 21 days ago

(ii) Clinical evidence of **PIMS-TS**:

- significant systemic disease with persistent pyrexia[1]; and
- C-reactive protein ≥75 mg/L

**(iii)** No medical history that might, in the opinion of the attending clinician, put the patient at significant risk if he/she were to participate in this aspect of the RECOVERY trial.

The organisation of children's services for COVID-19 will involve transferring children to regional tertiary units for specialist services and/or paediatric intensive care should their condition satisfy the above criteria, where interventions like tocilizumab (hence this second randomisation) will be considered. A copy of the RECOVERY trial consent form and first randomisation allocation sheet should be sent with the child on transfer.

The current trial web-based computer system only allows participants to be "second randomised" at the site where they were first recruited into the trial. Therefore, the following procedure must be followed to allow children who have been recruited at a referring hospital and subsequently transferred to a tertiary centre to be entered into this second randomisation. **The RECOVERY paediatric lead at the tertiary centre/PICU will assume trial responsibility for the child upon arrival.**

### Procedure

1. **Tertiary centre/PICU RECOVERY team** contact referring hospital RECOVERY team (ideally the referring hospital's RECOVERY paediatric lead if possible) to discuss second randomisation and agree that it is reasonable to proceed.

2. If agreed, **Tertiary Centre/PICU RECOVERY team** send baseline information required for second randomisation to referring hospital. This information includes:
   - Name of treating clinician (at PICU)
   - Current oxygen and ventilation requirements
   - Whether participant has significant systemic disease with persistent pyrexia
   - Latest laboratory results for CRP, ferritin and creatinine (copies of laboratory reports)

   The participant's study ID should be added to these documents. This information should be shared using NHSmail whenever possible. If other e-mail is used then any identifiers should be redacted.
3. **Referring hospital RECOVERY team** complete second randomisation on trial web-based randomisation system (indicating the name of the tertiary/PICU clinician and hospital in response to question A2 "Name of treating clinician").

4. **Referring hospital RECOVERY team** share PDF of allocation notification with tertiary unit/ PICU.

5. **Referring hospital RECOVERY team** store data received from tertiary unit/PICU in participant's medical record along with entry to describe second randomisation and a copy of the allocation notification from the RECOVERY trial web-based randomisation system.

[1] A small number of children (age <18 years) present with atypical features, including a hyperinflammatory state and evidence of single or multi-organ dysfunction. Some do not have significant lung involvement.
(see: https://www.rcpch.ac.uk/sites/default/files/2020-05/COVID-19-Paediatric-multisystem-%20inflammatory%20syndrome-20200501.pdf)

6. **Tertiary unit/PICU RECOVERY team** prescribe tocilizumab if necessary and document second randomisation process in medical record (with copy of allocation notification).

7. At the earliest of discharge, death or 28 days after first randomisation, Tertiary/**PICU RECOVERY team** contact referring hospital RECOVERY team to support completion of trial follow-up form (unless child has been transferred back to referring hospital prior to discharge).

## Trial drugs supply and administration

<table>
<tr><th>Drug</th><th>Specific administration issues</th></tr>
<tr><td>Baricitinib</td><td>Baricitinib will be sourced by local pharmacy procurement team via their normal routes. Baricitinib is available as 2mg and 4mg film coated tablets. A Blueteq form will need to be completed for each patient to ensure that costs can be reimbursed to hospital trusts. The Blueteq form can be completed in retrospect.<br><br>Instructions for administration for patients who are unable to swallow whole tablets:<br><br>- The dispersion volume is listed as per table below.<br>- Disperse the required number of tablets in water with gentle swirling.<br>- Tablets may be crushed to facilitate dispersion.<br>- Dispersed tablets are stable in water for up to 4 hours.<br>- Ensure the tablet(s) are sufficiently dispersed to allow free passage through the tip of the syringe.<br>- Withdraw the required volume from the container into an appropriate size syringe and administer.<br>- Rinse container (rinse volume as per table below), withdraw the contents into the syringe and administer.<br><br><table><tr><th>Administration via</th><th>Dispersion volume</th><th>Container rinse volume</th></tr><tr><td>Oral dispersion</td><td>10 mL (5 mL minimum)</td><td>10 mL (5 mL minimum)</td></tr><tr><td>Gastrostomy tube</td><td>15 mL (10 mL minimum)</td><td>15 mL (10 mL minimum)</td></tr><tr><td>Nasogastric tube</td><td>30 mL</td><td>15 mL</td></tr></table><br>Mixing with food: In adults, administration of baricitinib with meals was not associated with a clinically relevant effect on exposure. Therefore, mixing with a small amount of juice or squash would be considered expectable to aid administration.<br><br>There is no data on NJ administration.</td></tr>
<tr><td>Tocilizumab</td><td>Approval has been given for sites to use tocilizumab from local hospital stock by NHSE (and equivalent bodies in devolved nations). Charged via specialised commissioning (no blueteq required)<br><br>Based on vial size availability, doses can be rounded. Refer to Roche dosing guide in order to minimise wastage and to allow doses to be measured accurately. Refer to page 7 of https://www.medicines.org.uk/emc/rmm/1393/Document<br><br>Concentrate for solution for infusion 20 mg/mL</td></tr>
</table>

| | |
|---|---|
| | **< 30 kg**<br>- Calculate the volume of tocilizumab concentrate required for the patient's dose.<br>- Withdraw a volume of sodium chloride 0.9% from a 50 mL infusion bag, equal to the volume of tocilizumab concentrate required for the patient's dose.<br>- The required amount of tocilizumab concentrate should be withdrawn from the vial and placed in the 50 mL infusion bag.<br>Set the infusion pump and administer as an intravenous infusion over 60 minutes. The infusion rate can be adjusted in line with local practice.<br><br>**≥ 30 kg**<br>- Calculate the volume of tocilizumab concentrate required for the patient's dose.<br>- Withdraw a volume of sodium chloride 0.9% from a 100 mL infusion bag, equal to the volume of tocilizumab concentrate required for the patient's dose.<br>- The required amount of tocilizumab concentrate should be withdrawn from the vial and placed in the 100 mL infusion bag.<br>- Set the infusion pump and administer as an intravenous infusion over 60 minutes. The infusion rate can be adjusted in line with local practice.<br><br>After dilution, the prepared solution for infusion is physically and chemically stable at 30°C for 24 hours (storage at 2 - 8°C would be preferred). |
| **Anakinra** | Anakinra will be sourced by local pharmacy procurement team via their normal routes. Charged via specialised commissioning (no blueteq required)<br><br>Instructions for intravenous administration (if clinically required): Round dose to the nearest 5mg. Dilute in a suitable volume of sodium chloride 0.9% (10mL would be a suitable volume but 5mL may be used if very fluid restricted) and administer as intravenous bolus over 3 to 5 minutes.<br><br>Can be given peripheral or central line but it should not be mixed with other drugs. |

## Annex A: Trial drugs in children

There is clinical experience around using all the listed trial drugs for other conditions in children. The trial website provides broader discussions on the different interventions and their rationale with respect to COVID-19 (https://www.recoverytrial.net/for-site-staff/site-teams). Information relating to paediatric dosing is summarised below.

**Baricitinib –** Baricitinib is licensed in adults for the treatment of rheumatoid arthritis and atopic dermatitis at a recommended dose of 2 to 4mg once daily. Limited data informing baricitinib dosing (at doses 1 to 4mg once daily) in paediatric patients comes from ongoing clinical trials for the treatment of chronic autoimmune disorders requiring long-term treatment including different forms of juvenile idiopathic arthritis and atopic dermatitis. Through an expanded access program, baritictinib is also being used in the management of patients with type 1 interferonopathies (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6026004/). Paediatric patients with type 1 interferonopathies typically receive doses higher than 4 mg once daily dose (mean dose of 6 mg/day) and have been monitored over an extended period of time (up to 7 years).

**Tocilizumab -** Tocilizumab is licensed for the treatment of juvenile idiopathic polyarthritis and chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome (CRS) in children 2 years of age and older. A phase I PK study (n=11) showed tocilizumab 12mg/kg every 2 weeks provide comparable PK, PD and efficacy (with respect to JIA) between patients younger than 2 years (range: 0.8 - 1.8) and those aged 2 to 17 years (https://doi.org/10.1186/s12969-019-0364-z), although there is possibly a higher incidence of serious hypersensitivity in under 2.

**Anakinra** – Anakinra is licensed in children (aged 8 months and older with a body weight of 10 kg or above) for the treatment of cryopyrin-associated periodic syndromes, familial mediterranean fever, and Still's disease.

**Change control**

| Version | Changes |
|---|---|
| Version 2<br>(6th May2020) | Eligibility adaptation for paediatrics – signposting to FAQs<br>New and amended FAQs: Recruitment and randomisation Q1, Q2 and Q3<br>New FAQ: Clinical management Q1 |
| Version 3<br>(21st May 2020) | Clarification on hydrocortisone option<br>New FAQs: Recruitment and randomisation Q7, Q10, and Q11<br>New FAQ: Clinical management Q5<br>Inclusion of dosing tables from protocol version 6<br>Minor non-substantive edits made for consistency and clarity |
| Version 4<br>(27th May 2020) | Update: Recruitment and randomisation Q7<br>New section: Second randomisation of paediatric participants |
| Version 5<br>(2nd July 2020) | Hydroxychloroquine and lopinavir-ritonivir info removed from FAQ<br>Hydroxychloroquine and lopinavir-ritonivir info removed from section - Randomisation: intervention-specific considerations<br>Hydroxychloroquine and lopinavir-ritonivir info removed from section - Trial drugs administration<br>Hydroxychloroquine and lopinavir-ritonivir info removed from Annex A<br>New FAQ: Clinical management Q6 and Q7 (dose adjustment in renal impairment and infusion rate for convalescent plasma)<br>New FAQs: Recruitment and randomisation Q9 and Q10 (updated for dexamethasone and convalescent plasma) |
| Version 6<br>(23 July 2020) | Randomisation arms have been updated.<br>Amendment of corticosteroid dosing for children with PIMS-TS phenotype.<br>New FAQs on intravenous immunoglobulin and high dose methylprednisolone<br>Intravenous immunoglobulin info added to section - Randomisation: intervention-specific considerations<br>Trial drugs administration section changed to Trial drugs supply and administration<br>Intravenous immunoglobulin info added to section - Trial drugs supply administration<br>Intravenous immunoglobulin and high dose methylprednisolone info added to Annex A<br>Scenario flowcharts |
| Version 7<br>(06 Oct 2020) | Addition of randomisation arm: Synthetic neutralising antibodies (REGN10933 + REGN10987)<br>New FAQ: Recruitment and randomisation Q13<br>Dosing table – minor amendments for clarification |

| | |
|---|---|
| Version 8<br>(16th Dec 2020) | Information on azithromycin removed as this arm has now closed.<br>Option to proceed to 2nd stage randomisation if a child with PIMS-TS has already received a dose of intravenous immunoglobulin (IVIg) and steroids<br>New FAQ to provide clarification on IVIg dose calculation and administration.<br>Approval from NHSE to allow the use of hospital stock of tocilizumab. |
| Version 9<br>(13th Jan 2021) | Additional consideration when assessing suitability for tocilizumab randomisation: Children with alanine aminotransferase (ALT) or aspartate aminotransferase (AST) > 3 x Upper Limit of Normal are unsuitable. |
| Version 10<br>(28 Jan 2021) | Information convalescent plasma removed<br>Addition of baricitinib information<br>Addition of anakinra information |
| Version 10.1 | Correct exclusion criteria for baricitinib; "<1.5 x $10^9$/L" correct to <0.5 x $10^9$/L.<br>Additional intravenous preparation instructions for anakinra<br>Flowcharts moved to page 2 and 3<br>Removed reference to randomisation part A/B/C/D to minimise confusion<br>Removed "no additional treatment" from table on paediatric dosing information. |
| Version 11 | Randomisation stage 1 (comparing steroids, intravenous immunoglobulin, and no additional treatment) closed on the 16th July 2021.<br>Synthetic neutralising antibodies (REGN10933 + REGN10987) arm is closed. |