Management of children in hospital with Acute COVID-19

SARS CoV-2 RT-PCR Positive

Undertake SARS-CoV-2 antibody testing as soon as possible

All patients with pneumonitis requiring supplementary oxygen to achieve target saturations
(Above baseline oxygen requirement for children on long-term oxygen therapy)

Develops pneumonitis with oxygen requirement

Hospital-acquired COVID-19 with no new oxygen requirement

Patients fulfilling ALL the criteria below

- High Risk groups (see Page 3)
- Aged 12 and above
- Weight 40 kg and above
- Hospitalised for indications other than acute COVID-19
- Clinical deterioration from COVID-19 infection
- **No new oxygen requirement due to COVID-19**
- SARS-CoV-2 infection confirmed by PCR within last 5 days
- SARS-CoV-2 antibody test done (results not required)

Sotrovimab prophylaxis (within 5 days of symptom onset)
[If Sotrovimab is contraindicated/not possible/antiviral is the preferred clinical option, use **Remdesivir (3-day course)**

Dexamethasone
(Use Hydrocortisone in infants below 36 weeks corrected gestational age)

Venous thrombo embolism (VTE) prophylaxis

Age 12 years and above and Weight 40 kg and above

Remdesivir
On low-flow oxygen and within 10 days of onset of illness

(*Remdesivir is available for children below 12 years weighing at least 3.5kg, and 12-18 years weighing below 40kg, through company's compassionate scheme)

Viral pneumonia*

Viral pneumonia*

Age 12 years and above and Weight 40 kg and above

RECOVERY trial
Sotrovimab Vs Standard of Care

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

OR

Ventilated: Oxygenation index: 4 ≤ 16 / Oxygenation saturation index: 5 ≤ 12.3

(Consider recruitment early, when started on low dose dexamethasone).

Viral pneumonia*

MDT discussion required – contact Drs Hackett/Welch via UHB switchboard

Baricitinib

Age 2 years and above with features of Viral Pneumonia syndrome*
(*Typical symptoms (e.g. influenza-like illness with fever and muscle pain, or respiratory illness with cough and shortness of breath) **AND** compatible chest X-ray findings (consolidation or ground-glass shadowing) **AND** alternative causes considered unlikely or excluded (e.g. heart failure, bacterial pneumonia).

Baricitinib should not routinely be co-administered (given simultaneously) with an IL-6 inhibitor. However, if requiring critical care support or patient has deteriorated despite treatment, clinical judgement may deem co-administration appropriate.
A patient may be additively given an IL-6 inhibitor after treatment with Baricitinib has been commenced (or vice versa), according to clinical judgement.

Clinical deterioration

MDT discussion in severely ill patients – contact Drs Hackett/Welch via UHB switchboard

Il-6 INHIBITORS

Tocilizumab (Age 1 year and above)

(Sarilumab: Age 12 years and above and Weight 40 kg and above - if Tocilizumab is not available or cannot be used)

Requiring Low flow Oxygen AND CRP above 75
OR
Within 48 hours of commencing respiratory support*

(*High-flow nasal oxygen, continuous positive airway pressure, non-invasive ventilation or invasive mechanical ventilation)

MEDICATIONS

Medication	Dosage	Contraindications & cautions
Dexamethasone	**Dose:** 150 micrograms/kg once daily maximum 6 mg **Route**: PO or IV **Duration:** 10 days or discharge whichever is earlier.	
Hydrocortisone	**Dose:** 0.5 mg/kg every 12 hours for 7 days and then 0.5mg/kg once daily for 3 days **Route:** IV **Duration:** 10 days or until discharge if sooner.	
Sotrovimab	**Dose:** 500 milligrams **Route:** IV **Duration:** Single dose **(Note: Dose in RECOVERY trial is 1000 milligrams)**	• Known hypersensitivity reaction to the active substances or excipients • No dose adjustment required for renal or hepatic impairment
Remdesivir	**Dose:** Weight 3.5 - 40 kg: 5 mg/kg/ once daily on day 1, followed by 2.5 mg/kg/once daily Weight over 40 kg: 200 mg on day 1, followed by 100 mg once daily **Route:** IV **Duration:** 5 days (3 days in Hospital-acquired COVID-19)	• Estimated glomerular filtration rate (eGFR) below 30 ml/minute • Alanine aminotransferase (ALT) above 5 times the upper limit of normal at baseline Monitor liver and renal function daily, as dose adjustment/cessation might be required.
Baricitinib	**Dose:** Age 2 to <9 years: 2mg once daily Age ≥ 9 years: 4 mg daily **Route:** Oral **Duration:** 10 days or until discharge if sooner	• Known hypersensitivity to Baricitininb • eGFR <15 mL/min/1.73m^2 ([If the patient is below 9 years of age, this exclusion criteria should be eGFR <30 mL/min/1.73m^2] • Receiving dialysis or haemofiltration • Absolute neutrophil count less than 0.5 x 10^9 cells/L • Active tuberculosis • Pregnancy or breastfeeding (undertake pregnancy testing in females of childbearing potential prior to administration) • Dose adjustments required in renal impairment and co-administration with certain medications (seek advice from Pharmacy)
Tocilizumab	**Dose:** Weight below 30 kg: 12 mg/kg single dose Weight above 30 kg 8 mg/kg (max 800 mg) single dose **Route:** IV **Duration**: Single dose	• Known hypersensitivity to tocilizumab • Liver enzymes [alanine aminotransferase (ALT) or aspartate aminotransferase (AST)] more than ten times the upper limit of normal (caution if more than 1.5 times upper limit of normal) • Absolute neutrophil count of less than 1 x 10^9 /L • Platelet count of less than 50 x 10^3 /µL • Co-existing infection that might be worsened by tocilizumab • A pre-existing condition or treatment resulting in ongoing immunosuppression Note: Clinical (fever) and biochemical (CRP) responses to infection might be attenuated post -Tocilizumab. • Inform GP and family at discharge of the need to avoid pregnancy and live vaccines for at least 3 months post-Tocilizumab.
Sarilumab	**Dose**: 400mg **Route:** IV **Duration:** Single dose	• Should not have received another IL-6 inhibitor • Known hypersensitivity to sarilumab • Liver enzymes (ALT or AST) more than 5 times upper limit of normal • Platelet count of less than 150 x 10^9 /L • All the above cautions and contraindications as for Tocilizumab
RECOVERY trial medications	Refer to RECOVERY trial protocol https://www.recoverytrial.net/	• **Note: Sotrovimab dose in RECOVERY trial is 1000 milligrams**

High risk groups: Conditions listed below indicate increased risk for progression to severe COVID-19; however, these criteria are neither prescriptive nor restrictive.

Please discuss queries and severely ill patients with Paediatric Infectious Diseases service (Drs Hackett/Welch via UHB switchboard).

RCPCH guidance

CYP at significant risk

Neuro-disability

- Complex life-limiting neuro-disability with recurrent respiratory infections/ compromise

CYP at significant risk if 2 or more of these risk factors are present

Primary immunodeficiency

- Common variable immunodeficiency (CVID)
- Primary antibody deficiency on immunoglobulin (or eligible for immunoglobulin replacement)
- Hyper-IgM syndromes
- Good's syndrome (thymoma plus B-cell deficiency)
- Severe Combined Immunodeficiency (SCID)
- Autoimmune polyglandular syndromes /autoimmune polyendocrinopathy, candidiasis, ectodermal dystrophy (APECED syndrome)
- Primary immunodeficiency associated with impaired type I interferon signalling
- X-linked agammaglobulinaemia (and other primary agammaglobulinaemias)

Secondary immunodeficiency

- HIV CD4 count <200 cells/mm3
- Solid organ transplant
- HSCT within 12 months, or with GVHD
- CAR-T therapy in last 24 months
- Induction chemotherapy for acute lymphoblastic leukaemia (ALL), non-Hodgkin's lymphoma, chemotherapy for acute myeloid leukaemia (AML), relapsed and /or refractory leukaemia or lymphoma

Immunosuppressive treatment

- Chemotherapy within the last 3 months
- Cyclophosphamide within the last 3 months
- Corticosteroids >2mg/kg/day for 28 days in last 4 weeks
- B cell depleting treatment in the last 12 months

Other conditions

- High BMI (>95th Centile)
- Severe respiratory disease (e.g. CF or bronchiectasis with FEV1 <60%)
- Tracheostomy or long term ventilation
- Severe asthma (PICU admission in 12 months)
- Neurodisability and/or neurodevelopmental disorders
- Severe cardiac disease
- Severe chronic kidney disease
- Severe liver disease
- Sickle Cell disease or other severe haemoglobinopathy
- Trisomy 21
- Complex genetic or metabolic conditions associated with significant comorbidity
- Multiple congenital anomalies associated with significant comorbidity

NHSE guidance

Cohort	Description
Down's syndrome	All patients with Down's syndrome
Sickle cell disease	All patients with a diagnosis of sickle cell disease
Patients with a solid cancer	• Active metastatic cancer and active solid cancers (at any stage) • All patients receiving chemotherapy within the last 3 months • Patients receiving group B or C chemotherapy 3-12 months prior • Patients receiving radiotherapy within the last 6 months
Patients with a haematologic malignancy	• Allogeneic haematopoietic stem cell transplant (HSCT) recipients in the last 12 months or active graft vs host disease (GVHD) regardless of time from transplant (including HSCT for non-malignant diseases) • Autologous HSCT recipients in the last 12 months (including HSCT for non-malignant diseases) • Individuals with haematological malignancies who have o received chimaeric antigen receptor (CAR)-T cell therapy in the last 24 months, or o radiotherapy in the last 6 months • Individuals with haematological malignancies receiving systemic anti-cancer treatment (SACT) within the last 12 months except patients with chronic phase chronic myeloid leukaemia (CML) in molecular response or first or second line tyrosine kinase inhibitors (TKI). • All patients with myeloma (excluding MGUS) or chronic B-cell lymphoproliferative disorders (e.g. chronic lymphocytic leukaemia, follicular lymphoma) or myelodysplastic syndrome (MDS) who do not fit the criteria above. • All patients with sickle cell disease. • Individuals with non-malignant haematological disorder (e.g. aplastic anaemia or paroxysmal nocturnal haemoglobinuria) receiving B-cell depleting systemic treatment (e.g. anti-CD20, anti-thymocyte globulin [ATG] and alemtzumab) within the last 12 months.
Patients with renal disease	• Renal transplant recipients (including those with failed transplants within the past 12 months), particularly those who: o Received B cell depleting therapy within the past 12 months (including alemtuzumab, rituximab [anti-CD20], anti-thymocyte globulin) o Have an additional substantial risk factor which would in isolation make them eligible for nMABs or oral antivirals o Not been vaccinated prior to transplantation • Non-transplant patients who have received a comparable level of immunosuppression • Patients with chronic kidney stage (CKD) 4 or 5 (an eGFR less than 30 ml/min/1.73m2) without immunosuppression
Patients with liver disease	• Patients with cirrhosis Child's-Pugh class B and C (decompensated liver disease). • Patients with a liver transplant • Liver patients on immune suppressive therapy (including patients with and without liver cirrhosis) • Patients with cirrhosis Child's-Pugh class A who are not on immune suppressive therapy (compensated liver disease)
Patients with immune-mediated inflammatory disorders (IMID)	• IMID treated with rituximab or other B cell depleting therapy in the last 12 months • IMID with active/unstable disease on corticosteroids, cyclophosphamide, tacrolimus, cyclosporin or mycophenolate. • IMID with stable disease on either corticosteroids, cyclophosphamide, tacrolimus, cyclosporin or mycophenolate. • IMID patients with active/unstable disease including those on biological monotherapy and on combination biologicals with thiopurine or methotrexate
Primary immune deficiencies	• Common variable immunodeficiency (CVID) • Undefined primary antibody deficiency on immunoglobulin (or eligible for Ig) • Hyper-IgM syndromes • Good's syndrome (thymoma plus B-cell deficiency) • Severe Combined Immunodeficiency (SCID) • Autoimmune polyglandular syndromes/autoimmune polyendocrinopathy, candidiasis, ectodermal dystrophy (APECED syndrome) • Primary immunodeficiency associated with impaired type I interferon signalling • X-linked agammaglobulinaemia (and other primary agammaglobulinaemias)
HIV/AIDS	• Patients with high levels of immune suppression, have uncontrolled/untreated HIV (high viral load) or present acutely with an AIDS defining diagnosis • On treatment for HIV with CD4 <350 cells/mm3 and stable on HIV treatment or CD4>350 cells/mm3 and additional risk factors (e.g. age, diabetes, obesity, cardiovascular, liver or renal disease, homeless, those with alcohol-dependence)
Solid organ transplant recipients	• All recipients of solid organ transplants not otherwise specified above
Rare neurological conditions	• Multiple sclerosis • Motor neurone disease • Myasthenia gravis • Huntington's disease

References: (contains detailed information for guiding clinical care)

1. **NICE** COVID-19 guidance: https://www.nice.org.uk/guidance/ng191/resources/covid19-rapid-guideline-managing-covid19-pdf-51035553326
2. **RCPCH** COVID-19 guidance: https://www.rcpch.ac.uk/resources/covid-19-guidance-acute-settings
3. MHRA-CAS Clinical pathway: Therapies for patients hospitalised due to COVID-19 https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103203
4. Interim Clinical Commissioning Policy: **Baricitinib** for patients hospitalised due to COVID-19 (adults and children aged 2 years and over) 5 May 2022 https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103203
5. Interim Clinical Commissioning Policy: **Neutralising monoclonal antibodies and intravenous antivirals** in the treatment of COVID-19 in hospitalised patients https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103196
6. NHSE clinical commissioning policy for **Remdesivir** https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103197
7. NHSE clinical commissioning policy for **Tocilizumab** https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103194
8. NHSE clinical commissioning policy for **Sarilumab**: https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103194
9. **RECOVERY trial**: https://www.recoverytrial.net/
10. Local **Anticoagulation** policy

Dr Deepthi Jyothish (deepthi.jyothish@nhs.net)
Rhian Isaac (rhian.isaac@nhs.net)

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