GHA Clinical Decision Guide: Choosing Pre-emptive COVID Treatment for Non Hospitalised Clinically Vulnerable COVID Patients

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A: Basic Eligibility Criteria (ALL must be fulfilled):

- Within 5 days of onset of symptoms (i.e. patient MUST be symptomatic)
- PCR-test confirmed COVID-19 (if LFT positive only, the patient needs a PCR)
- Aged 12 years or over
- Not severely unwell (not admitted to hospital, no new or increased oxygen requirement)
- COVID-vulnerable patient meeting at least **one** of the criteria in Box B

B: High-Risk COVID Vulnerable Criteria (at least ONE must be met): (see Box G1 & Box G2 for specific criteria)

- Down's syndrome & other genetic disorders
- Current active solid cancer including patients having had chemotherapy in past 12 months & radiotherapy in past 6 months
- Haematological diseases: active, current diseases such as blood cancers: (leukaemia, lymphoma, myeloma, MDS), aplastic anaemia, paroxysmal nocturnal haemoglobinuria (PNH) being treated with chemotherapy, radiotherapy
- Patients who have had a stem cell (bone marrow) transplant
- Sickle cell disease
- Kidney (renal) disease: dialysis, kidney transplant, or those with chronic kidney disease (CKD) stage 4 or 5
- Liver disease: cirrhosis, liver transplant, autoimmune liver disease
- Immune mediated inflammatory diseases (auto-immune disease) on certain immunomodulators and/or higher dose steroids or unstable disease with other comorbidity
- Respiratory disease: severe asthma on oral steroids/immunesuppressants,COPD on NIV or long-term oxygen,interstitial lung disease, home non-invasive ventilation, pulm hypertension
- Patients with an immunodeficiency
- HIV patients
- Any solid organ transplant patient
- Neurological disease: motor neurone disease, Duchenne's muscular dystrophy, multiple sclerosis, myasthenia gravis, dementia & neurodegenerative disorders when associated with severe frailty (score of 7 or above) includes: Alzheimer's, vascular, Lewy body, frontotemporal atrophy, Parkinsons, Huntingdons, progressive supranuclear palsy & multiple system atrophy

C: ALL must be met: Consider Paxlovid

Age 18 years or over
Not pregnant & given & will comply with contraceptive advice
NO decompensated cirrhosis & NOT in CKD stage 4-5

D1: NOT for Paxlovid, FOR molnupiravir

- Age 18 years or over
- NOT Pregnant AND will comply with contraceptive advice
- NOT breastfeeding (or can pause until course completed & resume 5-days after stopping molnupiravir)

E: Child age under 18 years: refer to Paediatric Consultant see Box I

F: Assess for Paxlovid Drug Interaction (see BNF or use COVID-19 Drug Interactions website https://www.covid19-druginteractions.org/checker

NO interactions=Paxlovid. **YES to Interaction(s)**=Box D1/D2

D2: NOT for Paxlovid & NOT for Molnupiravir= consider sotrovimab via CALPE ward

Pregnant (likely)/ non-compliant with contraception OR unwilling to pause breastfeeding
OR
Paxlovid AND molnupiravir BOTH contra-indicated

BOX G1	Specifics https://www.gov.uk/government/publications/higher-risk-patients-eligible-for-covid-19-treatments-independent-advisory-group-report-march-2023/defining-the-highest-risk-clinical-subgroups-upon-community-infection-with-sars-cov-2-when-considering-the-use-of-neutralising-monoclonal-antibodies
Down's syndrome	All patients with Down's syndrome & other immune disorders known to affect immune competence
Patients with solid cancer	Active metastatic cancer or locally advanced inoperable cancer – Lung cancer (at any stage) - All patients receiving chemotherapy (including antibody-drug conjugates), PI3K inhibitors or radiotherapy within 12 months – People with cancer resected within 3 months and had no adjuvant chemo- or radiotherapy – People with cancer resected between 3-12 months and receiving no adjuvant chemo- or radiotherapy (lower risk but still eligible)
Patients with haematological disease and stem cell transplant recipients	- 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 - received chimaeric antigen receptor (CAR)-T cell therapy in the last 24 months. or radiotherapy in the last 12 months - Individuals with haematological malignancies receiving systemic anti-cancer treatment (SACT) within the last 12 months - All patients not meeting criteria above and diagnosed with myeloma (excluding MGUS), AL amyloidosis, chronic B-cell lymphoproliferative disorders (e.g., chronic lymphocytic leukaemia, follicular lymphoma), myelodysplastic syndrome (MDS), chronic myelomonocytic leukaemia (CMML) & myelofibrosis - All patients with sickle cell disease – people with thalassemia or rare inherited anaemia with severe cardiac iron overload or severe to moderate iron overload plus additional co-morbidity - 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), 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-Pugh class A, B and C whether receiving immune suppressive therapy or not (those with decompensated liver disease at Child-Pugh class B & C are at highest risk). Patients with a liver transplant . Liver patients on immune suppressive therapy (including patients with and without liver cirrhosis
Patients with immune-mediated inflammatory disorders	Patients with treated B cell depleting therapy (anti-CD20 drug e.g., rituximab, ocrelizumab, ofatumab, obinutuzumab) in the last 12 months Patients treated with cyclophosphamide (iv or oral) in 6 months prior to positive COVID PCR. Patients on corticosteroids (equivalent to >10mg/day of prednisolone for at least the 28 days prior to a positive PCR result), Patients on current treatment with tacrolimus, ciclosporin or mycophenolate mofetil, azathioprine/mercaptopurine (for kidney,liver & lung disease) or methotrexate (for lung disease). IMID patients with uncontrolled or clinically active disease (requiring dose inc. or new drug and/or other high risk co-morbidities (e.g. BMI >30, diabetes mellitus, hypertension, major organ involvement (kidney, liver, lung with impaired organ function)
Respiratory disease	Asthmatics on oral corticosteroids (equivalent to >10mg/day of prednisolone for at least the 28 days prior to a positive PCR result) or any immunosuppressants COPD on long term home non invasive ventilation (NIV). COPD patients on long term oxygen. COPD patients with moderate or severe disease (FEV1≥50% predicted) who have required 4 or more courses of prednisolone of 30mg for ≥ 5 days in last 12 months. Interstitial lung disease (ILD) such as idiopathic pulmonary fibrosis and ILD sub-types e.g sarcoidosis, hypersensitivity pneumonitis, connective tissue disease related All patients on NIV (regardless of the underlying disorder) Pulmonary hypertension (PH) – groups 1 and 4 from PH classification

BOX G2	Specifics https://www.gov.uk/government/publications/higher-risk-patients-eligible-for-covid-19-treatments-independent-advisory-group-report-march-2023/defining-the-highest-risk-clinical-subgroups-upon-community-infection-with-sars-cov-2-when-considering-the-use-of-neutralising-monoclonal-antibodies
Immune deficiencies	- Primary immunodeficiency associated with impaired type I interferon signalling. - Good's syndrome (thymoma plus B-cell deficiency) - X-linked agammaglobulinaemia (and other primary agammaglobulinaemias) - Any patient with a secondary immunodeficiency receiving, or eligible for, immunoglobulin replacement therapy - Common variable immunodeficiency (CVID) - Undefined primary antibody deficiency on immunoglobulin (or eligible for Ig) - Hyper-IgM syndromes - Severe Combined Immunodeficiency (SCID) - Autoimmune polyglandular syndromes /autoimmune polyendocrinopathy, candidiasis, ectodermal dystrophy (APECED syndrome)
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	All recipients of solid organ transplants not otherwise specified above
Neurological conditions	Conditions associated with neuromuscular respiratory failure: motor neurone disease, Duchenne's muscular dystrophy Conditions requiring immunotherapies: multiple sclerosis, myasthenia gravis, other immune mediated disorders Dementia and neurodegenerative disorders when associated with severe frailty (Clinical Frailty Score of 7 or more): Alzheimer's, Vascular dementia, Lewy body disease, frontotemporal atrophy, Parkinson's disease, Huntingdon's disease, progressive supranuclear palsy, multiple system atrophy.

Box I pathway for PCR-positive symptomatic non-hospitalized cases aged older than 12 and younger than 18 years, greater than 40kg weight, and clinical concern. All cases should be discussed with a Consultant Paediatrician.

Consultant Paediatrician should refer to tertiary paediatric ID centre for MDT case discussion through local established pathways, who will confirm eligibility and consider risk benefit and whether to proceed with offer of treatment.

Category	Specifics
Children and young people at substantial risk	Complex life-limiting neurodisability with recurrent respiratory infections or compromise.
Children and young people at significant risk if 2 or more of these risk factors are present	
Primary Immunodeficiency	- Primary immunodeficiency associated with impaired type I interferon signalling - Good's syndrome (thymoma plus B-cell deficiency) - X-linked agammaglobulinaemia (and other primary agammaglobulinaemias) - Common variable immunodeficiency (CVID) - Primary antibody deficiency on immunoglobulin (or eligible for Ig) - Hyper-IgM syndromes - Severe Combined Immunodeficiency (SCID) - Autoimmune polyglandular syndromes /autoimmune polyendocrinopathy, candidiasis, ectodermal dystrophy (APECED syndrome)
Secondary Immunodeficiency	-HIV CD4 count less than 200 cells per mm3 – Solid organ transplant – HSCT within 12 months or with GVHD -CAR-T therapy in past 24 months – induction chemotherapy for ALL, non-Hodgkin's lymphoma, chemotherapy for AML, relapsed and/or refractory leukaemia & lymphoma
Immunosuppressive Treatment	- Chemotherapy within last 3 months – Cyclophosphamide within last 3 months - Corticosteroids greater than 2mg/kg/day for 28 days in last 4 weeks – B-cell depleting treatment in last 12 months
Other Conditions	- High BMI (greater than 95th centile) - Severe Respiratory disease (e.g., Cystic Fibrosis or bronchiectasis with FEV1 less than 60%) -Tracheostomy or long-term ventilation - Severe asthma (paediatric ICU admission in last 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 (Down's syndrome) - complex or chromosomal genetic or metabolic conditions associated with significant comorbidity - Multiple congenital anomalies associated with significant comorbidity - bronchopulmonary dysplasia - decisions should be made taking in to account degree of prematurity at birth and chronological age - infants less than 1 year with congenital heart disease (CHD): cyanotic congenital heart disease, haemodynamically significant acyanotic CHD and history of prematurity, those due for corrective surgery, to avoid complications or delay due to SARS-CoV-2 infection