Patients Considered to be at the Highest Risk of Adverse Outcomes from COVID-19

The following adult patient cohorts were determined by an Independent Advisory Group (IAG) commissioned by the Department of Health and Social Care to be at the highest risk of an adverse COVID-19 outcome, namely hospitalisation and death. The report was updated on 31 March 2023 based on the latest evidence.

A further update of the IAG report in June 2023 was published in '*Section 5: Supporting information on risk factors for progression to severe COVID-19'* of NICE TA878 (https://www.nice.org.uk/guidance/ta878/chapter/5-Supporting-information-on-risk-factors-for-progression-to-severe-COVID-19). These changes are shown in **bold**.

Section	Description	Footnotes
Down's syndrome and other genetic disorders	All individuals with Down's syndrome or other chromosomal disorders known to affect immune competence.	
Solid cancer	• metastatic or locally advanced inoperable cancer • lung cancer (at any stage) • people receiving any chemotherapy (including antibody-drug conjugates), PI3K inhibitors or radiotherapy within 12 months • people who have had cancer resected within 3 months and who received no adjuvant chemotherapy or radiotherapy • people who have had cancer resected within 3 to 12 months and receiving no adjuvant chemotherapy or radiotherapy are expected to be at less risk (and thus less priority) but still at increased risk compared with the non-cancer populations	
Haematological diseases and recipients of	• allogeneic HSCT recipients in the last 12 months or active graft versus host disease (GVHD) regardless of time from transplant (including HSCT for non-	

haematological stem cell transplant (HSCT)	malignant diseases)
	• autologous HSCT recipients in the last 12 months (including HSCT for non-malignant diseases)
	• individuals with haematological malignancies who have received CAR-T cell therapy in the last 24 months, or until the lymphocyte count is within the normal range *(may exceed 24 months)*
	• individuals with haematological malignancies receiving systemic anti-cancer treatment (SACT) within the last 12 months, or radiotherapy within the last 12 months
	• all people who do not fit the criteria above, and are diagnosed with:
	  ○ myeloma (excluding monoclonal gammopathy of undetermined significance [MGUS])
	  ○ AL amyloidosis
	  ○ chronic B-cell lymphoproliferative disorders (chronic lymphocytic leukaemia, follicular lymphoma)
	  ○ myelodysplastic syndrome (MDS)
	  ○ chronic myelomonocytic leukaemia (CMML)
	  ○ myelofibrosis
	  ○ any mature T-cell malignancy
	• all people with sickle cell disease
	• people with thalassaemia or rare inherited anaemia with any of the following:
	  ○ severe cardiac iron overload (T2 * less than 10ms)
	  ○ severe to moderate iron overload (T2 * greater than or equal to 10ms) plus an additional co-morbidity of concern (for example, diabetes, chronic liver disease or severe hepatic iron load on MRI)
	• individuals with non-malignant haematological disorders (for example, aplastic anaemia or paroxysmal nocturnal haemoglobinuria) receiving B-cell depleting systemic treatment (for example, anti-CD20, anti-thymocyte globulin [ATG] and alemtuzumab) within the last 12 months	

Renal disease	• renal transplant recipients (including those with failed transplants within the past 12 months), particularly those who have:
	  ○ received B cell depleting therapy within the past 12 months (including alemtuzumab, rituximab [anti-CD20], anti-thymocyte globulin)
	  ○ an additional substantial risk factor which would in isolation make them eligible for monoclonals or oral antivirals
	• non-transplant renal patients who have received a comparable level of immunosuppression (*see IMIDs section*)
	• patients with chronic kidney disease (CKD) stage 4 or 5 (an estimated glomerular filtration rate [eGFR] less than 30ml per min per 1.73m^2) without immunosuppression	

Liver diseases	• people with cirrhosis Child-Pugh (CP) class A, B and C, whether receiving immune suppressive therapy or not. Those with decompensated liver disease (CP B and C) are at greatest risk • people with a liver transplant • people with liver disease on immune suppressive therapy (including people with and without cirrhosis)	
Solid organ transplant recipients	Solid organ transplant recipients not in any other categories.	
Immune-mediated inflammatory disorders (IMIDs)[1]	• people who have received a B-cell depleting therapy (anti-CD20 drug for example, rituximab, ocrelizumab, ofatumab, obinutuzumab) in the last 12 months. • people who have been treated with cyclophosphamide (IV or oral) in the 6 months prior to positive PCR or relevant COVID test • people who are on corticosteroids (equivalent to **or** greater than 10 mg per day of prednisolone) for at least the 28 days prior to positive COVID test • **people who are on biologics or small molecule JAK inhibitors** • people who are on current treatment with mycophenolate mofetil, oral	1. Diseases in which auto-immune or auto-inflammation based pathways are implicated in disease, for example, inflammatory arthritis, connective tissue diseases, inflammatory skin diseases, inflammatory gastrointestinal disease.

	tacrolimus, azathioprine, mercaptopurine, **or similar agents** (for major organ involvement such as kidney, gastro-intestinal tract, liver, **lung, brain**), methotrexate (for interstitial lung disease or asthma *(see Respiratory section)* only) and/or ciclosporin. No minimum dose threshold is suggested. • **people who are on current treatment (or within the last 6 months) with S1P modulators (fingolimod, ponesimod or siponimod), or alemtuzumab or cladribine within the last 12 months** • people who exhibit at least one of: a) uncontrolled or clinically active disease (that is, required recent increase in dose or initiation of new immunosuppressive drug or IM steroid injection or course of oral steroids within the 3 months prior to positive PCR); and/or b) other high-risk comorbidities (for example, body mass index [BMI] greater than 30, diabetes mellitus, hypertension, major organ involvement such as significant kidney, liver, **nervous system** or lung inflammation or significantly impaired renal, liver, **nervous system** and/or lung function)	
Respiratory	• asthma in people on oral corticosteroids (*as defined in IMID section*) or with frequent exacerbations requiring 4 or more courses of prednisolone per year. • any asthma patient taking immunosuppressants for their asthma including but not exclusively methotrexate, ciclosporin • COPD on long term home non-invasive ventilation (NIV). Patients on long term oxygen therapy. People with moderate or severe disease (FEV1 **less** than or equal to 50% predicted) who have required 4 or more courses of prednisolone 30mg for 5 days or greater in last 12 months • interstitial lung disease (ILD) – all patients with idiopathic pulmonary fibrosis • sub-types of ILD, for example, connective tissue disease related, sarcoidosis, hypersensitivity pneumonitis, NSIP (non-specific interstitial pneumonia) who have received a B-cell depleting therapy in last 12 months, or IV or oral	2. Patients using continuous positive airway pressure (CPAP) only for treatment of obstructive sleep apnoea (OSA) are not deemed to be particularly high risk and do not require prioritised access to treatments for COVID-19 disease. 3. All PH patients are likely at risk, but other classifications may be covered by other sections.

	cyclophosphamide in the 6 months prior to testing positive for COVID-19. Any ILD patient on current treatment with corticosteroids, mycophenolate mofetil, azathioprine, tacrolimus, ciclosporin or methotrexate. No minimum dose criteria • any people with any type of ILD who may not be on treatment due to intolerance but has severe disease with an FVC predicted less than 60% • NIV **and tracheostomy ventilated** – all patients requiring this type of support regardless of the underlying disorder (which might include COPD, obesity hypoventilation syndrome, scoliosis, bronchiectasis, **neurodisability** and genetic muscular diseases *[see Neurology section]*)[2] • lung cancer patients (*see Solid Cancer section*) • lung transplant patients (*see Solid Organ Transplant section*) • pulmonary hypertension (PH): groups 1 and 4 from PH classification[3]	
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 or autoimmune polyendocrinopathy, candidiasis, ectodermal dystrophy (APECED syndrome) • primary immunodeficiency associated with impaired type 1 interferon signalling • X-linked agammaglobulinaemia (and other primary agammaglobulinaemias) • any person with secondary immunodeficiency receiving, or eligible for, immunoglobulin replacement therapy	
HIV/AIDS	• people with high levels of immune suppression, have uncontrolled or untreated HIV (high viral load) or present acutely with an AIDS defining diagnosis • people on treatment for HIV with CD4 less than 350 cells per mm^3 and stable on HIV treatment or CD4 greater than 350 cells per mm^3 and at least one additional	4. The use of CD4 counts to assess eligibility for treatment applies only to those patients for whom CD4 counts are used to monitor for treatment compliance and/or levels of immune

	risk factor (for example, age >55, diabetes, obesity, cardiovascular, liver or renal disease, homeless, alcoholic dependency)[4].	compromise. Where CD4 counts are not known, but concerns remain around potential immune compromise, discussion with the patient's HIV team is advised.

Neurological disorders	• Conditions associated with neuromuscular respiratory failure requiring chronic ventilatory support:
	  ○ motor neurone disease
	  ○ Duchenne muscular dystrophy
	• Conditions that require use of specific immunotherapies (*see IMIDs section*)
	  ○ multiple sclerosis (MS)
	  ○ myasthenia gravis (MG)
	  ○ other immune-mediated disorders[5]
	• Dementia, neurodegenerative and **neuroimmune** disorders when associated with severe frailty (for example, level 7 or 8 on Clinical Frailty Scale):
	  ○ Alzheimer's disease, vascular disease, Lewy body disease, or frontotemporal atrophy
	  ○ Parkinson's Disease
	  ○ Huntington's disease
	  ○ progressive supranuclear palsy and multiple system atrophy
	  ○ **motor neurone disease**
	  ○ **multiple sclerosis and other immune-mediated neurological disorders**
		5. Other immune-mediated disorders may include rarer conditions such as neuromyelitis optica (NMO), refractory autoimmune encephalitis, and rare peripheral neuropathies.