Sherwood Forest Hospitals
NHS Foundation Trust

COVID-19 TREATMENT GUIDELINE FOR HOSPITALISED ADULTS

Decisions regarding treatment may need to be made based around individual patient.
Contact the Hot Respiratory phone 07813 567456 for the advice and guidance

1 GUIDELINE DETAILS

Severity of disease	Treatment recommendation (See Appendix 1 for treatment summary)
No Supplemental oxygen	Supportive care High risk patients* – as per NICE guidance – Risk factors for progression to severe COVID-19 – Consider antiviral or neutralising monoclonal antibodies (nMABs) (see details below) *** Decision to treat should be at consultant level (speciality leading the care of the patient) with support from multi-disciplinary colleagues in cases of uncertainty. Discussions with respiratory, microbiology or intensive care consultants in regards to eligibility should not be required.**
Supplemental oxygen	Supportive care Dexamethasone Consider Tocilizumab / AND/OR Baricitinib (see details below)
Non-invasive or mechanical ventilation	Supportive care Dexamethasone Consider IL-6 Inhibitors (Tocilizumab) and Baricitinib

SUPPORTIVE CARE
All patients

- Prevention & Evaluation of venous thromboembolism with enoxaparin (see page 6)
- Hydration – Aim Euvolaemic
- Oxygen (Aim SpO_2 > 92%, COPD patients 88-92%)
- Paracetamol
- Pneumonia Management as per Local guidelines
- Consider Early discharge / Escalation (Discuss with ACCU consultant if needed) / RESPECT Form

Antiviral and Neutralising Monoclonal Antibodies (nMABs)
Symptomatic with COVID-19* and showing no signs of clinical recovery without an escalating oxygen requirement / clinical deterioration attributed to COVID-19 ("mild" COVID) and deemed high risk of deterioration as per NICE guidance – Risk factors for progression to severe COVID-19.

FIRST LINE - Paxlovid® (nirmatrelvir plus ritonavir)

Eligibility Criteria:

- Treatment is commenced within 5 days of symptom onset
- The patient does NOT have a history of advanced decompensated liver cirrhosis or stage 4-5 chronic kidney disease
  - d/w specialists if deemed necessary to treat with Paxlovid®
- Paxlovid® (nirmatrelvir plus ritonavir) treatment has been deemed safe following guidance from the appropriate specialty team(s)

Exclusion criteria and cautions

- Known hypersensitivity reaction to the active substances or to any of the excipients of the products as listed in the respective Summary of Product Characteristics
- Children aged less than 18 years
- Pregnancy
- Patient taking an interacting medicine. Check www.covid19-druginteractions.org for up-to-date interaction information (see Appendix 2)
- Breast-feeding should be discontinued during treatment with Paxlovid® and for 7 days after the last dose of Paxlovid®

Dosage and administration
The recommended dosage is:

- **300 mg** nirmatrelvir – 2 x 150 mg tablets with
- **100 mg** ritonavir (1 x 100 mg tablet)

all taken together orally twice daily for 5 days.

Stage 3 CKD, the dose should be reduced:

- **150mg** nirmatrelvir – 1 x 150 mg tablets with
- **100mg** ritonavir 100 mg (1 x 100 mg tablet)

all taken together orally twice daily for 5 days.

- **Use the pre-defined dose sentences on EPMA to prescribe. If using in a non-EPMA area prescribe as separate medicines on the medicines chart to enable dose adjustment as required above.**
- **To** be taken with or without food. The tablets should be swallowed whole and not chewed, broken or crushed.
- A missed dose should be taken as soon as possible and within 8 hours of the scheduled time, and the normal dosing schedule should be resumed. If more than 8 hours has elapsed, the missed dose should not be taken and the treatment should resume according to the normal dosing schedule.
- If patient develops severe or critical COVID-19 after starting treatment with Paxlovid® the patient should complete the full 5-day treatment course at the discretion of the senior clinician

Antiviral and Neutralising Monoclonal Antibodies (nMABs)

<u>SECOND LINE</u> – Sotrovimab

Eligibility Criteria:

- Treatment with Paxlovid® (nirmatrelvir plus ritonavir) is contraindicated or not possible
- Treatment is delivered within 5 days of symptom onset

Exclusion criteria and cautions

- Known hypersensitivity reaction to the active substances or to any of the excipients of the products as listed in the respective Summary of Product Characteristics
- Children aged less than 12 years old
- Adolescents (aged 12-17 years) weighing less than 40kg

Pregnancy – use when benefit outweighs risk

Dosage and administration

500mg diluted in a 100mL bag of 0.9% sodium chloride to be administered as a single intravenous infusion over a minimum of 30 minutes. Administration needs to be via a **0.2micron** filter.

Repeat doses should not be administered

Ward-based preparation only. See Summary of Product Characteristics or Injectable Medicines Reference Guide (Medusa)

Adverse effects and monitoring

- Hypersensitivity reactions, including anaphylaxis
  - Manage in line with trust policies
- Infusion-related reactions (IRRs)
  - Typically observed during or within 24 hours of infusion
  - Commonly - nausea, chills, dizziness (or syncope), rash, urticaria and flushing
  - But not limited and potential for life-threatening IRRs
  - If an IRR occurs the infusion should be either;
    - paused and the patient monitored and if necessary initiate appropriate medications and/or supportive care
    - slow the infusion rate down to complete the administration, this should be completed in a step-wise pragmatic approach e.g. run over 60 minutes rather than 30 minutes.
    - If IRRs continue despite multiple pauses and slowing the infusion rate down then discontinue administration and initiate appropriate medications and/or supportive care

Monitor patient for 60 minutes after the infusion has ended.

Be aware of the risk of delayed reactions up to 24 hours after the infusion has ended.

DEXAMETHASONE
All suspected and Covid swab positive patients
All patients requiring supplemental oxygen
Dexamethasone IV or oral 6mg per day for up to 10 days or until hospital discharge, whichever comes first,
If dexamethasone not available, the total daily dose equivalencies are:

- Prednisone 40mg (administer once daily or in two divided doses daily)
- Methylprednisolone 32mg (administer once daily or in two divided doses daily)
- Hydrocortisone 160mg (administer in two to four divided doses daily)

TOCILIZUMAB (Approval by Respiratory and Critical Care Consultants)
Sarilumab no longer recommended as Tocilizumab is now the IL-6 inhibitor licensed for treatment of COVID.

Eligibility criteria:
Patients must meet all of the eligibility criteria and none of the exclusion criteria.

- COVID-19 positive within previous 10 days (Point of care or PCR including community specimen
- Radiology pattern on imaging consistent with Covid-19 (chest x-ray or CT scan)
- Oxygen saturation of <92% on room air OR requirement for supplemental oxygen;
- C-reactive protein level of at least 75mg/L;
- Assessed within 24-72 hours of admission with failure to improve.

Exclusion criteria:

- Known hypersensitivity to Tocilizumab
- Co-existing infection2 that might be worsened by Tocilizumab
- More than 24 hours has elapsed since ACCU admission or more than 24 hours after starting respiratory support (whichever is the greater)
- A baseline alanine aminotransferase (ALT) or aspartate aminotransferase (AST) more than 5 times the upper limit of normal (caution is recommended if hepatic enzymes are more than 1.5 times the upper limit of normal)
- A baseline platelet count of less than 50 x 10^9 /L (caution is recommended if platelet count is less than 100 x $10^{9/}$L)
- A baseline absolute neutrophil count of less than 2 x 10^9 /L
- A pre-existing condition or treatment resulting in on-going immunosuppression

Pregnancy – use when benefit outweighs risk

Dosing information:

- A single dose of 8mg/kg in 100ml 0.9% sodium chloride to be administered as an intravenous infusion over 60 minutes. The total dose should not exceed 800mg.

Repeat doses are not routinely recommended.

Ward-based preparation only. See Summary of Product Characteristics or Injectable Medicines Reference Guide (Medusa)

Ongoing clinical monitoring
Treatment with tocilizumab can lower the ability of the immune system to fight infections. This could increase the risk of getting a new infection or make any infection the patient contracts worse. It also causes prolonged depression of CRP levels , making CRP a less reliable marker of active infection. It would be expected that following a single dose this risk would persist for a 3 month period. It should be clearly documented in the patient's notes and actively handed over at all transitions of care both in secondary care and on discharge back to primary care.

Baricitinib

Eligibility Criteria:
Patients must meet all of the eligibility criteria and none of the exclusion criteria.

- Covid -19 swab positive or strong clinical and/or radiological features suggestive of COVID 19 by MDT AND
- Viral pneumonia syndrome AND
    - Typical symptoms (e.g Influenza like illness with fever and muscle pains,or respiratory illness with cough and shortness of breath) &
    - Compatible CXR findings (consolidation or ground glass shadowing &
    - Alternative causes have been considered unlikely or excluded (e.g Heart failure and bacterial pneumonia)
- Receiving supplemental oxygen or respiratory support for treatment of covid 19 AND
- Receiving dexamethasone or equivalent corticosteroid unless contraindicated.

Exclusion criteria and cautions
Baricitinib should not be administered in the following circumstances

- Known hypersensitivity to baricitinib
- eGFR < 15 ml/min
- Receiving dialysis or hemofiltration
- Absolute neutrophil count to less than 0.5 x 109 cells/l
- Active TB
- Pregnancy or breastfeeding

Dosage and administration
The recommended dose id 4 mg once daily for 10 days (Or until discharge is sooner)

Dose should be halved to 2 mg once daily if
eGFR is 30 to 60 ml/min OR
co administration of an organic anion transporter 3 (OAT3) with a strong inhibition potential such as probenecid
Dose should be reduced further to 2 mg alternate days with e GFR 15 – 30 mL/min

Co administration:
Use of Baricitinib in the treatment of covid 19 should be considered as “additive” to the use of IL-6 inhibitors (Tocilizumab rather than an alternative. In other words, patient may be given IL-6 inhibitor treatment after treatment with Baricitinib has been commenced (or vice versa) according to clinical judgement.
Baricitinib should not routinely be co administered with an IL-6 inhibitor (where co administration means given simultaneously). However in severe illness requiring critical care support or patient deteriorated despite treatment, clinical judgement may deem co administration appropriate.

Remdesivir
Remedesivir should not be considered as a treatment option for “mild” or symptomatic COVID-19. This will reviewed in line with NICE guidance updates.

Molnupiravir
Molnupiravir should not be considered as a treatment option for “mild” COVID-19. This will reviewed in line with NICE guidance updates.

IF HIGH PROBABILITY FOR PE, START THERAPEUTIC DOSE CLEXANE - CONSIDER CTPA ON ADMISSION
OTHERWISE THROMBOPROPHYLAXIS AS PER STANDARD TRUST GUIDELINES
(For 7 days minimum – If discharged before 7 days consider self-administration Enoxaparin by patient OR 2.5 mg Apixaban BD)
FOR POST ACCU PATIENT (Enhanced dose) – To be continued until discharged

Discharge information

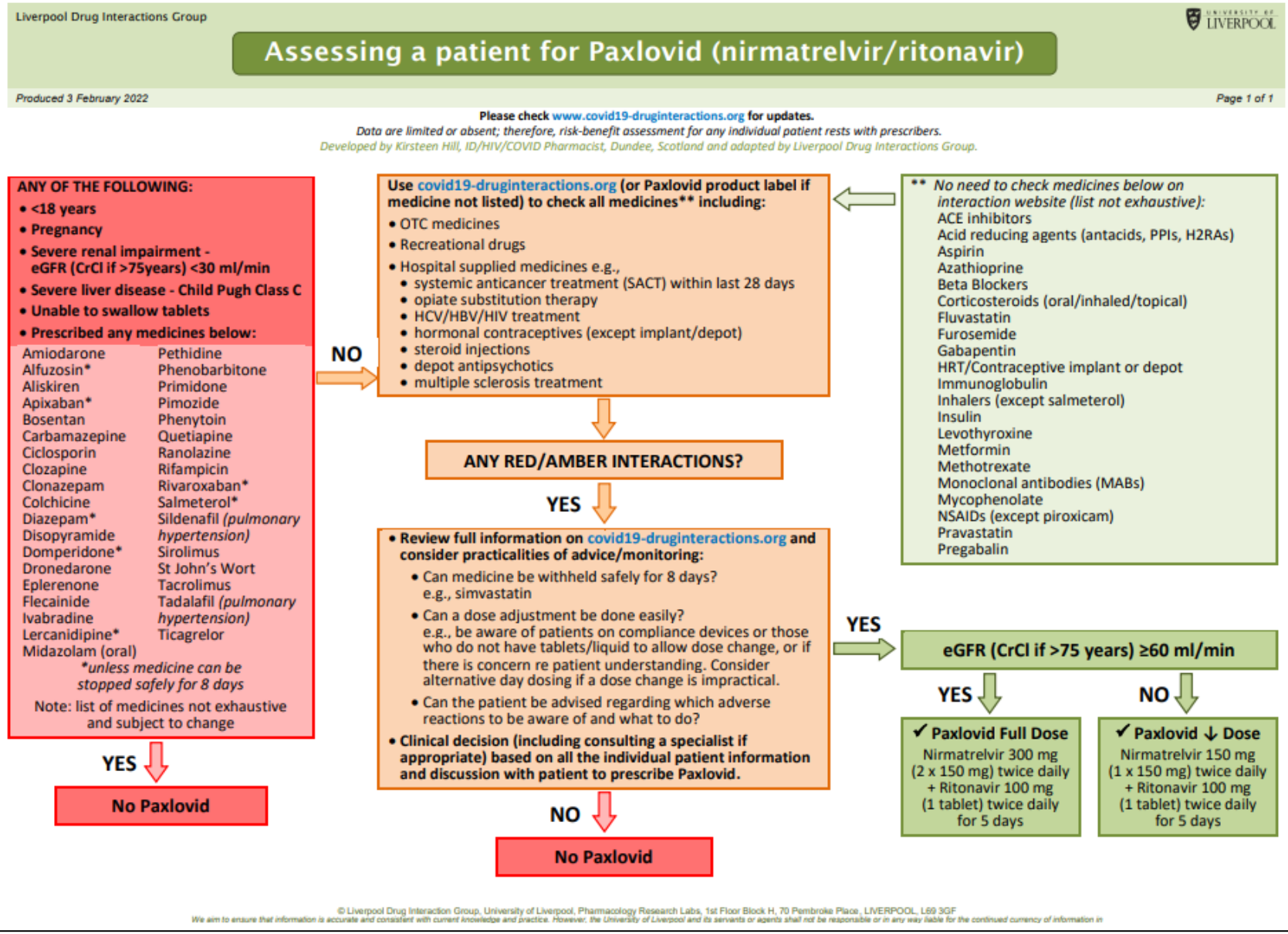
Medical and Pharmacy teams need to ensure that it is documented on the discharge letter when treatment for COVID (either mild or severe) was provided (dose and date of administration for each medicine) to ensure primary care teams are informed.

Appendix 1: Decision making tool on which therapeutic option to use

	Treatment of "mild" COVID-19		Treatment of severe COVID-19		
	Paxlovid® Nirmatrelvir / Ritonavir	**Sotrovimab (Xevudy®)**	**Dexamethasone**	**Tocilizumab**	**Baricitinib**
Drug classification	Antiviral (dual therapy)	Neutralising monoclonal antibody (nMAB)	Corticosteroid	Interluekin-6 (IL-6) inhibitor	Janus Kinase (JAK) inhibitor
% Relative Risk Reduction of Hospitalisation	88	85	N/A	N/A	N/A
Dose / administration	Oral: 3 tablets twice a day for 5 days	Intravenous: 500mg single infusion	Oral or intravenous: 6mg once daily for up to 10 days	Intravenous: 8mg/kg (max. 800mg) single infusion	Oral: 4mg once daily for up to 10 days
Age	Adults only (aged 18 years and over)	Adults and adolescents (aged 12 years and over and weighing at least 40kg)	All patients	Adults only (aged 18 years and over)	Adults and children (aged 2 years and over)
Symptom onset	Evidence based on treatment within 5 days of symptom onset	Evidence based on treatment within 5 days of symptom onset	New or increased supplemental oxygen	As per senior clinician decision	
Pregnancy	Not recommended in pregnancy	May be used in pregnancy where benefits of treatment outweigh risks	Can be used in pregnancy	May be used in pregnancy where benefits of treatment outweigh risks	Not recommended in pregnancy
Breast-feeding	Breast-feeding should be discontinued during treatment and for 7 days after last dose	No specific advice on discontinuation of breast-feeding during treatment	Can be continued in breast-feeding	No specific advice on discontinuation of breast-feeding during treatment	Recommended not to be used during breast-feeding
Liver and renal impairment	Dose reduction in moderate renal impairment Contraindicated in severe liver and kidney disease	No dose adjustment required in liver or renal impairment	No dose adjustment required in liver or renal impairment	No dose adjustment required in liver or renal impairment	Dose reduction required in renal impairment eGFR: Dose 30-60 ml/min: 2mg once daily 15-30 ml/min: 2mg alternate days
Drug-drug interactions	Multiple significant drug-drug interactions (see Appendix 2)	No significant drug-drug interactions	No significant drug-drug interactions	No significant drug-drug interactions	OAT3 inhibitor with strong inhibition potential e.g. probenecid, increases baricitinib levels – dose reduction required

Appendix 2 Drug – Drug interactions with Paxlovid® Nirmatrelvir plus Ritonavir

Please use www.covid19-druginteractions.org to check for up-to-date Paxlovid® (Nirmatrelvir/Ritonavir)drug interactions



2 EVIDENCE BASE/ REFERENCES

- National Institute for Health and Care Excellence. Technology Appraisal [TA878] Last updated 22 June 2023 Overview | Casirivimab plus imdevimab, nirmatrelvir plus ritonavir, sotrovimab and tocilizumab for treating COVID-19 | Guidance | NICE
- National Institute for Health and Care Excellence. NICE guideline [NG191] Last updated 30 November 2023 Overview | COVID-19 rapid guideline: managing COVID-19 | Guidance | NICE

3 EQUALITY IMPACT ASSESSMENT

- Guidance on how to complete an Equality Impact Assessment
- Sample completed form

Name of service/policy/procedure being reviewed: COVID-19 Treatment Guideline for Hospitalised Adult Patients			
New or existing service/policy/procedure: Replaces 3 previously separated guidelines			
Date of Assessment: January 2024			
For the service/policy/procedure and its implementation answer the questions a – c below against each characteristic (if relevant consider breaking the policy or implementation down into areas)			
Protected Characteristic	a) Using data and supporting information, what issues, needs or barriers could the protected characteristic groups' experience? For example, are there any known health inequality or access issues to consider?	b) What is already in place in the policy or its implementation to address any inequalities or barriers to access including under representation at clinics, screening?	c) Please state any barriers that still need to be addressed and any proposed actions to eliminate inequality
The area of policy or its implementation being assessed:			
Race and Ethnicity:	None	None	None
Gender:	None	None	None
Age:	None	None	None
Religion:	None	None	None
Disability:	None	None	None
Sexuality:	None	None	None
Pregnancy and Maternity:	None	None	None
Gender Reassignment:	None	None	None
Marriage and Civil Partnership:	None	None	None

Socio-Economic Factors (i.e. living in a poorer neighbourhood / social deprivation):	None	None	None

What consultation with protected characteristic groups including patient groups have you carried out? • No potential areas of impact identified that require discussion
What data or information did you use in support of this EqIA? • The guidance will be applied to all adult inpatients equally, and protected characteristics will not impact on this.
As far as you are aware are there any Human Rights issues be taken into account such as arising from surveys, questionnaires, comments, concerns, complaints or compliments? • None

Level of impact

From the information provided above and following EqIA guidance document please indicate the perceived level of impact:

Low Level of Impact

For high or medium levels of impact, please forward a copy of this form to the HR Secretaries for inclusion at the next Diversity and Inclusivity meeting.

Name of Responsible Person undertaking this assessment: Dr Noor
Signature:
Date: January 2024

Amendments from previous version(s)

Version	Issue Date	Section(s) involved (author to record section number/ page)	Amendment (author to summarise)
1.0	Jan-2024	Whole document	• Reviewed in line with updated NICE guidance • Combines 3 previously separate guidelines for COVID-19 pneumonia, nMABs and IL-6 inhibitors (as recorded on governance sheet). • Information on Sarilumab is no longer in the NICE guidance as it has no license for COVID.
			•

TITLE: COVID-19 TREATMENT GUIDELINE FOR HOSPITALISED ADULTS

Document Category:	**CLINICAL**
Document Type:	**GUIDELINE**

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Version:	Issue Date:	Review Date:
1.0	24th January 2024	January 2025

Supersedes:	• COVID-19 pneumonia – treatment in adult inpatients guideline, v2.1, Issued 29th July 2022 to Review Date April 2024 (RO[1]) • Neutralising Monoclonal Antibodies (nMAB) and intravenous antiviral treatment for patients with COVID-19 guideline, v2.0, Issued 31st March 2022 to Review Date February 2024 • Covid-19 and IL-6: Guideline for the use of Interleukin-6 (IL-6) inhibitors (tocilizumab and sarilumab) for COVID-19 pneumonia (adults) in Respiratory Medicine and Critical Care, v4.0, Issued 4th October 2022 to Review Date December 2023 (ext[1])		
Approved by (committee/group):	• v1.0, Drugs and Therapeutics Committee	**Date Approved:**	5th January 2024

Scope/ Target Audience: (delete as applicable and/ or describe)	**Trustwide**

Evidence Base/ References:	• See Section 2, page 9

Lead Division:	Medicine
Lead Specialty/ Department: **(Or Division if 'divisionally' owned)**	Respiratory
Lead Author: **(position/ role and name)**	• Dr Z Noor, Consultant in Respiratory Medicine, and • Mark Clymer, Assistant Chief Pharmacist • Tom Bell, Lead Pharmacist Surgery and Critical Care
Co-Author(s): **(position/ role and name if applicable)**	• Dr J Hutchinson, Consultant in Respiratory Medicine
Sponsor (position/ role):	Head of Service, Respiratory

Name the documents here or record not applicable *(these are documents which are usually developed or reviewed/ amended at the same time – ie a family of documents)*	
Associated Policy	Not Applicable
Associated Procedure(s)	Not Applicable
Associated Pathway(s)	Not Applicable
Associated Standard Operating Procedure(s)	Not Applicable
Other associated documents e.g. documentation/ forms	Not Applicable

Consultation Undertaken:	v1.0 • Respiratory Consultants • Assistant Chief Pharmacist (MC)

Template control:	v2.0 September 2023