



HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19

This document is intended for use by healthcare professionals only.

This guidance is specific to the management of patients with COVID-19 disease.

While the guidance is intended to strengthen clinical management of these patients it does not replace clinical judgment or specialist consultation.

This guidance should be read in conjunction with the [National HSE Infection Prevention and Control Guidance and Framework](#).



Table of Contents

1.	Summary of Amendments	2
2.	Background	3
3.	Summary of Recommendations	3
4.	Available Therapies	8
4.1	Systemic Corticosteroids	8
4.2	Intravenous Remdesivir - Antiviral	11
4.3	Intravenous Sotrovimab - Neutralising Monoclonal Antibody	14
4.4	Intravenous Tocilizumab –Anti-IL6 Receptor Monoclonal Antibody	15
4.5	Venous Thromboembolism (VTE) Prophylaxis	18
5.	Pregnancy and Treatments used in COVID-19	18
6.	Paediatrics and Treatments used in COVID-19	21
7.	Therapies not or no longer recommended in COVID-19	22
	References	22
	Appendices	26

1. Summary of Amendments

Table 1: Summary of amendments from previous edition version 1.0

Therapy Section	Amendment
Sotrovimab	New addition
Recommendations in Paediatrics	New addition
Tocilizumab	Licensed information included
Remdesivir	Early treatment with remdesivir included
Recommendations in Pregnancy	Updated
VTE prophylaxis	Website link to guidance updated
Systemic corticosteroids (in children)	Updated
IVIg (in adults)	No longer recommended
Lopinavir/ritonavir	No longer recommended
Hydroxychloroquine +/- Azithromycin	No longer recommended

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 2 of 35
Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/			

This is the second version of a living guideline and it replaces the first version (31st March 2021). Many pharmacological therapies are being used and many emerging therapeutics are being considered for the treatment of coronavirus disease 2019 (COVID-19). This document aims to support clinicians and other healthcare professionals in their decision about treatment and management of patients with COVID-19. It is developed from published evidence and recommendations of the COVID-19 Therapeutic Advisory Group (TAG). The purpose of the TAG is to provide clinical advice and recommendations to the Chief Clinical Officer on the use of all existing and emerging COVID-19 therapeutic medications. This is a living document which will be reviewed and updated as emerging treatments become available for use in Ireland or if there are changes to the dominant variant.

Clinical Trials

Patients should continue to be consented for enrolment in clinical trials, where available. This will support the generation of relevant data to help inform evidence-based guidance and support clinicians and other healthcare professionals in the management of patients with COVID-19. A record of registered and ongoing clinical trials for COVID-19 is available from the Infectious Diseases Data Observatory, through their living systematic review of COVID-19 clinical trial registrations and the WHO website, available from <https://covid-nma.com/>.

3. Summary of Recommendations

EVIDENCE FOR COVID-19 THERAPIES	
<p>The strongest evidence available to date is for venous thromboembolism prophylaxis, corticosteroid use and for the use of tocilizumab in rapidly deteriorating patients.</p> <p>The evidence base for the novel agents, such as sotrovimab, and novel indications, such as early use remdesivir, is limited:</p> <ul style="list-style-type: none"> • These trials were carried out in unvaccinated populations and prior to the emergence and spread of new variants of concern (i.e. omicron) • Given the paucity of strong evidence, some clinicians may wish not to prescribe these novel therapies and this is a valid clinical management strategy. • This guideline will be updated as further data emerges and matures. 	

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 3 of 35
<p>Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer</p> <p>This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/</p>			



Vaccines reduce harm caused by COVID-19 infection and are superior to the treatments listed in this document. Treatments should not be considered as an alternative to vaccination. It is recommended that everyone continue to take precautions to prevent infection with COVID-19.

If available and appropriate, advice should be sought from Infectious Diseases or Microbiology colleagues prior to prescribing novel agents for the treatment of COVID-19, and from Respiratory and Critical Care specialists, especially when considering steroids or tocilizumab. Serology testing may be carried out in advance, where locally available, for patients who despite vaccination are unlikely to have generated protective immunity. This should not be viewed as a requirement for treatment at this time.

A number of models have been developed internationally to categorise COVID-19 disease severity. In Ireland, the HSE National Clinical Programme for Respiratory Medicine/Irish Thoracic Society developed the COVID Respiratory Scale (CRS) (see Appendix 4).

Clinical Prioritisation

There may be global logistical or supply constraints that make it impossible to offer the available therapy to all eligible patients who could potentially benefit, making patient triage and prioritisation necessary. There is a limited global supply of intravenous tocilizumab and judicious consideration is advised before use. Use should be restricted to clinical scenarios with potential for treatment benefit.

The TAG recommends prioritising patients by risk group as described in Appendix 2 when considering sotrovimab and remdesivir treatment. Adult patients with conditions highlighted in **red** and unvaccinated patients are at the highest risk of severe disease as per the Clinical Risk Factor table (Appendix 3). They are expected to receive the greatest benefit from early intervention therapies and should be prioritised in situations of severely limited supply.

For the purposes of this document, the following terminology will be used:

- Unvaccinated: meaning COVID-19 vaccination schedule not commenced or incomplete.
- Vaccinated: meaning COVID-19 vaccine primary series completed and / or booster dose administered

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 4 of 35
Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/			



Table 2: Visual Summary of Recommendations using a Modified COVID-19 Respiratory Scale (CRS)

Taken from the Respiratory Management of Patients with COVID-19 V2 January 2021, Irish Thoracic Society

HOSPITALISED PATIENTS						
Non-Hospitalised Patients	CRS A1	CRS A2	CRS B	CRS C1	CRS C2	CRS D
NO O ₂ REQUIREMENT SaO ₂ >94%, RR<20	NO O ₂ REQUIREMENT SaO ₂ >94%, RR<20	NASAL CANNULA ≤3L SaO ₂ >94%, RR<20	NASAL CANNULA >3L min OR VENTURI 24-60% SaO ₂ <94%, RR>20 but respond well to nasal cannula	HIGH FLOW NASAL O ₂ (AIRVO) SaO ₂ <94%, RR>20: POOR RESPONSE TO VENTURI MASK	NON-INVASIVE VENTILATION SaO ₂ <94%, RR>20: POOR RESPONSE TO VENTURI MASK	ICU +/- INTUBATE SaO ₂ <94%, RR>20: POOR RESPONSE TO HFNO/NIV
		CORTICOSTEROIDS				
EARLY REMDESIVIR- 3 DAY COURSE						
		REMDESIVIR - 5 DAY COURSE				
SOTROVIMAB						
				TOCILIZUMAB		
	VTE PROPHYLAXIS					

Table 3: Summary of recommendations in alphabetical order.

Intervention	Patient Cohort	Recommendation
Corticosteroids (Systemic)	Hospitalised patients with new oxygen requirement	Systemic corticosteroids should be considered in selected patients
	Classified as CRS A2 on oxygen/B/C1/C2/D as defined in appendix 4	<i>Refer to Section 4.1 for further information</i>
	PIMS Paediatric patients	Paediatric Inflammatory Multisystem Syndrome (PIMS) has been reported following SARS-CoV2 infection. WHO recommends systemic corticosteroids in this cohort of

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 5 of 35
Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/			



		<p>patients. All cases of suspected PIMS should be discussed with the Paediatric Infectious Diseases team in CHI</p> <p><i>Refer to Section 4.1 for further information.</i></p>
Intravenous Immunoglobulin (IVIg)	Adult Patients	IVIg is not recommended for the treatment of COVID-19 in this population.
	Paediatric Patients	Paediatric Inflammatory Multisystem Syndrome (PIMS) has been reported following SARS-CoV2 infection. IVIg is used in this cohort of patients. All cases of suspected PIMS should be discussed with the Paediatric Infectious Diseases team in CHI
Remdesivir - 3 Day Course (Intravenous)	Unvaccinated patients aged 18 years and older at high risk of progression to severe COVID-19 infection not requiring supplemental oxygen	<p>A 3 day course of remdesivir should be considered in selected patients</p> <p>It should be initiated within 7 days of symptom onset and within 4 days of a confirmed diagnosis of COVID-19 (PCR or another high specificity method approved by hospital laboratory director)</p> <p><i>Refer to Section 4.2 for further information.</i></p>
	Immunocompromised patients aged 18 years and older at high risk of progression to severe COVID-19 infection not requiring supplemental oxygen	
Remdesivir - 5 Day Course (Intravenous)	<p>Hospitalised patients aged 12 years and older requiring supplemental oxygen +/- high-flow oxygen +/- non-invasive ventilation</p> <p>(CRS A on oxygen/B/C1/C2 as defined in Appendix 4)</p>	<p>A 5 day course of remdesivir should be considered in selected patients</p> <p><i>Refer to Section 4.2 for further information.</i></p>
Sotrovimab (Intravenous)	Unvaccinated patients aged 12 years and older at risk of progression to severe COVID-19 infection not requiring supplemental oxygen	<p>A single dose of sotrovimab should be considered in selected patients.</p> <p>It should be given within 5 days of symptom onset in patients with a confirmed diagnosis of COVID-19 (PCR or another high specificity method approved by hospital laboratory director).</p>

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 6 of 35
<p>Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer</p> <p>This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/</p>			



	(Tier 1 and Tier 2 as defined in Appendix 2)	Refer to Section 4.3 for further information.
	Immunocompromised patients aged 12 years and older at risk of progression to severe COVID-19 infection not requiring supplemental oxygen	
	(Tier 1 as defined in Appendix 2)	
Tocilizumab (Intravenous)	Recently hospitalised adult patients not in an ICU with rapidly increasing oxygen needs requiring either high-flow oxygen or non-invasive ventilation and significantly increased markers of inflammation.	Intravenous tocilizumab should only be considered for the management of COVID-19 disease in non-ICU adult patients with an inadequate clinical response to systemic corticosteroid therapy.
	(Note: The RECOVERY trial inclusion criterion for inflammation was a CRP greater than or equal to 75 mg/L).	Benefit has not been demonstrated with tocilizumab monotherapy, systemic corticosteroids should continue as adjunctive therapy.
	(CRS C1 or C2 as defined in Appendix 4)	If treatment is being considered outside of the ICU setting, it should only be initiated after consultant-level discussion in a multidisciplinary setting that includes at least two consultants from critical care medicine, haematology, infection specialists, or respiratory medicine, and with patient engagement (or their relevant person, by phone if appropriate and possible).
		Refer to Section 4.4 for further information.
	Adult patient admitted to ICU with severe pneumonia and requiring respiratory support.	Intravenous tocilizumab should be considered for the management of COVID-19 disease in ICU adult patients
	(CRS C1, C2 and D as defined in Appendix 4)	Tocilizumab should be administered in addition to corticosteroids therapy, not as a substitute for, unless contraindications to corticosteroid exist.
		Refer to Section 4.4 for further information.
VTE Prophylaxis	All hospitalised patients with COVID-19.	Risk assessment and provision of appropriate VTE prophylaxis and patient information is recommended for all patients hospitalised with COVID-19.
		Refer to Section 4.5 for further information

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 7 of 35
Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/			



4. Available Therapies

The authors of this guidance observe in general that, the decision to treat a patient should be at the medical opinion of the individual clinician and in discussion with a multidisciplinary team and/or colleagues and that the treatment options be discussed with the patient. It is not mandatory to apply these suggestions. The guideline does not override the responsibility of the clinician to make decisions appropriate to the circumstances of the individual patient.

Some of the Covid-19 treatments are newly licensed medications, being used for unlicensed indications or unlicensed. Many of them are subject to additional monitoring as the clinical evidence base is less well developed.

Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system and HPRa Pharmacovigilance website (www.hpra.ie). This will allow early identification of new safety signals and further inform the safe and effective use of these medicines. The incident and all actions taken must be recorded and the relevant National Incident Management Report Form (NIRF) completed as soon as is practicable after the event occurs and within one working day.

National Incident Report form can be found here <https://www.hse.ie/eng/about/who/nqpsd/qps-incident-management/nims/>.

Healthcare professionals should refer to the Summary of Product Characteristics and drug-drug interaction databases (e.g. Stockley's Interaction Checker) to check for drug-drug interactions. The University of Liverpool have developed an online database for checking drug-drug interactions with the experimental COVID-19 specific medicinal products; available online at <https://www.covid19-druginteractions.org/checker>

4.1 Systemic Corticosteroids

HSE Recommendations for Systemic Corticosteroid Therapy in Treatment of Hospitalised Patients with Severe or Critical COVID-19	
Refer to Summary of Product Characteristics (SmPCs) of respective medicinal products for full prescribing information. ^{1,2}	
<u>Inclusion Criteria for Systemic Corticosteroid Therapy</u>	
<ul style="list-style-type: none"> Systemic corticosteroid therapy should only be considered for the management of COVID-19 disease in hospitalised patients requiring: <ul style="list-style-type: none"> Mechanical ventilation (CRS D – see Appendix 4) 	
OR	

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 8 of 35
Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/			



- Supplemental oxygen but who are not mechanically ventilated (**CRS A on oxygen, B, C1, C2**)

*Systemic corticosteroids should **not** be used for the management of patients with COVID-19 who do not require respiratory support, unless another indication for corticosteroid therapy exists*

- Initiated after consultant-level discussion in a multidisciplinary setting when available.

Exclusion Criteria for Systemic Corticosteroid Therapy

- Any contraindications to systemic corticosteroid therapy including acute severe infection from sources other than COVID-19

Systemic (i.e. intravenous or oral) corticosteroid therapy (e.g. dexamethasone orally or intravenously or hydrocortisone intravenously) for 7 to 10 days.

Recommended Dexamethasone Dose Schedule

Oral

Dexamethasone 6mg daily for 7 to 10 days³ or until discharge (whichever is sooner).

Intravenous

Dexamethasone phosphate 8mg (equivalent to dexamethasone 6.6mg) daily for 7 to 10 days

- Note: In the RECOVERY trial dexamethasone was prescribed as dexamethasone base⁴
- Dexamethasone phosphate (salt) 4 mg in 1 mL injection is equivalent to dexamethasone (base) 3.3mg in 1ml injection.^{5,6}
- Check with local pharmacy department for available formulation.
- No conversion is required for oral formulations of dexamethasone.

Recommended Intravenous Hydrocortisone Dose Schedule

Hydrocortisone 50mg every 6 to 8 hours intravenously for 7 to 10 days.³

Considerations for Route of Administration Based on Level of Care

(All patients must satisfy the criteria for systemic corticosteroid therapy regardless of level of care)

Intensive Care Unit (ICU) Patients

Hospitalised patients requiring escalation to ICU within 24 hours of admission and not already commenced on dexamethasone should be considered for treatment with intravenous hydrocortisone.

Non-ICU Patients

Hospitalised patients not requiring admission to an ICU should be considered for treatment with parenteral corticosteroids

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 9 of 35
Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/			



	(dexamethasone or hydrocortisone) for the first 48 hours followed by a review to oral therapy. (<i>Expert Opinion of Therapeutic Guideline Group</i>)
Pregnancy Recommendations	Should be reviewed on a case by case basis. Please see section 5 below.
Paediatric Recommendations*	Corticosteroids, in addition to supportive care, should be considered for children with severe or critical COVID-19. This decision should be made following discussion with paediatric Infectious Diseases in CHI. Dexamethasone 150 micrograms/kg IV or PO (maximum 6mg) once daily for 10 days ⁷

Additional Information

- This guidance does not apply to the use of systemic corticosteroids for indications other than COVID-19 (e.g. exacerbations of asthma or COPD).
- Patients with COVID-19 who are receiving corticosteroids must be monitored for adverse effects (e.g. hyperglycaemia, secondary infections; see Summary of Product Characteristics for full information on adverse events). It would be prudent to monitor glucose levels in patients with severe and critical COVID-19, regardless of whether the patient is known to have diabetes. Consideration needs to be given to the need for appropriate gastro-protection according to local hospital policy.
- Suspected co-infection with pathogens other than COVID-19 should be investigated and treated empirically as per local antimicrobial policy with consideration of the principles of antimicrobial stewardship Further information available from: <https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/infectionpreventionandcontrolguidance/antimicrobialstewardship/>.
- Use of systemic corticosteroids may increase the risk of reactivation of latent infections (e.g., hepatitis B virus, herpes viruses, and tuberculosis).
- For patients prescribed systemic corticosteroids at the time of hospital admission, the dose should be increased to a dose therapeutically equivalent to that detailed in the recommended dose schedules above. Corticosteroid anti-inflammatory dose equivalencies⁸ are:

Dexamethasone base 6 mg
 ≡ Hydrocortisone 160 mg
 ≡ Methylprednisolone 32 mg
 ≡ Prednisolone 40 mg

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 10 of 35
Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/			



- Once the course of treatment with systemic corticosteroids indicated for COVID 19 is completed, assess clinical need to recommence the previous corticosteroid prescription.

*While acknowledging a lack of substantial evidence for their use, the WHO recommends the addition of systemic corticosteroids in the care of children and adolescents (aged between 0 - 18) who fit the diagnostic criteria of Paediatric Inflammatory Multisystem Syndrome (PIMS) and Kawasaki disease. The rationale for this advice results from the outcome that the potential harms of systemic corticosteroids were fewer than the potential benefits of their use in this population⁹. The decision to treat should be made following discussion with paediatric Infectious Diseases in CHI.

4.2 Intravenous Remdesivir - Antiviral

HSE Recommendations for Remdesivir in the Management of Patients with COVID-19

Refer to Summary of Product Characteristics (SmPC) of remdesivir for full prescribing information¹

Recommended Treatments:

1. Early remdesivir for patients who are COVID-19 positive (3 day treatment course)
2. Remdesivir for patients who are COVID-19 positive and are requiring supplemental oxygen (5 day treatment course)

1. Early remdesivir for patients who are COVID-19 positive (3 day treatment course)^{2,3}:

Inclusion Criteria

- Unvaccinated patients at risk of progressing to severe COVID 19 infection. (Clinical Prioritisation Framework for the Use and Prescribing of Emerging Novel COVID -19 Therapeutics Tier 1 and Tier 2 – See Appendix 2)

OR

- Immunocompromised patients at risk of progressing to severe COVID 19 infection who despite vaccination are unlikely to have generated protective immunity (Clinical Prioritisation Framework for the Use and Prescribing of Emerging Novel COVID -19 Therapeutics Tier 1 – See Appendix 2)

AND

- Less than or equal to 7 days of symptom onset

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 11 of 35
Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/			



- **Less than or equal to 4 days of confirmed diagnosis of COVID-19** (PCR or another high specificity method approved by hospital laboratory director)
- 18 years and over
- not requiring supplemental oxygen

Exclusion Criteria

- Any contraindications to remdesivir as listed in the SmPC.
- Sign / symptoms of severe COVID-19 (see Appendix 5)

2. Remdesivir for patients who are COVID-19 positive and are requiring supplemental oxygen (5 day treatment course):

Inclusion Criteria

- Hospitalised with COVID-19
- Patients with pneumonia requiring supplemental oxygen at the start of treatment (low- or high-flow oxygen or other non-invasive ventilation)
- 12 years and over
- Greater than or equal to 40kg

Exclusion Criteria

- Any contraindications to remdesivir as listed in the SmPC.
- Patients requiring invasive forms of ventilatory support at the start of treatment.

Drug Name	Remdesivir ▼
HSE Approved Indications	1. Early remdesivir treatment for adults who are COVID-19 positive who meet the inclusion criteria and none of the exclusion criteria outlined above.
	2. Remdesivir treatment for patients who are COVID-19 positive requiring supplemental oxygen and meet the inclusion criteria and none of the exclusion criteria outlined above.
Pregnancy Recommendations	Should be reviewed on a case by case basis. Please see section 5 below.
Paediatric Recommendations	1. Early use of remdesivir is not licensed for paediatric use. 2. Remdesivir is indicated for the treatment of COVID-19 in paediatrics (aged 12 years and older and weighing greater than or equal to 40 kg) with pneumonia requiring supplemental oxygen (low or high-flow oxygen or other non-invasive ventilation at start of treatment).
Formulation	100 mg powder for concentrate for solution for infusion.
Route of Administration	Intravenous infusion

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 12 of 35
Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/			



Dose and Duration of therapy	1. Early remdesivir for adults who are COVID-19 positive (3 day treatment course)				
	Day 1	Day 2	Day 3		
	200 mg loading dose	100 mg once daily	100 mg once daily		
	2. Remdesivir for patients who are COVID-19 positive and are requiring supplemental oxygen (5 day treatment course)				
	Day 1	Day 2	Day 3	Day 4	Day 5
	200 mg loading dose	100 mg once daily	100 mg once daily	100 mg once daily	100 mg once daily
Method of Administration	Please see Remdesivir (Veklury®) SmPC for administration details https://www.ema.europa.eu/en/documents/product-information/veklury-epar-product-information_en.pdf				
Funding	HSE (via United Drug)				

Additional Information

- Remdesivir should not be used in patients with eGFR less than 30 mL/min¹
- Transaminase elevations have been observed in clinical trials. Liver function should be determined in all patients prior to starting remdesivir and should be monitored while receiving it as clinically appropriate
 - Remdesivir should not be initiated in patients with alanine aminotransferase (ALT) greater than or equal to 5 x ULN at baseline
 - Remdesivir should be discontinued in patients who, during treatment, develop¹:
 - i. ALT greater than or equal to 5 x ULN. It may be restarted when ALT is less than 5 x ULN OR
 - ii. ALT elevation accompanied by signs or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or international normalised ratio (INR)
- Women of child-bearing potential should be advised to use effective contraception during treatment.
- Multi-disciplinary team assessment should determine if patients not suitable for escalation, would benefit from initiation of treatment with remdesivir. If patients on remdesivir require escalation, continuation of the drug should be considered by multi-disciplinary team assessment.

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 13 of 35
Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/			



- Available evidence has shown no incremental benefit of 10 days treatment over 5 days⁴.
- Monitor patients for hypersensitivity reactions during and following administration of remdesivir as clinically appropriate. Hypersensitivity reactions including infusion-related and anaphylactic reactions have been observed during and following administration of remdesivir. Slower infusion rates, with a maximum infusion time of up to 120 minutes, can be considered to potentially prevent these signs and symptoms.¹

4.3 Intravenous Sotrovimab - Neutralising Monoclonal Antibody

HSE Recommendations for Sotrovimab in the Management of Unvaccinated Patients and Immunocompromised Patients with COVID-19

For full prescribing information refer to the Summary of Prescribing Characteristics (SmPC) for sotrovimab¹

Inclusion Criteria for use of Sotrovimab^{2,3}

- Unvaccinated patients at risk of progressing to severe COVID 19 infection. (Clinical Prioritisation Framework for the Use and Prescribing of Emerging Novel COVID -19 Therapeutics Tier 1 and Tier 2 - See Appendix 2)

OR

- Immunocompromised patients at risk of progressing to severe COVID 19 infection who despite vaccination are unlikely to have generated protective immunity (Clinical Prioritisation Framework for the Use and Prescribing of Emerging Novel COVID -19 Therapeutics Tier 1 - See Appendix 2)

AND

- COVID-19 confirmed with a positive PCR (or another high specificity method approved by hospital laboratory director) **within the last 5 days**
- 12 years and over
- Greater than or equal to 40 kg
- Less than or equal to 5 days of symptom onset
- Patient does not require supplemental oxygen

Exclusion Criteria for use of Sotrovimab

- Sign / symptoms of severe COVID-19 (see Appendix 5)
- Any contraindications to sotrovimab as listed in the SmPC.

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 14 of 35
Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/			



Drug Name	Sotrovimab ▼
HSE Approved Indication	Treatment of unvaccinated or immunocompromised patients at risk of progressing to severe COVID-19 disease who meet the inclusion criteria and none of the exclusion criteria outlined above.
Pregnancy Recommendations	Eligible patients should be reviewed on a case by case basis. Please see section 5 below.
Paediatric Recommendations	Decision to treat patients aged 12 and over should be made in consultation with the paediatric Infectious Diseases team at CHI
Formulation	500 mg/ 8ml concentrate for solution for infusion
Route of Administration	Intravenous infusion over 30 minutes
Dose	500 mg
Duration of therapy	Single dose
Method of Administration	Please see Sotrovimab (Xevudy®) SmPC for administration details https://www.ema.europa.eu/en/documents/product-information/xevudy-epar-product-information_en.pdf
Funding	HSE (via United Drug)
Additional Information <ul style="list-style-type: none"> Patients should be monitored during and for at least 1 hour after infusion is complete. Hypersensitivity reactions, including anaphylaxis, have been reported with administration of sotrovimab. If signs or symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, administration should be discontinued immediately and appropriate medications and/or supportive care should be given. Infusion-related reactions (IRRs) have been observed with intravenous administration of monoclonal antibodies. These reactions may be severe or life threatening. If an IRR occurs, the infusion may be interrupted, slowed or stopped. 	

4.4 Intravenous Tocilizumab –Anti-IL6 Receptor Monoclonal Antibody

HSE Recommendations for Tocilizumab in the Management of Patients with Severe COVID-19 Disease	
Refer to Summary of Product Characteristics (SmPC) of tocilizumab for full prescribing information ¹	
<u>Inclusion Criteria for use of Intravenous Tocilizumab</u>	

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 15 of 35
Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/			



- Intravenous tocilizumab should only be considered for the management of COVID-19 disease in hospitalised adult patients:

- ICU admission with severe pneumonia and requiring respiratory support **(CRS C1, C2 and D)**

OR

- Recently hospitalised patients not in an ICU with rapidly increasing oxygen needs requiring either high-flow oxygen or non-invasive ventilation and significantly increased markers of inflammation. **(CRS C1 or C2)**

Note: The RECOVERY trial inclusion criterion for inflammation was a CRP greater than or equal to 75 mg/L^{2,3}

If treatment is being considered outside of the ICU setting, it should only be initiated after consultant-level discussion in a multidisciplinary setting that includes at least two consultants from critical care medicine, haematology, infection specialists, or respiratory medicine, and with patient engagement (or their relevant person, by phone).

AND

- The following parameters are met:
 - Liver enzymes less than 10 ULN
 - Absolute neutrophil count greater than $1 \times 10^9 / L$
 - Platelet count greater than $50 \times 10^9 / L$

Exclusion Criteria for use of Intravenous Tocilizumab

- Any contraindications to tocilizumab as listed in the SmPC, including acute severe infection from sources other than SARS-CoV2.

Drug Name	Tocilizumab
HSE Approved Indication	<p>Treatment of hospitalised patients with COVID-19 who meet the inclusion criteria and none of the exclusion criteria outlined above.</p> <p>Tocilizumab should not be administered to COVID-19 patients who are not receiving systemic corticosteroids as an increase in mortality cannot be excluded in this subgroup.</p>
Pregnancy Recommendations	Eligible patients should be reviewed on a case by case basis.
Paediatric Recommendations	<p>Tocilizumab is not currently licensed for use in paediatric patients for the treatment of COVID-19</p> <p>If treatment with tocilizumab is being considered it must be discussed on a case by case basis with paediatric Infectious Diseases team at CHI.</p>
Formulation	20 mg / mL concentrate for solution for infusion

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 16 of 35
<p>Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer</p> <p>This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/</p>			



Route of Administration	Intravenous infusion
Dose	8mg/kg (maximum 800mg per dose). Dose rounding to the nearest whole vial is recommended. Vial sizes available may include 80mg, 200mg, and 400mg.
Duration of therapy	Single dose. In exceptional circumstances, one additional dose may be considered no sooner than 8 hours after the initial dose if there has not been sufficient clinical improvement. The decision to administer a second dose must only be made following consultant-level multidisciplinary specialist input and not considered routine clinical practice.
Method of Administration	Please see the tocilizumab (RoActemra®) SmPC for details https://www.ema.europa.eu/en/documents/product-information/roactemra-epar-product-information_en.pdf
Funding	Hospital

Additional Information

- HSE guidance for the use of tocilizumab in the intensive care unit (ICU) setting is informed by the REMAP-CAP^{2,4,5} trial which demonstrates benefit with the use of tocilizumab, in combination with systemic corticosteroids and standard of care, in critically ill patients with COVID-19 receiving organ support (respiratory or cardiac) in an ICU.
- HSE guidance for the use of tocilizumab in the non-ICU setting is informed by results from the RECOVERY^{3,5} study. Results from the RECOVERY study demonstrated benefit in a subset of hospitalised patients with severe COVID-19 outside of the ICU setting who demonstrate evidence of progressive COVID-19 characterised by an inflammatory phenotype (CRP greater than or equal to 75 mg/L) and hypoxaemia (oxygen saturation less than 92% on air or requiring oxygen therapy).
- Use of tocilizumab outside of the ICU setting should only be considered after consultant-level discussion in a multidisciplinary setting that includes at least two consultants from critical care medicine, haematology, infection specialists, or respiratory medicine, and with patient engagement (or their relevant person, by phone).
- Tocilizumab should not be administered if there is a concurrent untreated severe active infection other than COVID-19.
- There may be a risk of reactivation of latent infections (e.g., hepatitis B virus, and tuberculosis).¹

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 17 of 35
Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/			



- Patients should be monitored for hepatotoxicity and haematological abnormalities. Tocilizumab is not recommended if ALT or AST are above 10 x ULN, absolute neutrophil count less than $1 \times 10^9 / L$ or platelet count less than $50 \times 10^9 / L$.¹
- Hypersensitivity reactions, including anaphylaxis, have been reported with administration of tocilizumab. If signs or symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, administration should be discontinued immediately and appropriate medications and/or supportive care should be given.¹

4.5 Venous Thromboembolism (VTE) Prophylaxis

Being hospitalised with COVID-19 is associated with a high risk of venous thromboembolism (VTE). Provision of appropriate prophylaxis and patient information is recommended for all patients, (unless contraindicated) with COVID-19 admitted to hospital. Refer to the *HSE COVID 19 Interim Clinical Guidance for VTE protocol and Patient Information for Acute Hospitals*¹

<https://hse-ie.libguides.com/c.php?g=679077&p=4866382>

5. Pregnancy and Treatments used in COVID-19

Vaccination remains the most effective method of preventing severe COVID-19 disease in pregnancy.

Pregnant women appear no more or less likely to contract COVID-19 than the general population¹. At present, the approach to prevention, evaluation, diagnosis, and treatment of pregnant women with suspected COVID-19 should be similar to that in non-pregnant individuals. The priority for medical care should be to stabilise the woman's condition with standard therapies.¹ As highlighted in multiple maternal death enquiries from Ireland and the UK, pregnant or postpartum women with medical problems should not be denied investigations and treatment because they are pregnant or breastfeeding and should be treated the same as non-pregnant women unless there is a clear contra-indication.²

The management of pregnant women with acute respiratory infection with COVID-19 should be in line with national guidance for non-pregnant patients, as detailed in the main body of this document. The use of pharmacological agents in the treatment of COVID-19 should only be used in a pregnant patient if the potential risk of maternal infection with COVID-19 is considered to be greater than any potential or unknown risks to the mother or the foetus from the drug. If treatment is indicated, pregnant and postpartum women should not be excluded from clinical trials unless there is a clear contra-indication.²

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 18 of 35
Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/			



The use of pharmacological agents outside of a clinical trial should balance the limited evidence of the safety of these agents in pregnancy with the uncertain efficacy. If treatment is being considered outside of a clinical trial, it must only be initiated after consultant-level discussion with multidisciplinary input with from relevant specialities, including Infectious Diseases / Microbiology / Obstetrics / Respiratory and patient engagement.

Seek pharmacy advice on available products, choice of agent, and potential drug-drug interactions.

Systemic Corticosteroids

The RECOVERY trial demonstrated a significant reduction in 28-day mortality for individuals with COVID-19 requiring oxygen who were given corticosteroid therapy. The RECOVERY trial protocol for pregnancy patients recommended oral prednisolone or IV hydrocortisone, instead of dexamethasone treatment.^{1,3} Prednisolone and hydrocortisone, unlike dexamethasone, are extensively metabolised in the placenta with minimal transmission to the foetus.¹ The decision to use systemic corticosteroids in pregnant patients with COVID-19 should be a shared decision involving a multidisciplinary approach and the patient, and should be considered separate to the administration of antenatal steroids to promote fetal lung maturity.

Intravenous Remdesivir – Antiviral

Extremely limited information is available on the use of remdesivir in human or animal pregnancy. Nonclinical reproductive toxicity studies demonstrated no adverse effect on embryofetal development when remdesivir was administered to pregnant rats and rabbits at exposure that was 4 times the recommended human dose (RHD).⁴ A randomised controlled trial of remdesivir use in the treatment of EBOLA included 6 women who had a positive pregnancy test (timing of exposure is unreported). No information on adverse pregnancy outcomes is described.⁵

A number of case reports⁶⁻⁸ and two case series including 17⁹ and 67¹⁰ women, have described the use of remdesivir in pregnant women.^{9, 10} No particular concerns have been reported in relation to the safety of remdesivir in pregnancy; however the absence of data on the use of remdesivir in the first trimester limits these conclusions.

The decision to use remdesivir in pregnant patients with COVID-19 should be a shared decision involving a multidisciplinary approach and the patient.

Intravenous Sotrovimab – Neutralising Monoclonal Antibody

Sotrovimab is a monoclonal antibody that has been authorised by the European Medicines Agency for the treatment of adults and adolescents (aged 12 years and over and weighing at least 40 kg) who are

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 19 of 35
Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/			



positive for COVID-19 confirmed with PCR (or alternative molecular testing technique) within the last 5 days, within 5 days of symptom onset, who do not require oxygen supplementation and who are at high risk of progressing to severe COVID-19. Studies suggest that it may prevent progression to severe disease in those at highest risk of same.

Key points for pregnancy clinical teams:

1. Currently, there are no data on the use of sotrovimab in pregnant women.¹¹ Other monoclonal antibodies have been safely used in pregnant women for a variety of conditions.¹² Due to its mechanism of action, there is a low theoretical risk to the foetus associated with its use in pregnancy.^{11,13}
2. Sotrovimab can be considered for use in pregnancy in line with the clinical prioritisation framework (Appendix 2.0) if the potential risk of maternal infection with COVID-19 is considered to be greater than any potential or theoretical risks to the mother or the foetus from the drug.
3. Treatment with sotrovimab in pregnancy should not be withheld on account of pregnancy when a benefit from treatment is perceived by the treating clinician(s).^{1,12,14}
4. Most pregnant women infected with SARS-CoV-2 will be either asymptomatic or have mild to moderate disease. Severe disease appears to be more common in later pregnancy.¹
5. There is data suggesting that COVID-19 infected pregnant women have a higher risk of severe disease and a higher instance of mortality and morbidity, including higher rates of intensive care unit (ICU) admission and higher needs for ventilation and extracorporeal membrane oxygenation (ECMO), compared to COVID-19 infected non-pregnant women.¹
 - There is pre-omicron data suggesting that among pregnant women, those who have COVID-19 have:
 - higher instance of mortality and morbidity compared to pregnant women who do not have COVID-19.¹⁵
 - increased risk of preterm birth and small for gestational age. Babies born to women with COVID-19 in pregnancy are more likely to be admitted to the Neonatal Intensive Care Unit (NICU).¹⁵
 - worse maternal outcomes, including an increased risk of death.¹⁵ Approximately 100,000 babies have been born in Ireland throughout the COVID-19 period.¹⁶ The TAG Pregnancy Subgroup are not aware of any maternal deaths to date from COVID-19 throughout the period. However, between 27/06/21 and 22/01/22 (waves 4 and 5) 38 pregnant or recently pregnant women with COVID-19 were admitted to ICU (representing 39% of COVID ICU admissions among females aged 15-44 years).¹⁷
 - approximately doubled risk of stillbirth.¹⁸ Since January 2021, there have been cases of COVID-19 placentitis in Ireland, resulting in 6 cases of stillbirth and one case of second trimester miscarriage due to placentitis.^{19,20} In addition, five fetal

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 20 of 35
Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/			



deaths greater than 20 weeks and two early neonatal deaths have been attributed to placentitis in the delta wave period September to December 2021.²⁰

Please note that the data gathered for points above refer to data pre-omicron. Initial observations suggest that the omicron variant may have less impact on maternal morbidity than previous variants. At the present time, the lesser impact of omicron on fetal outcome is unclear.

6. There does not appear to be a correlation between severity of maternal symptoms and placentitis.¹⁹ There is no evidence at this point that this therapy would impact placentitis.

Currently, 19 units deliver maternity care Ireland. It is likely that most of the women recommended to receive this treatment will be attending one of the larger hospitals due to their underlying disease, and consequently, it is appropriate that expertise in delivering this medication is located in the larger units.

Clinical Prioritisation Framework for the Use and Prescribing of Sotrovimab for COVID-19 in Pregnant Women (see also Appendix 2.0)

Every eligible woman will require a risk assessment and participate in shared decision making.

1. Tier 1: Regardless of vaccine status, Immunocompromised + pregnant = recommend
2. Tier 2: Unvaccinated + additional risk factors + pregnant = consider and decision after case discussion (e.g. obstetrics, infection consultant, and pharmacy).

Note: Pregnancy alone does not qualify for consideration for therapeutic intervention at this time, until more about the safety and efficacy profile of this therapeutic agent becomes known.

*Pregnancy additional risks includes but are not exclusive to obesity (BMI over 35), BAME (Black Asian Mixed Ethnicity), diabetes mellitus, hypertension, cardiovascular disease, chronic lung disease and clinical risk factor conditions not meeting full definition for inclusion in Tier 1.

The TAG Pregnancy Subgroup believe the number of pregnant women who may benefit from sotrovimab to be very small.

6. Paediatrics and Treatments used in COVID-19

The only proven way to prevent progression to severe COVID-19 in the paediatric population is vaccination.

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 21 of 35
Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/			



Children have a significantly lower risk than adults of developing severe COVID-19 even when additional risks are present. The numbers who will require targeted therapy will be small. The evidence to date on the use of these therapies in children is minimal and guidance may change as more data become available. Any decisions to treat children should always be made in consultation with the paediatric ID team at CHI. Unlicensed use of COVID-19 therapies may be considered in children and should always be discussed on a case by case basis with the paediatric infectious disease team at CHI.

7. Therapies not or no longer recommended in COVID-19

The therapies below should not be administered for the treatment of COVID-19 outside of an approved clinical trial. It should be noted that this list is not exhaustive and if a therapy is omitted from this list it should not be implied that it is recommended.

Some of the therapies outlined below are novel and evidence is emerging. When requested, the TAG will review these data and make recommendations to the CCO. There are many emerging therapies under review for the treatment of COVID-19, once further evidence is published and these treatments become available, they will be reviewed for use in line with this guideline.

Lopinavir/ritonavir	Lopinavir/ritonavir is not recommended for the management of COVID-19
Hydroxychloroquine +/- Azithromycin	Hydroxychloroquine +/- azithromycin is not recommended for the management of COVID-19
Ivermectin	Ivermectin is not recommended for the management of COVID-19 outside of the REMAP CAP trial

References

References for 4.1 Systemic Corticosteroids

- Summary of Product Characteristics. Dexamethasone 2 mg Tablet. Available from: http://www.hpra.ie/img/uploaded/swedocuments/LicenseSPC_PA1691-014-001_15032018112037.pdf. Accessed 4.2.2022
- Summary of Product Characteristics. Solu-Cortef Powder for Solution for Injection or Infusion 100 mg. Available from: https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA0822-137-001_26102021141816.pdf. Accessed 4.2.2022
- World Health Organisation. Corticosteroids for COVID-19. Living Guidance. 02 Sep 2020. Available online at: <https://www.who.int/publications/i/item/WHO-2019-nCoV-Corticosteroids-2020.1>. Accessed on 4.2.2022
- Randomised Evaluation of COVID-19 thERapY (RECOVERY) Clinical Trial Protocol. 2020. Available from: <https://www.recoverytrial.net/files/recovery-protocol-v7-0-2020-06-18.pdf>. Accessed 20 July 2020.
- Medicines Complete. Injectable Drugs Guide: Dexamethasone. Available online at: <https://www.medicinescomplete.com/>. Accessed 20 July 2020.

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 22 of 35
Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer . This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/			



6. Electronic Medicines Compendium. *Summary of Product Characteristics: Dexamethasone 3.3 mg/ml solution for injection*. Available online at: <https://www.medicines.org.uk/emc/product/4659/smpc>. Accessed: 4.2.2022
 7. Royal College of Paediatrics and Child Health. COVID-19 - guidance for management of children admitted to hospital and for treatment of non-hospitalised children at risk of severe disease. Available online at: <https://www.rcpch.ac.uk/resources/covid-19-management-children-hospital-and-non-hospitalised#treatment-criteria-for-covid-19-specific-therapy>. Accessed: 28.01.22
 8. Joint Formulary Committee. (2020). British national formulary. Available online at: <https://www.medicinescomplete.com/>. Accessed 09 Sep 2020.
 9. World Health Organisation. Living Guidance for Clinical Management of COVID-19. Available online at: <https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2021-2>. Accessed 17 Jan 2022
- The RECOVERY Collaborative Group. Dexamethasone in hospitalized patients with Covid-19 - preliminary report. *N Engl J Med*. DOI: 10.1056/NEJMoa2021436.
 - Dequin PF, Heming N, Meziani F, et al. Effect of hydrocortisone on 21-day mortality or respiratory support among critically ill patients with COVID-19: a randomized clinical trial. *JAMA*. Published online September 2, 2020. doi:10.1001/jama.2020.16761.
 - Tomazini BM, Maia IS, Cavalcanti AB, et al. Effect of Dexamethasone on Days Alive and Ventilator-Free in Patients With Moderate or Severe Acute Respiratory Distress Syndrome and COVID-19: The CoDEX Randomized Clinical Trial. *JAMA*. Published online September 02, 2020. doi:10.1001/jama.2020.17021.
 - The Writing Committee for the REMAP-CAP Investigators. Effect of Hydrocortisone on Mortality and Organ Support in Patients With Severe COVID-19: The REMAP-CAP COVID-19 Corticosteroid Domain Randomized Clinical Trial. *JAMA*. Published online September 02, 2020. doi:10.1001/jama.2020.17022.
 - The WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group. Association Between Administration of Systemic Corticosteroids and Mortality Among Critically Ill Patients With COVID-19: A Meta-analysis. *JAMA*. Published online September 02, 2020. doi:10.1001/jama.2020.17023
 - Randomised Evaluation of COVID-19 thERapY (RECOVERY) Clinical Trial Protocol. 2020. Available online at: <https://www.recoverytrial.net/files/recovery-protocol-v7-0-2020-06-18.pdf>. Accessed 20 July 2020.
 - Surviving Sepsis Campaign: Guidelines on the Management of Critically Ill Adults with Coronavirus Disease 2019 (COVID-19). Available online at: <https://www.esicm.org/wp-content/uploads/2020/03/SSC-COVID19-GUIDELINES.pdf>. Accessed 11 Sep 2020.

References for 4.2 Intravenous Remdesivir – Antiviral

1. Summary of Product Characteristics. Veklury 100 mg powder for concentrate for solution for infusion. Available online at: https://www.ema.europa.eu/en/documents/product-information/veklury-epar-product-information_en.pdf. Accessed: 19.01.2022
2. HSE Therapeutics Guideline Group: Recommendations from the COVID-19 Therapeutics Guideline Group to the Therapeutics Advisory Group: Remdesivir & Sotrovimab, January 20th 2022, version 2.0.
3. Gottlieb R.L., Vaca C.E., Paredes R., et. Al. “Early Remdesivir to Prevent Progression to Severe COVID-19 in Outpatients”. *NEJM*, December 22, 2021. DOI: 10.1056/NEJMoa2116846
4. COVID-19 ERG Rapid Evidence Review for “Clinical evidence for the use of antivirals in the treatment of COVID-19 v14. Available online at: <http://www.ncpe.ie/research/covid-19/>. Accessed 24.1.2022

References for 4.3 Intravenous Sotrovimab – Neutralising Monoclonal Antibody

1. Summary of Product Characteristics. Xevudy 500 mg concentrate for solution for infusion. Available from: https://www.ema.europa.eu/en/documents/product-information/xevudy-epar-product-information_en.pdf. Accessed 14.1.22.

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 23 of 35
Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer . This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/			



2. HSE Therapeutics Guideline Group: Recommendations from the COVID-19 Therapeutics Guideline Group to the Therapeutics Advisory Group: Remdesivir & Sotrovimab, January 20th 2022, version 2.0.
3. Gupta A, Gonzalez-Rojas, Y, Juarez E, et al. Early Treatment for COVID-19 with SARS-CoV-2 Neutralising Antibody Sotrovimab. NEJM. Published online October 27th 2021. DOI: 10.1056/NEJMoa2107934.

References for 4.4 Intravenous Tocilizumab – Anti-IL6 Receptor Monoclonal Antibody

1. Summary of Product Characteristics. RoActemra 20 mg/mL concentrate for solution for infusion. Available online at: https://www.ema.europa.eu/en/documents/product-information/roactemra-epar-product-information_en.pdf. Accessed 13.1.2022
2. NCPE Rapid Evidence Review: Tocilizumab in the management of COVID-19. A rapid evidence review, version 6. 25th Feb 2021. Available online from: <https://www.ncpe.ie/wp-content/uploads/2021/03/COVID-19-Evidence-Review-Group-Tocilizumab-V6-Final-Version.pdf>. Accessed 13.1.2022
3. Abani O, Abbas A, Abbas F et. al. Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. Lancet, May 2021. DOI: 10.1016/S0140-6736(21)00676-0.
4. REMAP-CAP Study Protocol. *Domain-Specific Appendix: COVID-19 Immune Modulation Therapy*. Available online at: <https://www.remapcap.org/protocol-documents>. Accessed 04.01.2022
5. NCPE Rapid Evidence Review: Tocilizumab in the management of COVID-19. A rapid evidence review, version 6. 25th Feb 2021. Available online at: <http://www.ncpe.ie/research/covid-19/>). Accessed 13.1.2022

References for 4.5 Venous Thromboembolism (VTE) Prophylaxis

1. HSE, Interim Clinical Guidance for VTE protocol and Patient Information for Acute Hospitals. Available from: <https://hse.ie/libguides.com/c.php?g=679077&p=4866382>. Accessed on 20.01.2022

References for Section 5: Pregnancy and Treatments used in COVID-19

1. Royal College of Obstetricians and Gynaecologists and the Royal College of Midwives. Coronavirus (COVID-19) Infection in Pregnancy. Version 14.3. 11th January 2022. Available online at: <https://www.rcog.org.uk/en/guidelines-research-services/guidelines/coronavirus-pregnancy/>. Accessed on 19.01.22.
2. Knight M, Bunch K, Cairns A, Cantwell R, Cox P, Kenyon S, Kotnis R, Lucas DN, Lucas S, Marshall L, Nelson-Piercy C, Page L, Rodger A, Shakespeare J, Tuffnell D, Kurinczuk JJ on behalf of MBRRACE-UK. Saving Lives, Improving Mothers' Care Rapid Report: Learning from SARS-CoV-2-related and associated maternal deaths in the UK March – May 2020 Oxford: National Perinatal Epidemiology Unit, University of Oxford 2020.
3. ClinicalTrials.gov. Randomised Evaluation of COVID-19 Therapy (RECOVERY). 2020. Available online at: <https://clinicaltrials.gov/ct2/show/NCT04381936>. Accessed 3.2.2022
4. Food and Drug Administration (FDA). Fact sheet for health care providers Emergency Use Authorisation (EUA) for Remdesivir (GS-5734™). Accessed online at: [fda.gov](https://www.fda.gov). Date accessed 20 May 2020.
5. Mulangu S, Dodd LE, Davey RTJ, Tshiani Mbaya O, Proschan M, Mukadi D, et al. A Randomized, Controlled Trial of Ebola Virus Disease Therapeutics. N Engl J Med. 2019 Dec; 381(24):2293–303.
6. Maldarelli GA, Savage M, Mazur S, Oxford-Horrey C, Salvatore M, Marks KM. Remdesivir treatment for severe COVID-19 in third-trimester pregnancy: Case report and management discussion. Open forum infectious diseases 2020 Sep;7(9).

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 24 of 35
Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/			



7. Naqvi M, Zakowski P, Glucksman L, Smithson S, Burwick RM. Tocilizumab and Remdesivir in a pregnant patient with coronavirus disease 2019 (COVID-19). *Obstetrics & Gynecology*. 2020 Nov 1;136(5):1025-9.
8. Anderson J, Schauer J, Bryant S, Graves CR. The use of convalescent plasma therapy and remdesivir in the successful management of a critically ill obstetric patient with novel coronavirus 2019 infection: A case report. *Case Reports in Women's Health*. 2020 May 16:e00221.
9. Pierce-Williams RA, Burd J, Felder L, Khoury R, Bernstein PS, Avila K, Penfield CA, Roman AS, DeBolt CA, Stone JL, Bianco A. Clinical course of severe and critical COVID-19 in hospitalized pregnancies: a US cohort study. *American Journal of Obstetrics & Gynecology Mfm*. 2020 May 8:100134.
10. Burwick RM, Yawetz S, Stephenson KE, Collier AR, Sen P, Blackburn BG, Kojic EM, Hirshberg A, Suarez JF, Sobieszczyk ME, Marks KM. Compassionate use of remdesivir in pregnant women with severe COVID-19. *Clinical Infectious Diseases*. 2020 Oct 8.
11. Summary of Medicinal Product Characteristics (SmPC). Xevudy 500 mg concentrate for solution for infusion. Accessed online at <https://www.ema.europa.eu/en/medicines/human/EPAR/xevudy>. Accessed 19.01.22.
12. American College of Obstetricians and Gynaecologists (ACOG). COVID-19 FAQs for Obstetrician-Gynecologists, Obstetrics. Accessed online at: <https://www.acog.org/clinical-information/physician-faqs/covid-19-faqs-for-ob-gyns-obstetrics>. Accessed 19.01.22.
13. UK Teratology Information Services (UKTIS). Accessed online at Toxbase.org. Accessed 19.01.22
14. National Institutes of Health. The COVID-19 Treatment Guidelines. Panel's Statement on Therapies for High-Risk, Non-hospitalized Patients With Mild to Moderate COVID-19. Accessed online at: <https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-therapies-for-high-risk-nonhospitalized-patients/>. Accessed: 19/01/22
15. Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ (Clinical research ed)* 2020; **370**: m3320-m
16. Central Statistics Office. Births, Deaths and Marriages. Available online at: <https://www.cso.ie/en/statistics/birthsdeathsandmarriages/vitalstatistics/>. Accessed 04.02.22
17. Health Protection Surveillance Centre. Epidemiology of Intensive Care Admissions in Cases of COVID-19 in Ireland (among those aged 15 years and older) 27/06/2021 – 22/01/2022. Available online at: <https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/surveillance/covid-19intensivecareadmissions/>. Accessed 04.02.2022
18. DeSisto CL, Wallace B, Simeone RM, et al. Risk for Stillbirth Among Women With and Without COVID-19 at Delivery Hospitalization – United States, March 2020 – September 2021. *MMWR Morbidity and Mortality Weekly Report* 2021; 70: 1640 – 1645. DOI: <http://dx.doi.org/10.15585/mmwr.mm7047e1>. Available online at: <https://www.cdc.gov/mmwr/volumes/70/wr/mm7047e1.htm#suggestedcitation>. Accessed 04/02/22
19. Royal College of Physicians of Ireland. Covid Placentalitis: Statement from the RCPI Faculty of Pathology and the Institute of Obstetricians and Gynaecologists, 13th April 2021. Available online at: <https://www.rcpi.ie/news/releases/covid-placentalitis-statement-from-the-rcpi-faculty-of-pathology-and-the-institute-of-obstetricians-and-gynaecologists/>. Accessed 04.02.22
20. Prof. Keelin O'Donoghue. Stillbirth, Surveillance of Fetal Wellbeing and SARS-CoV-2 Infection – January 2022 Update. Available online at: <https://rcpi-live-cdn.s3.amazonaws.com/wp-content/uploads/2022/01/Stillbirth-Fetal-Wellbeing-and-SARS-CoV-2-120122.pdf>. Accessed 04.02.22

References for Section 6: Paediatrics and Treatments used in COVID-19

1. <https://www.rcpch.ac.uk/resources/covid-19-management-children-hospital-and-non-hospitalised#treatment-criteria-for-covid-19-specific-therapy> [Accessed: 28.01.2022]
2. Consensus guidance for management of PIMS [https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642\(20\)30304-7/fulltext](https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(20)30304-7/fulltext) [Accessed: 31.01.2022]

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 25 of 35
Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer . This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/			



Appendices

Appendix 1: A Proposed Core Outcome Measure Set for Clinical Studies of COVID-19 Infection.

Graphic contains recommendations from the WHO Clinical Characterization and Management Working Group, <http://www.comet-initiative.org/Studies/Details/1528> . Refer to HSE COVID 19 Dataset specification for additional information on clinical coding detail.

<https://www.hse.ie/eng/services/news/newsfeatures/covid19-updates/covid-19-dataset-specification-for-patient-assessment-and-tracking.pdf>

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 26 of 35
Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/			



Viral burden

Semiquantitative viral RNA of severe acute respiratory syndrome coronavirus 2 as measured by quantitative PCR or cycle threshold; nasopharyngeal swabs are associated with the highest viral load

Survival

All-cause mortality at hospital discharge or at 60 days

Clinical progression

WHO Clinical Progression Scale measured daily over the course of the study

Patient State	Descriptor	Score
Uninfected	Uninfected; no viral RNA detected	0
Ambulatory mild disease	Asymptomatic; viral RNA detected	1
	Symptomatic; independent	2
	Symptomatic; assistance needed	3
Hospitalised: moderate disease	Hospitalised; no oxygen therapy*	4
	Hospitalised; oxygen by mask or nasal prongs	5
Hospitalised: severe diseases	Hospitalised; oxygen by NIV or high flow	6
	Intubation and mechanical ventilation, $pO_2/FiO_2 \geq 150$ or $SpO_2/FiO_2 \geq 200$	7
	Mechanical ventilation $pO_2/FiO_2 < 150$ ($SpO_2/FiO_2 < 200$) or vasopressors	8
	Mechanical ventilation $pO_2/FiO_2 < 150$ and vasopressors, dialysis, or ECMO	9
Dead	Dead	10

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 27 of 35
<p>Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer</p> <p>This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/</p>			



Appendix 2: Therapeutic Advisory Group: Clinical Prioritisation Framework for the Use and Prescribing of Emerging Novel Therapeutics for COVID-19

This is interim guidance on which individuals might receive the greatest benefit from emerging therapeutics. When it becomes necessary to prioritise patients for receipt of therapies, the TAG suggests prioritising by risk group as described in this document. The treating physician will need to consider all co-morbidities and therapies to gauge for cumulative immune suppressing effect.

Tier	Risk Group
1	<p>Immunocompromised adult patients not expected to mount an adequate immune* response to COVID-19 vaccination or SARS-coV-2 infection due to their underlying conditions, regardless of vaccine status (see Clinical Risk Factors)</p> <p>Immunosuppressed adult patients taking rituximab within 12 months** and other B cell or T cell depleting therapies OR high dose steroids defined as adults receiving over 40mgs/day for more than 1 week or over 20mgs/day for two weeks within the last three months</p> <p>Children‡ with profound immunodeficiency (e.g. peri-transplant or CAR-T treatment) or who have specific congenital immune disorders (APECED, Interferon pathway disorders)</p> <p>Unvaccinated adult patients at the highest risk of severe disease (adults aged over 75 years or adults aged over 55 years with additional risks***)</p>
2	<p>Unvaccinated adult patients at risk of severe disease not included in Tier 1 (adults aged over 65 years or adults aged under 55 years with additional risks***)</p> <p>Unvaccinated children who are under hospital supervision for conditions such as severe complex neurodisability with multiple medical needs OR complex medical needs with multiple co-morbidities (e.g. technology dependent – tracheostomy, home ventilation etc)</p>
3	<p>Vaccinated adult patients at high risk of severe disease (adults aged over 75 years or adults aged over 65 years with additional risks***)</p> <p>Note: Vaccinated adult patients who have not received a COVID-19 vaccine booster dose are likely at higher risk for severe disease; patients in this situation within this tier should be prioritised for treatment</p>
4	<p>Vaccinated adult patients at risk of severe disease (adults aged over 65 years or adults aged under 65 with additional risks***)</p> <p>Note: Vaccinated adult patients who have not received a COVID-19 vaccine booster dose are likely at higher risk for severe disease; patients in this situation within this tier should be prioritised for treatment</p>
Pregnancy	<p>Every eligible woman will require a risk assessment and participate in shared decision making.</p> <p>Tier 1: Regardless of vaccine status, Immunocompromised (as defined in Tier 1) + pregnant = recommend</p> <p>Tier 2: Unvaccinated + additional risk factors + pregnant = consider and decision after case discussion (e.g. obstetrics, infection consultant, and pharmacy).</p>

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 28 of 35
<p>Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer</p> <p>This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/</p>			



Note: Pregnancy alone does not qualify for consideration for therapeutic intervention at this time, until more about the safety and efficacy profile of this therapeutic agent becomes known

*Pregnancy additional risks include but are not exclusive to obesity (BMI over 35), BAME (Black Asian Mixed Ethnicity), diabetes mellitus, hypertension, cardiovascular disease, chronic lung disease and clinical risk factor conditions not meeting full definition for inclusion in Tier 1.

The TAG Pregnancy Subgroup believe the number of pregnant women who may benefit from sotrovimab to be very small.

*baseline or pre-treatment serology is not required but this guideline may change with evolving practice

** Extended effect may occur and impact may be supported by consideration for serology testing

*** **Additional risks** include obesity (BMI over 35), diabetes mellitus, hypertension, cardiovascular disease, chronic lung disease, clinical risk factor conditions not meeting full definition for inclusion in Tier 1

¥Note that children have a significantly lower risk than adults of developing severe COVID-19, even when additional risks are present. Any decisions to treat are made in consultation with the paediatric ID team at CHI.

Appendix 3: Therapeutic Advisory Group: Clinical Prioritisation Framework for the Use and Prescribing of Emerging Novel Therapeutics for COVID-19

In addition to unvaccinated patients at highest risk of severe disease, patients with conditions highlighted in **red** are those who might receive the greatest benefit from early intervention therapies and should be prioritised in situations of limited supply.

Clinical Risk Factors: Tier 1 Conditions (Clinical risk factors of immunocompromised individuals)

Clinical Risk Factors: Tier 1 Conditions -Adults	
PRIMARY IMMUNODEFICIENCY	
Diagnosis-based	CVID
	SCID / Combined Immunodeficiency
	Hypogammaglobulinaemia, associated with recurrent infections AND immunoglobulin replacement /prophylactic antibiotics
	Good's (thymoma + B cell deficiency)
	HyperIgM
	Autoimmune polyglandular syndromes
	IFN type 1 pathway defects / autoantibodies
SECONDARY IMMUNODEFICIENCY	
Solid organ transplant	Any
	Lung

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 29 of 35
Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/			



	Within 1 year of solid organ transplant
<i>HIV</i>	AIDS presentation or uncontrolled HIV infection
	Untreated (high viral load) with CD4<50
	CD4 <200
IMMUNE-MEDIATED INFLAMMATORY DISORDERS (IMID)	
<i>Treatment-based</i>	B- cell depleting Rx (eg rituximab) within 12 months; or where B cell reconstitution has not occurred
	Tacrolimus (systemic therapy - Excludes topical tacrolimus or other topical calcineurin inhibitors)
	Corticosteroids (Long term use of > 5mg/day prednisolone, or intermittent high dose within the previous 3 months)
	Cyclophosphamide (within last 6 months)
	Cyclosporin
	Mycophenolate Mofetil, Mycophenolic acid
	Biologic monotherapy with agents associated with significantly impaired vaccine response
	Biologic <u>PLUS</u> AZA (thiopurine) or Biologic <u>PLUS</u> MTX
	Abatacept
HAEMATOLOGY	
<i>Diagnosis-based</i>	HSCT < 12 months, OR where B cell reconstitution has not occurred
	GVHD active
	Chronic B cell lymphoproliferative disease
	Myeloma (<u>NOT</u> MGUS) (MGUS with impaired immune function, but not fulfilling myeloma definition)
	Myelodysplastic syndrome
<i>Treatment-based</i>	CART (Chimeric Receptor T-cell Therapy) within 2 years
	B-cell depletion Rx (anti-CD20, daratumumab) within 12 months OR where B cell reconstitution has not occurred
	T-cell depleting therapies (alemtuzumab, ATG) within 12 months
	Radiotherapy within 6 months
	Systemic anti-cancer therapy within 12 months (excluding tyrosine kinase inhibitors) for haem malignancy (<u>NOT</u> stable CML)
<i>Non-malignant</i>	Sickle cell disease
	Haem disorders receiving B-cell or T-cell depletion Rx within 12 months (anti-CD20, alemtuzumab, ATG)
ONCOLOGY	
<i>Diagnosis-based</i>	Active solid/metastatic cancer
<i>Treatment-based</i>	Radiotherapy within 6 months

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 30 of 35
<p>Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer</p> <p>This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/</p>			



	Chemotherapy within 3 months
RENAL	
<i>Diagnosis-based</i>	Renal transplant
	CKD 4 or 5
<i>Treatment-based</i>	B cell depleting Rx within 12 months OR where B cell reconstitution has not occurred
LIVER	
<i>Diagnosis-based</i>	Cirrhosis (Childs C)
	Liver transplant
<i>Treatment-based</i>	Any immunosuppression for liver disease (Excluding low dose corticosteroids)
NEUROLOGY	
<i>Diagnosis-based</i>	Huntington's
	MND on immune therapies
	MS on immune based therapies
	Myasthenia gravis on immune based therapies

Reference

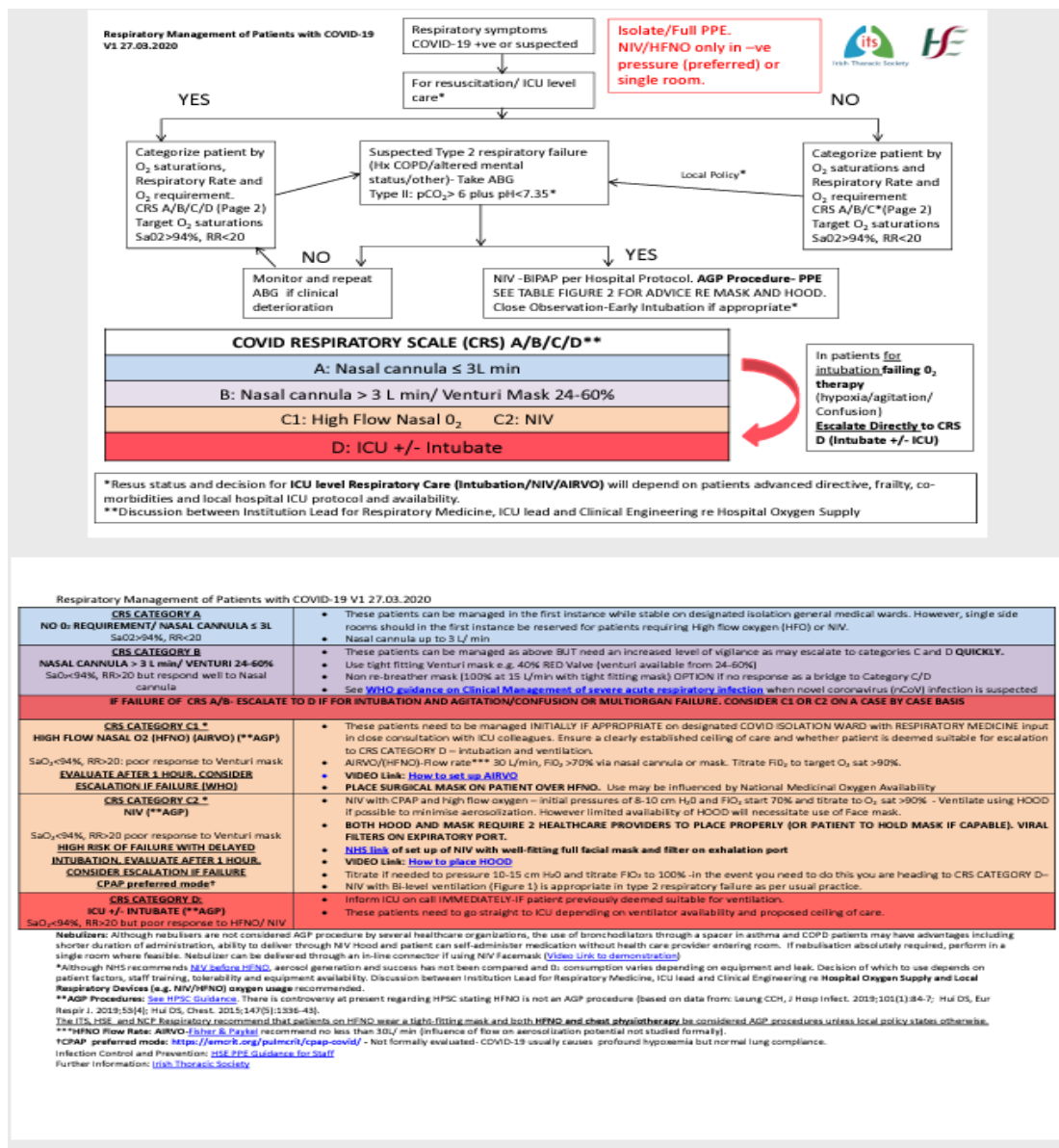
1. Therapeutic Advisory Group - Interim Statement and Guidance: The Clinical Prioritisation Framework for the Use and Prescribing of Emerging Novel Therapeutics for COVID-19, Version 1. 18th Jan 2022

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 31 of 35
Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/			



Appendix 4: Irish Thoracic Society – COVID-19 Respiratory Scale (CRS)

Taken from the Respiratory Management of Patients with COVID-19 V2 January 2021, Irish Thoracic Society



HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 32 of 35
<p>Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer</p> <p>This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/</p>			



- A. Use of Steroids: For hospitalized patients with COVID-19 requiring oxygen, the suggested regimen of corticosteroid use is 6 mg of dexamethasone (oral or intravenous (check equivalence with oral dose)) daily, intravenous hydrocortisone 50mg tid or equivalent for 7-10 days.
Link: [HSE Interim Guidance for the use of systemic corticosteroids in the management of hospitalised patients with severe COVID-19 disease.](#)
Do not routinely use corticosteroids to treat COVID-19 in adults who do not require oxygen unless there is another indication e.g. co-existent Asthma or COPD.
- B. Use prophylactic doses of anticoagulants, preferably low molecular weight heparin (LMWH) (e.g. enoxaparin 40 mg once daily) in adults with moderate COVID-19 or other indications, unless there is a contraindication, such as risk for major bleeding: <https://www.hse.ie/eng/about/who/acute-hospitals-division/drugs-management-programme/covid19-evidence-review-group-for-medicines-ref-for-thromboprophylaxis-in-the-management-of-covid19.pdf>
- C. Prone position for awake, spontaneously breathing patients may also improve oxygenation and the ventilation/perfusion ratio. For adults with COVID-19 who are receiving any form of supplemental oxygen therapy and have not yet been intubated, consider prone positioning for at least 3 hours per day as tolerated. When positioning a patient in prone, ensure it is used with caution and accompanied by close monitoring of the patient. Use of prone positioning should not delay endotracheal intubation and mechanical ventilation in patients with COVID-19 who are deteriorating
- D. Nebulizers: Although nebulisers are not considered AGP procedure, the use of bronchodilators through a spacer in asthma and COPD patients may have advantages including shorter duration of administration, ability to deliver through NIV Hood and patient can self-administer medication without health care provider entering room. If nebulization absolutely required, perform in a single room where feasible. Nebulizer can be delivered through an in-line connector if using NIV Facemask ([Video Link to demonstration](#))

Reference

1. The Irish Thoracic Society, Managing Respiratory Care during the COVID-19 Pandemic V2, January 2021. Available here <https://irishthoracicsociety.com/wp-content/uploads/2020/03/Respiratory-Mgt-Guideline-V2-Jan-2021.20.01.pdf>.

Accessed 17.1.2022

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 33 of 35
Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/			



Appendix 5.0 WHO COVID-19 Disease Severity Classification

For further information see <https://apps.who.int/iris/bitstream/handle/10665/338882/WHO-2019-nCoV-clinical-2021.1-eng.pdf?sequence=1&isAllowed=y>

Critical COVID-19	Defined by the criteria for acute respiratory distress syndrome (ARDS), sepsis, septic shock, or other conditions that would normally require the provision of life-sustaining therapies such as mechanical ventilation (invasive or non-invasive) or vasopressor therapy.
Severe	Defined by any of: <ul style="list-style-type: none"> • Oxygen saturation < 90% on room air. • Respiratory rate: <ul style="list-style-type: none"> ○ > 30 breaths/min in adults and children > 5 years old; ○ ≥ 60 breaths/min in children < 2 months old; ○ ≥ 50 in children 2–11 months old ○ ≥ 40 in children 1–5 years old. • Signs of severe respiratory distress (accessory muscle use, inability to complete full sentences, and, in children, very severe chest wall indrawing, grunting, central cyanosis, or presence of any other general danger signs).
Non-severe	Defined as absence of any criteria for severe or critical COVID-19.

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 34 of 35
Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/			



Appendix 6.0 Membership of COVID-19 Therapeutic Guideline Subgroup Members:

Co-chairs:

Dr Mike O'Connor, National Clinical Advisor and Group Lead and Dr Catherine Fleming, National Infectious Diseases Programme.

Members:

Professor Colm Bergin, National Infectious Diseases Programme.

Prof Alistair Nichol, National Clinical Programme for Critical Care nominee:

Dr Alan Gaffney, National Clinical Programme for Critical Care nominee.

Dr Des Murphy, Respiratory Consultant Cork University Hospital.

Prof Paul Browne, Irish Haematology Society nominee.

Dr Larry Bacon, Irish Haematology Society nominee.

Dr Roisín Adams, COVID 19 Evidence Review Group Lead.

Dr Paul Ryan, General Practitioner and Community Nominee.

Professor Marie Keogan, Immunology Consultant.

Dr Niamh Ennis, HPRA Representative.

Fionnuala King, Chief Pharmacist Acute Hospitals Drug Management Programme (AHDMP).

Rhona O'Neill, Chief II Pharmacist, Acute Hospitals Drug Management Programme (AHDMP).

Nina Acosta, Senior Pharmacist, Acute Hospitals Drug Management Programme (AHDMP).

HSE Interim Guidance for the Pharmacological Management of Patients with COVID-19.		Published: 14.02.2022 Review: 14.07.2022	Version number: 2
Protocol Code: COVID19	Approved by: COVID 19 Therapeutic Advisory Group	Guideline review group: COVID-19 Therapeutic Guideline Subgroup	Page 35 of 35
Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer This information is valid only on the day of printing, for any updates please check: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/			