



Specific Antiviral Therapy in the Clinical Management of Acute Respiratory Infection with SARS-CoV-2 (COVID-19).

Version 1.0: Recommendations in this document are based on the latest available evidence on 12th March 2020. If using a printed copy the information is valid only on the day of printing. The document is subject to change in response to emerging new evidence; for the most recent version of the document please check: <https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/guidanceforhealthcareworkers/>

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Protocol Code: COVID19	Approved by: Dr Vida Hamilton, HSE National Clinical Advisor and Group Lead, Acute Hospitals	Contributors: Prof C Bergin, M Philbin, P Gilvarry, M O'Connor, F King	Page 1 of 15
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Scope

This document is intended for use by healthcare professionals. The recommendations are specific to the management of acute respiratory infection when SARS-CoV-2 COVID-19 infection is confirmed. While the recommendations are intended to strengthen clinical management of these patients they do not replace clinical judgment or specialist consultation.

Comprehensive information for members of the public and healthcare professional on the prevention, diagnosis and management COVID-19 is available from the following sources:

- Department of Health: <https://www.gov.ie/en/publication/472f64-covid-19-coronavirus-guidance-and-advice/#treatment>
- European Centre for Disease Prevention and Control: <https://www.ecdc.europa.eu/en/novel-coronavirus-china>
- Health Service Executive (HSE): <https://www2.hse.ie/conditions/coronavirus/coronavirus.html#Treatment>
- HSE Health Protection Surveillance Centre (HPSC): <https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/>
- World Health Organisation:
 - <https://www.who.int/health-topics/coronavirus>
 - [https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-\(ncov\)-infection-is-suspected](https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected)

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Specific Antiviral Therapy in SARS-CoV-2 (COVID-19)

There is a paucity of clinical evidence for any disease-specific treatment. However, there are a number of medicinal products under investigation and may be considered in severely ill patients or those at risk of severe disease. There are no comparative studies between different treatments; access to individual medicinal products may need consideration in the treatment selection process. See **Tables 3-7** for information on medicinal products.

Treat empirically for community acquired pneumonia as per local guidelines and consider antivirals as below.

Table 1 lists criteria for specific antiviral therapy in SARS-CoV-2 (COVID-19). Clinical judgment will be required for all cases; specialist consultation with local Infectious Disease and Microbiology teams is recommended for those cases not meeting criteria listed in **Table 1**.

Table 1. Criteria for Specific Antiviral Therapy in SARS-CoV-2 (COVID-19)	
1.	<p>Confirmed COVID-19 disease (confirmed using test recommended by HPSC; available from: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/laboratoryguidance/)</p> <p style="text-align: center;">AND</p> <p>Critical Care Admission</p>
2.	<p>Confirmed COVID-19 disease (confirmed using test recommended by HPSC; available from: https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/laboratoryguidance/)</p> <p style="text-align: center;">AND</p> <p>NEWS Score ≥ 5</p> <p>Consider treatment in patients with NEWS Score ≥ 4 and significant co-morbidities or risk factors for severe disease, including:</p> <ul style="list-style-type: none"> • Cardiovascular Disease • Diabetes Mellitus • Immunocompromised • Chronic Kidney Disease • Pre-existing Respiratory Disease

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Table 2 Differential diagnoses of respiratory infections in presentation of suspected community transmission of Covid-19 (adapted from St James’s Hospital Protocol).

DIFFERENTIAL DIAGNOSES OF RESPIRATORY INFECTIONS IN PRESENTATION OF SUSPECTED COMMUNITY TRANSMISSION OF COVID-19		
	Investigations	Treatment
Community Acquired Pneumonia	<ul style="list-style-type: none"> - Arterial blood gases - Chest X-ray - Full Blood Count - Urea and electrolytes - Blood cultures - Sputum cultures - Urine for Legionella antigen 	Treat according to local antimicrobial prescribing policy.
Healthcare Associated Pneumonia	<ul style="list-style-type: none"> - Arterial blood gases - Chest X-ray - Full Blood Count - Urea and electrolytes - Blood cultures - Sputum cultures - 12 lead ECG 	Treat according to local antimicrobial prescribing policy.
Acute Infective Exacerbation of Chronic Obstructive Pulmonary Disease (COPD)	<ul style="list-style-type: none"> - Arterial blood gases - Chest X-ray - Full Blood Count - Urea and electrolytes - Blood cultures - Sputum cultures - 12 lead ECG - Pulmonary Function Tests 	Treat according to local antimicrobial prescribing policy.
Viral Influenza	<ul style="list-style-type: none"> - Arterial blood gases - Chest X-ray - Full Blood Count - Urea and electrolytes - Blood cultures - Sputum cultures - Nasopharyngeal aspirate 	<p>Treat according to local antimicrobial prescribing policy.</p> <p>AND</p> <p>National <i>Guidance on the use of antiviral agents for the treatment and prophylaxis of influenza (2019-2020)</i> available from: https://www.hpsc.ie/a-z/respiratory/influenza/seasonalinfluenza/guidance/antiviraltreatmentandprophylaxisguidance/Antivirals%20guidance%20for%20treatment%20and%20prophylaxis%20of%20influenza.pdf</p>
Suspected Covid-19 Infection	<ul style="list-style-type: none"> - Test as per most recent guidance from HPSC. 	See Table 3.

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Table 3 Diagnostics and pharmacological management of patients with confirmed COVID-19 Infection (adapted from St James’s Hospital Protocol).

	Investigations	Treatment
Confirmed COVID-19 Infection.	As per Table 2 to exclude bacterial co-infection.	<p>Refer to Tables 4, 5, 6 and 7 for further information on individual medicinal products. There is a paucity of clinical evidence for the use of any medicinal product in the treatment of COVID-19.</p> <p>The following are experimental COVID-19 treatment options (used as monotherapy) in adults:</p> <p>There is no paediatric dosing available at this time. Where clinically appropriate, children ≥ 12 years may be considered for adult dosing.</p> <p>Listed alphabetically:</p> <ul style="list-style-type: none"> - Chloroquine (oral): 500mg TWICE daily for 10days (see Table 4) Note: Highly toxic in overdose, especially in children <p style="text-align: center;">OR</p> <ul style="list-style-type: none"> - Hydroxychloroquine (oral): <u>Day 1</u>: 400mg TWICE a day, then <u>Days 2-5</u>: 200mg TWICE a day (total duration 5 days). (see Table 5) Note: Highly toxic in overdose, especially in children <p style="text-align: center;">OR</p> <ul style="list-style-type: none"> - Lopinavir/ritonavir (oral) 400mg/100mg TWICE daily up to a maximum of 14 days. (see Table 6) <p style="text-align: center;">OR</p> <ul style="list-style-type: none"> - Remdesivir (intravenous): 200mg ONCE daily on Day 1, then 100mg ONCE daily for a total of 10days. (available on Compassionate Use basis only from Gilead) (see Table 7)

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Evidence Summary

COVID-19 is a novel coronavirus and there is very limited clinical evidence for the use of any medicinal product and there is currently no licensed treatment available. Recommendations in this document are based on the latest available evidence (as of **12th March 2020**) which is summarised below.

Chloroquine

In the early *in vitro* studies, chloroquine was found to block COVID-19 infection.⁵ The anti-viral and anti-inflammatory activities of chloroquine may account for its potent efficacy in treating patients with COVID-19 pneumonia. A recent study by Wang *et al.* revealed that remdesivir and chloroquine were highly effective in the control of 2019-nCoV *in vitro*.²

Lopinavir/ritonavir

One article reports that the use of Kaletra® for the treatment of SARS was associated with a better outcome.³ Zhang *et al.* also reported a successful case of MERS-CoV disease treated with triple combination therapy LPV/RTV, ribavirin, and IFN-alpha 2a. Currently, Zhang *et al.* recommend Kaletra® as part of triple therapy with ribavirin and interferon.³ Young *et al.* describes the use of Kaletra® in 5 out of 18 patients.⁴ Five patients were treated with Kaletra® within 1 to 3 days of desaturation, but evidence of clinical benefit was equivocal. While defervescence occurred within 1 to 3 days of Kaletra® initiation, it was unable to prevent progressive disease in 2 patients. Decline in viral load as indicated by the cycle threshold value from nasopharyngeal swabs also appeared similar between those treated and not treated with Kaletra.⁴

Remdesivir

Reported to inhibit human and zoonotic coronavirus *in vitro* and to restrain severe acute respiratory syndrome coronavirus (SARS-CoV) *in vivo*.³ The antiviral activity of remdesivir and IFN-beta was found to be superior to that of LPV/RTV-IFN-beta against MERS-CoV *in vitro* and *in vivo*.³ In one case report (n=1), on hospital day 7 (illness day 11) following radiographic findings of atypical pneumonia remdesivir was administered.⁵ On hospital day 8 (illness day 12), the patient's clinical condition improved. Nasopharyngeal & oropharyngeal specimens obtained on illness days 11 & 12 showed a trend toward decreasing levels of virus.⁵ Both these outcomes may be reflective of the virus burning out rather than specifically related to the efficacy of remdesivir. A small number of patients with COVID-19 have received intravenous remdesivir for compassionate use outside of a clinical trial setting. A randomized placebo-controlled clinical trial of remdesivir for treatment of hospitalized patients with pneumonia and COVID-19 has been implemented in China.

Risk Factors for Severe Disease

A number of potential risk factors, including advanced age and a high SOFA (Sequential Organ Failure Assessment) score, have been reported as possible factors to identify patients with poor prognosis at an early stage.⁶

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Drug-Drug Interactions

Clinically significant drug-drug interactions may occur with the medicinal products used to treat COVID-19. A thorough medication history (including alternative and herbal medicines) should be obtained prior to initiation of treatment. 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 www.covid19-druginteractions.org.

Dose Adjustments

Where a dose reduction is recommended in hepatic or renal impairment it is recommended to prescribe the upper end of the dose range in the context of acute respiratory infection with SARS-CoV-2 (COVID-19) to avoid under dosing.

Administration of Medicinal Products in the Treatment of COVID-19

Timely initiation of medicinal products used for the treatment of COVID-19, at the recommended dose and frequency, is recommended to maximise efficacy, or the development of viral resistance. Delayed or omitted doses should be avoided, unless on the advice of the treating physician.

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Table 4 Chloroquine for the treatment for confirmed COVID-19 (adapted from St James's Hospital Protocol).							
Drug Chloroquine	Proposed MOA in COVID-19	Contra-indications	Monitoring	Renal/Hepatic Impairment	Side-Effects	Drug-Drug Interactions	Preparation & Sourcing
<p>Unlicensed indication, recommended from expert consensus (published ahead of trial results).</p> <p>Recommended Dose: Chloroquine phosphate 500mg twice daily for 10 days for patients diagnosed as mild, moderate and severe cases.</p>	<p>A weak base that increases the endosomal pH of acidic vesicles required for virus/cell fusion as well as interfering with glycosylation of cellular receptors of SARs-CoV.</p>	<p>Known hypersensitivity to chloroquine or any of the excipients.</p> <p>Concomitant use with amiodarone (due to increased risk of ventricular arrhythmia; see also Drug Interactions)</p>	<p>Full Blood Count: Myelosuppression may occur rarely; monitor if pre-existing myelosuppression or if receiving other myelosuppressive agents concomitantly.</p> <p>ECG: QTc prolongation may occur. Use with caution if pre-existing QTc prolongation and/or known risk factors for prolongation of the QTc interval (including concomitant administration of other QTc prolonging agents).</p> <p>Blood glucose: may cause hypoglycaemia.</p> <p>Epilepsy: may lower seizure threshold</p> <p>G6PD: Caution advised in patients with G6PD deficiency, may be risk of haemolysis. If status unknown, do not delay initiation of treatment in the context of moderate or severe COVID-19.</p>	<p>Renal Impairment: Use with caution. Dose reduced if CrCl <10ml/min; use 50% of normal dose.</p> <p>For patients on continuous veno-venous hemodialysis (CVVHD) no dose adjustment is necessary - dose as in normal renal function.</p> <p>Hepatic Impairment: No dose adjustment recommended in Avloclor® Summary of Product Characteristics. Use with caution in hepatic impairment, particularly when associated with cirrhosis.</p>	<p>See Summary of Product Characteristics (SmPC) for full list of side-effects; available from: https://www.medicines.org.uk/emc/product/5490/smpc.</p> <p>Chloroquine is highly toxic in overdose and children are particularly susceptible to toxic side effects. Ref Medicines for Children 2003 RCPCH</p>	<p>Refer to SmPC and drug-drug interaction databases e.g. Stockley's and University of Liverpool online (http://www.covid19-druginteractions.org/)</p> <p>Caution with concomitant QTc prolonging agents</p> <p>Caution with anti-convulsants; chloroquine may lower seizure threshold</p> <p>Possible potentiation of neuromuscular blockade with aminoglycoside antibiotics</p> <p>Antacids (aluminium, magnesium, and calcium salt) and adsorbents (e.g. kaolin) may reduce absorption of chloroquine; separate administration by at least 4 hours</p> <p>Chloroquine may increase levels of ciclosporin and digoxin (monitor levels)</p> <p>Thyroid medication: may increase Thyroid Stimulating Hormone levels with concomitant levothyroxine.</p>	<p>Details of availability and supply process to be confirmed.</p> <p>Tablets can be crushed and dispersed in water for administration.</p> <p>Bioavailability is increased when dose given with food</p> <p>Without crushing they will disperse in one to five minutes (different brands may vary).</p>

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Table 5 Hydroxychloroquine (HCQ) for the treatment for COVID-19.							
Drug Hydroxychloroquine (HCQ)	Proposed MOA in COVID-19	Contra-indications	Monitoring	Renal/Hepatic Impairment	Side-Effects	Drug-Drug Interactions	Preparation & Sourcing
<p>Unlicensed indication, recommended from expert consensus (published ahead of trial results).</p> <p>Recommended Dose:</p> <p>Day 1: 400mg TWICE a day, then Days 2-5 200mg TWICE a day (total duration 5 days).</p>	<p>Chloroquine analogue (see Table 3).</p> <p>Reported to have anti-SARS-CoV activity <i>in vitro</i> suggesting potential pharmacological agent for the treatment of COVID-19 infection.</p> <p><i>In vitro</i> study reported more potent inhibition of SARS-CoV-2 with HCQ compared to chloroquine.¹</p>	<p>Hypersensitivity to active ingredients or any of the excipients.</p> <p>Known hypersensitivity to 4-aminoquinoline compounds.</p> <p>Pre-existing maculopathy of the eye.</p> <p>Pregnancy.</p> <p>Children aged <6 years of age</p> <p>(200mg tablets not adapted for weight <35kg).</p> <p><i>Contd. next page</i></p>	<p>Full Blood Count:</p> <p>Myelosuppression may occur rarely; monitor if pre-existing myelosuppression or if receiving other myelosuppressive agents concomitantly.</p> <p>ECG: QTc prolongation may occur. Use with caution if pre-existing QTc prolongation and/or known risk factors for prolongation of the QTc interval (including concomitant administration of other QTc prolonging agents).</p> <p>Blood glucose: may cause hypoglycaemia.</p> <p>Epilepsy: may lower seizure threshold.</p> <p><i>Contd. next page</i></p>	<p>Renal Impairment:</p> <p>CrCl 30-50mL/min: 75% of dose</p> <p>CrCl 10-30mL/min: 25-50% of dose.</p> <p>CrCl <10mL/min: 25-50% of dose.</p> <p>CVVHD: 25-50% of dose.</p> <p>Recommend using upper dose range in context of COVID-19 infection.</p> <p>Extending dose intervals rather than dose reductions may be necessary for practical reasons.</p> <p><i>Contd. next page</i></p>	<p>See Summary of Product Characteristics (SmPC) for full list of side-effects; available from: https://www.medicines.ie/medicines/plaquenil-tablets-33380/smpc</p> <p>Hydroxychloroquine is highly toxic in overdose and children are particularly susceptible to toxic side effects. Ref Medicines for Children 2003 RCPCH</p>	<p><i>Refer to SmPC and drug-drug interaction databases e.g. Stockley's.</i></p> <p>Caution with concomitant QTc prolonging agents</p> <p>Caution with anti-convulsants; HCQ may lower seizure threshold</p> <p>Possible potentiation of neuromuscular blockade with aminoglycoside antibiotics.</p> <p>Antacids (aluminium, magnesium, and calcium salt) and adsorbents (e.g. kaolin) may reduce absorption of chloroquine; separate administration by at least 4 hours</p> <p>Avoid concomitant use of HCQ with drugs known to induce retinal toxicity.</p> <p><i>Contd. next page</i></p>	<p>Available as Plaquenil® (Sanofi-Aventis) from All-Phar.</p> <p>Details of ordering process are pending confirmation and will be provided direct to Chief Pharmacists.</p> <p>No data available for enteral tube administration of tablet formulation.</p>

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Table 5 (continued from previous page) Hydroxychloroquine (HCQ) for the treatment for COVID-19.

Drug Hydroxychloroquine (HCQ)	Proposed MOA in COVID-19	Contra- indications	Monitoring	Renal/Hepatic Impairment	Side-Effects	Drug-Drug Interactions	Preparation & Sourcing
		<p><i>Contd.</i></p> <p>Lapp lactase deficiency or glucose-galactose malabsorption.</p>	<p><i>Contd.</i></p> <p>G6PD: Caution advised in patient with G6PD deficiency, may be risk of haemolysis. If status unknown, do not delay initiation of treatment in the context of moderate or severe COVID-19.</p> <p>Retinal toxicity: Due to low risk with recommended dose and duration of treatment, ophthalmological examination not required in context of COVID-19 infection.</p>	<p><i>Contd.</i></p> <p>Hepatic Impairment:</p> <p>No specific dose adjustments recommended – use with caution.</p>		<p><i>Contd.</i></p> <p>Caution if co-administering medicines which may cause adverse ocular or skin reactions</p> <p>HCQ may increase levels of ciclosporin and digoxin (monitor levels)</p> <p>Caution with anti-convulsants; HCQ may lower seizure threshold</p>	

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Table 6 Lopinavir/ritonavir (Kaletra®) for the treatment for COVID-19 (adapted from St James's Hospital Protocol).							
Drug	Proposed MOA in COVID-19	Contra-indications	Monitoring	Renal/Hepatic Impairment	Side-Effects	Drug-Drug interactions	Preparation & Sourcing
<p>Lopinavir/ritonavir (Kaletra®)</p> <p>Unlicensed indication, recommended from expert consensus (published ahead of trial results).</p> <p>Recommended Dose: lopinavir/ritonavir (Kaletra®) 400mg/100mg TWICE a day administered as:</p> <p>Kaletra® 200mg/50mg Tablets: TWO tablets TWICE a day (with or without food).</p> <p>OR</p> <p>Kaletra® (80mg/20mg per mL) Oral Solution: 5mL TWICE a day (with food).</p>	<p>Lopinavir and ritonavir were initially hypothesised to inhibit the 3-chymotrypsin-like protease of SARS and MERS.</p> <p>This combined agent has in vitro activity against the SARS-CoV and appears to have some activity against MERS-CoV in animal studies.</p> <p>The use of this agent for treatment of COVID-19 has been described in case reports.</p>	<p>Hypersensitivity to active ingredients or any of the excipients.</p> <p>Severe hepatic insufficiency.</p> <p>Co-administration with medicinal products that are highly dependent on CYP3A for clearance and for which elevated plasma concentrations are associated with serious and/or life threatening events.</p> <p><i>Contd. next page.</i></p>	<p>Liver Function Tests (LFTs): deranged liver function tests and hepatic dysfunction have been reported; monitor LFTs before and during treatment.</p>	<p>Renal Impairment: negligible renal clearance and increased plasma concentrations are not expected in renal impairment.</p> <p>Lopinavir and ritonavir are highly protein-bound; unlikely to be significantly removed by haemodialysis or peritoneal dialysis.</p> <p><i>Contd. next page.</i></p>	<p>See Summary of Product Characteristics (SmPC) for full list of side-effects; available from: https://www.medicines.ie/medicines/kaletra-200-mg-50-mg-film-coated-tablets-32560/smpc.</p>	<p><i>Refer to SmPC and drug-drug interaction databases e.g. Stockley's and University of Liverpool online (http://www.covid19-druginteractions.org/)</i></p> <p>Lopinavir and ritonavir are both inhibitors of cytochrome P450 enzyme isoform CYP3A.</p> <p>Co-administration of medicinal products primarily metabolised by CYP3A may result in increased plasma concentrations of the other medicinal product, which could increase or prolong its therapeutic and adverse reactions (see also contraindications).</p> <p><i>Contd. next page</i></p>	<p>Available as oral formulations only (tablets and oral solution).</p> <p>Contact wholesaler and specific form to be completed by the pharmacy department.</p> <p>Crushing tablets significantly reduces exposure of both lopinavir and ritonavir (↓AUC by 45% and 47% respectively). Avoid crushing lopinavir/ritonavir tablets, if possible.</p> <p><i>Contd. next page</i></p>

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Table 6 (continued from previous page) Lopinavir/ritonavir (Kaletra®) for the treatment for COVID-19 (adapted from St James's Hospital Protocol).

Drug Lopinavir/ritonavir (Kaletra®)	Proposed MOA in COVID-19	Contra-indications	Monitoring	Renal/Hepatic Impairment	Side-Effects	Drug-Drug interactions	Preparation & Sourcing
		<p><i>Contd.</i></p> <p>Kaletra® oral solution contains propylene glycol and 42% v/v alcohol; contraindicated in children <14 days, pregnant women, patients with hepatic or renal failure and patients treated with disulfiram or metronidazole due to the potential risk of toxicity from the excipient propylene glycol.</p>		<p><i>Contd.</i></p> <p>Hepatic Impairment:</p> <p>Possible increased exposure in mild or moderate impairment; not expected to be clinically significant.</p> <p>Avoid in severe hepatic impairment.</p>		<p><i>Contd.</i></p> <p>Clinically significant drug-drug interactions are extensive. A thorough medication history (including alternative and herbal medicines) should be obtained prior to initiation of treatment.</p>	<p><i>Contd.</i></p> <p>If the oral solution is not available and it is considered necessary to crush tablets; a consideration of increasing dose to THREE tablets TWICE a day may be reasonable (unlicensed dose).</p> <p>No data available for enteral tube administration of tablet formulation.</p> <p>Oral solution is preferable in patients unable to swallow solid dosage forms.</p>

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Table 7 Remdesivir for the treatment for COVID-19.		
Drug	Proposed MOA in COVID-19	Key Information
<p>Remdesivir</p> <p>Unlicensed medicinal product, only available on compassionate use basis from manufacturer.</p> <p>Recommended Dose (as intravenous infusion):</p> <p>200mg on Day 1; then 100mg on Days 2-10 (total duration 10 days).</p> <p>Refer to the manufacturer's information for reconstitution and administration details.</p> <p><i>Contd. on next page</i></p>	<p>Remdesivir (GS-5734) is a phosphoramidate prodrug of an adenine derivative with a chemical structure similar to tenofovir alafenamide.</p> <p>Broad-spectrum activities against RNA viruses such as MERS and SARS in vitro in cell cultures and animal models, and has been tested in a clinical trial for Ebola.</p>	<p>Refer to the product information provided by Gilead as part of the compassionate use programme for detailed information.</p> <ul style="list-style-type: none"> - Remdesivir is an investigational medicinal product only available on a compassionate use basis direct from the manufacturer (Gilead). - Requests for supply of this medicine must be submitted <u>by the treating physician</u> on an individual patient basis via the online portal: https://rdvcu.gilead.com/ - In order to access remdesivir a number of documents must be completed and submitted to the manufacturer. The following documents are required and may be prepared in advance to expedite the ordering process for individual patients: <ol style="list-style-type: none"> 1. Signing of a Confidential Disclosure Agreement 2. Signing of Prescriber Agreement 3. Communication from Hospital CEO or Ethics Committee to approve the use of a Compassionate Access Medicine in the hospital <p>Key Inclusion Criteria (subject to change at discretion of manufacturer):</p> <ul style="list-style-type: none"> - Hospitalization - Confirmed SARS-CoV-2 by PCR - Mechanical ventilation <p>Key Exclusion criteria include (subject to change at discretion of manufacturer):</p> <ul style="list-style-type: none"> - Evidence of multi-organ failure - Pressor requirement to maintain blood pressure - ALT (alanine transaminase) levels > 5 x ULN (Upper Limit of Normal) - Creatinine Clearance <30 mL/min <u>or</u> dialysis <u>or</u> Continuous Veno-Venous Hemofiltration - Remdesivir cannot be used in conjunction with other experimental antiviral agents for COVID-19 (e.g., lopinavir/ritonavir) <p>The above criteria are subject to change and requests may be subject to additional considerations and limitations. Further information is available on the online portal: https://rdvcu.gilead.com/</p> <p><i>Contd. on next page</i></p>

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<p>NOTE: Available in two formulations, solution for injection (requires storage in freezer) and a lyophilised version (does not require storage in freezer).</p> <p>Follow manufacturer's storage instructions.</p>		<p><i>Contd.</i></p> <p>Renal Impairment: Caution in renal impairment as contains SBECD (sulfobutylether-β-cyclodextrin) which is renally cleared and accumulates in renal impairment. Not recommended in moderate to severe renal impairment. Monitor renal function; if eGFR decreases ≥50% permanent discontinuation of remdesivir treatment should be considered.</p> <p>Hepatic Impairment: Transient elevations in hepatic transaminases; monitor Liver Function Tests.</p> <p>Drug-drug Interactions: Co-administration of other antivirals is not recommended as there may be antagonism, synergy or no effect. Refer to product information from the manufacturer and the University of Liverpool online resource for further information; available from www.covid19-druginteractions.org.</p>
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Other Medicinal Products in the Clinical Management of Acute Respiratory Infection with SARS-CoV-2 (COVID-19)

There is emerging data for medicinal products in the clinical management of COVID-19 that are not anti-viral in their mechanism of action. These would only be considered in the same clinical setting of an elevated NEWS score and only after discussion between critical care medicine and infection specialists.

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