Sir Charles Gairdner Hospital

Quick Reference Medication Guide for current COVID-19 Therapies

A guide for currently recommended pharmacotherapies for management of COVID-19

Note: these recommendations serve as a guide only and clinical judgement should take precedence for each individual case.

Key Terms									
NS	Sodium chloride 0.9% (normal saline)	SAS	Special Access Scheme	OAT	Organic anion transporter	MATE	Multi-drug and toxic extrusion protein	OATP	Organic anion transporting polypeptide
G5%	Glucose 5% (dextrose 5%)	mg	Milligrams	OCT	Organic cationic transporter	ATSI	Aboriginal and Torres Strait Islander		
WFI	Water for Injections	mcg	Micrograms	BRCP	Breast cancer resistance protein	NIV	Non-invasive Ventilation		

DISEASE SEVERITY	ESTABLISHED DEFINITION	OXYGEN REQUIREMENTS	THERAPEUTIC OPTIONS
Mild illness *Confirmed COVID-19 infection without evidence of viral pneumonia or hypoxia*	No clinical features suggestive of moderate or more severe disease • No or mild symptoms and signs (fever, cough, sore throat, headache, myalgia, loss of taste/smell) • No new shortness of breath or difficult breathing on exertion • No evidence of lower respiratory tract disease during clinical assessment or on imaging	Not requiring oxygen	• **Budesonide (inhaled)** ✓ For non-hospitalised patients within 14 days of symptom onset and at risk of disease progression • **Sotrovimab** (refer to **Appendix 1**) ✓ Not fully vaccinated individuals within 5 days of symptom onset with one or more risk factors for disease progression ✓ Immunosuppressed individuals ✓ Pregnancy (especially if unvaccinated or immunosuppressed) ✓ ATSI > 35 yo with high risk co-morbidities • **Casirivimab plus Imdevimab (Ronapreve)** **Subject to availability** ✓ Alternative to sotrovimab for patients who are not infected with Omicron variant
Moderate illness *Confirmed COVID-19 infection with clinical signs of pneumonia (fever, cough, dyspnoea, tachypnoea) but not requiring oxygen*	A stable patient with evidence of lower respiratory tract disease during clinical assessment including • Oxygen saturation 92-94% on room air at rest • Desaturation or breathlessness with mild exertion OR evidence on imaging	Not requiring oxygen	• **Budesonide (inhaled)** ✓ For non-hospitalised patients within 14 days of symptom onset and at risk of disease progression • **Sotrovimab** (refer to **Appendix 1**) ✓ Not fully vaccinated individuals within 5 days of symptom onset with one or more risk factors for disease progression ✓ Immunosuppressed individuals ✓ Pregnancy (especially if unvaccinated or immunosuppressed) ✓ ATSI > 35 yo with high risk co-morbidities • **Casirivimab plus Imdevimab (Ronapreve)** **Subject to availability** ✓ Alternative to sotrovimab for patients who are not infected with Omicron variant
Severe illness *Confirmed COVID-19 infection with clinical signs of pneumonia AND requiring oxygen but NOT ventilation*	A patient with signs of moderate disease who is deteriorating OR A patient who meets any of the criteria below • Respiratory rate ≥ 30 breaths/min • Oxygen saturation ≤ 92% on room air at rest or requiring oxygen • Lung infiltrates > 50% of lung field	Requiring oxygen but NOT ventilation	• **Corticosteroids (eg dexamethasone)** ✓ For all patients requiring oxygen ✓ If pregnant, use prednisolone or hydrocortisone • **Remdesivir** - Commence if within 7 days of symptom onset If features of systemic inflammation*, or progression despite steroids +/- remdesivir consider: • **Baricitinib** (1st line) • **Tocilizumab** (2nd line – reserved for pregnant patients, eGFR< 15mls/min)

Critical illness
Confirmed COVID-19 infection requiring ventilation
	A patient meeting any of the criteria below
	• Respiratory failure
	  • Severe respiratory failure (PaO_2/FiO_2 < 200)
	  • Respiratory distress or acute respiratory distress syndrome (ARDS)
	  • Deteriorating despite non-invasive forms of respiratory support (eg NIV, HFNO)
	  • Requiring mechanical ventilation
	• Hypotension or shock
	• Impairment of consciousness
	• Other organ failure
		Requiring ventilation	• **Corticosteroids** (eg dexamethasone)
			  • For all patients requiring oxygen
			  • If pregnant, use prednisolone or hydrocortisone
			If features of systemic inflammation*, consider:
			• **Baricitinib** (1st line)
			• **Tocilizumab** (2nd line – reserved for pregnant patients, eGFR< 15mls/min)

*systemic inflammation defined as
For baricitinib – elevated levels of CRP, ferritin, LDH or D-dimer
For tocilizumab – CRP > 75

COVID-19 PHARMACOTHERAPEUTIC GUIDE (CURRENTLY AVAILABLE THERAPIES)

MEDICATION	WHEN TO USE OR COMMENCE	USE IN RELATION TO OXYGEN REQUIREMENTS				DOSAGE	DOSAGE ADJUSTMENTS	CONTRA-INDICATIONS / PRECAUTIONS	PREGNANCY/ BREASTFEEDING	POTENTIAL DRUG INTERACTIONS (see relevant appendices for details)	ACCESS/ APPROVAL
		Not on oxygen	SUPPLEMENTAL	VENTILATED							
			Low/High flow oxygen	NIV	Invasive mechanical ventilation						
ANTIVIRAL AGENTS											
REMDESIVIR	**SEVERE ILLNESS** Consider in patients with severe illness who require supplemental oxygen but NOT invasive or non-invasive ventilation	Do not use	Start therapy	Continue if already receiving Do not initiate	Continue if already receiving Do not initiate	Currently a 5-day course is recommended **Day 1** = 200mg **Days 2-5** = 100mg daily	**RENAL** CrCl < 30ml/min - Caution with use due to accumulation of cyclodextrin **HEPATIC** - No data	Hypersensitivity to any of the excipients Eg sulfobutyl betadex sodium CrCl < 30ml/min ALT/AST ≥ 5 x ULN NIV or Invasive Ventilation	Pregnancy - Category B2 - Considered safe to use Breastfeeding - Limited data	Avoid concomitant use with chloroquine/ hydroxychloroquine Substrate for • CYP2C8 / 2D6 / 3A4 • OATP1B1 • P-gp Inhibitor of • CYP3A4 • OATP1B1 / 1B3 Inducer of • CYP1A2 / 3A4	**Applicable to Common-wealth stock only** Consultant approval to commence Retrospective streamlined IPA required
SOTROVIMAB	**MILD ILLNESS** **MODERATE ILLNESS** Consider in not fully vaccinated patients with mild or moderate illness who are not requiring supplemental oxygen and have one or more risk factors for disease progression. Also consider in immunocompromised patients, pregnancy (2nd or 3rd trimester, esp if unvaccinated or immunocompromised) or ATSI > 35yo with co-morbidities **Refer to Appendix 1**	Consider starting if meets inclusion criteria	Do not use	Do not use	Do not use	A **single** 500mg IV dose	No dosage adjustments required for organ impairment - Metabolised by tissue proteolytic enzymes	Hypersensitivity to any of the excipients First trimester of pregnancy Known reaction to prior monoclonal antibodies	Pregnancy - Category B2 - Considered safe to use Breastfeeding - Limited data	Unlikely to involve interactions with cytochromeP450 enzymes , P-gp or other transporter systems	ID Consultant approval and REDCap form completion. Only available through National Medicines Stockpile
CASIRIVIMAB plus IMDEVIMAB **SUBJECT TO AVAILABILITY**	**MILD ILLNESS** **MODERATE ILLNESS** An alternative to sotrovimab therapy in patients infected with non-Omicron variant only	Consider starting as an alternative to sotrovimab for non-Omicron cases only	Do not use	Do not use	Do not use	1200mg (600mg of casirivimab + 600mg of imdevimab) as a **single** IV dose Subcutaneous route is an option when used as prophylaxis For treatment – use IV route	No dosage adjustments required for organ impairment - Metabolised by tissue proteolytic enzymes	Infection with Omicron variant Hypersensitivity to any of the excipients, including monoclonal antibodies First trimester of pregnancy	Pregnancy - Category B2 - Considered safe to use Breastfeeding - Limited data	Unlikely to involve interactions with cytochromeP450 enzymes , P-gp or other transporter systems	Not currently available

MEDICATION	WHEN TO USE OR COMMENCE	USE IN RELATION TO OXYGEN REQUIREMENTS				DOSAGE	DOSAGE ADJUSTMENTS	CONTRA-INDICATIONS / PRECAUTIONS	PREGNANCY/ BREASTFEEDING	POTENTIAL DRUG INTERACTIONS (see relevant appendices for details)	ACCESS/ APPROVAL
		Not on oxygen	SUPPLEMENTAL	VENTILATED							
			Low/High flow oxygen	NIV	Invasive mechanical ventilation						
IMMUNOMODULATING AGENTS											
CORTICOSTEROIDS Eg dexamethasone, hydrocortisone, prednisolone	**SEVERE ILLNESS** **CRITICAL ILLNESS** Use in all patients with severe or critical illness who are either requiring supplemental oxygen or ventilation	Do not use	Start therapy	Start therapy or continue if already receiving	Start therapy or continue if already receiving	Dexamethasone 6mg daily (IV / oral) for up to 10 days If pregnant, the preferred options (as placental transfer is limited) are Hydrocortisone 50mg IV every 6 hours for up to 10 days Prednisolone 50mg oral daily for up to 10 days If at risk of preterm birth; if foetal lung maturation is indicated then Dexamethasone is preferred	No dosage adjustments required for renal or hepatic impairment	Hypersensitivity to dexamethasone	Pregnancy - Category C - Preferred options are hydrocortisone or prednisolone Breastfeeding - Limited data - Alternative options available (Prednisolone, Hydrocortisone)	Dexamethasone is a substrate for CYP3A4 Theoretical interaction with CYP3A4 inducers - May increase metabolism to ↓ dexamethasone levels CYP3A4 inhibitors - May decrease metabolism to ↑ dexamethasone levels	Unrestricted
BUDESONIDE (INHALED)	**MILD ILLNESS** **MODERATE ILLNESS** Use in patients with mild to moderate illness within 14 days of symptom onset who do not require supplemental oxygen and are at risk for disease progression	Start if meets inclusion criteria	Do not use	Do not use	Do not use	Use breath-actuated inhaler (eg Symbicort®, Pulmicort®) 800microg twice a day for up to 14 days	No dosage adjustments required	Hypersensitivity to budesonide	Pregnancy - Category A - Safe to use Breastfeeding - Safe to use	Nil regarded as significant given the minimal systemic absorption following inhaled administration	Unrestricted
BARICITINIB	**SEVERE ILLNESS** **CRITICAL ILLNESS** Consider use in patients with severe or critical illness who are either requiring supplemental oxygen or ventilation and showing signs of systemic inflammation. (CRP>75, Ferritin >500, D-dimer >0.5)	Do not use	Consider starting therapy	Consider starting therapy or continue if already receiving	Consider starting therapy or continue if already receiving	4mg daily orally for up to 14 days Always use in combination with corticosteroids	**RENAL** CrCl 30-60ml/min • 2mg daily CrCl 15-30ml/min • 1mg daily Not recommended if CrCl <15ml/min or requiring RRT	Avoid with Pregnancy or lactation Avoid combining with other immune-modulating agents (except corticosteroids)	Pregnancy - Avoid use - Category D Breastfeeding - Limited data - Not recommended	In vitro, baricitinib is a substrate for • CYP3A4 • OAT3 • P-gp • BCRP • MATE2-K Baricitinib exhibits negligible effect on cytochrome P450	Consultant approval to commence Retrospective Streamlined IPA required

	Perform latent infection screen but do not delay commencement (Eg Hep B, Hep C, HIV serology- consider TB QuantiFERON® and Strongyloides serology based on risk)						**HEPATIC** No dosage adjustment in mild to moderate hepatic impairment Avoid in severe hepatic impairment	Avoid when cytopaenic: Neut< 1.0 Lymph <0.2 Hb <80		enzymes , P-gp, OAT, BCRP or MATE Caution when combining with other • Immunosuppressants • Immunomodulators • Clozapine • Live vaccines	
MEDICATION	**WHEN TO USE OR COMMENCE**	**USE IN RELATION TO OXYGEN REQUIREMENTS**				**DOSAGE**	**DOSAGE ADJUSTMENTS**	**CONTRA-INDICATIONS / PRECAUTIONS**	**PREGNANCY/ BREASTFEEDING**	**POTENTIAL DRUG INTERACTIONS** (see relevant appendices for details)	**ACCESS/ APPROVAL**
		Not on oxygen	**SUPPLEMENTAL**	**VENTILATED**							
			Low/High flow oxygen	**NIV**	**Invasive mechanical ventilation**						
TOCILIZUMAB	**SEVERE ILLNESS** **CRITICAL ILLNESS** Consider use in patients with severe or critical illness who are either requiring supplemental oxygen or ventilation and showing signs of systemic inflammation (CRP>75, Ferritin >500, D-dimer >0.5) # Generally reserved for use as an alternative in patients where baricitinib is not clinically suitable Perform latent infection screen but do not delay commencement (Eg Hep B, Hep C, HIV serology- consider TB QuantiFERON® and Strongyloides serology based on risk)	Do not use	Consider starting therapy #	Consider starting therapy# or continue if already receiving	Consider starting therapy# or continue if already receiving	Dosage is weight based (use actual body weight) as a single IV dose >90kg: 800mg 66-90kg: 600mg 41-65kg: 400mg ≤40kg: 8mg/kg Doses are capped at 800mg (max) A request for a second dose 12-24 hours after the first dose may be considered, taking into account patient status and stock availability	No dosage adjustments for renal or hepatic impairment or age have been established	Hypersensitivity to any component of the product Known reaction to prior monoclonal antibodies Hypersensitivity to Chinese hamster ovary cell products Use with caution in patients who are neutropenic, thrombo-cytopaenic or significantly immuno-suppressed	Pregnancy - Category C - Preferred agent over baricitinib Breastfeeding - Limited data - Preferred agent over baricitinib	Tocilizumab has no inhibitory or inducing effects on cytochrome P450 enzymes No clinically relevant pharmacological interactions have been noted Caution when combining with other • Immunosuppressants • Immunomodulators • Clozapine • Live vaccines	Consultant approval to commence Retrospective Streamlined IPA required

APPENDIX 1

Due to uncertainty regarding stock availability with emerging COVID-19 pharmacological therapies such as Sotrovimab, prioritisation for access to this medication has been devised into 3 categories based on eligibility criteria established by specialist working groups, with reference to the COMET-ICE trial results.

To ensure equity of access to all groups and preserving the limited stock for patients at highest risk of disease progression, allocation of Sotrovimab will be prioritised based on this eligibility criteria/assessment tool and release of stock will follow a staged process (which will be dictated by stock availability and supply)

SOTROVIMAB AVAILABILITY STAGE	ACCESSIBILITY
STAGE 1	Limited supply available; access only granted to TIER 1 risk categories
STAGE 2	Steady supply available; access granted to TIER 1 and TIER 2 risk categories
STAGE 3	Unrestricted supply available; access granted to TIER 1, TIER 2 and TIER 3 risk categories

SOTROVIMAB PRIORITY ASSESSMENT TOOL

TIER system based on National Institutes of Health Statement on Patient Prioritisation for Outpatient Therapies

TIER	AT RISK GROUP	ELIGIBILITY / CRITERIA
TIER 1	**UNVACCINATED WITH RECOGNISED RISK FACTOR/S**	**Unvaccinated** AND **age greater than 75 years** OR **Unvaccinated** AND **age greater than 65 years** WITH at least one other **recognised clinical risk factor** (refer to Appendix 1A) OR **Unvaccinated ATSI** patient AND age **greater than 35 years** WITH at least one **recognised clinical risk factor** (refer to Appendix 1A) *There is a cumulative increase in risk of progression to severe disease with each additional risk factor, which may further impact eligibility at times of extreme product shortage.*
	PREGNANT WOMEN IN SECOND OR THIRD TRIMESTER	**Unvaccinated or partially vaccinated** (received first dose only) **Any vaccination status** AND **immunocompromised** (refer to Appendix 1B and Appendix 1C)
	SEVERE IMMUNO-COMPROMISED STATE	**Severe immunocompromise** (refer to Appendix 1B) regardless of age or vaccination status
	PAEDIATRIC PATIENTS	**Paediatric Infectious Diseases Specialist review** required (PCH) to determine appropriateness of adolescent risk factors. *NB. Patients within 2 years of receiving Hematopoietic Stem-Cell Transplantation (HSCT) or Solid Organ Transplant, regardless of vaccination status will be prioritised.*
TIER 2	**UNVACCINATED OR PARTIALLY VACCINATED WITH RECOGNISED RISK FACTOR/S**	**Unvaccinated** AND age **greater than 55 years** OR **Partially vaccinated** (received first dose only) AND age **greater than 55 years** WITH at least one other **recognised clinical risk factor** (refer to Appendix 1A) OR **Partially vaccinated** (received first or second dose only) AND **moderate immunocompromise** (refer to Appendix 1C), regardless of age or recognised clinical risk factors
	PREGNANCY (ANY TRIMESTER)	**Any vaccination status** WITH at least one **recognised clinical risk factor** (refer to Appendix 1A) NB. Gestational diabetes requiring medication therapy is also included as a risk factor in addition to Appendix 1A for this patient group Limited data pertaining to use in 1st trimester – clinical benefit/risk assessment should be undertaken
	PAEDIATRIC PATIENTS	**Paediatric Infectious Diseases Specialist (PCH) review** required and referral of unvaccinated or partially vaccinated adolescents with paediatric clinical risk factors (refer to Appendix 1D)
TIER 3	**MODERATE RISK OF PROGRESSION TO SEVERE DISEASE**	**Moderate immunocompromise** (refer to Appendix 1C), regardless of age or vaccination status **Unvaccinated** WITH at least one **recognised clinical risk factor** (refer to Appendix 1A), regardless of age

APPENDIX 1A

RECOGNISED CLINICAL RISK FACTORS FOR DISEASE PROGRESSION (per COMET-ICE trial) ADAPTED FROM COMET-ICE CRITERIA FOR UNVACCINATED ADULTS AND ADULTS AT HIGH RISK OF SEVERE DISEASE
Age ≥ 55 years
Chronic kidney disease (eg eGFR < 60)
Chronic obstructive pulmonary disease (includes history of chronic bronchitis, chronic obstructive lung disease, or emphysema with dyspnoea on physical exertion)
Chronic heart failure (NYHA class II or greater)
Diabetes (requiring pharmacological treatment)
Moderate to severe asthma (on regular inhaled steroid therapy or prescribed a course of oral steroids within past 12 months for management of asthma)
Obesity (BMI ≥ 30 kg/m^2)

APPENDIX 1B

APPENDIX 1C

SEVERE IMMUNOCOMPROMISE STATUS	MODERATE IMMUNOCOMPROMISE STATUS
Subset of immunocompromised persons as per ATAGI Recommendations on the use of a 3rd primary dose of COVID-19 vaccine in individuals who are severely immunocompromised	

• Patients who are within 1 year of receiving B-cell depleting therapies (e.g., rituximab, ocrelizumab, ofatumumab, alemtuzumab)
• Patients receiving Bruton tyrosine kinase inhibitors
• Chimeric antigen receptor T cell recipients
• Post-hematopoietic stem cell transplant recipients who have chronic graft versus host disease or who are taking immunosuppressive medications for another indication
• Patients with hematologic malignancies who are on active therapy
• Lung transplant recipients
• Patients who are within 1 year of receiving a solid-organ transplant (other than lung transplant) or haematopoietic stem cell transplant
• Solid-organ transplant recipients with recent treatment for acute rejection with T or B cell depleting agents
• Patients with certain primary immunodeficiencies
  ○ PIDs affecting cellular and humoral immunity (severe and other combined immunodeficiencies (https://doi.org/10.1007/s10875-019-00737-x)
  ○ PIDs with profoundly decreased or absent B cell number or function
  ○ PIDs with impaired interferon responses
• Patients with untreated HIV who have a CD4 T lymphocyte cell count <50 cells/mm^3
• Patients on any of the following agents not already listed
  ○ Anti-CD20 antibodies rituximab, obinutuzumab, ocrelizumab, ofatumumab
  ○ BTK inhibitors ibrutinib, acalabrutinib, zanubrutinib
  ○ Sphingosine 1- phosphate receptor modulators fingolimod, siponimod
  ○ Anti-CD52 antibodies alemtuzumab
  ○ Anti-complement antibodies eculizumab
  ○ Anti-thymocyte globulin
	○ Primary immunodeficiency including combined immunodeficiency and syndromes, major antibody deficiency (e.g. common variable immune deficiency (CVID) or agammaglobulinemia), defects of innate immunity (including phagocytic cells), defects of immune regulation, complement deficiencies and phenocopies of primary immunodeficiencies
	○ Haematologic neoplasms: leukaemias, lymphomas, myelodysplastic syndromes
	○ Solid organ transplant on immunosuppressive therapy
	○ Greater than 12 months post-transplant: solid organ transplant (on immunosuppressive therapy) or haematopoietic stem cell transplant.
	○ Advanced or untreated HIV with CD4 counts <200/microL, or those with a higher CD4 count unable to be established on effective anti-retroviral therapy, recent (within 12 months) AIDS-defining condition, or persistent/recurrent viraemia OR not on ART (excluding elite controllers).
	○ Haemodialysis or peritoneal dialysis
	○ Immunosuppressive therapy (current or recent) examples include:
	  ○ Chemotherapy or radiotherapy
	  ○ JAK inhibitors - tofacitinib, baricitinib, ruxolitinib
	  ○ High-dose corticosteroids (≥20 mg of prednisone per day, or equivalent) for ≥14 days in a month, or pulse corticosteroid therapy
	○ Biologic and targeted therapies that are anticipated to reduce the immune response to COVID-19 vaccine
	○ Selected conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDS) including mycophenolate, methotrexate (>0.4 mg/kg/week), leflunomide, azathioprine (≥ 3mg/kg day), 6-mercaptopurine (≥ 1.5mg/kg/day), alkylating agents (e.g. cyclophosphamide, chlorambucil), and systemic calcineurin inhibitors (e.g. cyclosporin, tacrolimus).

APPENDIX 1D

PAEDIATRIC CLINICAL RISK FACTORS
• paediatric chronic complex condition, • obesity (>95th centile for age and gender based on CDC growth charts), • severe asthma, • chronic obstructive lung disease, • diabetes (on insulin), • severe cardiac disease, • end stage renal disease, • sickle cell disease, PA • immune deficiency

ADDITIONAL INFORMATION

AGENTS THAT ARE NOT CONSIDERED TO IMPART ANY INCREASED IMMUNOSUPPRESSIVE RISK
▪ Anti-integrins natalizumab, vedolizumab ▪ Anti-TNF-α antibodies infliximab, adalimumab, etanercept, golimumab, certolizumab ▪ Anti-IL1 antibodies anakinra ▪ Anti-IL6 antibodies tocilizumab ▪ Anti-IL17 antibodies secukinumab, ixekizumab ▪ Anti-IL4 antibodies dupilumab Anti-IL23 antibodies ustekinumab ▪ Immune checkpoint inhibitors nivolumab, pembrolizumab, ipilimumab, atezolizumab

DEFINING VACCINATION STATUS (as per current ATAGI statement February 2022)			
Patient Group	**Unvaccinated**	**Partially Vaccinated**	**Up to Date or Fully Vaccinated**
General Population (immunocompetent, including pregnant patients)	Patient has not received a TGA approved or other recognised COVID-19 vaccine	Patient has received only 1 dose of a TGA approved or other recognised vaccine	Patient has received 2 doses (considered a primary course) of a TGA approved or other recognised vaccine
Immunocompromised patients (moderate-severely immunocompromised)	Patient has not received a TGA approved or other recognised COVID-19 vaccine	Patient has received only 1 or 2 doses of a TGA approved or other recognised vaccine	Patient has received 3 doses of a TGA approved or other recognised vaccine
Individuals with evidence of previous SARS-CoV-2 infection	Patient has not received a TGA approved or other recognised COVID-19 vaccine	Individuals with previous COVID-19 infection are still recommended to complete their vaccination schedule. Evidence suggests that prior infection with Delta or other variants is not completely protective against re-infection with Omicron. ATAGI recommends boost doses for all individuals with previous COVID-19. If infected with COVID-19 prior to commencing vaccination or during vaccination schedule the next dose can be deferred for up to 4 months.	

APPENDIX 2A

REMDESIVIR - POTENTIAL DRUG INTERACTIONS					
ADVICE ▪ These are theoretical interactions only, co-administration of these agents has NOT been studied ▪ As a precaution any potentially interacting therapies listed should be withheld or avoided temporarily where possible					
	CYP2C8 inhibitors	**CYP2D6 inhibitors**	**CYP3A4 inhibitors**	**P-gp inhibitors**	**OATP1B1 inhibitors**
Interactions that may ↑ remdesivir levels	Clopidogrel^{+++} Gemfibrozil^{+++} trimethoprim	amiodarone bupropion^{+++} celecoxib, cinacalcet^{++}, cobicistat duloxetine^{++} fluoxetine^{+++} haloperidol methadone, metoclopramide, midodrine, mirabegron^{++} paroxetine^{+++} terbinafine^{+++}	amiodarone, aprepitant^{++}, atazanavir^{++} ciclosporin^{++}, ciprofloxacin^{++}, clarithromycin^{+++}, cobicistat^{+++} darunavir, diltiazem^{++} erythromycin^{++} fluconazole^{++}, fluvoxamine^{++} imatinib, isavuconazole, itraconazole^{+++}, ketoconazole^{+++} letermovir^{++}, lopinavir palbociclib, posaconazole^{+++} quinine ribociclib, ritonavir^{+++} saquinavir tacrolimus, ticagrelor, verapamil^{++}, verapamil^{+++}	amiodarone, azithromycin carvedilol, ciclosporin, clarithromycin, cobicistat erythromycin, everolimus glecaprevir with pibrentasvir isavuconazole, itraconazole ketoconazole lapatinib, ledipasvir osimertinib ritonavir ticagrelor, tolvaptan vandetanib, velpatasvir, vemurafenib, venetoclax, verapamil, voxilaprevir	atazanavir, clarithromycin cyclosporine erythromycin gemfibrozil lopinavir rifampicin, ritonavir simepravir
	CYP2C8 inducers	**CYP2D6 inducers**	**CYP3A4 inducers**	**P-gp inducers**	**OATP1B1 inducers**
Interactions that may ↓ remdesivir levels	rifampicin $^{++}$	dexamethasone rifampicin haloperidol	apalutamide^{+++}, aprepitant bosentan^{++} carbamazepine^{+++}, clobazam, corticosteroids (eg dexamethasone, prednisolone, hydrocortisone) dabrafenib efavirenz^{++}, encorafenib, enzalutamide^{+++}, etravirine^{++} lorlatinib^{++}, lumacaftor^{+++} modafinil^{++} nevirapine phenobarbitone, phenytoin^{+++} rifabutin, rifampicin^{+++}, ritonavir St John's Wort^{+++} tipranavir, topiramate vemurafenib	apalutamide carbamazepine lorlatinib phenytoin rifampicin St John's Wort tipranavir	No OATP inducers have been identified

REMDESIVIR - POTENTIAL DRUG INTERACTIONS		
	CYP3A4 substrates (levels may potentially be ↑ or ↓ by remdesivir)	**OATP1 B1 / B3 substrates**
Drug that may have their levels ↑ by concurrent administration of remdesivir	abiraterone, alprazolam, amitriptyline, apalutamide, apixaban, aprepitant, aripiprazole, atorvastatin betamethasone, bictegravir, bortezomib, brentuximab, budesonide carbamazepine, ciclosporin, cinacalcet, clarithromycin, clopidogrel, cobicistat, codeine, colchicine, cyclophosphamide dabrafenib, darunavir, dasatinib, dexamethasone, diazepam, diltiazem, docetaxel, domperidone, donepezil elvitegravir, encorafenib, enzalutamide, eplerenone, erythromycin, esomeprazole, etoposide, etravirine, everolimus felodipine, fentanyl, haloperidol, hydrocortisone ibrutinib, ifosfamide, imatinib, irinotecan, isavuconazole, itraconazole, ivabradine, ivacaftor ketoconazole lercanidipine, lidocaine, lopinavir, lorlatinib, lurasidone methylprednisolone, midazolam, midostaurin, mirabegron, mirtazapine nifedipine, nilotinib, nimodipine omeprazole, ondansetron, oxycodone paclitaxel, palbociclib, pazopanib, pomalidomide, propranolol quetiapine, quinine reboxetine, ribociclib, rifabutin, rilpivirine, risperidone, ritonavir, rivaroxaban, romidepsin, ruxolitinib sildenafil, simvastatin, sirolimus, solifenacin, sorafenib, sunitinib tacrolimus, tadalafil, tamoxifen, ticagrelor, tofacitinib, tolvaptan, tramadol vandetanib, velpatasvir, vemurafenib, venetoclax, venlafaxine, verapamil, vinblastine, vincristine, vinorelbine, voriconazole, voxilaprevir warfarin (R-isomer) ziprasidone, zolpidem	atorvastatin bosentan digoxin empagliflozin, ezetimibe fexofenadine, fluvastatin glecaprevir, grazoprevir levothyroxine methotrexate olmesartan pravastatin rifampicin, rifaximin, rosuvastatin simvastatin telmisartan valsartan, velpatasvir, voxilaprevir

	CYP1A2 substrates
Drugs that may have their levels ↓ by concurrent administration of remdesivir	agomelatine, amitriptyline, asenapine, axitinib bendamustine clopidogrel, clozapine duloxetine erlotinib fluvoxamine haloperidol imipramine lidocaine melatonin olanzapine, ondansetron paracetamol, pomalidomide, propranolol rasagiline, ropinirole, ropivacaine stiripentol tamoxifen, theophylline warfarin (R-isomer) zolmitriptan

APPENDIX 2B

CORTICOSTEROIDS (SYSTEMIC) - POTENTIAL DRUG INTERACTIONS	
ADVICE ▪ As a precaution any potentially interacting therapies listed should be withheld or avoided temporarily where possible	
Interactions that may ↑ corticosteroid levels	**CYP3A4 inhibitors**
	amiodarone, aprepitant[++], atazanavir[++] ciclosporin[++], ciprofloxacin[++], clarithromycin[+++], cobicistat[+++] darunavir, diltiazem[++] erythromycin[++] fluconazole[++], fluvoxamine[++] imatinib, isavuconazole, itraconazole[+++], ketoconazole[+++] letermovir[++], lopinavir palbociclib, posaconazole[+++] quinine ribociclib, ritonavir[+++] saquinavir tacrolimus, ticagrelor, verapamil[++], verapamil[+++]
Interactions that may ↓ corticosteroid levels	**CYP3A4 inducers**
	apalutamide[+++], aprepitant bosentan[++] carbamazepine[+++], clobazam, corticosteroids (eg dexamethasone, prednisolone, hydrocortisone) dabrafenib efavirenz[++], encorafenib, enzalutamide[+++], etravirine[++] lorlatinib[++], lumacaftor[+++] modafinil[++] nevirapine phenobarbitone, phenytoin[+++] rifabutin, rifampicin[+++], ritonavir St John's Wort[+++] tipranavir, topiramate vemurafenib

APPENDIX 2C

BARICITINIB - POTENTIAL DRUG INTERACTIONS

ADVICE

- Majority of these are theoretical interactions only
- Extensive study of their concurrent administration together has not been performed. In the limited studies performed no clinically significant impact on drug levels has been observed.
- As a precaution any potentially interacting therapies listed should be withheld or avoided temporarily where possible

	CYP3A4 inhibitors	OAT3 inhibitors*	BCRP inhibitors*	P-gp inhibitors	MATE2-K inhibitors*
Interactions that may ↑ baricitinib levels	amiodarone, aprepitant^{++}, atazanavir^{++} ciclosporin^{++}, ciprofloxacin^{++}, clarithromycin^{+++}, cobicistat^{+++} darunavir, diltiazem^{++} erythromycin^{++} fluconazole^{++}, fluvoxamine^{++} imatinib, isavuconazole, itraconazole^{+++} ketoconazole^{+++} letermovir^{++}, lopinavir palbociclib, posaconazole^{+++} quinine ribociclib, ritonavir^{+++} saquinavir tacrolimus, ticagrelor, verapamil^{++}, verapamil^{+++}	balsalazide cabotegravir ethacrynic acid irbesartan ketorolac nitazoxanide probenecid rifampicin valsartan	curcumin cyclosporin eltrombopag	amiodarone, azithromycin carvedilol, ciclosporin, clarithromycin, cobicistat erythromycin, everolimus glecaprevir with pibrentasvir isavuconazole, itraconazole ketoconazole lapatinib, ledipasvir osimertinib ritonavir ticagrelor, tolvaptan vandetanib, velpatasvir, vemurafenib, venetoclax, verapamil, voxilaprevir	cimetidine ciprofloxacin dolutegravir isavuconazole nizatidine pyrimethamine trimethoprim vandetanib

*very limited evidence exists for these potential interactions and their clinical significance

	CYP3A4 inducers	OAT3 inducers	BCRP inducers	P-gp inducers	MATE2-K inducers
Interactions that may ↓ baricitinib levels	apalutamide^{+++}, aprepitant bosentan^{++} carbamazepine^{+++}, clobazam, corticosteroids (eg dexamethasone, prednisolone, hydrocortisone) dabrafenib efavirenz^{++}, encorafenib, enzalutamide^{+++}, etravirine^{++} lorlatinib^{++}, lumacaftor^{+++} modafinil^{++} nevirapine phenobarbitone, phenytoin^{+++} rifabutin, rifampicin^{+++}, ritonavir St John's Wort^{+++} tipranavir, topiramate vemurafenib	There is limited information available relating to OAT3 inducers	There is limited information available relating to BCRP inducers	apalutamide carbamazepine lorlatinib phenytoin rifampicin St John's Wort tipranavir	There is limited information available relating to MATE2-K inducers

Authorisation & Version Control

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For full details regarding, development, review, consultation, approval, endorsement - contact the Policy Officer for the submission form