Clinical guidelines for management of non-hospitalised patients with COVID-19

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Treatment of non-hospitalised adults with COVID-19 (nMABs and antivirals)

ELIGIBILITY CRITERIA

- Positive COVID-19 PCR/lateral flow test
- **AND** Symptomatic with COVID-19 and showing no signs of clinical recovery
- **AND** member of a highest risk group (see Appendix 1 for list of qualifying conditions)

EXCLUSION CRITERIA

- Requires hospital care for the management of acute COVID-19 illness
- New requirement for supplemental oxygen
- Children < 12 years of age
- Adolescents (aged 12-17) weighing < 40 kg
- Known sensitivity to any of the nMABs or Remdesivir

1st Line → PF-07321332 (nirmatrelvir) plus ritonavir (Paxlovid) OR Sotrovimab

2nd Line → Remdesivir

3rd Line → Molnupiravir

Adolescents aged 12-17 years may be considered for treatment with Remdesivir or Sotrovimab only

If patients do not meet eligibility criteria consider recruitment to PANORAMIC trial

Combination treatment with an nMAB and an antiviral is NOT routinely recommended.

Read in conjunction with UK Interim Clinical Commissioning Policy: Therapies for symptomatic non-hospitalised patients with COVID-19

1st Line treatment for non-hospitalised patients with COVID-19: PF-07321332 (nirmatrelvir) plus ritonavir

PF-07321332 (nirmatrelvir) plus ritonavir (Paxlovid)

ELIGIBILITY CRITERIA

- Positive COVID-19 PCR/lateral flow test
- **AND** symptomatic with COVID-19 and showing no signs of clinical recovery
- **AND** member of a highest risk group (see Appendix 1 & 2 for list of qualifying conditions)
- **AND** clinical judgment is that treatment with an antiviral is the preferred treatment option
- **AND** treatment is commenced within 5 days of symptom onset
- **AND** no history of decompensated liver cirrhosis or stage 4-5 chronic kidney disease
- **AND** treatment is deemed safe by specialty team (see full clinical guidance)

EXCLUSION CRITERIA

- Age < 18 years
- Pregnancy
- The patient is not taking any of the medications listed in Appendix 3
- Requires hospital care for the management of acute COVID-19 illness
- New requirement for supplemental oxygen

- Prescribe **PF-07321332 (nirmatrelvir) plus ritonavir (Paxlovid)** 300 mg (2x 150 mg tablets) PF-07321332 (nirmatrlevir) with 100mg ritonavir taken together orally twice daily for 5 days

- **Serious risk of adverse reactions with other medicines**
- Caution in patients with pre-existing liver disease or liver enzyme abnormalities - causes raised liver transaminases, hepatitis and jaundice
- May decrease efficacy of combined hormonal contraceptives. Advise patients to use an effective alternative contraceptive method or an additional barrier method of contraception during treatment and until after one complete menstrual cycle after stopping treatment.

Read in conjunction with UK Interim Clinical Commissioning Policy: Therapies for symptomatic non-hospitalised patients with COVID-19

1st Line treatment for non-hospitalised patients with COVID-19: PF-07321332 (nirmatrelvir) plus ritonavir

Drug interactions

PF-07321332 (nirmatrelvir) plus ritonavir is a CYP3A inhibitor. This can cause increased plasma concentrations of other drugs metabolised by CYP3A. If new medications are started that inhibit or induce CYP3A they may increase or decrease concentrations of PF-07321332 (nirmatrelvir).

These interactions may lead to:

- Clinically significant adverse reactions, potentially leading to severe, life-threatening or fatal events from greater exposures of concomitant medicinal products
- Clinically significant adverse reactions from greater exposures of PF-07321332 (nirmatrelvir) plus ritonavir
- Loss of therapeutic effect of PF-07321332 (nirmatrelvir) plus ritonavir and possible development of viral resistance

Liver function

Hepatic transaminase elevations, clinical hepatitis and jaundice have occurred in patients receiving ritonavir. Therefore, caution should be exercised when administering PF-07321332 (nirmatrelvir) plus ritonavir to patients with pre-existing liver diseases, liver enzyme abnormalities or hepatitis.

Contraception

Use of ritonavir may reduce the efficacy of combined hormonal contraceptives. Patients using combined hormonal contraceptives should be advised to use an effective alternative contraceptive method or an additional barrier method of contraception during treatment and until after one complete menstrual cycle after stopping PF-07321332 (nirmatrelvir) plus ritonavir.

1st Line treatment for non-hospitalised patients with COVID-19: Sotrovimab

Sotrovimab

ELIGIBILITY CRITERIA

- Positive COVID-19 PCR/lateral flow test
- **AND** symptomatic with COVID-19 and showing no signs of clinical recovery
- **AND** member of a highest risk group (see Appendix 1 & 2 for list of qualifying conditions)
- **AND** clinical judgment is that treatment with an nMAB is the preferred treatment option
- **AND** treatment is commenced within 5 days of symptom onset

- Prescribe **Sotrovimab** 500mg IV
- Dilute in 100mls 0.9% saline and infuse over 30 minutes
- Do not give concomitantly with other IV drugs

- Monitor for sign of hypersensitivity reactions such as nausea, chills, dizziness, rash, urticaria and anaphylaxis up to 1 hour post infusion.
- For minor reactions consider changing the infusion rate to one hour.
- For anaphylaxis stop the infusion and treat appropriately

EXCLUSION CRITERIA

- Age < 12 years
- Adolescents (aged 12-17) weighing < 40 kg
- Requires hospital care for the management of acute COVID-19 illness
- New requirement for supplemental oxygen
- Known sensitivity to nMABs

Patients considered for treatment with sotrovimab should have samples taken for serology testing against SARS-CoV-2 prior to treatment. However, serology results are not a requirement for treatment.

2nd Line treatment for non-hospitalised patients with COVID-19: Remdesivir

Remdesivir

ELIGIBILITY CRITERIA

- Positive COVID-19 PCR/lateral flow test
- **AND** symptomatic with COVID-19 and showing no signs of clinical recovery
- **AND** member of a highest risk group (see Appendix 1 & 2 for list of qualifying conditions)
- **AND** clinical judgment is that treatment with an antiviral is the preferred treatment option
- **AND** Treatment with PF-07321332 (nirmatrelvir) plus ritonavir is contraindicated or not possible
- **AND** treatment is commenced within 7 days of symptom onset

- Prescribe **Remdesivir** 200mg IV loading dose followed by 100mg IV days 2 and 3
- Dilute in 100 or 250mls 0.9% saline and infuse over a minimum of 30 minutes

- Not recommended in individuals with ALT ≥ 5 times the upper limit of normal or eGFR < 30 ml/min
- Monitor for sign of hypersensitivity reactions such as nausea, chills, dizziness, rash, urticaria and anaphylaxis up to 1 hour post infusion.
- For mild to moderate reactions consider slowing the infusion rate up to a maximum infusion time of 120 minutes.
- For anaphylaxis stop the infusion immediately and treat appropriately

EXCLUSION CRITERIA

- Age < 12 years
- Adolescents (aged 12-17) weighing < 40 kg
- Requires hospital care for the management of acute COVID-19 illness
- New requirement for supplemental oxygen
- Known sensitivity to Remdesivir

Use of remdesivir in children aged 12-17 years would be off-label

3rd Line treatment for non-hospitalised patients with COVID-19: Molnupiravir

Molnupiravir

ELIGIBILITY CRITERIA

- Positive COVID-19 PCR/lateral flow test
- **AND** symptomatic with COVID-19 and showing no signs of clinical recovery
- **AND** member of a highest risk group (see Appendix 1 & 2 for list of qualifying conditions)
- **AND t**reatment with PF-07321332 (nirmatrelvir) plus ritonavir, remdesivir AND sotrovimab are contraindicated or not possible
- **AND** treatment is commenced within 5 days of symptom onset

- Prescribe **Molnupiravir** 800mg (4x200 mg tablets) orally every 12 hours for 5 days

- Individuals of childbearing potential should use effective contraception for the duration of treatment and 4 days after the last dose of molnupiravir

EXCLUSION CRITERIA

- Age < 18 years
- Pregnancy
- Requires hospital care for the management of acute COVID-19 illness
- New requirement for supplemental oxygen

Clinical Evidence: Antivirals

Antiviral medications inhibit viral replication and prevent progression of infection.

PF-07321332 (NIRMATRELVIR) PLUS RITONAVIR (PAXLOVID)

Final results from the EPIC HR trial indicate that the dual oral antiviral PF-07321332 (nirmatrelvir) plus ritonavir resulted in a relative risk reduction of hospitalisation or death by 89% (within 3 days of symptom onset) and 88% (within 5 days of symptom onset) compared to placebo in non-hospitalised, high-risk adults with COVID-19

REMDESIVIR

Remdesivir is an adenosine nucleotide pro-drug that is metabolised intracellularly to form the pharmacologically active substrate remdesivir triphosphate which inhibits SARS-CoV-2 RNA polymerase and perturbs viral replication

A three-day intravenous course of remdesivir administered within 7 days of COVID-19 symptom onset to non-hospitalised patients with risk factors for disease progression, resulted in a relative risk reduction of 87% in hospitalisation or death at day 28 (Gottlieb et al, 2021).

MOLNUPIRAVIR

Final results from the Phase 3 MOVe-OUT trial show that the oral antiviral molnupiravir administered within 5 days of COVID-19 symptom onset to high-risk, non-hospitalised patients resulted in a relative risk reduction of 30% in the composite primary outcome of hospitalisation or death at day 29 (Bernal et al, 2021).

Clinical Evidence: Monoclonal Antibodies

Neutralising MABs (nMABs) are synthetic monoclonal antibodies that bind to the spike protein of SARS-CoV-2, preventing subsequent entry of the virus into the host cell and its replication. This effectively 'neutralises' the virus particle.

SOTROVIMAB

Interim analysis of the COMET-ICE trial, which studied sotrovimab administered intravenously to non-hospitalised patients with mild-to-moderate disease and at least one risk factor for disease progression, showed a relative risk reduction in hospitalisation or death at day 29 by 85% in patients treated with sotrovimab compared with placebo (Gupta et al, 2021a). The final analysis of this study has shown a relative risk reduction in hospitalisation or death at day 29 by 79% in patients treated with sotrovimab compared with placebo (Gupta et al, 2021b).

Appendix 1: Patient cohorts considered at highest risk from COVID-19 and to be prioritised for treatment with nMABs and antivirals

Cohort	Description
Down's syndrome	All patients with Down's syndrome
Patients with a solid cancer	• Active metastatic cancer and active solid cancers (at any stage) • All patients receiving chemotherapy within the last 3 months • Patients receiving group B or C chemotherapy 3-12 months prior (see Appendix 3) • Patients receiving radiotherapy within the last 6 months
Patients with haematological diseases and stem cell transplant recipients	• Allogeneic haematopoietic stem cell transplant (HSCT) recipients in the last 12 months or active graft vs host disease (GVHD) regardless of time from transplant (including HSCT for non-malignant diseases) • Autologous HSCT recipients in the last 12 months (including HSCT for non-malignant diseases) • Individuals with haematological malignancies who have o received chimaeric antigen receptor (CAR)-T cell therapy in the last 24 months, or o radiotherapy in the last 6 months • Individuals with haematological malignancies receiving systemic anti-cancer treatment (SACT) within the last 12 months except patients with chronic phase chronic myeloid leukaemia (CML) in molecular response or first or second line tyrosine kinase inhibitors (TKI). • All patients with myeloma (excluding MGUS) or chronic B-cell lymphoproliferative disorders (e.g. chronic lymphocytic leukaemia, follicular lymphoma) or myelodysplastic syndrome (MDS) who do not fit the criteria above. • All patients with sickle cell disease. • Individuals with non-malignant haematological disorder (e.g. aplastic anaemia or paroxysmal nocturnal haemoglobinuria) receiving B-cell depleting systemic treatment (e.g. anti-CD20, antithymocyte globulin [ATG] and alemtzumab) within the last 12 months.

Patients with renal disease	• Renal transplant recipients (including those with failed transplants within the past 12 months), particularly those who:
	  • Received B cell depleting therapy within the past 12 months (including alemtuzumab, rituximab [anti-CD20], anti-thymocyte globulin)
	  • Have an additional substantial risk factor which would in isolation make them eligible for nMABs or oral antivirals
	  • Not been vaccinated prior to transplantation
	• Non-transplant patients who have received a comparable level of immunosuppression
	• Patients with chronic kidney stage (CKD) 4 or 5 (an eGFR less than 30 ml/min/1.73m2) without immunosuppression

Cohort	Description
Patients with liver disease	• Patients with cirrhosis Child's-Pugh class B and C (decompensated liver disease). • Patients with a liver transplant • Liver patients on immune suppressive therapy (including patients with and without liver cirrhosis) • Patients with cirrhosis Child's-Pugh class A who are not on immune suppressive therapy (compensated liver disease)
Patients with immune-mediated inflammatory disorders (IMID)	• IMID treated with rituximab or other B cell depleting therapy in the last 12 months • IMID with active/unstable disease on corticosteroids*, cyclophosphamide, tacrolimus, cyclosporin or mycophenolate. • IMID with stable disease on either corticosteroids*, cyclophosphamide, tacrolimus, cyclosporin or mycophenolate. • IMID patients with active/unstable disease including those on biological monotherapy and on combination biologicals with thiopurine or methotrexate
Immune deficiencies	• Common variable immunodeficiency (CVID) • Undefined primary antibody deficiency on immunoglobulin (or eligible for Ig) • Hyper-IgM syndromes • Good's syndrome (thymoma plus B-cell deficiency) • Severe Combined Immunodeficiency (SCID) • Autoimmune polyglandular syndromes/autoimmune polyendocrinopathy, candidiasis, ectodermal dystrophy (APECED syndrome) • Primary immunodeficiency associated with impaired type I interferon signalling • X-linked agammaglobulinaemia (and other primary agammaglobulinaemias) • Any patient with a secondary immunodeficiency 14 receiving, or eligible for, immunoglobulin replacement therapy
HIV/AIDS	• Patients with high levels of immune suppression, have uncontrolled/untreated HIV (high viral load) or present acutely with an AIDS defining diagnosis • On treatment for HIV with CD4 350 cells/mm3 and additional risk factors (e.g. age, diabetes, obesity, cardiovascular, liver or renal disease, homeless, those with alcohol-dependence)
Solid organ transplant recipients	• All recipients of solid organ transplants not otherwise specified above
Rare neurological conditions	• Multiple sclerosis • Motor neurone disease • Myasthenia gravis • Huntington's disease

Appendix 2: Group B and C chemotherapeutic agents

Group B 10-50% risk of grade 3/4 febrile neutropenia or lymphopenia

- Etoposide based regimens; CMF
- Irinotecan and Oxaliplatin based regimens
- Cabazitaxel
- Gemcitabine
- Chlorambucil
- Temozolomide
- Daratumumab#
- Rituximab
- Obinutuzumab
- Pentostatin
- Proteosome inhibitors
- IMIDs
- PI3Kinase inhibitors
- BTK inhibitors
- JAK inhibitors
- Venetoclax
- Trastuzumab-emtansine
- Anthracycline-based regimens
- Fluorouracil, epirubicin and cyclophosphamide (FEC)
- Methotrexate, vinblastine, adriamycin/doxorubicin, cisplatin (MVAC)
- Adriamycin/doxorubicin, bleomycin, vinblastine, dacarbazine (ABVD)
- Cyclophosphamide, doxorubicin, vincristine, prednisolone (CHOP)
- Bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine and prednisolone (BEACOPP)
- Liposomal doxorubicin
- Taxane – 3-weekly
- Nab-paclitaxel
- Carboplatin-based regimens • Ifosphamide-based regimens
- Bendamustine 12
- Cladrabine
- Topotecan
- Cyclophosphamide/Fludarabine combinations
- Ifosphamide, carboplatin, etoposide (ICE)
- Gemcitabine, dexamethasone, cisplatin (GDP)
- Isatuximab
- Polatuzumab
- Acalabrutinib
- Dexamethasone, cytarabine, cisplatin (DHAP)
- Etoposide, methylprednisolone, cytarabine, cisplatin (ESHAP)
- Cyclophosphamide, vincristine, doxorubicin, dexamethasone (CVAD)
- Dacarbazine-based regimens
- Lomustine
- Magalizumab
- Brentuximab vedotin
- Asparaginase-based regimens

Group C >50% risk of grade 3/4 febrile neutropenia or lymphopenia

- All acute myeloid leukaemia/acute lymphocytic regimens
- Bleomycin, etoposide and platinum
- Highly immunosuppressive chemotherapy (e.g. FluDAP, high dose Methotrexate & Cytarabine)
- Trifluradine/ Tipiracil
- KTE-X19
- Gilteritinib

Appendix 3: Drug-drug interactions involving PF-07321332 (nirmatrelvir) plus ritonavir.

NHS Borders

Table 1: List of medicines indicating that PF-07321132 (nirmatrelvir) plus ritonavir is not an appropriate option to be prescribed together.

Specific medicines	Medicine used for	Use of PF-07321132 (nirmatrelvir) plus ritonavir
Abemaciclib	Cancer	Consider risks and benefits
Acalabrutinib	Cancer	Consider risks and benefits
Alfuzosin	Prostate gland enlargement	Do not use
Aliskiren	High blood pressure (hypertension)	Do not use*
Amiodarone	Irregular heartbeats	Do not use
Apalutamide	Cancer	Consider risks and benefits
Apixaban	Treating or preventing blood clots	Do not use
Avanafil	Erection problems	Do not use
Bedaquiline	Infections	Consider risks and benefits
Bosentan	Pulmonary arterial hypertension	Do not use
Budesonide (inhaled, nasal spray)	Relieving asthma or COPD, or cold- like symptoms caused by allergic rhinitis	Consider risks and benefits
Carbamazepine	Epilepsy, nerve pain or trigeminal neuralgia	Do not use
Ceritinib	Cancer	Consider risks and benefits
Ciclosporin	Immunosuppressant	Do not use
Cisapride	Gastrointestinal motility problems	Do not use
Clonazepam	Epilepsy or anxiety	Do not use
Clopidogrel	Treating or preventing blood clots	Do not use*
Clozapine	Schizophrenia	Do not use
Colchicine	Gout	Do not use
Contraception, hormonal	Contraception	Consider risks and benefits
Dabigatran	Treating or preventing blood clots	Consider risks and benefits
Delamanid	Infections	Consider risks and benefits
Dexamphetamine	Narcolepsy or attention deficit hyperactivity disorder (ADHD)	Consider risks and benefits
Diazepam	Anxiety, muscle spasms or fits	Do not use
Digoxin	Irregular heartbeats or heart failure	Consider risks and benefits
Dihydroergotamine	Cluster headaches	Do not use
Disopyramide	Irregular heartbeats	Do not use*
Dronedarone	Irregular heartbeats	Do not use
Eletriptan	Migraines	Consider risks and benefits
Encorafenib	Cancer	Consider risks and benefits
Enzalutamide	Cancer	Consider risks and benefits

Specific medicines	Medicine used for	Use of PF-07321132 (nirmatrelvir) plus ritonavir
Eplerenone	Heart failure	Do not use*
Ergotamine	Cluster headaches	Do not use
Everolimus	Cancer or immunosuppressant	Do not use
Exviera (contains dasabuvir)	Hepatitis C	Consider risks and benefits
Fentanyl	Pain	Consider risks and benefits
Flecainide	Irregular heartbeats	Do not use
Flurazepam	Anxiety or problems sleeping	Do not use
Fluticasone propionate (inhaled or nasal spray)	Relieving asthma or COPD Cold-like symptoms caused by allergic rhinitis	Consider risks and benefits
Fostamatinib	Blood disorder	Consider risks and benefits
Fusidic acid (oral)	Infections	Do not use
Ibrutinib	Cancer	Consider risks and benefits
Illegal drugs	Substance abuse	Check advice in University of Liverpool COVID-19 Drug Interaction checker
Ivabradine	Heart failure or angina	Do not use*
Ketoconazole	Infections	Consider risks and benefits
Lamotrigine	Epilepsy or bipolar disorder	Consider risks and benefits
Lercanidipine	High blood pressure (hypertension)	Do not use*
Letermovir	Transplant	Consider risks and benefits
Levothyroxine	Underactive thyroid (hypothyroidism)	Consider risks and benefits
Lomitapide	Lowering cholesterol	Do not use
Lurasidone	Schizophrenia	Do not use
Maviret (contains glecaprevir and pibrentasvir)	Hepatitis C	Do not use
Methadone	Heroin dependence	Consider risks and benefits
Methylphenidate	Narcolepsy or attention deficit hyperactivity disorder (ADHD)	Consider risks and benefits
Midazolam	Epilepsy	Do not use
Neratinib	Cancer	Do not use
Pethidine	Pain	Do not use
Phenobarbital	Epilepsy	Do not use
Phenytoin	Epilepsy	Do not use
Pimozide	Schizophrenia	Do not use
Piroxicam	Pain	Do not use
Propafenone	Irregular heartbeats	Do not use
Propoxyphene	Analgesics	Do not use

Specific medicines	Medicine used for	Use of PF-07321132 (nirmatrelvir) plus ritonavir
Quetiapine	Bipolar disorder, depression, schizophrenia	Do not use
Quinidine	Antiarrhythmic	Do not use
Ranolazine	Heart failure or angina	Do not use
Rifabutin	Infections	Consider risks and benefits
Rifampicin	Infections	Do not use
Riociguat	Pulmonary arterial hypertension	Consider risks and benefits
Rivaroxaban	Treating or preventing blood clots	Do not use
Rosuvastatin	Lowering cholesterol	Consider risks and benefits
Salmeterol (inhaled)	Relieving asthma or COPD	Do not use
Sildenafil	Erection problems or pulmonary arterial hypertension	Do not use
Simvastatin	Lowering cholesterol	Do not use
Sirolimus	Immunosuppressant	Do not use*
Sodium fusidate (oral)	Infections	Do not use
St. John's Wort (Hypericum perforatum)	Herbal medicine	Do not use
Tacrolimus	Immunosuppressant	Do not use
Tadalafil	Erection problems or pulmonary arterial hypertension	Do not use
Theophylline	Relieving asthma or COPD	Consider risks and benefits
Ticagrelor	Treating or preventing blood clots	Do not use*
Vardenafil	Erection problems	Do not use
Valproic acid	Bipolar disorder, epilepsy or migraine	Consider risks and benefits
Venetoclax	Cancer	Do not use
Viekirax (contains ombitasvir, paritaprevir and ritonavir)	Hepatitis C	Consider risks and benefits
Vinblastine	Cancer	Consider risks and benefits
Vincristine	Cancer	Consider risks and benefits
Voriconazole	Infections	Consider risks and benefits
Warfarin	Treating or preventing blood clots	Consider risks and benefits
Zepatier (contains elbasvir and grazoprevir)	Hepatitis C	Do not use*

The information in this appendix is based on SPS guidance and is correct at the time of publication. Please refer to the SPS guidance for the most up to date information.

Table 2: Medications interacting with PF-07321332 (nirmatrelvir) plus ritonavir

What the medicine is used for	Specific medicine	Use of PF-07321132 (nirmatrelvir) plus ritonavir
Underactive thyroid (hypothyroidism)	Levothyroxine	Consider risks and benefits
Lowering cholesterol	Lomitapide Rosuvastatin Simvastatin	Do not use Consider risks and benefit Do not use
Treating or preventing blood clots	Apixaban Clopidogrel Dabigatran Rivaroxaban Ticagrelor Warfarin	Do not use Do not use* Consider risks and benefits Do not use Do not use* Consider risks and benefits
Relieving asthma or COPD (inhaled or oral)	Budesonide Fluticasone propionate Salmeterol Theophylline	Consider risks and benefits Consider risks and benefits Do not use Consider risks and benefits
Bipolar disorder, schizophrenia, epilepsy, migraine or cluster headaches	Carbamazepine Clonazepam Clozapine Dihydroergotamine Eletriptan Ergotamine Lamotrigine Lurasidone Phenobarbital Phenytoin Pimozide Quetiapine Valproic acid Midazolam	Do not use Do not use Do not use Do not use Consider risks and benefits Do not use Consider risks and benefits Do not use Do not use Do not use Do not use Do not use Consider risks and benefits Do not use

Specific medicines	Medicine used for	Use of PF-07321132 (nirmatrelvir) plus ritonavir
Erection problems	Avanafil Sildenafil Tadalafil Vardenafil	Do not use Do not use Do not use Do not use
Contraception. hormonal	Elicit name of medication and check COVID-19 Drug Interaction checker.	Consider risks and benefits
Irregular heartbeats	Amiodarone Digoxin Disopyramide Dronedarone Flecainide Propafenone Quinidine	Do not use Consider risks and benefits Do not use* Do not use Do not use Do not use Do not use
High blood pressure (hypertension)	Aliskiren Lercanidipine	Do not use* Do not use*
Prostate gland enlargement	Alfuzosin	Do not use
Cold-like symptoms caused by allergic rhinitis (nasal spray)	Budesonide Fluticasone propionate	Consider risks and benefits Consider risks and benefits
Pain	Fentanyl Midazolam Pethidine Propoxyphene Piroxicam	Consider risks and benefits Do not use Do not use Do not use Do not use
Nerve pain or trigeminal neuralgia	Carbamazepine	Do not use

Specific medicines	Medicine used for	Use of PF-07321132 (nirmatrelvir) plus ritonavir
Heart failure or angina	Eplerenone Ivabradine Ranolazine Digoxin	Do not use* Do not use* Do not use Consider risks and benefits
Gout	Colchicine	Do not use
Heroin dependence	Methadone	Consider risks and benefits
Substance abuse	Various illicit drugs	Check COVID-19 Drug Interaction checker
Herbal medicines	St. John's Wort (Hypericum perforatum)	Do not use
Infections	Bedaquiline Delamanid Fusidic acid/ sodium fusidate (oral) Ketoconazole Rifabutin Rifampicin Voriconazole	Consider risks and benefits Consider risks and benefits Do not use Consider risks and benefits Consider risks and benefits Do not use Consider risks and benefits
Pulmonary arterial hypertension	Bosentan Riociguat Sildenafil (Revatrio) Tadalafil	Do not use* Consider risks and benefits Do not use Do not use
Anxiety, problems sleeping, muscle spasms, fits, attention deficit hyperactivity disorder (ADHD) or narcolepsy	Diazepam Flurazepam Clonazepam St John's Wort Dexamphetamine Methylphenidate	Do not use Do not use Do not use Do not use Consider risks and benefits Consider risks and benefits

Specific medicines	Medicine used for	Use of PF-07321132 (nirmatrelvir) plus ritonavir
Immunosuppressant medications which can be used in a range of conditions	Ciclosporin Everolimus Sirolimus Tacrolimus	Do not use* Do not use* Do not use* Do not use*
Transplant	Letermovir	Consider risks and benefits
Hepatitis C	Exviera (contains dasabuvir) Maviret (contains glecaprevir and pibrentasvir) Viekirax (contains ombitasvir, paritaprevir and ritonavir) Zepatier (contains elbasvir and grazoprevir)	Consider risks and benefits Do not use Consider risks and benefits Do not use*
Cancer	Abemaciclib Acalabrutinib Apalutamide Ceritinib Encorafenib Enzalutamid Everolimus Ibrutinib Neratinib Venetoclax Vinblastine Vincristine	Consider risks and benefits Consider risks and benefits Consider risks and benefits Consider risks and benefits Consider risks and benefits Consider risks and benefits Do not use Consider risks and benefits Do not use Do not use Consider risks and benefits Consider risks and benefits
Blood disorders	Fostamatinib	Consider risks and benefits

*Not listed in PF-07321132 (nirmatrelvir plus ritonavir SmPC but use NOT advised by *COVID-19 Drug Interaction checker*

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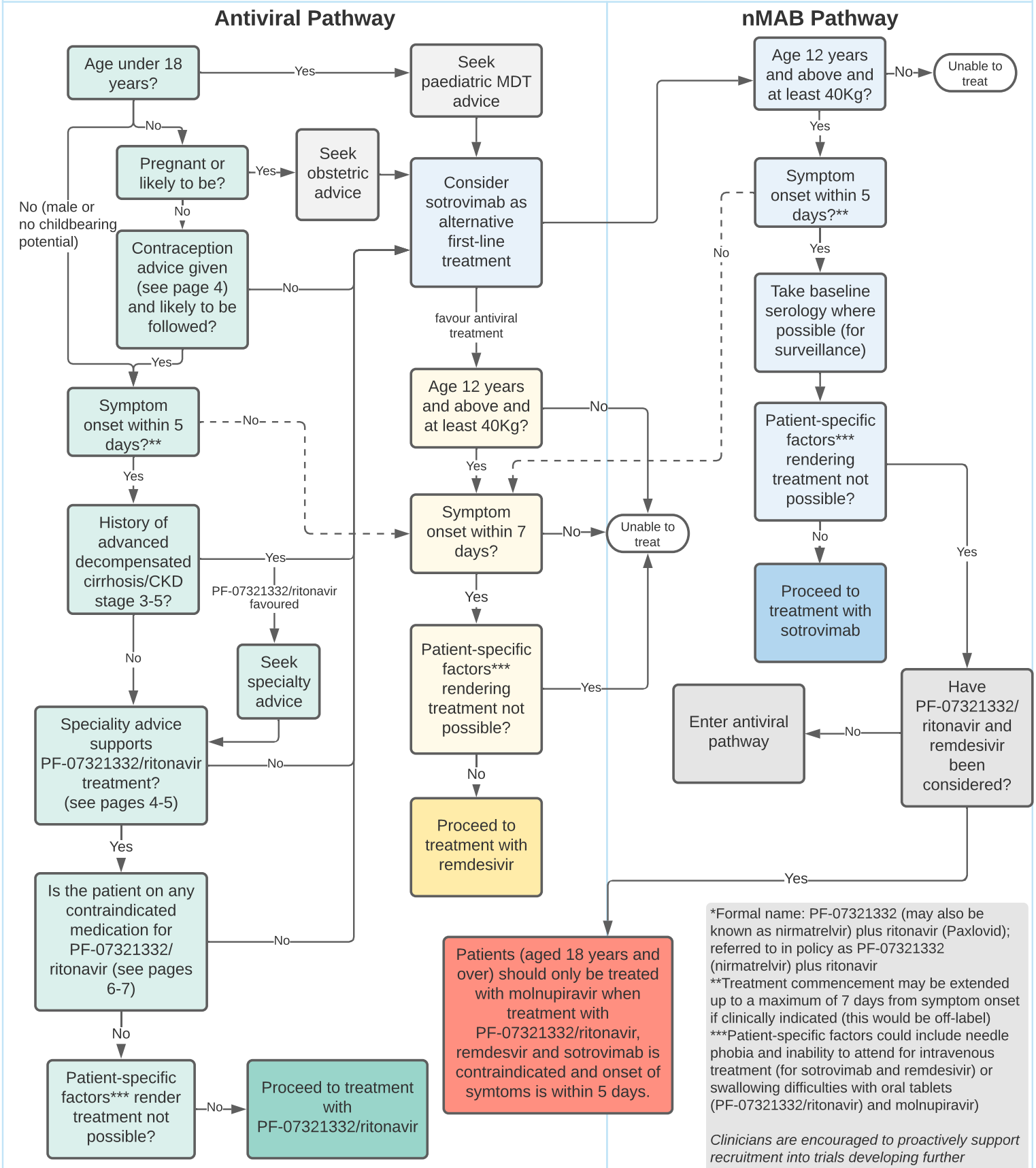
UK Interim Clinical Commissioning Policy:
Therapies for symptomatic non-hospitalised patients with COVID-19

Consider access to this clinical pathway for patients under the following conditions:

- Onset of symptoms of COVID-19 within the last 5 days (for PF-07321332/ritonavir*, sotrovimab and molnupiravir) or 7 days (for remdesivir), remains symptomatic and with no signs of clinical recovery
- SARS-CoV-2 infection is confirmed by either PCR or lateral flow test (registered via gov.uk)
- The patient is a member of a 'highest' risk group (see page 2)
- The patient is not hospitalised for COVID-19 and is not requiring new supplemental oxygen specifically for the management of COVID-19 symptoms

Consider the clinical suitability of antiviral or neutralising monoclonal antibody. PF-07321332/ritonavir and sotrovimab are first-line options and remdesivir is second-line. Molnupiravir should be considered a third-line treatment options. (see page 3 for further information on choosing between antiviral and nMAB).



*Formal name: PF-07321332 (may also be known as nirmatrelvir) plus ritonavir (Paxlovid); referred to in policy as PF-07321332 (nirmatrelvir) plus ritonavir
**Treatment commencement may be extended up to a maximum of 7 days from symptom onset if clinically indicated (this would be off-label)
***Patient-specific factors could include needle phobia and inability to attend for intravenous treatment (for sotrovimab and remdesivir) or swallowing difficulties with oral tablets (PF-07321332/ritonavir) and molnupiravir)

Clinicians are encouraged to proactively support recruitment into trials developing further evidence in the treatment of COVID-19

Clinical Guide: The 'highest risk' cohort for access to treatment

The following cohorts were determined by an independent advisory group commissioned by the Department of Health and Social Care (DHSC). Patients in these cohorts are determined to be at highest risk of adverse outcomes from COVID-19 and are to be prioritised for treatment with nMABs and antivirals.

Cohort	Definition
Down's syndrome	All patients with Down's syndrome
Patients with a solid cancer	Active metastatic cancer and active solid cancers (at any stage) • All patients receiving chemotherapy within the last 3 months • Patients receiving group B or C chemotherapy 3-12 months prior (see Appendix 3) • Patients receiving radiotherapy within the last 6 months
Patients with haematological disease and stem cell transplant recipients	• Allogeneic haematopoietic stem cell transplant (HSCT) recipients in the last 12 months or active graft vs host disease (GVHD) regardless of time from transplant (including (HSCT for non-malignant diseases) • Autologous HSCT recipients in the last 12 months (including (HSCT for non-malignant diseases) • Individuals with haematological malignancies who have ◦ received chimaeric antigen receptor (CAR)-T cell therapy in the last 24 months. or ◦ radiotherapy in the last 6 months • Individuals with haematological malignancies receiving systemic anti-cancer treatment (SACT) within the last 12 months except patients with chronic phase chronic myeloid leukaemia (CML) in molecular response; or first or second line tyrosine kinase inhibitors (TKI) • All patients with myeloma (excluding MGUS) or chronic B-cell lymphoproliferative disorders (e.g.chronic lymphocytic leukaemia, follicular lymphoma) or myelodysplastic syndrome (MDS) who do not fit the criteria above. • All patients with sickle cell disease. • Individuals with non-malignant haematological disorder (e.g.aplastic anaemia or paroxysmal nocturnal haemoglobinuria) receiving B-cell depleting systemic treatment (e.g.anti-CD20, anti-thymocyte globulin [ATG] andalemtzumab) within the last 12 months.
Patients with renal disease	• Renal transplant recipients (including those with failed transplants within the past 12 months), particularly those who: ◦ Received B cell depleting therapy within the past 12 months (including alemtuzumab, rituximab [anti-CD20], anti-thymocyte globulin) ◦ Have an additional substantial risk factor which would in isolation make them eligible for nMABs or oral antivirals ◦ Not been vaccinated prior to transplantation • Non-transplant patients who have received a comparable level of immunosuppression • Patients with chronic kidney stage (CKD) 4 or 5 (an eGFR less than 30 ml/min/1.73m2) without immunosuppression
Patients with liver disease	Patients with cirrhosis Child's-Pugh class B and C (decompensated liver disease) • Patients with a liver transplant • Liver patients on immune suppressive therapy (including patients with and without liver cirrhosis) Patients with cirrhosis Child's-Pugh class A who are not on immune suppressive therapy (compensated liver disease)
Patients with immune-mediated inflammatory disorders	• IMID treated with rituximab or other B cell depleting therapy in the last 12 months • IMID with active/unstable OR stable disease on corticosteroids (equivalent to ≥10mg/day of prednisolone for at least the 28 days prior to a positive PCR result), cyclophosphamide, tacrolimus, cyclosporin or mycophenolate • IMID patients with active/unstable disease including those on biological monotherapy and on combination biologicals with thiopurine or methotrexate
Immune deficiencies	• Primary immunodeficiency associated with impaired type I interferon signalling • Good's syndrome (thymoma plus B-cell deficiency) • X-linked agammaglobulinaemia (and other primaryagammaglobulinaemias) • Any patient with a secondary immunodeficiency receiving, or eligible for, immunoglobulin replacement therapy • Common variable immunodeficiency (CVID) • Undefined primary antibody deficiency on immunoglobulin (or eligible for Ig) • Hyper-IgM syndromes • Severe Combined Immunodeficiency (SCID) • Autoimmune polyglandular syndromes /autoimmunepolyendocrinopathy, candidiasis, ectodermal dystrophy (APECED syndrome)
HIV/AIDS	• Patients with high levels of immune suppression, have uncontrolled/untreated HIV (high viral load) or present acutely with an AIDS defining diagnosis • On treatment for HIV with CD4 <350 cells/mm3 and stable on HIV treatment or CD4>350 cells/mm3 and additional risk factors (e.g. age, diabetes, obesity, cardiovascular, liver or renal disease, homeless, those with alcohol-dependence)
Solid organ transplant recipients	All recipients of solid organ transplants not otherwise specified above
Rare neurological conditions	Multiple sclerosis Motor neurone disease Myasthenia gravis Huntington's disease

Clinical Guide: Therapy characteristics when deciding on treatment choice

Use this guide to assist in decision making on which therapetic option to use:

- Three products have similar relative risk reduction of reducing hospitalistion: PF-07321332/ritoniavir, remdesivir; and sotrovimab
- Molnupiravir has a substantially lower level of efficacy - reserve when the others cannot be used
- Medicines availability will be monitored nationally and regionally, so unless otherwise directed do not consider supply issues in your decision making

PF-07321332/ritonavir (Paxlovid)	Remdesivir (Veklury)	Sotrovimab (Xevudy)
Antiviral (dual therapy)	Antiviral (monotherapy)	Neutralising monoclonal antibody
Administered **orally**: 3 tablets twice a day for 5 days	Administered **intravenously**: one infusion every 24 hours for 3 days	Administered **intravenously**: single infusion
Adults only (aged 18 years and over)	Adults and children (aged 12 years and over and weighing at least 40kg)	Adults and children (aged 12 years and over and weighing at least 40kg)
Evidence based on treatment within **5** days of symptom onset	Evidence based on treatment within **7** days of symptom onset	Evidence based on treatment within **5** days of symptom onset
Not recommended in pregnancy	May be used in **pregnancy** where benefits of treatment outweigh risks	May be used in **pregnancy** although there is no safety data available
Breast-feeding should be discontinued during treatment and for 7 days after last dose	No specific advice on discontinuation of breast-feeding during treatment	No specific advice on discontinuation of breast-feeding during treatment
Contraindicated in severe liver and kidney disease	Not recommended in individuals with ALT ≥5 times the upper limit of normal or eGFR <30ml/min	No dose adjustment recommended in liver or renal impairment*
Multiple significant drug-drug interactions (see page 4)	No significant drug-drug interactions	No significant drug-drug interactions
88% Relative Risk Reduction of Hospitalisation	87% Relative Risk Reduction of Hospitalisation	85% Relative Risk Reduction of Hospitalisation

Molnupiravir (Lageviro)

Antiviral (monotherapy)	Breast-feeding should be discontinued during treatment and for 4 days after last dose
Administered **orally**: 4 capsules twice a day for 5 days	May be used in severe liver and kidney disease (no dose adjustment recommended)
Adults only (aged 18 years and over)	No significant drug-drug interactions
Not recommended in pregnancy	

30% Relative Risk Reduction of Hospitalisation

For the key publications of trial results and licence click here

PF-07321332/ritonavir publication due	PF-07321332/ritonavir SmPC
Remdesevir NEJM Dec 2021	Remdesivir EU EPAR
Sotrovimab NEJM Nov 2021	Sotrovimab SmPC
Molnupiravir NEJM Dec 2021	Molnupiravir SmPC

*there are limited/no data on the use of sotrovimab in patients with a creatinine clearance of <30ml/min/1.73m^2 and those with severe elevations ALT (5 - <10 x upper limit of normal)

Version 1. 27 January 2022. Not valid if printed

Clinical Guide: Specialty advice for 'highest-risk' cohorts

Specialty-specific advice on the management of patients within each of the highest-risk cohorts (particularly around the use of PF-07321332/ritonavir) may be found in the table below. Contact your local specialist team for further guidance on issues not covered by this advice.

Cohort	Advice/guidance
Liver Disease	PF-07321332/ritonavir should not be administered to patients with advanced decompensated cirrhosis. Such patients can be identified by questioning or review of medical records. Patients should be asked if they have ever been admitted to hospital with liver disease and if they are currently receiving regular ascitic drainage. A positive response is a contraindication to PF-07321332/ritonavir. If blood tests are available a bilirubin >50 at any time is a contraindication to PF-07321332/ritonavir, if the jaundice is due to liver disease. Patients receiving rifaximin (only used in very advanced liver disease) should not receive PF-07321332/ritonavir.
Solid organ transplant (non-renal)	PF-07321332/ritonavir is currently contraindicated in both Solid Organ and Islet Transplant recipients due to significant harmful drug interactions especially anti-rejection medication. These patients should be triaged to receive sotrovimab.
Renal disease (including renal transplant)	Currently PF-07321332/ritonavir is not indicated in the majority of at-risk individuals with renal disease, due to lack of dosing information or drug interactions. These include patients with: CKD stage 4 and 5, including those on dialysis: and in transplant patients due to interactions with immunosuppressive therapy. PF-07321332/ritonavir requires dose modification in people with CKD stage 3 (see product information). When nMAbs are not indicated or available, clinicians can discuss alternative treatment options such as remdesivir with renal provider clinicians. Remdesivir may be used in patients with an eGFR of ≥30ml/min/1.73m^2 and in some patients on haemodialysis (discuss with renal clinicians for further guidance).
Solid cancer (including metastases); Haematological disease (including non-malignant conditions)	Specialist cancer and haematology teams are encouraged to establish a central provider email account to receive queries from clinicians treating patients with COVID-19 with antivirals and/or nMABs. For patients who are receiving SACT or complex supportive care for malignancy or stem cell transplantation, please ask whether the patient has already been contacted or reviewed by their specialist haematology/oncology/bone marrow transplant team. If the patient has not already been in contact with their specialist, please establish the location of the provider and consider referral to the respective specialist team via the central provider email where available. Please ask the patient to have details of their current medication available for any following consultation.
Rare neurological conditions	There are no specific needs for specialist neurology services to prescribe PF-07321332/ritonavir, though care should be taken with those who have difficulty swallowing or have supported feeding, and for those with behavioural or psychiatric concerns. If a patient is identified as eligible for PF-07321332/ritonavir due to neurology risk factors then ask about swallowing difficulties. Disease-specific advice is as follows: **Multiple Sclerosis (MS)** • In addition to the medicines listed in pages 6-7, avoid concurrent use of PF-07321332/ritonavir with the following: siponimod, cladribine and modafinil • For those patients taking oral or intravenous methylprednisolone discuss the steroid dose with the MS neurology team as PF-07321332/ritonavir may increase corticosteroid levels. **Myasthenia Gravis** • This includes muscle specific kinase (MUSK) myasthenia and the Lambert-Eaton Myasthenic Syndrome (LEMS). There are anecdotal reports of myasthenia gravis worsening in association with PF-07321332/ritonavir • There are no known specific drug interactions. Myasthenia can be aggravated by COVID-19 and COVID-19 vaccination and requires close monitoring given the risk of bulbar and respiratory failure. **Motor Neurone Disease (MND)** • Discuss patients on quinine with an MND physician • Levels of riluzole treatment may be increased by PF-07321332/ritonavir and should be temporarily suspended following discussion with an MND physician. **Huntington's Disease** • In addition to the medicines listed in pages 6-7, avoid concurrent use of PF-07321332/ritonavir with the following: primidone, tetrabenazine and trihexyphenidyl
Immunology	Considering commonly prescribed medications in immunology, there are no issues with concomitant immunoglobulin replacement therapy and PF-07321332/ritonavir and nMABs. Patients should be informed by specialist clinicians and clinical/patient networks to maintain a list of all medications including those prescribed in hospital. Patients may be taking prophylactic antimicrobials - please refer to the list of contraindicated medications on pages 6-7 for further reference.
Obstetrics and gynaecology	It is recommended that CMDU staff liaise with their Maternity COVID Champion, or dedicated clinician when assessing a pregnant patient with COVID. Please ensure that a full drug history and past medical history is taken as other specialists may also need to be involved, for example renal or transplant teams. Use of ritonavir may reduce the efficacy of combined hormonal contraceptives. Patients using combined hormonal contraceptives should be advised to use an effective alternative contraceptive method or an additional barrier method of contraception during treatment and until after one complete menstrual cycle after stopping PF-07321332/ritonavir.
Paediatrics	For paediatric/adolescent patients (aged 12-17 year inclusive), paediatric multidisciplinary team (MDT) assessment should be used to determine clinical capacity to benefit from treatment.

Clinical Guide: Specialty advice for 'highest-risk' cohorts

Specialty-specific advice on the management of patients within each of the highest-risk cohorts (particularly around the use of PF-07321332/ritonavir) may be found in the table below. Contact your local specialist team for further guidance on issues not covered by this advice.

Cohort	Advice/guidance
IMID	**Factors to be considered in IMID patients**: • Consistent with existing guidance on management of COVID-19 in patients with IMID, patients should temporarily suspend their conventional DMARD(s), biologic and/or JAK inhibitor until the course of antiviral treatment has been completed and symptoms of COVID-19 are improving (this will usually be between 1-3 weeks). For most patients this will not require specific contact with the specialty team. • Do not stop or decrease corticosteroids • Swallowing difficulties may preclude the use of oral antivirals e.g. in patients with dysphagia due to myositis, oesophageal dysmotility due to scleroderma/systemic sclerosis because of the size of the tablets (approximately 2cm long) • Do not delay antiviral treatment pending specialist advice The following links on speciality websites may be useful: • The British Society for Rheumatology website • COVID-19 guidance | British Society for Rheumatology • COVID-19 Guidance & Advice - The British Society of Gastroenterology (bsg.org.uk) • British Thoracic Society website: https://www.brit-thoracic.org.uk/covid-19/ • British Association of Dermatologists Advice for Dermatology HCPs during COVID-19 pandemic: https://www.bad.org.uk/healthcare-professionals/covid-19
HIV/AIDS	• It is recommended that each CMDU has details of their local HIV specialist service (both specialist HIV pharmacist and HIV physician) to discuss individuals where advice is needed. Specialty arrangements for referral to HIV specialist advice may be regional in some areas. • The majority of individuals living with HIV and referred to CMDUs for PF-07321332/ritonavir treatment should be managed in accordance with the guidance without the need for referral to the specialist centre. There are no antiretroviral treatment (ART) regimens that are a contraindication to PF-07321332/ritonavir treatment. No dose adjustment of any ART agent including ritonavir or cobicistat is needed. Interactions with other generalist co-medications prescribed should be assessed according to guidance including by reference to the Liverpool Covid drug interaction website. • Some individuals living with HIV do not disclose their HIV status to their GPs. It is therefore good practice to enquire of individuals during triage if they have any other medical conditions or take any other medications not managed directly by their GP. • CD4 counts are no longer routinely monitored in those with virological suppression and previous counts above 350 cells/mm3. These individuals will generally be assessed as not meeting the immunosuppression criteria although some patients may still meet the criteria that take account of other demographic factors and co-morbidities. We suggest using an age threshold of 55 years or older as an appropriate indicator for treatment in these circumstances as this was the inclusion criteria used in clinical studies.

Down's syndrome	• The following issues should be given due consideration when assessing a patient for treatment with a suitable antiviral or nMAB:
	  • The individual is likely to have impaired ability to understand the information given and they may be more likely to have hearing and communication difficulties
	  • There is significant potential for co-existence of significant health conditions
	  • There is a need for a corroborated and detailed collateral medical and drug history from an informant
	  • Mental capacity assessment is an essential part of the assessment/triage process in these individuals
	  • Other people cannot consent for an individual's treatment unless they are legally permitted to do so
	  • In patients iudged not to have capacity, a process of best interests decision-making should be pursued.
	• A person with Down's syndrome may be more likely to be taking medications that are contra-indicated or which may lead to interactions with PF-07321332/ritonavir e.g.:
	  • For heart conditions and high blood pressure
	  • Antipsychotic, antidepressants, anxiolytics A
	  • Anticonvulsants (anti-epileptics)
	  • Statins
	• PF-07321332/ritonavir tablets are relatively large (8-9mm diameter) and should not be crushed. Patients with swallowing difficulties will need support to ensure these are taken safely.
	• Contact the hospital learning disability liaison nurse (if available) or the local specialist learning disability service for clinical advice around psychotropic medications and the implication of contraindications and potential interactions

Clinical Guide: Medicines where PF-07321332/ritonavir is NOT an appropriate option

These tables show the medicines where there are contraindications with PF-07321332/ritonavir and cautions that are not easily managed. If a patient is currently prescribed any of these medicines, then PF-07321332/ritonavir is NOT a treatment option. Please refer to SPS Guidance here.

What the medicine is used for	Specific Medicines
Irregular heartbeats	Digoxin, Disopyramide, Amiodarone, Quinidine, Dronedarone, Flecainide, Propafenone
Treating and preventing blood clots	Apixaban, Dabigatran, Rivaroxaban, Warfarin, Clopidogrel, Ticagrelor
High blood pressure (hypertension)	Aliskiren, Lercanidipine
Lowering cholesterol	Rosuvastatin, Simvastatin, Lomitapide
Erection problems	Avanafil, Sildenafil, Tadalafil, Vardenafil
Inhalers Inhaled or oral medicines to relieve asthma and COPD	Salmeterol, Budesonide, Fluticasone Propionate, Theophylline
Cold-like symptoms caused by allergic rhinitis (nasal spray)	Budesonide, Fluticasone propionate
Underactive thyroid (hypothyroidism)	Levothyroxine
Prostate gland enlargement	Alfuzosin
Heart failure or angina	Ranolazine, Ivabradine, Eplerenone, Digoxin
Pain	Fentanyl, Midazolam, Pethidine, Piroxicam, Propoxyphene
Heroin dependence	Methadone
Bipolar disorder, schizophrenia, epilepsy, migraine or cluster headaches	Carbamazepine, Clozapine, Eletriptan, Lamotrigine, Lurasidone, Phenobarbital, Phenytoin, Quetiapine, Ergotamine, Dihydroergotamine, Valproic acid, Pimozide, Midazolam, Clonazepam
Nerve pain or trigeminal neuralgia	Carbamazepine
Gout	Colchicine
Pulmonary arterial hypertension (PAH)	Sildenafil, Bosentan, Riociguat, Tadalafil
Herbal medicines	St. John's Wort
Anxiety, problems sleeping, muscle spasms, fits, narcolepsy and ADHD	Flurazepam, Diazepam, Clonazepam, St John's Wort, Methylphenidate, Dexamphetamine

Clinical Guide: Medicines where PF-07321332/ritonavir is NOT an appropriate option

These tables show the medicines where there are contraindications with PF-07321332/ritonavir and cautions that are not easily managed. If a patient is currently prescribed any of these medicines, then PF-07321332/ritonavir is NOT a treatment option. Please refer to SPS Guidance here.

What the medicine is used for	Specific Medicines
Cancer	Abemaciclib, Acalabrutinib, Ceritinib, Encainide, Encorafenib, Enzalutamide, Everolimus, Apalutamide, Ibrutinib, Neratinib, Venetoclax, Vinblastine, Vincristine
Infections	Bedaquiline, Delamanid, Ketoconazole, Rifabutin, Rifampicin, Voriconazole, Fusidic acid / sodium fusidate
Transplant	Letermovir
Immunosuppressant medicines which can be used for a range of conditions	Ciclosporin, Sirolimus, Tacrolimus, Everolimus
Hepatitis C	Maviret (contains glecaprevir and pibrentasvir), Zepatier (contains elbasvir and grazoprevir), Exviera (contains dasabuvir), Viekierax (contains ombitasvir, paritaprevir and ritonavir)
Blood Disorder	Fostamatinib
Hormonal contraception	Check COVID-19 Drug Interaction Checker
Illegal substances	

A-Z: All medicines where PF-07321332/ritonavir is NOT an appropriate option

DO NOT USE | CONSIDER RISKS AND BENEFITS

Abemaciclib, Acalabrutinib, Alfuzosin, Aliskiren, Amiodarone, Apalutamaide, Apixaban, Avanafil, Bedaquiline, Bosentan, Budesonide, Carbamazepine, Ceritinib, Ciclosporin, Cisapride, Clonazepam, Clopidogrel, Clozapine, Colchicine, Contraception, hormonal, Dabigatran, Delamanid, Dexamphetamine, Diazepam, Digoxin, Dihydroergotamine, Disopyramide, Dronedarone, Elbasvir/grazoprevir (Zepatier), Eletriptan, Encorafenib, Enzalutamide, Eplerenone, Ergotamine, Everolimus, Exviera, Fentanyl, Flecainide, Flurazepam, Fluticasone, Fostamatinib, Fusidic acid, Glecaprevir/pibrentasvir (Maviret), Ibrutinib, Ivabradine, Ketoconazole, Lamotrigine, Lercanidipine, Letermovir, Levothyroxine, Lomitapide, Lurasidone, Methadone, Methylphenidate, Midazolam, Neratinib, Pethidine, Phenobarbital, Phenytoin, Pimozide, Piroxicam, Propafenone, Propoxyphene, Quetiapine, Quinidine, Ranolazine, Rifabutin, Rifampicin, Riociguat, Rivaroxaban, Rosuvastatin, Salmeterol, Sildenafil, Simvastatin, Sirolimus, Sodium fusidate, St. John's Wort, Tacrolimus, Tadalafil, Theophylline, Ticagrelor, Valproic acid, Vardenafil, Venetoclax, Viekirax, Vinblastine, Vincristine, Voriconazole, Warfarin

More detail of drug/drug interactions in found on the Liverpool COVID Drug Interaction Checker - Click Here