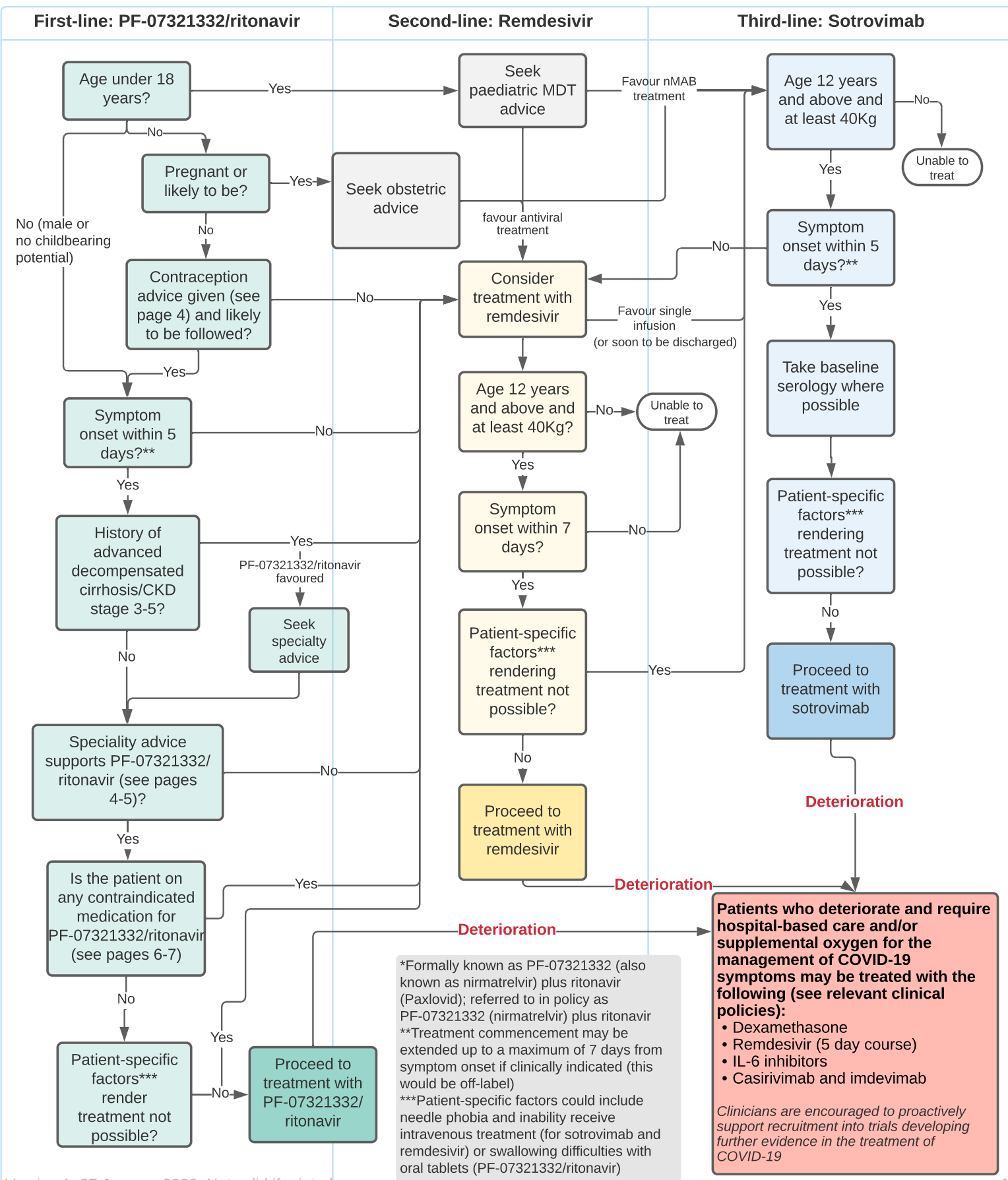


# UK Interim Clinical Commissioning Policy

## Therapies for patients with symptomatic hospital-onset COVID-19

### Consider access to this clinical pathway under the following conditions:

- Hospitalised for indications other than for the management of acute symptoms of COVID-19
- Onset of symptoms of COVID-19 within the last 5 days (for PF-07321332/ritonavir\* and sotrovimab) 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
- The patient is a member of a 'highest' risk group (see page 2) OR COVID-19 infection presents a material risk of destabilising a pre-existing condition or compromising recovery from a procedure (as determined by MDT assessment)
- The patient is not requiring new supplemental oxygen specifically for the management of COVID-19 symptoms



## 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                                             | <p>Active metastatic cancer and active solid cancers (at any stage)</p> <ul style="list-style-type: none"> <li>All patients receiving chemotherapy within the last 3 months</li> <li>Patients receiving group B or C chemotherapy 3-12 months prior (see Appendix 3)</li> <li>Patients receiving radiotherapy within the last 6 months</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| Patients with haematological disease and stem cell transplant recipients | <ul style="list-style-type: none"> <li>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)</li> <li>Autologous HSCT recipients in the last 12 months (including (HSCT for non-malignant diseases)</li> <li>Individuals with haematological malignancies who have <ul style="list-style-type: none"> <li>received chimaeric antigen receptor (CAR)-T cell therapy in the last 24 months. or</li> <li>radiotherapy in the last 6 months</li> </ul> </li> <li>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)</li> <li>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.</li> <li>All patients with sickle cell disease.</li> <li>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] andalemtuzumab) within the last 12 months.</li> </ul> |
| Patients with renal disease                                              | <ul style="list-style-type: none"> <li>Renal transplant recipients (including those with failed transplants within the past 12 months), particularly those who: <ul style="list-style-type: none"> <li>Received B cell depleting therapy within the past 12 months (including alemtuzumab, rituximab [anti-CD20], anti-thymocyte globulin)</li> <li>Have an additional substantial risk factor which would in isolation make them eligible for nMABs or oral antivirals</li> <li>Not been vaccinated prior to transplantation</li> </ul> </li> <li>Non-transplant patients who have received a comparable level of immunosuppression</li> <li>Patients with chronic kidney stage (CKD) 4 or 5 (an eGFR less than 30 ml/min/1.73m2) without immunosuppression</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| Patients with liver disease                                              | <p>Patients with cirrhosis Child's-Pugh class B and C (decompensated liver disease)</p> <ul style="list-style-type: none"> <li>Patients with a liver transplant</li> <li>Liver patients on immune suppressive therapy (including patients with and without liver cirrhosis)</li> </ul> <p>Patients with cirrhosis Child's-Pugh class A who are not on immune suppressive therapy (compensated liver disease)</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| Patients with immune-mediated inflammatory disorders                     | <ul style="list-style-type: none"> <li>IMiD treated with rituximab or other B cell depleting therapy in the last 12 months</li> <li>IMiD with active/unstable OR stable disease on corticosteroids, cyclophosphamide, tacrolimus, cyclosporin or mycophenolate</li> <li>IMiD patients with active/unstable disease including those on biological monotherapy and on combination biologicals with thiopurine or methotrexate</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Immune deficiencies                                                      | <ul style="list-style-type: none"> <li>Primary immunodeficiency associated with impaired type I interferon signalling</li> <li>Good's syndrome (thymoma plus B-cell deficiency)</li> <li>X-linked agammaglobulinaemia (and other primaryagammaglobulinaemias)</li> <li>Any patient with a secondary immunodeficiency receiving, or eligible for, immunoglobulin replacement therapy</li> <li>Common variable immunodeficiency (CVID)</li> <li>Undefined primary antibody deficiency on immunoglobulin (or eligible for Ig)</li> <li>Hyper-IgM syndromes</li> <li>Severe Combined Immunodeficiency (SCID)</li> <li>Autoimmune polyglandular syndromes /autoimmunepolyendocrinopathy, candidiasis, ectodermal dystrophy (APECED syndrome)</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| HIV/AIDS                                                                 | <ul style="list-style-type: none"> <li>Patients with high levels of immune suppression, have uncontrolled/untreated HIV (high viral load) or present acutely with an AIDS defining diagnosis</li> <li>On treatment for HIV with CD4 &lt;350 cells/mm3 and stable on HIV treatment or CD4&gt;350 cells/mm3 and additional risk factors (e.g. age, diabetes, obesity, cardiovascular, liver or renal disease, homeless, those with alcohol-dependence)</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Solid organ transplant recipients                                        | All recipients of solid organ transplants not otherwise specified above                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| Rare neurological conditions                                             | <p>Multiple sclerosis</p> <p>Motor neurone disease</p> <p>Myasthenia gravis</p> <p>Huntington's disease</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |

# Clinical Guide: Therapy characteristics when deciding on treatment choice

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

- Three products have similar relative risk reduction of reducing hospitalisation: PF-07321332/ritonavir, 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 <b>orally</b> : 3 tablets twice a day for 5 days                         | Administered <b>intravenously</b> : one infusion every 24 hours for 3 days                             | Administered <b>intravenously</b> : single infusion                        |
| Adults only (aged 18 years and over)                                                  | Adults and adolescents (aged 12 years and over and weighing at least 40kg)                             | Adults and adolescents (aged 12 years and over and weighing at least 40kg) |
| Evidence based on treatment within <b>5</b> days of symptom onset                     | Evidence based on treatment within <b>7</b> days of symptom onset                                      | Evidence based on treatment within <b>5</b> days of symptom onset          |
| <b>Not recommended in pregnancy</b>                                                   | May be used in <b>pregnancy</b> where benefits of treatment outweigh risks                             | May be used in <b>pregnancy</b> 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 $\geq 5$ times the upper limit of normal or eGFR $< 30$ ml/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 <b>orally</b> : 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                                                 |
| <b>Not recommended in pregnancy</b>                            |                                                                                       |
| 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 |
| Remdesivir NEJM Dec 2021              | Remdesivir SmPC            |
| 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  $< 30$ ml/min/1.73m<sup>2</sup> and those with severe elevations ALT (5 -  $< 10$  x upper limit of normal)

## 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 $\geq 30\text{ml/min/1.73m}^2$ and in some patients on haemodialysis (discuss with renal clinicians for further guidance).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| Solid cancer (including metastases);<br>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:<br><b>Multiple Sclerosis (MS)</b> <ul style="list-style-type: none"> <li>In addition to the medicines listed in pages 6-7, avoid concurrent use of PF-07321332/ritonavir with the following: siponimod, cladribine and modafinil</li> <li>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.</li> </ul> <b>Myasthenia Gravis</b> <ul style="list-style-type: none"> <li>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</li> <li>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.</li> </ul> <b>Motor Neurone Disease (MND)</b> <ul style="list-style-type: none"> <li>Discuss patients on quinine with an MND physician</li> <li>Levels of riluzole treatment may be increased by PF-07321332/ritonavir and should be temporarily suspended following discussion with an MND physician.</li> </ul> <b>Huntington's Disease</b> <ul style="list-style-type: none"> <li>In addition to the medicines listed in pages 6-7, avoid concurrent use of PF-07321332/ritonavir with the following: primidone, tetrabenazine and trihexyphenidyl</li> </ul> |
| 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            | <p><b>Factors to be considered in IMiD patients:</b></p> <ul style="list-style-type: none"> <li>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.</li> <li>Do not stop or decrease corticosteroids</li> <li>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)</li> <li>Do not delay antiviral treatment pending specialist advice</li> </ul> <p>The following links on speciality websites may be useful:</p> <ul style="list-style-type: none"> <li>The British Society for Rheumatology website</li> <li><a href="#">COVID-19 guidance   British Society for Rheumatology</a></li> <li><a href="#">COVID-19 Guidance &amp; Advice - The British Society of Gastroenterology (bsg.org.uk)</a></li> <li>British Thoracic Society website: <a href="https://www.brit-thoracic.org.uk/covid-19/">https://www.brit-thoracic.org.uk/covid-19/</a></li> <li>British Association of Dermatologists Advice for Dermatology HCPs during COVID-19 pandemic: <a href="https://www.bad.org.uk/healthcare-professionals/covid-19">https://www.bad.org.uk/healthcare-professionals/covid-19</a></li> </ul>                                                                                                                                                                          |
| HIV/AIDS        | <ul style="list-style-type: none"> <li>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.</li> <li>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.</li> <li>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.</li> <li>CD4 counts are no longer routinely monitored in those with virological suppression and previous counts above 350 cells/mm<sup>3</sup>. 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.</li> </ul>                                                |
| Down's syndrome | <ul style="list-style-type: none"> <li>The following issues should be given due consideration when assessing a patient for treatment with a suitable antiviral or nMAB: <ul style="list-style-type: none"> <li>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</li> <li>There is significant potential for co-existence of significant health conditions</li> <li>There is a need for a corroborated and detailed collateral medical and drug history from an informant</li> <li>Mental capacity assessment is an essential part of the assessment/triage process in these individuals</li> <li>Other people cannot consent for an individual's treatment unless they are legally permitted to do so</li> <li>In patients judged not to have capacity, a process of best interests decision-making should be pursued.</li> </ul> </li> <li>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.: <ul style="list-style-type: none"> <li>For heart conditions and high blood pressure</li> <li>Antipsychotic, antidepressants, anxiolytics A</li> <li>Anticonvulsants (anti-epileptics)</li> <li>Statins</li> </ul> </li> <li>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.</li> <li>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</li> </ul> |

## 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                        |
| Treating and preventing blood clots                                      | Quinidine, Dronedarone, Flecainide, Propafenone          |
| High blood pressure (hypertension)                                       | Apixaban, Dabigatran, Rivaroxaban, Warfarin, Clopidogrel |
| Lowering cholesterol                                                     | Ticagrelor                                               |
| Erection problems                                                        | Aliskiren, Lercanidipine                                 |
| Inhalers<br>Inhaled or oral medicines to relieve asthma and COPD         | Rosuvastatin, Simvastatin, Lomitapide                    |
| Cold-like symptoms caused by allergic rhinitis (nasal spray)             | Avanafil, Sildenafil, Tadalafil, Vardenafil              |
| Underactive thyroid (hypothyroidism)                                     | Salmeterol, Budesonide, Fluticasone Propionate           |
| Prostate gland enlargement                                               | Theophylline                                             |
| Heart failure or angina                                                  | Budesonide, Fluticasone propionate                       |
| Pain                                                                     | Levothyroxine                                            |
| Heroin dependence                                                        | Alfuzosin                                                |
| Bipolar disorder, schizophrenia, epilepsy, migraine or cluster headaches | Ranolazine, Ivabradine, Eplerenone, Digoxin              |
| Nerve pain or trigeminal neuralgia                                       | Fentanyl, Midazolam, Pethidine, Piroxicam                |
| Gout                                                                     | Propoxyphene                                             |
| Pulmonary arterial hypertension (PAH)                                    | Methadone                                                |
| Herbal medicines                                                         | Carbamazepine, Clozapine, Eletriptan, Lamotrigine        |
| Anxiety, problems sleeping, muscle spasms, fits, narcolepsy and ADHD     | Lurasidone, Phenobarbital, Phenytoin, Quetiapine         |
|                                                                          | Ergotamine, Dihydroergotamine, Valproic acid             |
|                                                                          | Pimozide, Midazolam, Clonazepam                          |
|                                                                          | Carbamazepine                                            |
|                                                                          | Colchicine                                               |
|                                                                          | Sildenafil, Bosentan, Riociguat, Tadalafil               |
|                                                                          | St. John's Wort                                          |
|                                                                          | 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), Viekirax (contains ombitasvir, paritaprevir and ritonavir) |
| Blood Disorder                                                          | Fostamatinib                                                                                                                                                                            |
| Hormonal contraception                                                  |                                                                                                                                                                                         |
| Illegal substances                                                      | Check COVID-19 Drug Interaction Checker                                                                                                                                                 |

### 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      | Apalutamide   | 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