FAQs on Prescribing relevant to COVID-19 Update 11th May 2022

What treatments should I use when novel coronavirus (SARS-CoV-2) infection is suspected ?

Microguide has a COVID-19 section under body systems>respiratory>COVID-19. In proven severe or critical infection (WHO definition) adults should be offered dexamethasone (or iv hydrocortisone, pregnant and breast feeding women have prednisolone/hydrocortisone)[29], and in most such patients baricitinib. Some hospitalised patients may benefit from IL-6 inhibitors, and/or neutralising monoclonal antibodies (nMABs), and/or remdesivir[11,12,25] . Selected patients at high risk of COVID-19 progression or in hospital practice of destabilising their condition will benefit up to 7 days from initial symptom onset from antiviral treatment. The oral antiviral Paxlovid® (nirmatrelvir plus ritonavir) is presently first line in the treatment pathways which include remdesivir, an nMAB or 4th line in community patients oral molnupiravir. Please see Adult Antimicrobial Guide COVID-19 section for more details of the standard of care involved in the use of these drugs. The latest NHS England guidance on treatment is at https://www.england.nhs.uk/coronavirus/secondary-care/management-confirmed-coronavirus-covid-19/clinical-medical-management/. Please ensure you have read our oxygen safety update as this is the proven and most important treatment in those hospitalised. This guidance will supplemented by updates in these FAQs and microguide as proven deliverable treatments that improve survival become known and available. Appendix 1 of this guide on availability of COVID-19 treatment options gives detail. There is now high quality evidence that hydroxychloroquine, azithromycin, lopinavir-ritonavir, convalescent plasma and interferon are ineffective in hospitalised patients[10]. At this time other medications with inhibitory proprieties on SARS-CoV-2 and combinations with low toxicity still have promise in treatment pathways for early disease but need proper clinical trials. The experience to date with chloroquine and hydroxychloroquine[13,14,15,16] and specific therapies directed at hyperimmune response[17,18] where therapy given too early is harmful but that given in a very defined sub-indication promptly is beneficial suggests that evidenced based health care practice and getting the basics right is the key to best outcome.

What treatments are available for prevention ?

Information on vaccines is in the Green Book chapter 14a, and links to national training materials can be accessed from formulary, in the Pharmacy Vaccination in COVID-19 Microguide section and the Trustnet COVID-19 vaccine section which also deals with staff vaccination. Other potentially preventative therapies are presently only available in clinical trials in the UK. The rare side effect of vaccine-induced immune thrombotic thrombocytopenia is subject to NICE guidance as it requires evolving specific and potentially complex assessment & treatment (see VITT guideline and pathway).

What treatments in suspected COVID-19 needing hospital admission are most important ?

Addressing oxygen, fluid and electrolyte issues and reviewing medications in the context of comorbid issues is essential. All patients must have oxygen charted as this can be needed at short notice, fluids charted for at least for first day and chemothromboprophylaxis charted unless contraindicated. Dexamethasone at correct dose in adults with proven COVID-19 requiring oxygen is proven to be effective at reducing mortality with an extra gain in reduction of mortality in those over 2 years old who can take safely baricitinib. In patients with a highly activated immune response or respiratory failure this can be supplemented by an IL-6 inhibitor. Sotrovimab is the only available nMAB with antiviral activity against the Omicron strain. Casirivimab and imdevimab reduces mortality in those with no anti-S (anti-Spike) antibody to SARS-CoV-2 delta strain hospitalised for acute COVID-19 and was also used where early SARS-CoV-2 infection is detected in high risk inpatients. Remdesivir reduces length of stay and if given early has an impact on mortality. **Nephrotoxic drugs must be withheld with acute kidney injury and dosages of renally excreted medicines changed**. In a patient with acute kidney injury renal excreted medications with a low therapeutic index, like digoxin and aminophylline preparations will need blood levels done. Diabetes is a

common comorbidity and its management is different in those with COVID-19. Guidelines for its management in the presence of COVID-19 can be accessed from Trust desktop and microguide. These have been updated as evidence is emerging that some diabetic medications but not others may be associated with poor outcome[1,2]. Sulfonylureas should be withheld with acute kidney injury. You must monitor the blood glucose carefully having done this using insulin preparations or titration of safe oral alternatives to maintain control. Hypotension is common and anti-hypertensive agents and alpha-blockers will need to be withheld if this occurs. **Anti-thrombotic management including extended prophylaxis has recently changed in COVID-19** – see Appendix 6, P11. Other medications such as immunosuppressive agents and other critical medications need identification of their significance, and patient specific decisions taken relevant to continuation and substitution. Most of these patients, even some that a moribund on admission, will recover with good basic care, so the medication decisions made must be clearly documented and all medications reviewed at discharge. Patients will present with rare complications of COVID-19 such as Guillain-Barre Syndrome or PMIS/MIS-C and must access promptly proven treatments.

Are antibiotics indicated in proven COVID-19 infection ?

By default **NO** if no other infection likely. While antibiotics are often initially indicated for inpatients (eg CAP/HAP - see end of Microguide COVID-19 section for important indications) their use should be re-evaluated at 48 hours and all subsequent usual review trigger points. If a patient is discharged please ensure your management is compliant with the NICE COVID-19 rapid guideline NG191: managing COVID-19.

For inpatients with significant COVID-19 disease should I prescribe low molecular weight heparin thromboprophylaxis ?

Please use at prophylactic dose, in hospitalised patients, even if clotting abnormalities develop, as in Wuhan this was associated with significantly better survival in disease with raised D-dimer and clotting abnormalities[3]. See COVID-19 specific Thrombosis Guidelines on Microguide or COVID 19 management of coagulopathy (Appendix 6 P11, below) for more details. ITU patients may need enhanced anticoagulation as per Trust guidelines. National guidelines exist.

What treatments should I use in palliation ?

The Trust in conjunction with Pilgrims Hospice has published guidance on the management of symptoms in palliation of the COVID-19 patient now v1.5. There is also a Guideline for the care of dying patients with COVID-19. Nice now covers this in NICE COVID-19 rapid guideline NG191: managing COVID-19. Appendix 3 is now accessible only via clickable link.

How do I prescribe in teleclinics ?

Please see the Procedure for issuing FP10HNC prescriptions for Clinics inc Telephone consultation clinics. See flowchart for getting FP10HNC forms but they will need to be signed out on this form if the teleclinic is not held in outpatients. Importantly as in this flowchart, if the item required is a hospital only medicine, controlled drug or even urgent the script must be done on a yellow outpatient prescription which the patient or a representative can only take to our internal pharmacy. Importantly the prescriber must keep a record on a special form of each script issued.

I have heard that there are drug shortages due to COVID-19. How will this affect patients?

Please read the patient orientated FAQ at https://icmanaesthesiacovid-19.org/drug-demand-supply-patient-faqs. More details are available for clinical staff in the documents Guidance on adaptations to

standard UK critical care medication prescribing and administration practices during pandemic emergency pressures and Guidance on potential changes to anaesthetic drug usage and administration during pandemic emergency pressures. Supply of most medications is only completely assured where historic usage is maintained. Drug supply is being coordinated nationally. Updates of ITU medication shortages are notified to ITU as they occur and an overview of the multiple current issues can be seen in the weekly medication shortage update at https://www.ekhuft.nhs.uk/staff/clinical/drugs-and-therapeutics-committee/antidote-drug-stock-lists/ There may be inconvenience to healthcare professionals and patients which are being mitigated as much as possible, in a situation where supply chains have been impacted at multiple points.

Is there access to Investigational Medicines ?

The Trust allows the use of IL-6 inhibitors, nMABs and remdesivir[11,12] which while licensed are still investigational, only available outside research where there is evidence of benefit, although they or other medications may be available for compassionate use. Prescribers will have to comply with the commissioning requirements of NHS England which are updated from time to time via the CAS alert system. The Trust is entering patients in the Randomised Evaluation Of COVID-19 Therapy (RECOVERY) trial. Prescribing guidance for the RECOVERY trial as on MicroGuide. The Trust has been stood down from ISARIC CCP data collection which took place between March 2020 to December 2021. The clinical trial situation is rapidly evolving and is coordinated through the Research and Innovation Department who must be contacted (Appendix 4, Appendix 5. Pages 8-10). A list of currently approved trials in the UK are at https://www.nihr.ac.uk/covid-19/urgent-public-health-studies-covid-19.htm. At the time of this update investigational drugs to treat COVID-19 are not available on compassionate grounds or outside formal protocols/trials agreed centrally. Such investigational drugs include those that prescribers might think there is a case for using out of license, particularly if there might be off label availability. WHO and multiple national organs have made statements on this issue, and national advice, Trust governance arrangements and expected practice by UK regulatory bodies of their registered health professionals is fully consistent with WHO[4] and pre-existing governance prior to the COVID-19 pandemic. Requests for such treatment related to COVID-19 will not be able to be fulfilled from Pharmacy at this time (see Appendix 1 Page 6) and where prescribing is identified as inappropriate will be subject to standard governance processes. Where a medication would usually be used exceptionally in an indication caused by COVID-19 infection the Trust will do its best to procure it. This would apply for example in COVID-19 associated Kawasaki like syndrome now termed paediatric inflammatory multisystem syndrome temporally associated with COVID-19 (PIMS-TS).

Should my prescribing for other conditions change ?

Generally not if the patient does not have active COVID-19 infection. There are already evidenced based changes in management of complications of COVID-19 infection and in co-morbid conditions such as diabetes mellitus. You must keep up to date with the latest Trust guidelines on microguide and latest national guidelines.

Otherwise please issue scripts unchanged from normal as to length of supply. An FAQ on medicines requiring monitoring or administration by injection by health care staff is later in this document.

A National clinical guide for the management of patients requiring immunoglobulin treatment during the coronavirus pandemic and management of supply should be adhered to.

Medicines that need to be prioritised for supporting the inpatient care of COVID-19 patients may have to be substituted where safe to do so and staff must take extra care that they are prescribed appropriately and without unnecessary wastage. Please see current national list.

As maintenance of supply chain plans are based on historic demand for medications, medications should only be changed for sound clinical reasons relevant to an individual. The risk of significant changes in supply are further shortages.

If your service makes a generalised prescribing recommendation with implications for other services there has to be coordination with other services that may be impacted and likely are facing issues you are not aware of. Needlessly to say the same applies for individual patient specific decisions. Many general issues are being handled at national level and by local well established mechanisms.

NICE has started issuing rapid guidance on aspects of COVID-19 care. Some important ones in context of ensuring correct prescribing decisions with hospital presentations are :

- NG191 Managing COVID-19 1 replaced NG159 Critical care in adults, NG173 Antibiotics for pneumonia in adults in hospital, NG165 Managing suspected or confirmed pneumonia in adults in the community, NG186 Reducing the risk of venous thromboembolism in over 16s with COVID-19, NG171 Acute myocardial injury, NG175 Acute kidney injury in hospital and NG163 managing symptoms (including at the end of life) in the community
- NG200 Vaccine-induced immune thrombocytopenia and thrombosis (VITT)
- NG177 Interstitial lung disease
- NG176 Chronic kidney disease
- NG 178 Renal transplantation
- NG161 Delivery of systemic anticancer treatments
- NG164 Haematopoietic stem cell transplantation
- NG166 Severe asthma
- NG 170 Cystic fibrosis
- NG168 Community-based care of patients with chronic obstructive pulmonary disease (COPD)
- NG167 Rheumatological autoimmune, inflammatory and metabolic bone disorders
- NG169 Dermatological conditions treated with drugs affecting the immune response
- NG 172 Gastrointestinal and liver conditions treated with drugs affecting the immune response
- NG 179 Arranging planned care in hospitals and diagnostic services
- NG 187 Vitamin D
- NG188 Managing the long-term effects of COVID-19

What do I do about therapy requiring regular monitoring or are administered by health care staff?

Where clinically indicated current arrangements should continue. Our experience is that some basic inpatient monitoring such as capillary glucose in diabetic patients is not being done when it can and must be. There is no community capacity to take on extra monitoring and individual risk assessment may be necessary. Changing patients to drugs not requiring monitoring or healthcare staff administration needs full appropriate consultation as this could impact on supply chain management. Please see Drug monitoring: factors to consider during Covid-19 at https://www.sps.nhs.uk/articles/drug-monitoring-factors-to-consider-during-covid-19/ for general national advice on the process you should go through that excludes the drug shortage issue which can only be resolved by pharmacy consideration. The pages for specific drugs are accessed at https://www.sps.nhs.uk/articles/drug-monitoring-in-primary-care-for-stable-patients-during-covid-19/ and currently specific information is available for safe extension of monitoring intervals and other details for the following medications:
Azathioprine, leflunomide, mercatopurine, and methotrexate
Penicillamine
Sulfasalazine
Hydroxychloroquine
Ciclosporin
Leflunomide and mycophenolate mofetil

Warfarin
Lithium
Clozapine
Hydroxocobalamin injection

Is it appropriate to use prescription chart to document patients COVID-19 status ?
Not under any circumstances. The Trust has communicated to staff how to document this.

Are there other treatments associated with harm or benefit in COVID-19 ?

Yes. The literature is now immense and while a number of medications are in advances stage 3 trials studies have repeatedly demonstrated that wrong drug or patient selection will do harm. Even virus variant can be important, as has probably been the case with some of the monoclonal antibodies and the now known to be net useless convalescent plasma approach. While undirected use of high dose steroids and immunoglobulin was associated with higher mortality[5], used at correct dosing where the indication is proven but associated with COVID-19 can be of benefit. The issues of increased incidence in diabetics with COVID-19 of hyperglycaemia with ketones and atypical presentations of diabetes emergencies (eg, mixed DKA and hyperosmolar states) mean all oral hypoglycaemic drugs must be reviewed against the latest national guidelines. The reasons for higher mortality in ventilated patients early in the Pandemic[6] are now better understood and should be incorporated into routine practice. There is now evidence from multiple studies that prior use of any RAAS modulating medicine is safe and these should only be withheld in acute kidney injury[1,2,15,21]. The Rheumatologists use a scoring system with their immunosuppressant therapy which is consistent with evidence to date. See https://www.ekhuft.nhs.uk/EasysiteWeb/getresource.axd?AssetID=486487&type=full&servicetype=Attachment

NHS advice based on NICE review is that use of ibuprofen and NSAIDs is safe[22,23]. See commissioning policy at https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2020/04/C0211-NSAIDs-RPS_14-April.pdf. The evidence is much weaker for other treatments so far. Oseltamivir does not work (as expected).

The view of the British Cardiovascular Society (BCS) and the British Society for Heart Failure (BSH) joint statement on the 16th March 2020 on the treatment of patients with ACEi or ARB in relation to COVID-19 was: "*that both organisations share the view of the European Society of Hypertension and the Renal Association that patients should continue treatment with ACEi and ARB unless specifically advised to stop by their medical team*." This advice can now be extended to all drugs inhibiting the renin-angiotensin-aldosterone system. Our cardiologists had issued advice, which is in Appendix 2 Page 7 of this document. The hypothesis that these medicines may be beneficial exists[7] and in the case of ACE inhibitors is backed by epidemiology showing prior use is associated with mortality reduction[1,2,15].

There is preliminary evidence that concurrent PPI (proton pump inhibitor) treatment is associated with poorer outcome in hospitalised patients with COVID-19[19,20]. This means that the risk benefit decision, particularly in the situation of new use for gastric protection and current absence of alternatives needs to be both individualised and weighed carefully with reference to the current literature. Established patients should at this time be continued on a PPI if there is a good indication, but as always PPI use should be reviewed. Many clinicians are unaware that long term use of PPIs prior to COVID-19 was associated with a general and condition dependent increase in mortality probably for complex reasons[21].

Where do I get further information ?

Information will change and you should regularly review the Trust Coronavirus (COVID-19) pages at https://www.ekhuft.nhs.uk/staff/news-centre/coronavirus/ and the NHS Coronavirus guidance for clinicians page at https://www.england.nhs.uk/coronavirus/ The NICE COVID-19 page is at https://www.nice.org.uk/covid-19 . At this time national guidance and speciality interim guidelines are being updated frequently and important changes have occurred. Established Trust sources of information like Formulary or Microguide are regularly updated with latest COVID-19 information (eg try a search string like "Covid-19").

What information is used to prepare this review ?

The peer reviewed literature is reviewed for every update. WHO now maintains a list of vaccines in development[8] and the development pipeline of pharmaceuticals is monitored by established NHS horizon spotting mechanisms. It is possible that non-peer reviewed and peer reviewed non-English publications will be missed and staff should draw these to the attention of the lead author/director of pharmacy with an English translation. In practice medicines management has become aware of significant advances in therapy before formal e-publication, or communication via well established local, national and international network arrangements.

Lead Author: Dr M L Jenkinson Lead Clinician Drugs & Therapeutics

APPENDICES FOLLOW:

Appendix 1. **AVAILABILITY OF COVID-19 TREATMENT OPTIONS**

Please be aware that the following medications, which have been proposed in literature as potential treatment options for COVID-19, are NOT available for routine use in COVID-19 this time (Green are routine in some specific COVID-19 presentations and dangerous or ineffective in others).:

1. Nirmatrelvir (PF-07321332) + ritonavir▼*®
2. Remdesivir▼*®?,10,9,10
3. Molnupiravir* ▼
4. Lopinavir + ritonavir (Kaletra)√*®11,12,30
5. Hydroxychloroquine√₸*® ‡10, 13,14,15,31
6. Azithromycin√*®‡
7. Chloroquine√10,14,16
8. Teicoplanin√‡
9. Chloramphenicol√
10. Tetracyclines√‡ - doxycycline is NICE recommended antibiotic of choice in CAP potentially associated with COVID-19*®
11. Isoniazid√‡
12. Ivermectin√
13. Itraconazole
14. Fluconazole√‡
15. Cefuroxime√‡
16. Cefamandole
17. Chlorhexidine√‡
18. Interferons including interferon beta√1?,10
19. Tocilizumab√?®17*▼
20. Sarilumab®*▼
21. Anakinra√?18 N▼
22. Any Sartan√*₸‡N
23. Any betablocker √‡
24. Colchicine √‡
25. Nicardipine√‡
26. Digoxin√‡
27. Alfuzosin√‡
28. JAK inhibitors such as Ruxolitinib√, Upadacitinib√, Filgotinib√ but not Baricitinib*®▼√
29. Pemetrexed√
30. Fludarabine√
31. Isotretinoin√
32. Intravenous Immunoglobulin√†1▼
33. Nitazoxanide®√
34. Systemic Steroids (Dexamethasone) ▼
35. Fludrocortisone √‡
36. Inhaled corticosteroids▼√® ‡
37. Estradiol√‡
38. Tibolone√‡
39. Montelukast√‡
40. Cromolyn
41. Theophylline√‡
42. Fluvoxamine* or any SSRI/σ-1 receptor (S1R) agonist √‡®
43. Thymidine
44. Any licensed antiviral not otherwise specified√
45. Oseltamivir (unless influenza√)
46. Darunavir/cobicistat
47. Bevacizumab*√
48. Convalescent plasma√®
49. Any monoclonal antibodies not specified. casirivimab/imdevimab▼*, Meplazumab® sotrovimab▼
50. Iloprost or epoprostenol ▼
51. Disulfram√‡
52. Eculizumab√‡
53. Griffithsin
54. Chlorphenesin carbamate
55. Dantrolene√‡
56. Pancuronium bromide√
57. Niclosamide
58. Levodropropizine
59. Bromocriptine√‡
60. Dabigatran√‡
61. Ascorbic acid/ Vitamin C√‡
62. Riboflavin√‡
63. Lutein
64. Chenodeoxycholic acid
65. XueBiJing® or other herbal medicines
66. Levosimendan▼
67. Nitric oxide(inhaled) √®
68. Sildenafil and analogues√?
69. Magnesium√
70. Zinc and zinc ionophores (eg pyrithione zinc)√‡
71. Famotidine√®‡
72. Omeprazole and other PPIs √‡19,20,21
73. Sulfasalazine√‡
74. Statins such as Simvastatin√‡
75. Melatonin√
76. Lenzilumab*
77. Avitadil®
78. Nintedanib*
79. Heparin/Low molecular weight heparins*®/DOACs*®

▼Needs use according to NHS commissioning criteria or ▼ individual patient medicines management approval for use
† Associated with marked increase in mortality from early non clinical trial data
Ŧ Associated with slight increase in mortality from overview of early studies possibly due to confounding
*Emerging RCT evidence, available in RCT in Trust or if made available in Trust outside RCTs will be subject to pre-license extension studies. Please see https://www.bio.org/policy/human-health/vaccines-biodefense/coronavirus/pipeline-tracker
®Published studies - not licensed/routinely available/used in RCT in Trust and/or significant harm, no significant benefit or benefit unclear. Please see https://www.bio.org/policy/human-health/vaccines-biodefense/coronavirus/pipeline-tracker
‡ May be appropriate to continue if patient on it prior to admission
√ Only available for use in other indications routinely used and commissioned prior to COVID-19
? Usage likely to be constrained by supply issues even in established indications. Being actively considered for indication but not available routinely. [N] NICE rapid evidence summary exists [18,22,23,24,25].
Numbered superscripts refer to references below. Medicines with good evidence for repurposed use are removed from the list[26,27,28].

The data supporting the use of these medications in COVID-19 indications is limited and there is currently not enough evidence available to show that the benefits of treatment outweigh the risks of these medications In addition, use for this indication has not been approved by the Drugs and Therapeutics Committee. There are mechanisms in place to rapidly add proven therapies such as dexamethasone[29] to the pathway of care and to note therapies without benefit[30,31].

Stock of many of these medications is controlled by central procurement teams across the country with the Trust under strict instructions not to use our 'local' stock for treating COVID-19. This is to preserve the limited stock we have available nationally for the long-term conditions for which they are intended.

Requests for treatment of COVID-19 will not be able to be fulfilled from Pharmacy at this time, including those on private prescriptions.

Lead Author: Will Willson, Director of Pharmacy Last updated: 06/03/2022

Appendix 2. **ACEI and ARBs and COVID 19**

There has been considerable attention drawn toward whether patient taking Ace-inhibitors, (such as ramipril, lisinopril, perindopril etc) Angiotensin Receptor Blockers (such as candesartan, olmersartan, losartan, valsartan etc) and Entresto (Valsartan/Sacubutril) are more susceptible to Coronovirus (COVID-19).

Having reviewed the evidence and recommendations from the European Society of Cardiology (ESC), the consensus statement from the East Kent Hospital's Cardiologists as of March 18th, 2020, is for patients on these medications for heart failure, diabetes or high blood pressure to continue taking them. There is no good quality evidence at present, that these medications make patients more susceptible to COVID-19 or lead to more severe infections in those already infected. Stopping these medications, particularly in patients with heart failure, is likely to lead to significant harm. We would advise against patients contacting or attending their surgeries to discuss making medication changes at this time.

In the event of new, good quality evidence being released which shifts the consensus opinion, information and recommendations will be cascaded through the existing channels to primary care. For now, it should be reiterated that patients should remain on their ace inhibitor, angiotensin receptor blocker and Entresto medications.

Dr Jane Fisher

Consultant Cardiologist and Clinical Lead for Cardiology, East Kent Hospitals University Foundation Trust

Dr Dominika Budzbon

Consultant Cardiologist, Heart Failure Lead, East Kent Hospitals University Foundation Trust

Appendix 3 – Management of symptoms in palliation of the Covid-19 patient is now at https://www.ekhuft.nhs.uk/EasysiteWeb/getresource.axd?AssetID=485744&type=full&servicetype=Attachment

Appendix 4. *Message from Ms Jessica Evans- Director of Research and Innovation - 2ND April 2020 (amended 11th April 2020 and 5th June 2020) Acknowledgements to Drs Neil Richardson and Christian Linares.*

Dear all

The level and extent to which healthcare professionals are coming forward and asking to be involved in COVID19 research has been fantastic!

As you will more than be aware there are a number of COVID19 studies, some portfolio and powered and selected to attain meaningful data, others that are less robust.
There are currently there are no approved treatments for COVID-19.
Any other treatment apart from oxygen is experimental, and should only be given within a trial setting.

Research during this phase of the COVID19 pandemic is key in halting its progress and is of the highest importance.
The research delivery teams based at each site have already reviewed and halted all non-essential research to prioritise COVID 19 research.
Their role is to set up and support clinical teams to undertake this research. They are usually easily recognisable by their purple uniforms!

Current status:

RECOVERY is a randomised trial and COVID-19 (amended suspected and proven) inpatients in the UK over the age of 18 may be enrolled. See the multiple critical updates on the RECOVERY Trial, as the protocol has changed .

MEMORANDUM

Appendix 5. **COVID-19 CLINICAL RECOVERY TRIAL**

TO: All Clinical Staff

FROM: Hayley Blackgrove, Lead Clinical Trials Pharmacy Technician

DATE: 21/04/2020 – updated 27/12/2020

This study aims to compare different treatments that may be useful for patients with COVID-19. These treatments have been recommended by the expert panel that advises the Chief Medical Officer in England. Although these treatments show promise, nobody knows if any of them will turn out to be more effective in helping patients recover than the usual standard of care. Patients suspected (as well as proven) SARS-CoV-2 infection are eligible for this study. Full information is available at https://www.recoverytrial.net/

Other information in this appendix has now been archived

Appendix 6.

COVID-19 and Haematology SOP v 4.6

The master copy of this Appendix is available from microguide

Appendix 7 Antiviral Agents -Prescribing updates Remdesivir, Dexamethasone, IL6-inhibitors and nMABs since start of Pandemic

These are now archived except for the latest one. Please see NICE COVID-19 rapid guideline: managing COVID-19 at https://www.nice.org.uk/guidance/ng191 as the NICE updates to this guideline are expected to be immediately implemented in Trust practice.

Updated clinical guidance for the treatment of hospitalised and non-hospitalised patients with Covid from 10th February 2022 09/02/2022 v1.1

The commissioned guidance for both cohorts of patients will be changing on the 10th of February 2022 to include the addition of Paxlovid®, an oral antiviral nirmatrelvir1 combined with a potent CYP3A4 inhibitor – ritonavir. This is now first line in treating patients who are at high risk of progression to serious COVID-19 have confirmed early SARS-CoV-2 infection. Please see and use microguide from 10th February which will be updated with details.

In contrast to other available COVID-19 treatments, Paxlovid, because of the ritonavir component, interacts with a significant number of other drugs likely to be prescribed in patients eligible for treatment.

Such interactions can be potentially very serious and prescribers must familiarise themselves with the risks of this, not only in adding such treatment to a patient's current medication but the subsequent effects on treatment having completed the 5-day treatment course. The changes are as follows

A) Hospitalised patients

1) Group 1. Patients hospitalised for acute COVID-19 illness:

Given the lack of effectiveness of Ronapreve (casirivimab and imdevimab) against the omicron variant there are no changes for patients admitted to hospital due to COVID-19 who are ineligible for casirivimab and imdevimab; however, they may be considered for entry into the RECOVERY trial, which is studying sotrovimab versus standard of care.

2) Group 2. Patients with hospital-onset COVID-19

Who meet the criteria for treatment will be eligible to receive with one of the following:

First-line: Paxlovid (nirmatrelvir plus ritonavir) – oral – 5-day course
Second-line: Remdesivir – intravenous 3-day course
Third-line: Sotrovimab – single dose

Accompanying this letter is the national pathway document for all these therapies for patients with symptomatic hospital-onset COVID-19 which has details including the pathway of assessment, details of the cohorts and interacting drugs for Paxlovid.

B) Non-hospitalised patients - via the Covid Medicines Delivery Unit (CMDU)

Those eligible patients will be eligible for treatment with any one of the four currently available medicines if SARS-CoV-2 infection is confirmed

First-line: Paxlovid (nirmatrelvir plus ritonavir) **or** sotrovimab, as clinically indicated

Second-line: Remdesivir
Third-line: Molnupiravir (oral antiviral)

Pharmacy will be available to support and advise on prescribing, especially given the significant risk of interactions with the prescribing of Paxlovid.

Given the eligibility criteria, it is imperative that teams from the key clinical specialties who have patients in the highest risk groups are familiar with the risks of paxlovid and available to

advise/support prescribing decisions that may have significant impact for their patients. The at risk groups while detailed in the accompanying document affect the following specialities:

- Renal medicine, dialysis and transplant
- Hepatology
- Clinical Haematology
- Oncology (in particular the acute oncology service)
- Immunology
- Rheumatology
- HIV
- Neurology
- Learning disability

In the case of hospitalised patients who acquire SARS-CoV2 while hospitalised the clinical team caring for the patient MUST assess as soon as the patient becomes symptomatic to see if the patient is in a high risk of progression group. This includes patients (in this group alone) where COVID-19 infection presents a material risk of destabilising a pre-existing condition or illness or compromising recovery from surgery or other hospital procedure (as determined by multidisciplinary team [MDT] assessment [2]).
Microguide will be updated with information and advice and the following documents are available providing additional information
1. Advice on prescribing interactions for paxlovid: https://www.sps.nhs.uk/wp-content/uploads/2022/01/Paxlovid-SPS-20220202.pdf

2. Interim clinical commissioning policy for hospitalised patients (CAS alert): https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103192

3. Interim clinical commissioning policy for non-hospitalised patients (CAS alert): https://www.cas.mhra.gov.uk/ViewandAcknowledgment/ViewAlert.aspx?AlertID=103191

[1] Also known as PF-07321332

[2] A minimal MDT would in hours (and these decisions can be in daylight hours 7 days a week) be 3 senior clinicians, such as the requesting consultant, a relevant other specialist, a microbiologist/lead clinician D&T or a senior pharmacist. The MDT team decision should be documented in the clinical record. MDT decision making is not required in adults when a patient falls in an at risk group as defined in the commissioning criteria. Paediatric patients always require a MDT decision.

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