**RECOVERY TRIAL - CLINICAL INFORMATION**

Eligibility

* Adult patients (18+ years old) hospitalised with confirmed COVID-19.

Prescriber

* Any doctor working within the hospital can prescribe for this study. They do not require GCP training and do not have to be on the delegation log; however they should have completed online Recovery study training.

Randomisation

* Randomisation will take place on a central web-based randomisation service and will be 2:1:1:1:1 to the following treatment arms
* The randomisation form should be **printed** and **attached** to the drug chart by the doctor or member of the research team doing the randomisation.

Prescription

* This will be prescribed on the drug chart using the stickers provided for standard dosing. Prescribers are permitted to modify or stop treatment if deemed to be in the patient’s best interest, this does not mean the patient must be withdrawn from the study as follow up can still continue.

Ordering a Supply

* Firstly check that the randomisation form matches the drug prescribed.
* Consider if a supply has been taken from the emergency drug cupboard (EDC) out of hours.
* If a supply needs to be ordered from the dispensary use the order form that has been created (unless there has been dose modification)
* Check the prescription on the drug chart matches the order form and tick the supply you need – send this to the dispensary
* Hospital stock of dexamethasone (all forms) is currently being used so if not already stock on the ward please request a supply of this – it does not need to be ordered via the order form or from dispensary. At some point this will be provided by PHE at which point it will be ordered from dispensary.

Storage on the ward

* No temperature monitoring is required
* Keep IMPs (hydroxychloroquine, lopinavir/ritonavir, interferon) separate from ward stock to prevent RECOVERY medications being used for patients not part of the RECOVERY trial – this is not necessary for dexamethasone as using normal hospital stock (see above).

Out of Hours (On-Call)

* A small supply of all open treatment arms will be available in the EDC – this will be stored on the right hand side of the shelving, in a ‘RECOVERY’ box with a form for nursing staff to record what has been taken.
* Currently the interferon arm is not open and Kaletra liquid is not available therefore no items should be in the EDC fridge at this time however, once these are open/ available a small supply will be available in a designated RECOVERY section of the EDC fridge.

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| **Treatment Arm** | **Dose**  **All for 10 days or until discharge (whichever is sooner)** | **Notes** | **Contraindications & Cautions** | **Renal / Hepatic dose adjustments** | **Interactions** | **Side Effects** |
| **Arm 1 - Standard treatment** | n/a | n/a | n/a | n/a | n/a | n/a |
| **Arm 2 – Lopinavir/ Ritonavir** | 400mg / 100mg BD PO | If liquid is needed only 1 x 60ml bottle should be ordered and the patient should be switched to tablets as soon as possible due to stock shortages.  Tablets cannot be crushed and the liquid is incompatible with polyurethane feeding tubes so PVC or silicone tubes should be used (dieticians are aware of this).  Liquid contains 42% v/v alcohol – avoid metronidazole with this.  Liquid is stored in the fridge but once removed is stable for up to 42 days at <25oC.  Protocol states it has been widely used in pregnant women. | C/I in severe liver impairment | No adjustment needed for renal impairment.  No dose adjustment needed for mild – moderate hepatic impairment. | Lopinavir/Ritonavir should not be co-administered with medicines that are dependent on CYP3A for clearance.  Alfuzosin, amiodarone, ranolazine, neratinib, colchicine, quetiapine, simvastatin, sildenafil, midazolam, ergot alkaloids, St John’s wort. (see SmPC for full list)  **It is essential to check individual interactions**  **SEE LIVERPOOL DRUG INTERACTIONS &**  **http://www.covid19-druginteractions.org** | Common - diarrhoea, nausea, vomiting.  Upper respiratory infection, hypersensitivity, blood glucose and lipid disorders, anxiety, headache, dizziness, insomnia, hypertension, neuropathy, hepatitis, myalgia, fatigue. (see SmPC) |
| **Arm 3 – Interferon beta 1-a** | 6MIU (0.5ml + 0.15ml overage) OD via nebulisation | Given via I-Neb (provided by sponsor)  Parenteral interferon has been used in pregnancy.  Stored in the fridge (2 – 8oC*)*  Inhaled interferon is unlicensed and is still under investigation. | C/I in severe liver impairment |  | n/a | For **systemic** use:  Flu-like symptoms, injection site reactions, decreased white blood cell count, hypertonia, chest pain. |
| **Arm 4 - Dexamethasone** | 6mg OD IV/ PO | 6mg dose is of dexamethasone base therefore 6mg IV = 1.8ml of the 3.3mg/ml IV solution. | Patients on long term (2+ months) corticosteroids should be excluded from this arm as they may need increased dose due to sick day rules. | No dose adjustments required. | n/a | Hyperglycaemia |
| **Arm 5 - Hydroxychloroquine** | 800mg at 0 + 6 hours, then 400mg at 12 and 24 hours. Then 400mg 12 hourly thereafter. | No dose adjustment needed for body weight.  Tablets may be crushed and dispersed in water to give via NG or in swallowing difficulties.  Doses are much higher than those seen in the BNF and SmPC but are in line with doses used by the WHO. | Contraindicated in prolonged QT interval.  Caution with other drugs that prolong QT interval (macrolides, quinolones) – consider ECG to check QT interval.  SmPC states contraindicated in pregnancy however protocol states prophylaxis of choice as anti-malarial. | Trial states no dose adjustment for renal impairment due to the short course needed. | Digoxin (increased levels), anti-diabetics (hypoglycaemia), antacids (reduce absorption), ciclosporin, tamoxifen. | Dyspepsia, nausea, vomiting (occasionally), visual disturbances, headache, urticaria.  Hypoglycaemia, rash, dizziness (uncommon), anorexia. (See SmPC for more) |

* Information in red is taken from the SmPC and not the trial protocol – see references below.
* Trial Protocol & Pharmacy Information is available at <https://www.recoverytrial.net/>

References

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