Pharmacy Technical Review Form for CTIMPs

Please note that Pharmacy Assurance will be provided based on the study documents listed in Section 2. Amendments will not be reviewed through Pharmacy Assurance.

Sponsors and participating sites: guidance is available on the IRAS website about how to provide feedback if you have a query or concern regarding the information provided in this form. See https://www.myresearchproject.org.uk/help/hlppharmacyassurance.aspx

Part 1: Study identification. To be completed by lead nation administrative support (All nations)

Section 1: Study Identification	
Pharmacy Specialisms	Adult Oncology ☐ Paediatric Oncology ☐ Adult Non-oncology ☒ Paediatric Non-oncology ☒ Radiopharmacy ☐ ATIMPs ☐
Full Protocol Title	Randomised Evaluation of COVID-19 Therapy (RECOVERY)
Study Acronym (if applicable)	RECOVERY
Sponsor Protocol Reference	NDPHRECOVERY
NRS ID Number (Scotland only)	N/A
EudraCT Number	2020-001113-21
IRAS Number	281712
Sponsor Organisation	University of Oxford

Section 2a: Documents reviewed as part of original submission		
Document	**Version Number**	**Date**
Corticosteroid [Dexamethasone 0.5mg tablets]	NA	16 May 2018
IB Interferon beta-1a (SNG001)	11	05 March 2020
IRAS_Form	N/A	13 March 2020
Lopinavir Ritonavir [Accord 200mg 50mg film-coated tablets]	N/A	09 March 2020
RECOVERY Protocol	2.0	23 March 2020
SNG001 IMPD	3	20 August 2019
Recovery Clinical Trial Pharmacy Breifing Document (FAQ online)	accessed 9am 23-Mar-2020	
Hydroxycholorquine SmPC		10 March 2020

Section 2b: Documents reviewed as part of SA3 14 April 2020 submission		
Document	**Version Number**	**Date**
Azithromycin 500mg tablets SmPC		Updated 25 September 2019
Hydrocortisone 100mg/ml solution for injection SmPC		Updated 02 November 2018
Prednisolone 10mg Tablets SmPC		Updated 18 February 2020
Tocilizumab 20 mg/mL concentrate for solution for infusion SmPC		
RECOVERY Protocol	4.0	14 April 2020
Recovery Clinical Trial Pharmacy Breifing Document (FAQ online)	4.0	22 April 2020

Section 2c: Documents reviewed as part of Protocol version 5 submission		
Document	**Version Number**	**Date**
RECOVERY Protocol	5.0	24th April 2020
RECOVERY Clinical Trial Pharmacy Breifing Document (FAQ online)	4	24th April 2020
RECOVERY Paediatric Guidance	2	7th May 2020
Methylprednsiolone SmPC	N/A	July/2019

Section 3: Details of Sites	
Number of sites in UK at initial submission	120
Total recruitment planned in UK at initial submission	See A59 in IRAS form
Does the study involve Primary Care?	No

Part 2: Technical pharmacy review. To be completed by HRA Pharmacy Reviewer(s) (All nations)

Section 4: Study Summary	
a) Description of study treatment regimen Brief summary to be used as a reference, include full information on doses, routes of administration, timing of administration, length of infusion (if applicable), blinding and placebos	Randomised trial in adults hospitalised for confirmed COVID-19. Treatment inteventions to be given alongside usual standard of care in hospital. Arms (randomised 2:1:1:1 ratio or where arm(s) not appropriate for participant/available at site this will change to 2:1:1 or 2:1 ratio): No updated infomration on the change of ratio based on there being 5 arms in protocol V2 Arm 1: No additional treatment Arm 2: Lopinavir-Ritonavir 400/100mg PO (or ng tube) every 12 hours for 10 days or until discharge Arm 3: Interferon -beta-1a - nebulised 6MIU (0.5ml of solution containing 12MIU/ml) OD for 10 days or until discharge Arm 4: Dexamethasone PO liquid or IV 6mg OD for 10 days or until discharge (permitted to switch between PO/IV according to clinical circumstances) Arm 5: hydroxychloroquine PO 800mg initial dose,, +6hrs 800mg, +12hours 400mg, +24hours 400mg, then 400mg ewvery 12 hours thereafter for 9 days Where not all treatments are available at the participating site fewer arms will be used. other arms may be added if evidence emerges for suitable treatments. Where there is a specific contraindication to one of the active treatment arms the patient will be excluded from randomisation to that arm Standard pharmacy reviews of patients (usually within 48hrs enrollment) will guide modifications to study treatment and use of concomitant medication (i.e.: for drug interactions) Amendment Protocol V4.0 (incorporating changes also made in V3 of protocol)- removal of interferon arm. Change of inclusion criteria to include suspected COVID patients. Inclusion of infomration regarding pregnant patients. Addition of

	Azithromycin 500mg OD by mouth (or ng tube) or IV for 10 days or until discharge (whichever occurs first) Second randomisation for patients with progressive COVID-19 to receive no additional treatment or tocilizumab (1:1). All doses given in 100ml NaCl 0.9% over 60min IV infusion >40 to <=65kg dose is 400mg >65 to <=90kg dose is 600mg >90 dose is 800mg for patients less than 40kg dose should be 8mg/kg and may be adminsitered in 50ml bag of NaCl 0.9% Pre-pregnancy weight should be used in pregnant participants Dose can be repeated >=12hours and <24hours later if patients condition has not improved. Patients must have been enrolled in RECOVERY no more than 21 days prior to date of planned second randomisation. Second randomisation may happen at any point after first being randomised and therefore may receive up to 2 study treatments In pregnant or breastfeeding women dexamethasone should be substituted for prednisolone 40mg PO OD (or IV hydrocortisone 80mg BD). It is permitted to switch between routes of administration according to clinical circumstances. Amendment Protocol V5.0: - Inclusion criteria of "aged at least 18 years" have been removed. Patients of all ages are now eligible for RECOVERY. - Protocol should be read in conjunction with the paediatric guidance. - Paediatric patients will be eligible for all arms. However, there are certain age restrictions for: Lopinavir-Ritonavir arm will not be open to preterm infants with a corrected gestation age of <42 weeks or neonates with postnatal age of < 14 days Corticosteroid arm will include different corticosteroid options (hydrocortisone for neonates <40 weeks, dexamethasone, prednisolone or methylprednisolone) at the discretion of the treating clinician. Hydroxychloroquine arm will not be open to infants with postnatal age of < 180 days. Paediatric dosings provided in Appendix 3 of the protocol

Section 5: Pharmacy Resources	
a) Type of Study	Dispensary ☒ Aseptic ☐ Radiopharmacy ☐
Set up, management and close-down costs	
a) Set Up/Close Down type	Type A ☒ Type B ☐ Type C ☐ Type D ☐
Additional resource information	
a) Dispensing schedule Include number of dispensing and frequency	once for the 10 days - if sites can and they are able to, the medication may be packed down into patient packs to enable easier recruitment/dispensing processes Amendment protocol V4.0 - second randomisation for tocilizumab - up to 2 doses per participant may be dispensed as detailed in section 4
b) Duration of treatment E.g. 13 days/6 cycles/2 years/until disease progression	10 days or until discharge cannot comment in the box below - randomisation etc canbe carried out 24/7 so provision for medication is required within 6 hours ideally (confirmed via email to Sponsor) Amendment protocol V4.0 - second randomisation may be started up to 21 days after first randomisation
c) Does the protocol dictate dispensing out of hours?	Yes ☒ No ☒

Section 6: Treatment allocation/Randomisation/Blinding	
a) Is Pharmacy blinded?	Yes ☐ No ☐ N/A ☒ open label
b) If local pharmacies will be involved in repackaging and/or relabelling open-label medication to blind, give details	N/A
c) Will Pharmacy be involved in treatment allocation?	Yes ☐ No ☒ N/A ☐ randomisation by clnician via web based system
d) How will Pharmacy be notified of treatment allocation details?	Select: Email sent to person randomising - suggest this is comminicated to pharmacies in whichever form is easiest for each individual site. Pharmacy not being cc'ed into email randomisation but information is available on website to any user - confirmed via email with Sponsor
e) Can randomisation be done in advance of patient visit?	No
f) Does dispensing need to be verified on IXRS by Pharmacy, and if so does it need to be done in real time?	Yes ☐ No ☒ N/A ☐

g) Can Pharmacy dispense from the IXRS system in advance of patient visits? If yes, specify the timescale for this.	Yes ☐ No ☐ N/A ☒

Section 7: Emergency Unblinding	
a) What is the process for emergency unblinding?	N/A
b) Will Pharmacy be involved in emergency unblinding?	Yes ☐ No ☐ N/A ☒

Section 8: General Funding	
a) Are there likely to be excess treatment costs or other local funding implications?	None expected - Kaletra and hydroxychloroquine FOC from Sponsor - this pandemic is a unique situation for a clinical trial to be in Amendment protocol V4.0 - Azithromycin and tocilizumab (in addition to lopinovir/ritonivir and hydroxychloroquine) to be supplied by site until the point of it being available FOC from DHSC via ImmForm
b) Where product(s) are not supplied free of charge, are they supplied at a discounted rate for the duration of the trial?	Yes ☐ No ☐ N/A
c) Is information given on compassionate use/ongoing supply after the trial finishes? Include arrangement details and whether there is written confirmation of the exit strategy.	Yes ☐ No ☐ N/A ☒ finite treatment course
d) Other/Comments	N/A

Section 9: Further Information on Study	
a) Method(s) permitted for calculating BSA (body surface area)	N/A ☒ Du Bois ☐ Mosteller ☐ Local practice ☐ Other (please specify) ☐
b) Method permitted for calculating dose based on weight	N/A ☐ IBW ☐ ABW ☒ Amendment protocol V4.0 - second randomisation for tocilizumab - estimated BW may be used if ABW not able to be measured. Amendment protocol V5.0 - Confirmed with sponsor that esimated BW may be used if unable to obtain ABW.

c) Are methods permitted for calculating BSA/weight detailed in the protocol?	N/A ☐ Yes ☒ No ☐ See above
d) Method(s) permitted for calculating GFR (glomerular filtration rate)	N/A ☒ Cockcroft-Gault ☐ Local practice ☐ Other (please specify) ☐
e) Blood test validity periods/Frequency specified	N/A

Section 10.1: Product Information	
Description and Product Type	
a) Description of Product Include name, strength, concentration, volume, form e.g. Drug A 100mg in 5ml Injection (10ml vial)	Lopinavir/Ritonavir 200mg/5mg film coated tablets -…these cannot be put down an ng tube. Liquid would be used to admin via ng. Also issue with using liquid with certain tubes - see liverpool HIV drug interation website. Solution not recommended for use with polyurathene feeding tubes. . Update 23-Apr-2020: PHE only have 100mg/25mg (pack size 120) and 200mg/50mg (pack size 60) in stock for sites to order Update 11-May-2020: Oral solution is still not available. 100/25 tablets will now be restricted to sites recruiting paediatric patients only. See FAQ V4 for details on obtaining/confirming compatible feeding tubes for liquid adminsistration If patient moved to ICU it is likely this medicaiton would need to cease due to inability to adminsiter via ng tube and potential to interact with ICU drugs i.e.: midazolam.
b) Is the product an IMP (investigational medicinal product) or AMP (auxiliary medicinal product)?	IMP ☒ AMP ☐
c) Are all the drug names correct (i.e. rINN)?	Yes ☒ No ☐
d) Route of administration (include detail of timing in relation to food and how to take etc.)	Oral every 12 hours with or without food. Liquid with food Protocol V5: Paediatric dosing added
e) Licence status	Licensed outside this indication
f) Properties of product requiring special attention	N/A ☒ Cytotoxic ☐ Monoclonal Antibody ☐ Cytotoxic Monoclonal Antibody ☐ Cytostatic ☐ Biological ☐ ATMP ☐ Radiopharmaceutical ☐ Other (please specify) ☐
g) Is it a controlled drug?	Yes ☐ No ☒ N/A ☐

If yes, include details of Sponsor's arrangements for safe and secure handling of drug	
h) If it is a controlled drug, which schedule is it in?	N/A ☒ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐
i) Will additional licenses be required?	Yes ☐ No ☐ N/A ☒
Dose banding and capping	
a) Is dose banding permitted? If nationally dose banded drug, is the use of national dose banding table permitted?	Yes ☐ No ☐ N/A ☒ Dosing in paeds provided as weight bands
b) What dose capping/rounding protocols are permitted?	N/A Weight based dose banding for paediatrics
Product Source	
a) Source of product	Other (please specify) Supply via specific route via PHE - see FAQ on website. Sponsor to clarify still the route of access for the devolved nations Amendment protocol V4.0 - liquid still not available for use via ImmForm (DHSC) 27th April 2020 - Oral solution still not available 11th May 2020 - Oral solution still not available
b) If the product is to be sourced from commercial stocks, will it be reimbursed?	Yes ☐ No ☐ N/A ☒
c) If the product is to be sourced from commercial stocks, can any brand be used?	Yes ☐ No ☐ N/A ☒
d) Is the use of pre-filled infusion bags and/or syringes procured through a third-party manufacturer permitted?	Yes ☐ No ☐ N/A ☒
Packaging and Storage	
a) Packaging of IMP E.g. Primary: in HDPE bottles with child resistant cap; Secondary: 1 carton (kit) contains 2 bottles. Dimensions: Kit dimensions – 12x20x10cm	Commercial supplies to be used supplied via centralised route - currently only tablets in stock for use. No information on kit dimensions. Info from FAQ online
b) Storage conditions of the product E.g. 2-8°C. Include details of temperature monitoring requirements and temperature deviation procedures	tablets as per SmPC - no specific requirements. Liquid store in fridge Update 23-Apr-2020 - Tablets from Mylan are in bottles and are stable out of the original container for up to 120 days Liquid can be stored out fo the fridge for up to 42 days - add date of removal from fridge to the bottle.

	query made to sponsor regarding the reduced expiry of pack down of the Hetero brand. Response from Sponsor by email - they are in discussions with PHE regarding this and how sites are to manage the stock appropriately.
c) Storage space requirements for initial supplies i.e. details on size of initial shipment	Likely that sufficient tablets covering 100 patients having a 10 day course will be supplied from central stock - info in FAQ online
Product Preparation	
a) Provide detailed information on methods of reconstitution/dilution/preparation Include information on diluents, time to dissolve/reconstitute, container compatibility, equipment (filters etc.) and safety handling requirements, detail on any drug/drug compatibility	N/A Amendment 23-Apr-2020: there is need to dispense required number of tablets for a patient or allocate to a wrd/area stock holding to be used for more than one patient. Do not dispense whole packs. Dispensing for adults: 200/50mg tablets - dispesne 40 tablets for the 10 day course 100/25mg tablets - dispense 80 tablets for the 10 day course 400/100mg in 5ml liquid - supply 60ml bottle initially and switch to tablets asap to limit wastage of stock.
b) Does the Sponsor require product preparation in an aseptically controlled environment, or can it be prepared using aseptic manipulation in a general area?	N/A
c) Stability and storage requirements of reconstituted/diluted/prepared product of those requiring aseptic manipulation E.g. Diluted solution to be stored at room temperature for no more than 12 hours after preparation	N/A
d) Are all drug formulations appropriate to the patient population (e.g. liquids for paediatrics)?	Yes ☒ No ☐ tablets and oral liquid (for ng administration) to be allowed
IMP/AMP Labelling	
a) Are the drug labels available for review?	Yes ☐ No ☐ N/A ☒
b) For IMP(s), are these compliant with Annexe 13?	Yes ☐ No ☐ N/A
c) Is there any other information that should be on the labels?	N/A
d) Are sites allowed to use their own labels in their local format?	Yes ☒ No ☐ sites are able to add their own labels in order to facilitate the management of the study however is most appropriate at their site - info from email from Sponsor

e) Are sites required or permitted to add their own dispensing labels?	Yes ☒ No ☐ as above
f) Is there consistency between drug names in the protocol and on the label?	Yes ☐ No ☐ N/A
Management of IMP/AMP	
a) Will the Sponsor provide prescription forms or is it permitted for sites to use their own? If it is permitted for a site to use their own, will the Sponsor need to approve the prescription forms?	sites to manage as usual methods - copies of prescription charts not expected to be placed in a pharmacy file/TMF - email confirmation from Sponsor
b) Accountability requirements Check if site's own accountability logs may be used	Nil - FAQ online
c) How will receipt and re-ordering of IMP/AMP be done?	Other (please specify) via ImmForm via Movianto - see FAQ for details.
d) How is the IMP transported from supplier to site? E.g. use of TempTale® device, requirement to return shipping box on receipt. Include any specific requirements for transportation of IMP from pharmacy to clinic on site	PHE to deliver next working day (M-F) on orders placed before 11.55am Orders before cut off Friday will be delivered Monday, after cut off delivery Tuesday. FAQ online. No details on type of shipment.
e) When will the initial shipment of IMP be sent? E.g. at site activation, at first patient screening, at first patient randomisation	site activation - site to arrange obtaining stock
f) What is the lead time for delivery of IMP to site once the order is placed?	See part d
g) Level of control required on trial stock E.g. dispensing of specific pack numbers, reporting stock balance	nil
h) Management of returned IMP Would pharmacy be responsible for a compliance count?	if stock used on wards/unused if patient is discharged early can be reused this would help with stock situation. Sites own decision based on Trust information on if medication which has been on a COVID-19 ward are able to be returned to pharmacy or not - confirmed via email with Sponsor.
i) Disposal arrangements	Local disposal sponsor approval not required - confirmed via email with Sponsor

Section 10.2: Product Information	
Description and Product Type	
a) Description of Product Include name, strength, concentration, volume, form e.g. Drug A 100mg in 5ml Injection (10ml vial)	Amendment protocol V4 - this is no longer an option as an arm SNG001 - Interferon-beta-1a ready to use nebuliser solution. Presented in disposible syringe 0.65ml of 44 microg/ml

b) Is the product an IMP (investigational medicinal product) or AMP (auxiliary medicinal product)?	IMP ☒ AMP ☐
c) Are all the drug names correct (i.e. rINN)?	Yes ☒ No ☐ but also known as SNG001
d) Route of administration (include detail of timing in relation to food and how to take etc.)	Other (please specify) inhaled
e) Licence status	Unlicensed
f) Properties of product requiring special attention	N/A ☒ Cytotoxic ☐ Monoclonal Antibody ☐ Cytotoxic Monoclonal Antibody ☐ Cytostatic ☐ Biological ☐ ATMP ☐ Radiopharmaceutical ☐ Other (please specify) ☐
g) Is it a controlled drug? If yes, include details of Sponsor's arrangements for safe and secure handling of drug	Yes ☐ No ☒ N/A ☐
h) If it is a controlled drug, which schedule is it in?	N/A ☒ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐
i) Will additional licenses be required?	Yes ☐ No ☐ N/A ☒
Dose banding and capping	
a) Is dose banding permitted? If nationally dose banded drug, is the use of national dose banding table permitted?	Yes ☐ No ☐ N/A ☒
b) What dose capping/rounding protocols are permitted?	N/A
Product Source	
a) Source of product	Supplied by sponsor
b) If the product is to be sourced from commercial stocks, will it be reimbursed?	Yes ☐ No ☐ N/A ☒
c) If the product is to be sourced from commercial stocks, can any brand be used?	Yes ☐ No ☐ N/A ☒
d) Is the use of pre-filled infusion bags and/or syringes procured through a third-party manufacturer permitted?	Yes ☐ No ☐ N/A ☒
Packaging and Storage	
a) Packaging of IMP E.g. Primary: in HDPE bottles with child resistant cap; Secondary: 1 carton (kit) contains 2 bottles. Dimensions: Kit dimensions – 12x20x10cm	Glass syringe - no further information. - Info from IB. Preparation and usage instructions to be provided in due course. COSHH/MSDS sent to HRA - to be sent to sites

b) Storage conditions of the product E.g. 2-8°C. Include details of temperature monitoring requirements and temperature deviation procedures	5 deg C +/- 3 degC. Stable at room temp for at least 3 months (25deg C) but sponosr to be informed if out of fridge for more than 8 hours - from IB. confirmed via email with Sponsor that information will be provided when this arm is ready to open
c) Storage space requirements for initial supplies i.e. details on size of initial shipment	Sponsor to clarify when arm ready to be opened - confirmed via email with Sponsor
Product Preparation	
a) Provide detailed information on methods of reconstitution/dilution/preparation Include information on diluents, time to dissolve/reconstitute, container compatibility, equipment (filters etc.) and safety handling requirements, detail on any drug/drug compatibility	nebuliser (I-Neb) to be provided to sites - more infomration when ready to open arm confirmed via email with Sponsor
b) Does the Sponsor require product preparation in an aseptically controlled environment, or can it be prepared using aseptic manipulation in a general area?	N/A
c) Stability and storage requirements of reconstituted/diluted/prepared product of those requiring aseptic manipulation E.g. Diluted solution to be stored at room temperature for no more than 12 hours after preparation	N/A
d) Are all drug formulations appropriate to the patient population (e.g. liquids for paediatrics)?	Yes ☒ No ☐ adults only
IMP/AMP Labelling	
a) Are the drug labels available for review?	Yes ☐ No ☒ N/A ☐
b) For IMP(s), are these compliant with Annexe 13?	Yes ☐ No ☐ unknown - no labels to review - confirmed via email with Sponsor that details will be decided prior to opening arm of study
c) Is there any other information that should be on the labels?	see above
d) Are sites allowed to use their own labels in their local format?	Yes ☐ No ☐ see kaletra answer
e) Are sites required or permitted to add their own dispensing labels?	Yes ☐ No ☐ see kaletra answer
f) Is there consistency between drug names in the protocol and on the label?	Yes ☐ No ☐ unable to comment
Management of IMP/AMP	

a) Will the Sponsor provide prescription forms or is it permitted for sites to use their own? If it is permitted for a site to use their own, will the Sponsor need to approve the prescription forms?	sites to manage as usual methods
b) Accountability requirements Check if site's own accountability logs may be used	No accountability required - simplified trial to allow ease of running trial at sites - confirmed via email with Sponsor
c) How will receipt and re-ordering of IMP/AMP be done?	Select: unsure - sponsor to clarify with more info when arm of study open
d) How is the IMP transported from supplier to site? E.g. use of TempTale® device, requirement to return shipping box on receipt. Include any specific requirements for transportation of IMP from pharmacy to clinic on site	unsure - sponsor to clarify with more info when arm of study open
e) When will the initial shipment of IMP be sent? E.g. at site activation, at first patient screening, at first patient randomisation	unsure - sponsor to clarify with more info when arm of study open
f) What is the lead time for delivery of IMP to site once the order is placed?	unsure - sponsor to clarify with more info when arm of study open
g) Level of control required on trial stock E.g. dispensing of specific pack numbers, reporting stock balance	unsure - sponsor to clarify with more info when arm of study open
h) Management of returned IMP Would pharmacy be responsible for a compliance count?	see kaletra answer
i) Disposal arrangements	Local disposal no permission for destruction required - sponsor confirmed via email

Section 10.3: Product Information	
Description and Product Type	
a) Description of Product Include name, strength, concentration, volume, form e.g. Drug A 100mg in 5ml Injection (10ml vial)	Dexamethasone
b) Is the product an IMP (investigational medicinal product) or AMP (auxiliary medicinal product)?	IMP ☒ AMP ☐
c) Are all the drug names correct (i.e. rINN)?	Yes ☒ No ☐
d) Route of administration (include detail of timing in relation to food and how to take etc.)	Oral and IV. PO take with food only SmPC for tablets sent for review, FAQ - 6mg base IV or oral to be prescribed - rounded IV to a measurable amount (i.e.: 3.3mg/ml - round to 1.8ml). Can dissolve tabs in water if liquid not availbale at sites. IV to be given bolus or infusion at prescribers discretion

	Protocol V5 - Paeditric dosing included. NOTE: communication with sponsor that there is currently a typo with the paediatric dexamethasone dosing. It should reaed 150 microgram/kg and not 100 microgram/kg.
e) Licence status	Licensed outside this indication
f) Properties of product requiring special attention	N/A ☒ Cytotoxic ☐ Monoclonal Antibody ☐ Cytotoxic Monoclonal Antibody ☐ Cytostatic ☐ Biological ☐ ATMP ☐ Radiopharmaceutical ☐ Other (please specify) ☐
g) Is it a controlled drug? If yes, include details of Sponsor's arrangements for safe and secure handling of drug	Yes ☐ No ☒ N/A ☐
h) If it is a controlled drug, which schedule is it in?	N/A ☒ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐
i) Will additional licenses be required?	Yes ☐ No ☐ N/A ☒
Dose banding and capping	
a) Is dose banding permitted? If nationally dose banded drug, is the use of national dose banding table permitted?	Yes ☐ No ☐ N/A ☒
b) What dose capping/rounding protocols are permitted?	N/A
Product Source	
a) Source of product	Dispensed from commercial stocks may come from DHSC ImmForm in due course - info from FAQ Update 11 May 2020 - Dexamethasone tablet, oral solution and injection are available on ImmForm
b) If the product is to be sourced from commercial stocks, will it be reimbursed?	Yes ☐ No ☒ N/A ☐ see above a
c) If the product is to be sourced from commercial stocks, can any brand be used?	Yes ☒ No ☐ N/A ☐
d) Is the use of pre-filled infusion bags and/or syringes procured through a third-party manufacturer permitted?	Yes ☐ No ☐ N/A ☒
Packaging and Storage	
a) Packaging of IMP E.g. Primary: in HDPE bottles with child resistant cap; Secondary: 1 carton (kit) contains 2 bottles. Dimensions: Kit dimensions – 12x20x10cm	Commerical product to be used Update 23-Apr-2020 : In near future PHE will supply ring fenced stock. Current stock at PHE: tablets (2mg pack size 50), oral solution (2mg/5ml pack size 150ml or 75ml)and IV amps (3.3mg/ml 20 x 1 ml amp pack size)

b) Storage conditions of the product E.g. 2-8°C. Include details of temperature monitoring requirements and temperature deviation procedures	as per smpc for products - no special storage conditions (tabs only available)
c) Storage space requirements for initial supplies i.e. details on size of initial shipment	unknown - depends on supply chain/route to sites - info in due course when supply from DHSC confirmed/not. interim use own hospital stock Update 23-apr-2020: PHE stock see info in lop/rit section
Product Preparation	
a) Provide detailed information on methods of reconstitution/dilution/preparation Include information on diluents, time to dissolve/reconstitute, container compatibility, equipment (filters etc.) and safety handling requirements, detail on any drug/drug compatibility	N/A Update 23-apr-2020: for PHE stock - need to dispense required number of tabs for a patient or allocate ward/area stock holding for multiple patients. Dex 2mg tablets, oral suspension, IV amps - dosage presumed incorrect in pharmacy FAQ as states BD dosing - Sponsor to confirm. Response from sponsor by email - this is to be corrected in FAQ and should be OD dosing.
b) Does the Sponsor require product preparation in an aseptically controlled environment, or can it be prepared using aseptic manipulation in a general area?	N/A
c) Stability and storage requirements of reconstituted/diluted/prepared product of those requiring aseptic manipulation E.g. Diluted solution to be stored at room temperature for no more than 12 hours after preparation	N/A
d) Are all drug formulations appropriate to the patient population (e.g. liquids for paediatrics)?	Yes ☒ No ☐
IMP/AMP Labelling	
a) Are the drug labels available for review?	Yes ☐ No ☐ N/A ☒ commercially available stock
b) For IMP(s), are these compliant with Annexe 13?	Yes ☐ No ☐ N/A
c) Is there any other information that should be on the labels?	unable to comment
d) Are sites allowed to use their own labels in their local format?	Yes ☒ No ☐ see kaletra
e) Are sites required or permitted to add their own dispensing labels?	Yes ☒ No ☐ see kaletra
f) Is there consistency between drug names in the protocol and on the label?	Yes ☐ No ☐ N/A
Management of IMP/AMP	

a) Will the Sponsor provide prescription forms or is it permitted for sites to use their own? If it is permitted for a site to use their own, will the Sponsor need to approve the prescription forms?	sites to manage as usual methods
b) Accountability requirements Check if site's own accountability logs may be used	None required
c) How will receipt and re-ordering of IMP/AMP be done?	Other (please specify) commercial product - sites own methods - possibly via DHSC in due course PHE systems as per ritonivir/lopinivir
d) How is the IMP transported from supplier to site? E.g. use of TempTale® device, requirement to return shipping box on receipt. Include any specific requirements for transportation of IMP from pharmacy to clinic on site	N/A - commercial supplies currently PHE systems as per rit/lop
e) When will the initial shipment of IMP be sent? E.g. at site activation, at first patient screening, at first patient randomisation	N/A - commercial supplies currently
f) What is the lead time for delivery of IMP to site once the order is placed?	N/A - commercial supplies currently Update 23-apr-2020: PHE stock as per lop/rit
g) Level of control required on trial stock E.g. dispensing of specific pack numbers, reporting stock balance	N/A - commercial supplies currently - no specific requirements
h) Management of returned IMP Would pharmacy be responsible for a compliance count?	see kaletra answer
i) Disposal arrangements	Local disposal permission to destroy not required from sponsor

Section 10.4: Product Information	
Description and Product Type	
a) Description of Product Include name, strength, concentration, volume, form e.g. Drug A 100mg in 5ml Injection (10ml vial)	Hydroxychloroquine (200mg tablets based on SmPC provided)
b) Is the product an IMP (investigational medicinal product) or AMP (auxiliary medicinal product)?	IMP ☒ AMP ☐
c) Are all the drug names correct (i.e. rINN)?	Yes ☒ No ☐
d) Route of administration (include detail of timing in relation to food and how to take etc.)	Oral 800mg initially, +6hr (after initial dose) 800mg, +12hrs (after initial dose) 400mg, +24hours (after initial dose) 400mg then 400mg every 12 hours for 9 days Updated 23-apr-2020

	Protocol V5: Paediatric dosing included
e) Licence status	Licensed outside this indication
f) Properties of product requiring special attention	N/A ☒ Cytotoxic ☐ Monoclonal Antibody ☐ Cytotoxic Monoclonal Antibody ☐ Cytostatic ☐ Biological ☐ ATMP ☐ Radiopharmaceutical ☐ Other (please specify) ☐
g) Is it a controlled drug? If yes, include details of Sponsor's arrangements for safe and secure handling of drug	Yes ☐ No ☒ N/A ☒
h) If it is a controlled drug, which schedule is it in?	N/A ☒ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐
i) Will additional licenses be required?	Yes ☐ No ☐ N/A ☒
Dose banding and capping	
a) Is dose banding permitted? If nationally dose banded drug, is the use of national dose banding table permitted?	Yes ☐ No ☐ N/A ☒
b) What dose capping/rounding protocols are permitted?	N/A
Product Source	
a) Source of product	Other (please specify) As per Kaletra
b) If the product is to be sourced from commercial stocks, will it be reimbursed?	Yes ☐ No ☐ N/A ☐ as per kaletra
c) If the product is to be sourced from commercial stocks, can any brand be used?	Yes ☐ No ☐ N/A ☐ as per kaletra
d) Is the use of pre-filled infusion bags and/or syringes procured through a third-party manufacturer permitted?	Yes ☐ No ☐ N/A ☒
Packaging and Storage	
a) Packaging of IMP E.g. Primary: in HDPE bottles with child resistant cap; Secondary: 1 carton (kit) contains 2 bottles. Dimensions: Kit dimensions – 12x20x10cm	commercial product, packs of 60 tablets (200mg)
b) Storage conditions of the product E.g. 2-8°C. Include details of temperature monitoring requirements and temperature deviation procedures	below 25 deg C - SmPC information
c) Storage space requirements for initial supplies i.e. details on size of initial shipment	can be supplied sufficient for 100 patients (48 tablets per treatment course)

Product Preparation	
a) Provide detailed information on methods of reconstitution/dilution/preparation Include information on diluents, time to dissolve/reconstitute, container compatibility, equipment (filters etc.) and safety handling requirements, detail on any drug/drug compatibility	N/A Updated 23-Apr-2020 There is a need to dispense required number of tablets for a patient or allocate ward/area stock holding for more than one patient. Do not dispense whole packs.
b) Does the Sponsor require product preparation in an aseptically controlled environment, or can it be prepared using aseptic manipulation in a general area?	N/A
c) Stability and storage requirements of reconstituted/diluted/prepared product of those requiring aseptic manipulation E.g. Diluted solution to be stored at room temperature for no more than 12 hours after preparation	N/A
d) Are all drug formulations appropriate to the patient population (e.g. liquids for paediatrics)?	Yes ☒ No ☐ hydroxychloroquine tablets can be crushed and dispersed in 15mL-30mL of water and the resulting solution can be administered down a enteral feeding tube if required - confirmed by email with Sponsor Paediatric guidance provide further information on administration part dosing.
IMP/AMP Labelling	
a) Are the drug labels available for review?	Yes ☐ No ☐ N/A ☒ commercial stocks
b) For IMP(s), are these compliant with Annexe 13?	Yes ☐ No ☐ N/A
c) Is there any other information that should be on the labels?	N/A
d) Are sites allowed to use their own labels in their local format?	Yes ☒ No ☐ As per Kaletra
e) Are sites required or permitted to add their own dispensing labels?	Yes ☒ No ☐ as above
f) Is there consistency between drug names in the protocol and on the label?	Yes ☐ No ☐ N/A - no lables
Management of IMP/AMP	
a) Will the Sponsor provide prescription forms or is it permitted for sites to use their own? If it is permitted for a site to use their own, will the Sponsor need to approve the prescription forms?	As kaletra
b) Accountability requirements	No accountability requirements

Check if site's own accountability logs may be used	
c) How will receipt and re-ordering of IMP/AMP be done?	Other (please specify) as per kaletra
d) How is the IMP transported from supplier to site? E.g. use of TempTale® device, requirement to return shipping box on receipt. Include any specific requirements for transportation of IMP from pharmacy to clinic on site	as per kaletra
e) When will the initial shipment of IMP be sent? E.g. at site activation, at first patient screening, at first patient randomisation	as per kaletra
f) What is the lead time for delivery of IMP to site once the order is placed?	as per kaletra
g) Level of control required on trial stock E.g. dispensing of specific pack numbers, reporting stock balance	as per kaletra
h) Management of returned IMP Would pharmacy be responsible for a compliance count?	As kaletra
i) Disposal arrangements	Local disposal no permission required for destruction

Section 10.5: Product Information	
Description and Product Type	
a) Description of Product Include name, strength, concentration, volume, form e.g. Drug A 100mg in 5ml Injection (10ml vial)	Update on 23-Apr-2020: Prednisolone 10mg tablets (SmPC) - sponsor to confirm sites can use any of their own stock no matter what strength to make up the required dose dose 40mg OD in place of dexamethasone for pregnant participants Response from sponsor by email - sites can use any stock/strength/brand to make the does required. Protocol V5: paediatric dosing included. Sites can use any stock/strength/formulation/brand to adminster the dose required.
b) Is the product an IMP (investigational medicinal product) or AMP (auxiliary medicinal product)?	IMP ☒ AMP ☐
c) Are all the drug names correct (i.e. rINN)?	Yes ☒ No ☐
d) Route of administration (include detail of timing in relation to food and how to take etc.)	Oral
e) Licence status	Licensed outside this indication

f) Properties of product requiring special attention	N/A ☒ Cytotoxic ☐ Monoclonal Antibody ☐ Cytotoxic Monoclonal Antibody ☐ Cytostatic ☐ Biological ☐ ATMP ☐ Radiopharmaceutical ☐ Other (please specify) ☐
g) Is it a controlled drug? If yes, include details of Sponsor's arrangements for safe and secure handling of drug	Yes ☐ No ☒ N/A ☐
h) If it is a controlled drug, which schedule is it in?	N/A ☒ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐
i) Will additional licenses be required?	Yes ☐ No ☐ N/A ☒
Dose banding and capping	
a) Is dose banding permitted? If nationally dose banded drug, is the use of national dose banding table permitted?	Yes ☐ No ☒ N/A ☐
b) What dose capping/rounding protocols are permitted?	N/A
Product Source	
a) Source of product	Dispensed from commercial stocks
b) If the product is to be sourced from commercial stocks, will it be reimbursed?	Yes ☐ No ☒ N/A ☐
c) If the product is to be sourced from commercial stocks, can any brand be used?	Yes ☒ No ☐ N/A ☐
d) Is the use of pre-filled infusion bags and/or syringes procured through a third-party manufacturer permitted?	Yes ☐ No ☐ N/A ☒
Packaging and Storage	
a) Packaging of IMP E.g. Primary: in HDPE bottles with child resistant cap; Secondary: 1 carton (kit) contains 2 bottles. Dimensions: Kit dimensions – 12x20x10cm	Commercial product - sites own stock to be used
b) Storage conditions of the product E.g. 2-8°C. Include details of temperature monitoring requirements and temperature deviation procedures	In line with site's own stock holding SmPC for 10mg tabs supplied states no specific temperature storage requirements
c) Storage space requirements for initial supplies i.e. details on size of initial shipment	Site own stock - N/A
Product Preparation	
a) Provide detailed information on methods of reconstitution/dilution/preparation	N/A

Include information on diluents, time to dissolve/reconstitute, container compatibility, equipment (filters etc.) and safety handling requirements, detail on any drug/drug compatibility	
b) Does the Sponsor require product preparation in an aseptically controlled environment, or can it be prepared using aseptic manipulation in a general area?	N/A
c) Stability and storage requirements of reconstituted/diluted/prepared product of those requiring aseptic manipulation E.g. Diluted solution to be stored at room temperature for no more than 12 hours after preparation	N/A
d) Are all drug formulations appropriate to the patient population (e.g. liquids for paediatrics)?	Yes ☒ No ☐
IMP/AMP Labelling	
a) Are the drug labels available for review?	Yes ☐ No ☐ N/A ☒ Site own commercial stock being used
b) For IMP(s), are these compliant with Annexe 13?	Yes ☐ No ☐ N/A - no specific labelling requirement
c) Is there any other information that should be on the labels?	sites to manage in line with own dispensing practice
d) Are sites allowed to use their own labels in their local format?	Yes ☒ No ☐
e) Are sites required or permitted to add their own dispensing labels?	Yes ☒ No ☐
f) Is there consistency between drug names in the protocol and on the label?	Yes ☐ No ☐ N/A
Management of IMP/AMP	
a) Will the Sponsor provide prescription forms or is it permitted for sites to use their own? If it is permitted for a site to use their own, will the Sponsor need to approve the prescription forms?	Sites to manage in line with own processes - use own prescriptions if needed
b) Accountability requirements Check if site's own accountability logs may be used	None required by sponsor
c) How will receipt and re-ordering of IMP/AMP be done?	Other (please specify) commerical stock holding
d) How is the IMP transported from supplier to site? E.g. use of TempTale® device, requirement to return shipping box on receipt. Include any specific requirements for transportation of IMP from pharmacy to clinic on site	N/A commercial supply

e) When will the initial shipment of IMP be sent? E.g. at site activation, at first patient screening, at first patient randomisation	N/A commercial supply
f) What is the lead time for delivery of IMP to site once the order is placed?	N/A commercial supply
g) Level of control required on trial stock E.g. dispensing of specific pack numbers, reporting stock balance	No accountability required by sponsor
h) Management of returned IMP Would pharmacy be responsible for a compliance count?	if stock used on wards/unused if patient is discharged early can be reused this would help with stock situation. Sites own decision based on Trust information on if medication which has been on a COVID-19 ward are able to be returned to pharmacy or not - confirmed via email with Sponsor.
i) Disposal arrangements	Local disposal no sponsor approval required

Section 10.6: Product Information	
Description and Product Type	
a) Description of Product Include name, strength, concentration, volume, form e.g. Drug A 100mg in 5ml Injection (10ml vial)	Update on 23-Apr-2020: Hydrocortisone 100mg/ml solution for injection (SmPC provided). Dose: 80mg BD IV in substitution for dexamethasone in pregnant participants. Protocol V5: paediatric dosing included for neonates ONLY. Sites can use any stock/strength/brand to give the required dose.
b) Is the product an IMP (investigational medicinal product) or AMP (auxiliary medicinal product)?	IMP ☒ AMP ☐
c) Are all the drug names correct (i.e. rINN)?	Yes ☒ No ☐
d) Route of administration (include detail of timing in relation to food and how to take etc.)	Intravenous Protocol V5: Neonatal dosing included
e) Licence status	Licensed outside this indication
f) Properties of product requiring special attention	N/A ☒ Cytotoxic ☐ Monoclonal Antibody ☐ Cytotoxic Monoclonal Antibody ☐ Cytostatic ☐ Biological ☐ ATMP ☐ Radiopharmaceutical ☐ Other (please specify) ☐
g) Is it a controlled drug? If yes, include details of Sponsor's arrangements for safe and secure handling of drug	Yes ☐ No ☒ N/A ☐

h) If it is a controlled drug, which schedule is it in?	N/A ☒ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐
i) Will additional licenses be required?	Yes ☐ No ☐ N/A ☒
Dose banding and capping	
a) Is dose banding permitted? If nationally dose banded drug, is the use of national dose banding table permitted?	Yes ☐ No ☐ N/A ☒
b) What dose capping/rounding protocols are permitted?	N/A
Product Source	
a) Source of product	Dispensed from commercial stocks Any stock on sites can be used to deliver appropriate dose to patients
b) If the product is to be sourced from commercial stocks, will it be reimbursed?	Yes ☐ No ☒ N/A ☐
c) If the product is to be sourced from commercial stocks, can any brand be used?	Yes ☒ No ☐ N/A ☐
d) Is the use of pre-filled infusion bags and/or syringes procured through a third-party manufacturer permitted?	Yes ☐ No ☐ N/A ☒
Packaging and Storage	
a) Packaging of IMP E.g. Primary: in HDPE bottles with child resistant cap; Secondary: 1 carton (kit) contains 2 bottles. Dimensions: Kit dimensions – 12x20x10cm	Sites own commercial stocks
b) Storage conditions of the product E.g. 2-8°C. Include details of temperature monitoring requirements and temperature deviation procedures	As per sites own commercial stock SmPc. SmPC provided states below 25deg C
c) Storage space requirements for initial supplies i.e. details on size of initial shipment	Sites own commercial stocks
Product Preparation	
a) Provide detailed information on methods of reconstitution/dilution/preparation Include information on diluents, time to dissolve/reconstitute, container compatibility, equipment (filters etc.) and safety handling requirements, detail on any drug/drug compatibility	N/A
b) Does the Sponsor require product preparation in an aseptically controlled environment, or can it be prepared using aseptic manipulation in a general area?	N/A

c) Stability and storage requirements of reconstituted/diluted/prepared product of those requiring aseptic manipulation E.g. Diluted solution to be stored at room temperature for no more than 12 hours after preparation	N/A
d) Are all drug formulations appropriate to the patient population (e.g. liquids for paediatrics)?	Yes ☒ No ☐
IMP/AMP Labelling	
a) Are the drug labels available for review?	Yes ☐ No ☐ N/A ☒ Site own commercial stock being used
b) For IMP(s), are these compliant with Annexe 13?	Yes ☐ No ☐ N/A - no specific labelling requirement
c) Is there any other information that should be on the labels?	sites to manage in line with own dispensing practice
d) Are sites allowed to use their own labels in their local format?	Yes ☒ No ☐
e) Are sites required or permitted to add their own dispensing labels?	Yes ☒ No ☐
f) Is there consistency between drug names in the protocol and on the label?	Yes ☐ No ☐ N/A
Management of IMP/AMP	
a) Will the Sponsor provide prescription forms or is it permitted for sites to use their own? If it is permitted for a site to use their own, will the Sponsor need to approve the prescription forms?	Sites to manage in line with own processes - use own prescriptions if needed
b) Accountability requirements Check if site's own accountability logs may be used	Not required by sponsor
c) How will receipt and re-ordering of IMP/AMP be done?	Other (please specify) Commercial stock holding at site being used
d) How is the IMP transported from supplier to site? E.g. use of TempTale® device, requirement to return shipping box on receipt. Include any specific requirements for transportation of IMP from pharmacy to clinic on site	N/A commercial supply
e) When will the initial shipment of IMP be sent? E.g. at site activation, at first patient screening, at first patient randomisation	N/A commercial supply
f) What is the lead time for delivery of IMP to site once the order is placed?	N/A commercial supply

g) Level of control required on trial stock E.g. dispensing of specific pack numbers, reporting stock balance	No accountability required by sponsor
h) Management of returned IMP Would pharmacy be responsible for a compliance count?	if stock used on wards/unused if patient is discharged early can be reused this would help with stock situation. Sites own decision based on Trust information on if medication which has been on a COVID-19 ward are able to be returned to pharmacy or not - confirmed via email with Sponsor.
i) Disposal arrangements	Local disposal

Section 10.7: Product Information	
Description and Product Type	
a) Description of Product Include name, strength, concentration, volume, form e.g. Drug A 100mg in 5ml Injection (10ml vial)	Update on 23-Apr-2020: Azithromycin 500mg OD for 10 days (500mg tablet SmPC supplied) Protocol V5: paediatric dosing included. Update on 11-May-2020: Oral suspension available on ImmForm. Restricted for sites recruiting for paediatric patients.
b) Is the product an IMP (investigational medicinal product) or AMP (auxiliary medicinal product)?	IMP ☒ AMP ☐
c) Are all the drug names correct (i.e. rINN)?	Yes ☒ No ☐
d) Route of administration (include detail of timing in relation to food and how to take etc.)	Oral or IV Protocol V5: Paediatric dosing included
e) Licence status	Licensed outside this indication
f) Properties of product requiring special attention	N/A ☒ Cytotoxic ☐ Monoclonal Antibody ☐ Cytotoxic Monoclonal Antibody ☐ Cytostatic ☐ Biological ☐ ATMP ☐ Radiopharmaceutical ☐ Other (please specify) ☐
g) Is it a controlled drug? If yes, include details of Sponsor's arrangements for safe and secure handling of drug	Yes ☐ No ☒ N/A ☐
h) If it is a controlled drug, which schedule is it in?	N/A ☒ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐
i) Will additional licenses be required?	Yes ☐ No ☐ N/A ☒
Dose banding and capping	
a) Is dose banding permitted?	Yes ☐ No ☐ N/A ☒

If nationally dose banded drug, is the use of national dose banding table permitted?	
b) What dose capping/rounding protocols are permitted?	N/A
Product Source	
a) Source of product	Other (please specify) PHE will supply stocks of azithromycin for the study. Until such stocks are available NHSE and equivalent in Wales and Scotland have approved use of NHS stocks for the trial. PHE stock will be 500mg tablets (3 pack) and 250mg capsules (6 pack) Discussions in place regarding procuring liquid and IV for the trial Update on 11-May-2020: Oral suspension available on ImmForm. Restricted for sites recruiting for paediatric patients. IV still not available.
b) If the product is to be sourced from commercial stocks, will it be reimbursed?	Yes ☐ No ☒ N/A ☐ sites to liaise with their finance dept to recoup costs via COVID 19 budget from govt
c) If the product is to be sourced from commercial stocks, can any brand be used?	Yes ☒ No ☐ N/A ☐
d) Is the use of pre-filled infusion bags and/or syringes procured through a third-party manufacturer permitted?	Yes ☐ No ☐ N/A ☒
Packaging and Storage	
a) Packaging of IMP E.g. Primary: in HDPE bottles with child resistant cap; Secondary: 1 carton (kit) contains 2 bottles. Dimensions: Kit dimensions – 12x20x10cm	PHE stock to be 250mg capsule (6 pack) and 500mg tablets (3 pack) Oral liquid: 200mg in 5mL Sandoz brand (30ml) IV preparations yet to be confirmed
b) Storage conditions of the product E.g. 2-8°C. Include details of temperature monitoring requirements and temperature deviation procedures	As per SmPC of brand received. SmPC reviewed states no specific storage conditions
c) Storage space requirements for initial supplies i.e. details on size of initial shipment	Stock holding still being determined. Likely to be sufficient for 100 patients 10 day course each. Update on 11-May-2020: Oral suspension restricted for sites recruiting paediatric patients only. Recommend initial order of 5 bottles and re-order as and when a patient is randomised.
Product Preparation	

a) Provide detailed information on methods of reconstitution/dilution/preparation Include information on diluents, time to dissolve/reconstitute, container compatibility, equipment (filters etc.) and safety handling requirements, detail on any drug/drug compatibility	Dispensing quantities 10 x 500mg tablets or 20 x 250mg capsules. There is the need to dispense specific quanitites or have a stock holding/area for multiple patients treatment to be accessed from
b) Does the Sponsor require product preparation in an aseptically controlled environment, or can it be prepared using aseptic manipulation in a general area?	N/a
c) Stability and storage requirements of reconstituted/diluted/prepared product of those requiring aseptic manipulation E.g. Diluted solution to be stored at room temperature for no more than 12 hours after preparation	N/A
d) Are all drug formulations appropriate to the patient population (e.g. liquids for paediatrics)?	Yes ☒ No ☐
IMP/AMP Labelling	
a) Are the drug labels available for review?	Yes ☐ No ☐ N/A ☒
b) For IMP(s), are these compliant with Annexe 13?	Yes ☐ No ☐ N/A commercial stocks and no labelling requirement stated
c) Is there any other information that should be on the labels?	sites to manage in line with own dispensing practice
d) Are sites allowed to use their own labels in their local format?	Yes ☒ No ☐
e) Are sites required or permitted to add their own dispensing labels?	Yes ☒ No ☐
f) Is there consistency between drug names in the protocol and on the label?	Yes ☐ No ☐ N/a
Management of IMP/AMP	
a) Will the Sponsor provide prescription forms or is it permitted for sites to use their own? If it is permitted for a site to use their own, will the Sponsor need to approve the prescription forms?	Sites to manage in line with own processes - use own prescriptions if needed
b) Accountability requirements Check if site's own accountability logs may be used	None required by sponsor
c) How will receipt and re-ordering of IMP/AMP be done?	Other (please specify) Currently NHS commercial stock being used. When PHE stock being supplied - see Lop/rit information regarding ImmForm
d) How is the IMP transported from supplier to site?	As above

E.g. use of TempTale® device, requirement to return shipping box on receipt. Include any specific requirements for transportation of IMP from pharmacy to clinic on site	
e) When will the initial shipment of IMP be sent? E.g. at site activation, at first patient screening, at first patient randomisation	As above
f) What is the lead time for delivery of IMP to site once the order is placed?	As above
g) Level of control required on trial stock E.g. dispensing of specific pack numbers, reporting stock balance	As above
h) Management of returned IMP Would pharmacy be responsible for a compliance count?	if stock used on wards/unused if patient is discharged early can be reused this would help with stock situation. Sites own decision based on Trust information on if medication which has been on a COVID-19 ward are able to be returned to pharmacy or not - confirmed via email with Sponsor.
i) Disposal arrangements	Local disposal No sponsor approval required

Section 10.8: Product Information	
Description and Product Type	
a) Description of Product Include name, strength, concentration, volume, form e.g. Drug A 100mg in 5ml Injection (10ml vial)	Update on 23-Apr-2020: Tocilizumab 200mg/10ml or 400mg/20ml solution for injection Updated on 11-May-2020: 80mg vials avilable on ImmForm restricted to sites recruiting paediatric patients.
b) Is the product an IMP (investigational medicinal product) or AMP (auxiliary medicinal product)?	IMP ☒ AMP ☐
c) Are all the drug names correct (i.e. rINN)?	Yes ☒ No ☐
d) Route of administration (include detail of timing in relation to food and how to take etc.)	Intravenous Protocol V5: Paediatric dosing included.
e) Licence status	Licensed outside this indication
f) Properties of product requiring special attention	N/A ☐ Cytotoxic ☐ Monoclonal Antibody ☒ Cytotoxic Monoclonal Antibody ☐ Cytostatic ☐ Biological ☐ ATMP ☐ Radiopharmaceutical ☐ Other (please specify) ☐
g) Is it a controlled drug?	Yes ☐ No ☒ N/A ☐

If yes, include details of Sponsor's arrangements for safe and secure handling of drug	
h) If it is a controlled drug, which schedule is it in?	N/A ☒ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐
i) Will additional licenses be required?	Yes ☐ No ☒ N/A ☐
Dose banding and capping	
a) Is dose banding permitted? If nationally dose banded drug, is the use of national dose banding table permitted?	Yes ☐ No ☐ N/A ☒ doses are banded in protocol Separate mg/kg dosing for paediatric patients
b) What dose capping/rounding protocols are permitted?	N/A
Product Source	
a) Source of product	Supplied by sponsor Updated on 11-May-2020: 80mg vials avilable on ImmForm restricted to sites recruiting paediatric patients.
b) If the product is to be sourced from commercial stocks, will it be reimbursed?	Yes ☐ No ☐ N/A ☒
c) If the product is to be sourced from commercial stocks, can any brand be used?	Yes ☐ No ☐ N/A ☒
d) Is the use of pre-filled infusion bags and/or syringes procured through a third-party manufacturer permitted?	Yes ☐ No ☒ N/A ☐
Packaging and Storage	
a) Packaging of IMP E.g. Primary: in HDPE bottles with child resistant cap; Secondary: 1 carton (kit) contains 2 bottles. Dimensions: Kit dimensions – 12x20x10cm	1 vial pack size of either 400mg/20ml or 200mg/10ml Updated on 11-May-2020: 80mg vials avilable on ImmForm restricted to sites recruiting paediatric patients.
b) Storage conditions of the product E.g. 2-8°C. Include details of temperature monitoring requirements and temperature deviation procedures	Refrigerated 2-8deg C
c) Storage space requirements for initial supplies i.e. details on size of initial shipment	limited stock available. limited sites will open to this arm of the study. Initial supply of 8 x 200mg and 16 x 400mg vials ordered per site Sites to ensure stock received is approprately segregated/identified as being for the RECOVERY study only.
Product Preparation	

a) Provide detailed information on methods of reconstitution/dilution/preparation Include information on diluents, time to dissolve/reconstitute, container compatibility, equipment (filters etc.) and safety handling requirements, detail on any drug/drug compatibility	Tocilizumab doses should be prepared in an IV infusion bag containing sodium chloride 0.9%. Do not use infusion bags containing any other diluents. Calculate the appropriate volume of tocilizumab solution for infusion to be added to the sodium chloride 0.9% infusion bag. Prior to the addition of the tocilizumab to the IV bag, remove the equivalent volume of saline from the sodium chloride 0.9% IV bag. The required volume of tocilizumab should be withdrawn from the vial(s) and added to the saline IV bag. To mix the solution, gently invert the infusion bag to avoid foaming. Inspect the bag for particulates and discard if present. If not used immediately, the prepared tocilizumab infusion may be stored at room temperature for up to 30 hours (see Tocilizumab SmPC and Medusa). Note - SmPC states store up to 30deg for up to 24 hours. Sponsor confirmed by email that FAQ will be amended to reflect this. Please use information on the SmPC and Medusa.
b) Does the Sponsor require product preparation in an aseptically controlled environment, or can it be prepared using aseptic manipulation in a general area?	Aseptic manipulation in a general area. no specific need for pharmacy to prepare the product.
c) Stability and storage requirements of reconstituted/diluted/prepared product of those requiring aseptic manipulation E.g. Diluted solution to be stored at room temperature for no more than 12 hours after preparation	See section a)
d) Are all drug formulations appropriate to the patient population (e.g. liquids for paediatrics)?	Yes ☒ No ☐
IMP/AMP Labelling	
a) Are the drug labels available for review?	Yes ☐ No ☐ N/A ☒
b) For IMP(s), are these compliant with Annexe 13?	Yes ☐ No ☐ N/A
c) Is there any other information that should be on the labels?	Standard dispensing practice/ward level infusion labelling practice to be utilised to comply with own site SOP/policies on injectable medicines
d) Are sites allowed to use their own labels in their local format?	Yes ☒ No ☐
e) Are sites required or permitted to add their own dispensing labels?	Yes ☒ No ☐
f) Is there consistency between drug names in the protocol and on the label?	Yes ☐ No ☐ N/A

Management of IMP/AMP	
a) Will the Sponsor provide prescription forms or is it permitted for sites to use their own? If it is permitted for a site to use their own, will the Sponsor need to approve the prescription forms?	Sites to manage in line with own processes - use own prescriptions if needed. Note Medusa states this is an NPSA 20 amber medication requiring risk reduction strategies for preparation out of pharmacy. Sites to use own procedures to comply with this. Note - preparation is consistent with detail on Medusa
b) Accountability requirements Check if site's own accountability logs may be used	None required by sponsor
c) How will receipt and re-ordering of IMP/AMP be done?	Other (please specify) See Rit/Lop information
d) How is the IMP transported from supplier to site? E.g. use of TempTale® device, requirement to return shipping box on receipt. Include any specific requirements for transportation of IMP from pharmacy to clinic on site	See Rit/Lop information
e) When will the initial shipment of IMP be sent? E.g. at site activation, at first patient screening, at first patient randomisation	depending on site being selected. Also see Rit/Lop information
f) What is the lead time for delivery of IMP to site once the order is placed?	See Rit/Lop information
g) Level of control required on trial stock E.g. dispensing of specific pack numbers, reporting stock balance	No accountability requirements
h) Management of returned IMP Would pharmacy be responsible for a compliance count?	if stock used on wards/unused due to change in circumsatances stock may be reused - this would help with stock situation. Sites own decision based on Trust information on if medication which has been on a COVID-19 ward are able to be returned to pharmacy or not - confirmed via email with Sponsor.
i) Disposal arrangements	Local disposal no approval from Sponsor required

Section 10.9: Product Information	
Description and Product Type	
a) Description of Product Include name, strength, concentration, volume, form e.g. Drug A 100mg in 5ml Injection (10ml vial)	Methylprednisolone sodium succinate (this is an option for paediatric patients only)
b) Is the product an IMP (investigational medicinal product) or AMP (auxiliary medicinal product)?	IMP ☒ AMP ☐
c) Are all the drug names correct (i.e. rINN)?	Yes ☒ No ☐

d) Route of administration (include detail of timing in relation to food and how to take etc.)	Intravenous
e) Licence status	Licensed outside this indication
f) Properties of product requiring special attention	N/A ☒ Cytotoxic ☐ Monoclonal Antibody ☐ Cytotoxic Monoclonal Antibody ☐ Cytostatic ☐ Biological ☐ ATMP ☐ Radiopharmaceutical ☐ Other (please specify) ☐
g) Is it a controlled drug? If yes, include details of Sponsor's arrangements for safe and secure handling of drug	Yes ☐ No ☒ N/A ☐
h) If it is a controlled drug, which schedule is it in?	N/A ☒ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐
i) Will additional licenses be required?	Yes ☐ No ☐ N/A ☒
Dose banding and capping	
a) Is dose banding permitted? If nationally dose banded drug, is the use of national dose banding table permitted?	Yes ☐ No ☒ N/A ☐
b) What dose capping/rounding protocols are permitted?	Max 32 mg
Product Source	
a) Source of product	Dispensed from commercial stocks
b) If the product is to be sourced from commercial stocks, will it be reimbursed?	Yes ☐ No ☒ N/A ☐
c) If the product is to be sourced from commercial stocks, can any brand be used?	Yes ☒ No ☐ N/A ☐
d) Is the use of pre-filled infusion bags and/or syringes procured through a third-party manufacturer permitted?	Yes ☐ No ☒ N/A ☒
Packaging and Storage	
a) Packaging of IMP E.g. Primary: in HDPE bottles with child resistant cap; Secondary: 1 carton (kit) contains 2 bottles. Dimensions: Kit dimensions – 12x20x10cm	Sites own commercial stocks
b) Storage conditions of the product E.g. 2-8°C. Include details of temperature monitoring requirements and temperature deviation procedures	Sites own commercial stocks - This product does not require any special temperature storage conditions. Keep the vials in the outer carton in order to protect from light.
c) Storage space requirements for initial supplies i.e. details on size of initial shipment	Sites own commercial stocks

Product Preparation	
a) Provide detailed information on methods of reconstitution/dilution/preparation Include information on diluents, time to dissolve/reconstitute, container compatibility, equipment (filters etc.) and safety handling requirements, detail on any drug/drug compatibility	Sites own commercial stocks - refer to individal SmPC
b) Does the Sponsor require product preparation in an aseptically controlled environment, or can it be prepared using aseptic manipulation in a general area?	Aseptic manupulation in a general area.
c) Stability and storage requirements of reconstituted/diluted/prepared product of those requiring aseptic manipulation E.g. Diluted solution to be stored at room temperature for no more than 12 hours after preparation	In line with local practice
d) Are all drug formulations appropriate to the patient population (e.g. liquids for paediatrics)?	Yes ☒ No ☐
IMP/AMP Labelling	
a) Are the drug labels available for review?	Yes ☐ No ☐ N/A ☒ Annex 13 labelling exemption
b) For IMP(s), are these compliant with Annexe 13?	Yes ☐ No ☐ Annex 13 labelling exemption
c) Is there any other information that should be on the labels?	Annex 13 labelling exemption
d) Are sites allowed to use their own labels in their local format?	Yes ☒ No ☐
e) Are sites required or permitted to add their own dispensing labels?	Yes ☒ No ☐
f) Is there consistency between drug names in the protocol and on the label?	Yes ☐ No ☐ N/A
Management of IMP/AMP	
a) Will the Sponsor provide prescription forms or is it permitted for sites to use their own? If it is permitted for a site to use their own, will the Sponsor need to approve the prescription forms?	Manage in line with local practice
b) Accountability requirements Check if site's own accountability logs may be used	No accountability requirements
c) How will receipt and re-ordering of IMP/AMP be done?	Other (please specify) Sites to manage as per routine commercial stock

d) How is the IMP transported from supplier to site? E.g. use of TempTale® device, requirement to return shipping box on receipt. Include any specific requirements for transportation of IMP from pharmacy to clinic on site	Sites to manage as per routine commercial stock
e) When will the initial shipment of IMP be sent? E.g. at site activation, at first patient screening, at first patient randomisation	Sites to manage as per routine commercial stock
f) What is the lead time for delivery of IMP to site once the order is placed?	Sites to manage as per routine commercial stock
g) Level of control required on trial stock E.g. dispensing of specific pack numbers, reporting stock balance	Sites to manage as per routine commercial stock
h) Management of returned IMP Would pharmacy be responsible for a compliance count?	Not required by sponsor
i) Disposal arrangements	Local disposal Sites to manage as per routine commercial stock

Section 11: Additional Information

For example, information on supportive care (pre or post medication requirements), specific consumables, potential issue e.g. gene therapy isolators, or any further requirements (drug interactions/contraindications, concomitant meds) which may affect pharmacy. Please include details if the study is a stratified CTIMP or additional arms are expected.

Additional information gathered from sponsor:
- all participants should receive standard care accoridng to their olocal protocol. Randomisation is in addition to this.
- co-enrolment into other COVID-19 studies is allowed as long as their randomisation does not directly conflict with RECOVERY
- No delegation logs will be applicable to this study
- next version of protocol to adjust wording regarding the 'standard pharmacy review within 48 hours of enrolment' to relieve onus on pharmacy staff doing this and make a 'medication review' that anyone appropriately qualified can perform.
- non-medical prescribers can prescribe medication as long as local SOPs allow
- supportive medication for Kaletra patients are at the discretion of managing team but recommend being responsive to side effects not routine prescribing
- CRA/contact for sponsor = recoverytrial@ndph.ox.ac.uk

I consider this review as complete as much as possible with the information currently available.
I consider the review on the amendment relating to protocol V4 as complete as possible with the information available

Part 3: Nation specific review. To be completed by Pharmacy Reviewer(s) (Devolved Administrations only, if applicable)

Section 12: Clinical Information	
a) Is appropriate guidance given of support/rescue medication e.g. antiemetics/pre-medications?	Yes ☐ No ☐ N/A ☐
b) Is information given on side-effects?	Yes ☐ No ☐ N/A ☐
c) Is information given on treatment of side-effects?	Yes ☐ No ☐ N/A ☐
d) Are cautions/contra-indications listed?	Yes ☐ No ☐ N/A ☐
e) Is information given on concomitant medication permitted/prohibited?	Yes ☐ No ☐ N/A ☐
f) Is appropriate information given on dose modifications/delays and interruptions?	Yes ☐ No ☐ N/A ☐
g) Is the drug information contained in the Participant Information Sheet complete and appropriate?	Yes ☐ No ☐ N/A ☐
h) Other/Comments	

Section 13: GP Letter	
a) Does the GP letter contain information regarding permitted/disallowed concomitant medications?	Yes ☐ No ☐ N/A ☐
b) Does the GP letter contain information regarding potential interactions and known side-effects as detailed in the study protocol?	Yes ☐ No ☐ N/A ☐
c) Is the GP required to see the patient in direct respect of their participation in the study? If yes – add detail.	Yes ☐ No ☐ N/A ☐
d) Is the GP required to prescribe any IMP or supportive medication as a result of patient participation in the study? If yes, add detail.	Yes ☐ No ☐ N/A ☐
e) Is the letter explicit on any GP activity required as a result of the patient's participation in the study? If yes – add detail	Yes ☐ No ☐ N/A ☐

Section 14: Commercial Costing Template/Fees Agreed	
a) State version of commercial template used.	Version
Set up, management and close-down costs	
a) Set Up/Close Down for each additional site	Yes ☐ No ☐ N/A ☐
b) IMP management fee	Yes ☐ No ☐ N/A ☐
Per Patient Costs Per Drug	
a) Number of drugs:	Standard Dispensing Aseptic Dispensing
b) Dispensing time for standard agent or IMP/AMP (excluding use of IVR/IWR)	Yes ☐ No ☐ N/A ☐
c) Aseptic dispensing agent time	Yes ☐ No ☐ N/A ☐
d) Controlled drug – additional dispensing time	Yes ☐ No ☐ N/A ☐
e) Use of IVR/IWR system for dispensing by Pharmacy (additional time)	Yes ☐ No ☐ N/A ☐
f) Pharmacy arrangement of IMP delivery or posting preparation time	Yes ☐ No ☐ N/A ☐
g) Patient drug accountability time/medicine reconciliation	Yes ☐ No ☐ N/A ☐
Variable Costs (only charged if applicable)	
a) Storage space over 0.5m² approx. (=one shelf 0.3m deep x 1.5m long) per month	Yes ☐ No ☐ N/A ☐
b) Waste disposal as hazardous waste per 50L container	Yes ☐ No ☐ N/A ☐
c) Waste disposal storage pending collection or disposal of all unused/unwanted/expired medicines originally supplied by Sponsor per month or part thereof (Chargeable only if not collected within 1 month of the first request to collect)	Yes ☐ No ☐ N/A ☐
Additional costs (to be met by Sponsor as required)	
a) Re-labelling and releasing of IMP batch (e.g. shelf life extension)	Yes ☐ No ☐ N/A ☐
b) CRA-requested dedicated Pharmacy staff time to support monitoring visits. Chargeable as additional to standard/routine service provision of basic access,	Yes ☐ No ☐ N/A ☐

hospitality, documentation provision and query response	
c) Revision of relevant SOPs or IMP documentation as a result of a substantial protocol amendment	Yes ☐ No ☐ N/A ☐
d) Non-standard reporting of or additional company requested stock or temperature checks	Yes ☐ No ☐ N/A ☐
Miscellaneous Costs	
a) IMP specific consumables (total cost)	Yes ☐ No ☐ N/A ☐
b) Equipment purchase for specific IMP requirements in storage space or conditions (total cost)	Yes ☐ No ☐ N/A ☐
Drug Costs	
a) Name of drug/product	
b) Drug reimbursement to be covered in contract	Yes ☐ No ☐ N/A ☐
Potential Fees that would be specific to individual sites and their agreement to commit to extra workload	
a) Courier/posting costs for IMPs (third party costs as required e.g. per patient)	Yes ☐ No ☐ N/A ☐
b) Out-of-hours working (Usual staff hourly rate + 100%)	Yes ☐ No ☐ N/A ☐
c) Extending working hours (Usual staff hourly rate + 50%)	Yes ☐ No ☐ N/A ☐
d) Other/Comments	

Section 15: Non-commercial Costing	
a) Are fees available for any activities relating to the placebo drug in the project?	Yes ☐ No ☐ N/A ☐
b) Other/Comments	

Section 16: General	
a) Any comments on study design?	
b) Are the archiving arrangements specified?	Yes ☐ No ☐ N/A ☐
c) Other/Comments	

Section 17: Identified Sites		
List all Potential Sites	**Local Pharmacy Contact**	**Contact Made**
		Yes ☐ No ☐ N/A ☐
		Yes ☐ No ☐ N/A ☐
		Yes ☐ No ☐ N/A ☐
		Yes ☐ No ☐ N/A ☐
		Yes ☐ No ☐ N/A ☐

Part 4: Review outcome. To be completed by HRA Pharmacy Reviewer(s) (All nations)

Section 18: Review form completion				
Completed By (Lead Reviewer)	**Employing Organisation/Health Board**	**HRA registered reviewer number**	**Date**	**Outcome**
Penny Bradley	The Newcastle upon Tyne Hospitals NHS Foundation Trust	HRA3729PA	updated 25-Mar-2020 Amendment update 23-Apr-2020	1 ☒ 2 ☐

Outcome

1 **Co-ordinated Review Completed** All risks managed & mitigated. Proceed to final local review

2 **Co-ordinated Review Completed** Some risks require local mitigation. Proceed to local review with clarification required

Completed By (Additional Reviewer)	**Employing Organisation/Health Board**	**HRA registered reviewer number**	**Date**
Mandy Wan	Guy's and St Thomas' NHS Foundation Trust	HRA2979PA	11 May 2020

Appendix: Paediatric dosing table

Taken from protocol version 5, 24 April 2020

Arm	Route	Weight [#]	Dose (Duration for all arms = 10 days or until discharge from hospital)
No additional treatment	-	-	-
Lopinavir-Ritonavir (Kaletra®) - 80/20mg in 1mL oral solution - 100/25mg tablet - 200/50mg tablet Tablets must NOT be crushed	Oral or Nasogastric	Preterm infants with a corrected gestation age of <42 weeks **or** neonates with postnatal age of < 14 days excluded	
		≤ 5 kg	0.2 mL/kg every 12 hours
		6 - 9 kg	1.5 mL every 12 hours
		10 - 13 kg	2 mL every 12 hours
		14 - 19 kg	2.5 mL every 12 hours or 200/50 mg every 12 hours
		20 - 24 kg	3 mL every 12 hours or 200/50 mg every 12 hours
		25 - 34 kg	4 mL every 12 hours or 300/75 mg every 12 hours
		≥ 35 kg	5 mL every 12 hours or 400/100 mg every 12 hours
Corticosteroid - Oral solution* - Tablet* - Soluble tablet* - Solution for injection* *various strengths available	Oral or Nasogastric or Intravenous	All Including pre-term neonates	**Hydrocortisone (IV) – Preterm infants with a corrected gestation age of <40 weeks ONLY:** 0.5 mg/kg every 12 hours for 7 days and then 0.5mg/kg once daily for 3 days or **Prednisolone (Oral/NG)**: 1 mg/kg once daily (max: 40 mg; doses can be rounded as per routine clinical practice) or **Methylprednisolone sodium succinate (IV):** 0.8 mg/kg once daily (max: 32 mg) or **Dexamethasone (Oral/NG/IV)**: 100 micrograms/kg (as base) once daily (max: 6 mg)

[#] Weight to be rounded to the nearest kg unless dosage expressed as mg/kg or mL/kg.

Arm	Route	Weight #	Dose (Duration for all arms = 10 days or until discharge from hospital)
Hydroxychloroquine sulfate <u>Dose expressed as hydroxychloroquine sulfate</u> - 200mg tablet (tablets may be crushed and dispersed in water to allow for aliquot dosing – see note below) **A baseline ECG (to check QTc interval) is recommended for paediatric patients randomised to hydroxychloroquine**	Oral <u>or</u> Nasogastric	Infants with postnatal age of < 180 days excluded	
		5 - 10 kg	Initial dose: 100 mg 6 hours after initial dose: 100 mg 12 hours after initial dose: 50 mg 24 hours after initial dose: 50 mg Then 50 mg every 12 hours
		11 - 20 kg	Initial dose: 200 mg 6 hours after initial dose: 200 mg 12 hours after initial dose: 100 mg 24 hours after initial dose: 100 mg Then 100 mg every 12 hours
		21 - 39 kg	Initial dose: 400 mg 6 hours after initial dose: 400 mg 12 hours after initial dose: 200 mg 24 hours after initial dose: 200 mg Then 200 mg every 12 hours
		≥ 40 kg	Initial dose: 800 mg 6 hours after initial dose: 800 mg 12 hours after initial dose: 400 mg 24 hours after initial dose: 400 mg Then 400 mg every 12 hours
Azithromycin - 40mg in 1mL oral suspension - 250mg tablet/capsule - 500mg tablet/capsule - 500mg powder for solution for infusion	Oral <u>or</u> Nasogastric <u>or</u> Intravenous	≤ 16 kg Including preterm neonates	10 mg/kg once daily
		17 - 25 kg	200 mg once daily
		26 - 35 kg	300 mg once daily
		36 - 45 kg	400 mg once daily
		≥ 46 kg	500 mg once daily

Weight to be rounded to the nearest kg unless dosage expressed as mg/kg or mL/kg.

Note: Hydroxychloroquine oral solution is not available as authorised medicinal product in the EU. The European Directorate for the Quality of Medicines and the European Paediatric Formulary (PaedF) Working Party have, in this exceptional situation, complied <u>existing knowledge on paediatric formulations for hydroxychloroquine</u>. As noted in their document, hydroxychloroquine sulfate is a highly soluble drug and it is expected that manipulation of the formulation will have minimal impact on bioavailability. The extemporaneously preparations described in literature is generally prepared by crushing of tablets and mixing with an aqueous base. On these basis and the urgent public health need of this trial, we propose that hydroxychloroquine tablets to be crushed and dispersed in water to allow for aliquot dosing in children if required**.**

2nd stage randomisation (Patients < 1 year of age will NOT be eligible)

Arm	Route	Weight	Dose
No additional treatment	-	-	-
Tocilizumab	Intravenous	Infants < 1 year excluded	
		< 30 kg	12 mg/kg A second dose may be given ≥12 and ≤24 hours later if, in the opinion of the attending clinicians, the patient's condition has not improved.
		≥ 30 kg	8 mg/kg (max 800 mg) A second dose may be given ≥12 and ≤24 hours later if, in the opinion of the attending clinicians, the patient's condition has not improved.