

REQUEST FOR AUTHORISATION OF A CLINICAL TRIAL ON A MEDICINAL PRODUCT FOR HUMAN USE TO THE COMPETENT AUTHORITIES AND FOR OPINION OF THE ETHICS COMMITTEES IN THE COMMUNITY

For official use:

Date of receiving the request:	Date of request for additional information:	Grounds for non acceptance / negative opinion :
Date of request for information to make it valid:		Give date:
Date of valid application :	Date of receipt of additional / amended information :	Authorisation / positive opinion:
Date of start of procedure :		Give date:
Competent authority registration number :		Withdrawal of application :
Ethics Committee registration number :		Give date :

A: Trial identification

A1. National Competent Authority:

UK - MHRA

A2. European Clinical Trials Database (EudraCT) number:

2020-001113-21

A3. Full title of the trial:

Randomised Evaluation of COVID-19 Therapy (RECOVERY)

A3-1. Title of the trial for lay people, in easily understood, i.e. non-technical, language

RANDOMISED EVALUATION OF COVID-19 THERAPY (RECOVERY)

A3-2. Name or abbreviated title of the trial where available:

RECOVERY trial

A4. Sponsor's protocol:

Number: NDPHRECOVERY

Version: 27.0

Date: 13/09/2023

A5-1. ISRCTN number, if available :

ISRCTN50189673

A5-2. US NCT number:
NCT04381936

A5-3. Who Universal Trial Reference Number (UTRN)

A5-4. Other Identifiers:

Name	Identifier

A6. Is this a resubmission?

Yes No

A7. Is the trial part of a Paediatric Investigation Plan?

Yes No Not Answered

B: Identification of the sponsor responsible for the request

B1. Sponsor

SP1
Contact person

Name of organisation University of Oxford
 Given name NA
 Family name NA
 Address Clinical Trials & Research Governance, 1st Floor, Boundary Brook House, Old Road, Headington
 Town/city OXFORD
 Post code OX3 7GB
 Country United Kingdom
 Telephone 00000
 Fax 00000
 E-mail rgea.sponsor@admin.ox.ac.uk

B2. Legal Representative for the purpose of this CTIMP.
A legal representative must be appointed for a clinical trial of an investigational medicinal product (CTIMP) if the sponsor is not established in the UK or on the MHRA approved country list (please refer to question specific guidance).

Legal Representative 1

Contact person

Name of organisation

Given name
Family name
Address
Town/city
Post code
Country
Telephone
Fax
E-mail

B3. Status of the sponsor: Non-Commercial

B.4 Source(s) of Monetary or Material Support for the clinical trial (repeat as necessary):

B.5 Contact point designated by the sponsor for further information on the trial:

Name of organisation
Functional name of contact point
Street Address
Town/city
Post code
Country
Telephone
Fax
E-mail

C: Applicant identification

C1. Request for the competent authority

C1-1. Who is responsible for the Clinical Trial Authorisation Application?

Sponsor

C1-4. Complete the details of the applicant below even if they are provided elsewhere on the form:

Contact person

Person or organisation name: University of Oxford

Contact person Given name **Ferdousi**

Contact person Family name **Chowdhury**

Address Research Governance, Ethics & Assurance, First Floor, Boundary Brook House

Town/city	Headington, Oxford
Post code	OX3 7GB
Country	United Kingdom
Telephone	00000
Fax	00000
E-mail	rgea.sponsor@admin.ox.ac.uk

C1-5. Do you want a xml file copy of the CTA form data saved on EudraCT?

Yes No Not Answered

C2.Request for ethics committee

C2-1. Who is responsible for the Clinical Trial Authorisation Application?

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C2-5. Complete the details of the applicant below even if they are provided elsewhere on the form

Person or organisation name:

Title:

Forename/Initials:

Surname:

Middlename:

Address:

Town/city:

Post code:

Country:

Telephone:

Fax:

E-mail:

Part D: Investigational Medicinal Products

D: Information on the IMPs

Information on each "bulk product" before trial-specific operations (blinding, trial specific packaging and labelling) should be provided in this section for each investigational medicinal product (IMP) being tested including each comparator, if applicable. If the trial is performed with several products please create a separate set of the following questions for each product. If the product is a combination product please give separate information for each active substance.

Click on the first row and enter details of the product in the following screens. When you have completed the details, click on the navigate button or the "See All" link and return to this section to enter details of the next product. When you have completed details of all products please move to question D7 using the navigation screen.

D. Investigational medicinal products

- PR7 [Hydrocortisone](#)
- PR8 [RoActemra](#)
- PR16 [Kineret](#)
- PR17 [Dexamethasone](#)
- PR19 [Prednisolone](#)
- PR21 [Empagliflozin](#)
- PR22 [Oseltamivir](#)
- PR23 [Baloxavir](#)
- PR24 [Sotrovimab](#)
- PR25 [Molnupiravir](#)
- PR26 [Nirmatrelvir/ritonavir](#)

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR7**
 Investigational medicinal product category:
 Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

Yes No Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

Yes No Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

Yes No Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

Yes No Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

Yes No Not Answered

D2-3. IMPD submitted:

Full IMPD

Yes No Not Answered

Simplified IMPD

Yes No Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

Yes No Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

Yes No Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

Yes No Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

Yes No Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

Yes No Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

Yes No Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable	Hydrocortisone
D.3.2 Product code where applicable	
D.3.3 ATC codes, if officially registered	H02AB09
D.3.4 Pharmaceutical form (use standard terms)	
D.3.4.1 Is this a specific paediatric formulation?	<input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Not Answered
D.3.5 Maximum duration of treatment of a subject according to the protocol	

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial	
D.3.6.1 Specify per day or total:	<input type="radio"/> per day <input type="radio"/> total <input type="radio"/> Not Answered
D.3.6.1 Specify total dose (number and unit)	
D.3.6.1 Route of administration (relevant to the first dose):	
D.3.6.2 Maximum dose allowed	1600 mg
D.3.6.2 Specify per day or total	<input type="radio"/> per day <input checked="" type="radio"/> total <input type="radio"/> Not Answered
D.3.6.2 Specify total dose (number and unit)	1600 mg milligram(s)
D.3.6.2 Route of administration (relevant to the maximum dose):	Intravenous use

D.3.7 Routes of administration for this IMP

Intravenous use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): Hydrocortisone
 CAS number:

Current sponsor code:
 Other descriptive name:
 Full Molecular formula
 Chemical/biological description
 of the Active Substance
Strength

Concentration unit:

Concentration type:

Concentration number (only
 use both fields for range):

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? Yes No Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) Yes No Not Answered

Is this a:

Advanced Therapy IMP (ATIMP) ⁽¹⁾ Yes No Not Answered

Combination product that includes a device, but does not involve an Advanced Therapy Yes No Not Answered

Radiopharmaceutical medicinal product? Yes No Not Answered

Immunological medicinal product (e.g. vaccine, allergen, immune serum)? Yes No Not Answered

Plasma derived medicinal product? Yes No Not Answered

Extractive medicinal product? Yes No Not Answered

Recombinant medicinal product? Yes No Not Answered

Medicinal product containing genetically modified organisms? Yes No Not Answered

Herbal medicinal product? Yes No Not Answered

Homeopathic medicinal product? Yes No Not Answered

Another type of medicinal product? Yes No Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action.

Immunomodulatory

Is it an IMP to be used in a first-in-human clinical trial? Yes No Not Answered

^(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

^(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

⁽⁴⁾ As defined in Article 2(1)(b) of Regulation 1394/2007/EC

⁽⁶⁾ Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

DRAFT

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR8**
 Investigational medicinal product category:
 Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

Yes No Not Answered

Trade name:

RoActemra

EV Product Code

Name of the MA holder:

Roche

MA number (if MA granted by a Member State):

EU/1/08/492/001

Is the IMP modified in relation to its MA?

Yes No Not Answered

Which country granted the MA?

UK - MHRA

Is this the Member State concerned with this application?

Yes No Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

Yes No Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

Yes No Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

Yes No Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

Yes No Not Answered

D2-3. IMPD submitted:

Full IMPD

Yes No Not Answered

Simplified IMPD

Yes No Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

Yes No Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

Yes No Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

Yes No Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

Yes No Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

Yes No Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

Yes No Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable RoActemra

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered L04AC07

D.3.4 Pharmaceutical form (use standard terms)

D.3.4.1 Is this a specific paediatric formulation? Yes No Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol

D.3.6 Dose allowed	
D.3.6.1 First dose for first-in-human clinical trial	
D.3.6.1 Specify per day or total:	<input type="radio"/> per day <input type="radio"/> total <input type="radio"/> Not Answered
D.3.6.1 Specify total dose (number and unit)	
D.3.6.1 Route of administration (relevant to the first dose):	
D.3.6.2 Maximum dose allowed 1600 mg	
D.3.6.2 Specify per day or total	<input type="radio"/> per day <input checked="" type="radio"/> total <input type="radio"/> Not Answered
D.3.6.2 Specify total dose (number and unit)	1600 mg milligram(s)
D.3.6.2 Route of administration (relevant to the maximum dose): Intravenous use	

D.3.7 Routes of administration for this IMP
Intravenous use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1	
Name of active substance (INN or proposed INN if available): Tocilizumab	
CAS number:	
Current sponsor code:	
Other descriptive name:	
Full Molecular formula	
Chemical/biological description of the Active Substance	
<i>Strength</i>	
Concentration unit:	mg/ml milligram(s)/millilitre
Concentration type:	equal
Concentration number (only use both fields for range):	20

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin?

Yes No Not Answered

- Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) Yes No Not Answered
- Is this a:*
- Advanced Therapy IMP (ATIMP) ⁽¹⁾ Yes No Not Answered
- Combination product that includes a device, but does not involve an Advanced Therapy Yes No Not Answered
- Radiopharmaceutical medicinal product? Yes No Not Answered
- Immunological medicinal product (e.g. vaccine, allergen, immune serum)? Yes No Not Answered
- Plasma derived medicinal product? Yes No Not Answered
- Extractive medicinal product? Yes No Not Answered
- Recombinant medicinal product? Yes No Not Answered
- Medicinal product containing genetically modified organisms? Yes No Not Answered
- Herbal medicinal product? Yes No Not Answered
- Homeopathic medicinal product? Yes No Not Answered
- Another type of medicinal product? Yes No Not Answered

Specify the mode of action for the active substance in this medicinal product
The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Anti-interleukin 6 receptor antagonist

Is it an IMP to be used in a first-in-human clinical trial? Yes No Not Answered

(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

(4) As defined in Article 2(1)(b) of Regulation 1394/2007/EC

(6) Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR16**
Investigational medicinal product category:
Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

Yes No Not Answered

Trade name:

Kineret

EV Product Code

Name of the MA holder:

Swedish Orphan Biovitrum Ltd

MA number (if MA granted by a Member State):

EU/1/02/203/005

Is the IMP modified in relation to its MA?

Yes No Not Answered

Which country granted the MA?

Sweden

Is this the Member State concerned with this application?

Yes No Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

Yes No Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

Yes No Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

Yes No Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

Yes No Not Answered

D2-3. IMPD submitted:

Full IMPD

Yes No Not Answered

Simplified IMPD

Yes No Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

Yes No Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

Yes No Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

Yes No Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

Yes No Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

Yes No Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

Yes No Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable

Kineret

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered

L04AC03

D.3.4 Pharmaceutical form (use standard terms)

Solution for injection

D.3.4.1 Is this a specific paediatric formulation?

Yes No Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol

D.3.6 Dose allowed	
D.3.6.1 First dose for first-in-human clinical trial	
D.3.6.1 Specify per day or total:	<input type="radio"/> per day <input type="radio"/> total <input type="radio"/> Not Answered
D.3.6.1 Specify total dose (number and unit)	
D.3.6.1 Route of administration (relevant to the first dose):	
D.3.6.2 Maximum dose allowed	
D.3.6.2 Specify per day or total	2 mg/kg for 7 days <input checked="" type="radio"/> per day <input type="radio"/> total <input type="radio"/> Not Answered
D.3.6.2 Specify total dose (number and unit)	2 mg/kg milligram(s)/kilogram
D.3.6.2 Route of administration (relevant to the maximum dose): Subcutaneous use	

D.3.7 Routes of administration for this IMP
Intravenous use
Subcutaneous use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances
<i>Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.</i>
<p>Active Substance 1</p> <p>Name of active substance (INN or proposed INN if available): Anakinra</p> <p>CAS number:</p> <p>Current sponsor code:</p> <p>Other descriptive name:</p> <p>Full Molecular formula</p> <p>Chemical/biological description of the Active Substance</p> <p><i>Strength</i></p> <p>Concentration unit: mg/ml milligram(s)/millilitre</p> <p>Concentration type: equal</p> <p>Concentration number (only use both fields for range): 150</p>

D3-11. Type of IMP
Does the IMP contain an active substance:
Of chemical origin? <input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Not Answered

- Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) Yes No Not Answered
- Is this a:*
- Advanced Therapy IMP (ATIMP) ⁽¹⁾ Yes No Not Answered
- Combination product that includes a device, but does not involve an Advanced Therapy Yes No Not Answered
- Radiopharmaceutical medicinal product? Yes No Not Answered
- Immunological medicinal product (e.g. vaccine, allergen, immune serum)? Yes No Not Answered
- Plasma derived medicinal product? Yes No Not Answered
- Extractive medicinal product? Yes No Not Answered
- Recombinant medicinal product? Yes No Not Answered
- Medicinal product containing genetically modified organisms? Yes No Not Answered
- Herbal medicinal product? Yes No Not Answered
- Homeopathic medicinal product? Yes No Not Answered
- Another type of medicinal product? Yes No Not Answered

Specify the mode of action for the active substance in this medicinal product
The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Human interleukin-1 receptor antagonist to reduce inflammation in PIMS-TS.

Is it an IMP to be used in a first-in-human clinical trial? Yes No Not Answered

(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

(4) As defined in Article 2(1)(b) of Regulation 1394/2007/EC

(6) Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR17**
 Investigational medicinal product category:
 Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

Yes No Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

Yes No Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

Yes No Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

Yes No Not Answered

Other :

Yes No Not Answered

D2-3. IMPD submitted:

Full IMPD

Yes No Not Answered

Simplified IMPD

Yes No Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

Yes No Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

Yes No Not Answered

Specify which Member States:

AUSTRIA	<input type="checkbox"/>	BELGIUM	<input type="checkbox"/>	BULGARIA	<input type="checkbox"/>
CROATIA	<input type="checkbox"/>	CYPRUS	<input type="checkbox"/>	CZECH REPUBLIC	<input type="checkbox"/>
DENMARK	<input type="checkbox"/>	ESTONIA	<input type="checkbox"/>	FINLAND	<input type="checkbox"/>

FRANCE	<input type="checkbox"/>	GERMANY	<input type="checkbox"/>	GREECE	<input type="checkbox"/>
HUNGARY	<input type="checkbox"/>	ICELAND	<input type="checkbox"/>	IRELAND	<input type="checkbox"/>
ITALY	<input type="checkbox"/>	LATVIA	<input type="checkbox"/>	LIECHTENSTEIN	<input type="checkbox"/>
LITHUANIA	<input type="checkbox"/>	LUXEMBOURG	<input type="checkbox"/>	MALTA	<input type="checkbox"/>
NETHERLANDS	<input type="checkbox"/>	NORWAY	<input type="checkbox"/>	POLAND	<input type="checkbox"/>
PORTUGAL	<input type="checkbox"/>	ROMANIA	<input type="checkbox"/>	SLOVAKIA	<input type="checkbox"/>
SLOVENIA	<input type="checkbox"/>	SPAIN	<input type="checkbox"/>	SWEDEN	<input type="checkbox"/>
UNITED KINGDOM	<input checked="" type="checkbox"/>				

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

Yes No Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

Yes No Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

Yes No Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

Yes No Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable	Dexamethasone
D.3.2 Product code where applicable	
D.3.3 ATC codes, if officially registered	H02AB02
D.3.4 Pharmaceutical form (use standard terms)	Concentrate for solution for infusion
D.3.4.1 Is this a specific paediatric formulation?	<input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Not Answered
D.3.5 Maximum duration of treatment of a subject according to the protocol	3 days

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial
 D.3.6.1 Specify per day or total: per day total Not Answered
 D.3.6.1 Specify total dose (number and unit)
 D.3.6.1 Route of administration (relevant to the first dose):

D.3.6.2 Maximum dose allowed 59.4 mg
 D.3.6.2 Specify per day or total per day total Not Answered
 D.3.6.2 Specify total dose (number and unit) 59.4 mg
 milligram(s)
 D.3.6.2 Route of administration (relevant to the maximum dose): Intravenous use

D.3.7 Routes of administration for this IMP

Intravenous use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): Dexamethasone

CAS number:

Current sponsor code:

Other descriptive name:

Full Molecular formula

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg milligram(s)

Concentration type: equal

Concentration number (only use both fields for range): 5

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? Yes No Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) Yes No Not Answered

Is this a:

- Advanced Therapy IMP (ATIMP) ⁽¹⁾ Yes No Not Answered
- Combination product that includes a device, but does not involve an Advanced Therapy Yes No Not Answered
- Radiopharmaceutical medicinal product? Yes No Not Answered
- Immunological medicinal product (e.g. vaccine, allergen, immune serum)? Yes No Not Answered
- Plasma derived medicinal product? Yes No Not Answered
- Extractive medicinal product? Yes No Not Answered
- Recombinant medicinal product? Yes No Not Answered
- Medicinal product containing genetically modified organisms? Yes No Not Answered
- Herbal medicinal product? Yes No Not Answered
- Homeopathic medicinal product? Yes No Not Answered
- Another type of medicinal product? Yes No Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Immune response modulation

Is it an IMP to be used in a first-in-human clinical trial? Yes No Not Answered

(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

(4) As defined in Article 2(1)(b) of Regulation 1394/2007/EC

(6) Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR19**
 Investigational medicinal product category:
 Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

Yes No Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

Yes No Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

Yes No Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

Yes No Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

Yes No Not Answered

D2-3. IMPD submitted:

Full IMPD

Yes No Not Answered

Simplified IMPD

Yes No Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

Yes No Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

Yes No Not Answered

Specify which Member States:

AUSTRIA

BELGIUM

BULGARIA

CROATIA	<input type="checkbox"/>	CYPRUS	<input type="checkbox"/>	CZECH REPUBLIC	<input type="checkbox"/>
DENMARK	<input type="checkbox"/>	ESTONIA	<input type="checkbox"/>	FINLAND	<input type="checkbox"/>
FRANCE	<input type="checkbox"/>	GERMANY	<input type="checkbox"/>	GREECE	<input type="checkbox"/>
HUNGARY	<input type="checkbox"/>	ICELAND	<input type="checkbox"/>	IRELAND	<input type="checkbox"/>
ITALY	<input type="checkbox"/>	LATVIA	<input type="checkbox"/>	LIECHTENSTEIN	<input type="checkbox"/>
LITHUANIA	<input type="checkbox"/>	LUXEMBOURG	<input type="checkbox"/>	MALTA	<input type="checkbox"/>
NETHERLANDS	<input type="checkbox"/>	NORWAY	<input type="checkbox"/>	POLAND	<input type="checkbox"/>
PORTUGAL	<input type="checkbox"/>	ROMANIA	<input type="checkbox"/>	SLOVAKIA	<input type="checkbox"/>
SLOVENIA	<input type="checkbox"/>	SPAIN	<input type="checkbox"/>	SWEDEN	<input type="checkbox"/>
UNITED KINGDOM	<input checked="" type="checkbox"/>				

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

Yes No Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

Yes No Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

Yes No Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

Yes No Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable	Prednisolone
D.3.2 Product code where applicable	
D.3.3 ATC codes, if officially registered	H02AB06
D.3.4 Pharmaceutical form (use standard terms)	Tablet
D.3.4.1 Is this a specific paediatric formulation?	<input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Not Answered
D.3.5 Maximum duration of treatment of a subject according to the protocol	10 days

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total: per day total Not Answered

D.3.6.1 Specify total dose (number and unit)

D.3.6.1 Route of administration (relevant to the first dose):

D.3.6.2 Maximum dose allowed 975 mg over 10 days

D.3.6.2 Specify per day or total per day total Not Answered

D.3.6.2 Specify total dose (number and unit) 975 mg milligram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Oral use

D.3.7 Routes of administration for this IMP

Oral use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): Prednisolone

CAS number:

Current sponsor code:

Other descriptive name:

Full Molecular formula

Chemical/biological description of the Active Substance

Strength

Concentration unit:

Concentration type:

Concentration number (only use both fields for range):

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin?

Yes No Not Answered

- Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) Yes No Not Answered
- Is this a:*
- Advanced Therapy IMP (ATIMP) ⁽¹⁾ Yes No Not Answered
- Combination product that includes a device, but does not involve an Advanced Therapy Yes No Not Answered
- Radiopharmaceutical medicinal product? Yes No Not Answered
- Immunological medicinal product (e.g. vaccine, allergen, immune serum)? Yes No Not Answered
- Plasma derived medicinal product? Yes No Not Answered
- Extractive medicinal product? Yes No Not Answered
- Recombinant medicinal product? Yes No Not Answered
- Medicinal product containing genetically modified organisms? Yes No Not Answered
- Herbal medicinal product? Yes No Not Answered
- Homeopathic medicinal product? Yes No Not Answered
- Another type of medicinal product? Yes No Not Answered

Specify the mode of action for the active substance in this medicinal product
The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action.
 Immunomodulatory

Is it an IMP to be used in a first-in-human clinical trial? Yes No Not Answered

^(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

^(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

⁽⁴⁾ As defined in Article 2(1)(b) of Regulation 1394/2007/EC

⁽⁶⁾ Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR21**
Investigational medicinal product category:
Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

Yes No Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

Yes No Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

Yes No Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

Yes No Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

Yes No Not Answered

D2-3. IMPD submitted:

Full IMPD

Yes No Not Answered

Simplified IMPD

Yes No Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

Yes No Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

Yes No Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

Yes No Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

Yes No Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

Yes No Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

Yes No Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable Empagliflozin

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered A10BK03

D.3.4 Pharmaceutical form (use standard terms) Film-coated tablet

D.3.4.1 Is this a specific paediatric formulation? Yes No Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol Duration of admission (average 15 days)

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total: per day total Not Answered

D.3.6.1 Specify total dose (number and unit) 10 mg
milligram(s)

D.3.6.1 Route of administration (relevant to the first dose): Oral use

D.3.6.2 Maximum dose allowed 10 mg once daily

D.3.6.2 Specify per day or total per day total Not Answered

D.3.6.2 Specify total dose (number and unit)	10	mg milligram(s)
D.3.6.2 Route of administration (relevant to the maximum dose): Oral use		

D.3.7 Routes of administration for this IMP

Oral use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): Empagliflozin

CAS number:

Current sponsor code:

Other descriptive name:

Full Molecular formula

Chemical/biological description of the Active Substance

Strength

Concentration unit:

Concentration type:

Concentration number (only use both fields for range):

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? Yes No Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) Yes No Not Answered

Is this a:

Advanced Therapy IMP (ATIMP) ⁽¹⁾ Yes No Not Answered

Combination product that includes a device, but does not involve an Advanced Therapy Yes No Not Answered

Radiopharmaceutical medicinal product? Yes No Not Answered

Immunological medicinal product (e.g. vaccine, allergen, immune serum)? Yes No Not Answered

Plasma derived medicinal product? Yes No Not Answered

Extractive medicinal product? Yes No Not Answered

- Recombinant medicinal product? Yes No Not Answered
- Medicinal product containing genetically modified organisms? Yes No Not Answered
- Herbal medicinal product? Yes No Not Answered
- Homeopathic medicinal product? Yes No Not Answered
- Another type of medicinal product? Yes No Not Answered

Specify the mode of action for the active substance in this medicinal product
The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Anti-inflammatory; anti-oxidant; haemodynamic

Is it an IMP to be used in a first-in-human clinical trial? Yes No Not Answered

(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

(4) As defined in Article 2(1)(b) of Regulation 1394/2007/EC

(6) Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR22**
Investigational medicinal product category:
Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

Yes No Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

Yes No Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

Yes No Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

The products to be administered as IMPs are defined as belonging to an ATC group

Yes No Not Answered

Other :

Yes No Not Answered

D2-3. IMPD submitted:

Full IMPD

Yes No Not Answered

Simplified IMPD

Yes No Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

Yes No Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

Yes No Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

Yes No Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

Yes No Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

Yes No Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

Yes No Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable Oseltamivir

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered J05AH02

D.3.4 Pharmaceutical form (use standard terms) Capsule, hard

D.3.4.1 Is this a specific paediatric formulation? Yes No Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol 10 days

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total: per day total Not Answered

D.3.6.1 Specify total dose (number and unit)

D.3.6.1 Route of administration (relevant to the first dose):

D.3.6.2 Maximum dose allowed 1500 mg

D.3.6.2 Specify per day or total per day total Not Answered

D.3.6.2 Specify total dose (number and unit) 1500 mg
milligram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Oral use

D.3.7 Routes of administration for this IMP

Oral use
Nasogastric use (Noncurrent)

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): Oseltamivir

CAS number:

Current sponsor code:

Other descriptive name:

Full Molecular formula

Chemical/biological description of the Active Substance

Strength

Concentration unit:

Concentration type:

Concentration number (only use both fields for range):

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? Yes No Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) Yes No Not Answered

Is this a:

Advanced Therapy IMP (ATIMP) ⁽¹⁾ Yes No Not Answered

Combination product that includes a device, but does not involve an Advanced Therapy Yes No Not Answered

Radiopharmaceutical medicinal product? Yes No Not Answered

Immunological medicinal product (e.g. vaccine, allergen, immune serum)? Yes No Not Answered

Plasma derived medicinal product? Yes No Not Answered

Extractive medicinal product? Yes No Not Answered

Recombinant medicinal product? Yes No Not Answered

Medicinal product containing genetically modified organisms? Yes No Not Answered

- Herbal medicinal product? Yes No Not Answered
- Homeopathic medicinal product? Yes No Not Answered
- Another type of medicinal product? Yes No Not Answered

Specify the mode of action for the active substance in this medicinal product
The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Antiviral therapy

- Is it an IMP to be used in a first-in-human clinical trial? Yes No Not Answered

(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

(4) As defined in Article 2(1)(b) of Regulation 1394/2007/EC

(6) Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

DRAFT

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR23**
 Investigational medicinal product category:
 Test IMP

D2. Status of the IMP if the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

Yes No Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

Yes No Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

Yes No Not Answered

The products to be administered as IMPs are defined as belonging to an ATC group

Yes No Not Answered

Other :

Yes No Not Answered

D2-3. IMPD submitted:

Full IMPD

Yes No Not Answered

Simplified IMPD

Yes No Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

Yes No Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

Yes No Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

Yes No Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

Yes No Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

Yes No Not Answered

CHMP = *Committee for Medicinal Products for Human Use*

From a MS competent authority?

Yes No Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable	Baloxavir
D.3.2 Product code where applicable	
D.3.3 ATC codes, if officially registered	J05AX25
D.3.4 Pharmaceutical form (use standard terms)	Film-coated tablet
D.3.4.1 Is this a specific paediatric formulation?	<input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Not Answered
D.3.5 Maximum duration of treatment of a subject according to the protocol	Two doses: day 1 and day 4

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial	
D.3.6.1 Specify per day or total:	<input type="radio"/> per day <input type="radio"/> total <input type="radio"/> Not Answered
D.3.6.1 Specify total dose (number and unit)	
D.3.6.1 Route of administration (relevant to the first dose):	
D.3.6.2 Maximum dose allowed	160 mg
D.3.6.2 Specify per day or total	<input type="radio"/> per day <input checked="" type="radio"/> total <input type="radio"/> Not Answered
D.3.6.2 Specify total dose (number and unit)	160 mg milligram(s)
D.3.6.2 Route of administration (relevant to the maximum dose):	Oral use

D.3.7 Routes of administration for this IMP

Oral use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): Baloxavir

CAS number:

Current sponsor code:

Other descriptive name:

Full Molecular formula

Chemical/biological description of the Active Substance

Strength

Concentration unit:

Concentration type:

Concentration number (only use both fields for range):

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? Yes No Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) Yes No Not Answered

Is this a:

Advanced Therapy IMP (ATIMP) ⁽¹⁾ Yes No Not Answered

Combination product that includes a device, but does not involve an Advanced Therapy Yes No Not Answered

Radiopharmaceutical medicinal product? Yes No Not Answered

Immunological medicinal product (e.g. vaccine, allergen, immune serum)? Yes No Not Answered

Plasma derived medicinal product? Yes No Not Answered

Extractive medicinal product? Yes No Not Answered

Recombinant medicinal product? Yes No Not Answered

Medicinal product containing genetically modified organisms? Yes No Not Answered

Herbal medicinal product? Yes No Not Answered

Homeopathic medicinal product?

Yes No Not Answered

Another type of medicinal product?

Yes No Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Anti-viral.

Is it an IMP to be used in a first-in-human clinical trial?

Yes No Not Answered

(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

(4) As defined in Article 2(1)(b) of Regulation 1394/2007/EC

(6) Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

DRAFT

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR24**
Investigational medicinal product category:
Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

Yes No Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

Yes No Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

Yes No Not Answered

The products to be administered as IMPs are defined as belonging to an ATC group

Yes No Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :

Yes No Not Answered

D2-3. IMPD submitted:

Full IMPD

Yes No Not Answered

Simplified IMPD

Yes No Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

Yes No Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

Yes No Not Answered

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

Yes No Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

Yes No Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

Yes No Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

Yes No Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable Sotrovimab

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered

D.3.4 Pharmaceutical form (use standard terms) Solution for infusion

D.3.4.1 Is this a specific paediatric formulation? Yes No Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol Single dose only

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial

D.3.6.1 Specify per day or total: per day total Not Answered

D.3.6.1 Specify total dose (number and unit)

D.3.6.1 Route of administration (relevant to the first dose):

D.3.6.2 Maximum dose allowed 1000 mg

D.3.6.2 Specify per day or total per day total Not Answered

D.3.6.2 Specify total dose (number and unit) 1000 mg milligram(s)

D.3.6.2 Route of administration (relevant to the maximum dose): Intravenous use

D.3.7 Routes of administration for this IMP

Intravenous use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): Sotrovimab

CAS number:

Current sponsor code:

Other descriptive name:

Full Molecular formula

Chemical/biological description of the Active Substance: Monoclonal antibody against SARS-CoV-2 spike protein.

Strength

Concentration unit: mg milligram(s)

Concentration type: equal

Concentration number (only use both fields for range): 500

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? Yes No Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) Yes No Not Answered

Is this a:

Advanced Therapy IMP (ATIMP) ⁽¹⁾ Yes No Not Answered

Combination product that includes a device, but does not involve an Advanced Therapy Yes No Not Answered

Radiopharmaceutical medicinal product? Yes No Not Answered

Immunological medicinal product (e.g. vaccine, allergen, immune serum)? Yes No Not Answered

Plasma derived medicinal product? Yes No Not Answered

Extractive medicinal product? Yes No Not Answered

Recombinant medicinal product? Yes No Not Answered

Medicinal product containing genetically modified organisms? Yes No Not Answered

- Herbal medicinal product? Yes No Not Answered
- Homeopathic medicinal product? Yes No Not Answered
- Another type of medicinal product? Yes No Not Answered

Specify the mode of action for the active substance in this medicinal product
The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Anti-SARS-CoV-2 spike protein human monoclonal IgG antibody

Is it an IMP to be used in a first-in-human clinical trial? Yes No Not Answered

(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

(4) As defined in Article 2(1)(b) of Regulation 1394/2007/EC

(6) Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

DRAFT

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR25**
 Investigational medicinal product category:
 Test IMP

D2. Status of the IMP if the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

Yes No Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?

Yes No Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?

Yes No Not Answered

The products to be administered as IMPs are defined as belonging to an ATC group

Yes No Not Answered

Other :

Yes No Not Answered

D2-3. IMPD submitted:

Full IMPD

Yes No Not Answered

Simplified IMPD

Yes No Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only

Yes No Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

Yes No Not Answered

Specify which Member States:

AUSTRIA	<input type="checkbox"/>	BELGIUM	<input type="checkbox"/>	BULGARIA	<input type="checkbox"/>
CROATIA	<input type="checkbox"/>	CYPRUS	<input type="checkbox"/>	CZECH REPUBLIC	<input type="checkbox"/>
DENMARK	<input type="checkbox"/>	ESTONIA	<input type="checkbox"/>	FINLAND	<input type="checkbox"/>
FRANCE	<input type="checkbox"/>	GERMANY	<input type="checkbox"/>	GREECE	<input type="checkbox"/>

HUNGARY	<input type="checkbox"/>	ICELAND	<input type="checkbox"/>	IRELAND	<input type="checkbox"/>
ITALY	<input type="checkbox"/>	LATVIA	<input type="checkbox"/>	LIECHTENSTEIN	<input type="checkbox"/>
LITHUANIA	<input type="checkbox"/>	LUXEMBOURG	<input type="checkbox"/>	MALTA	<input type="checkbox"/>
NETHERLANDS	<input type="checkbox"/>	NORWAY	<input type="checkbox"/>	POLAND	<input type="checkbox"/>
PORTUGAL	<input type="checkbox"/>	ROMANIA	<input type="checkbox"/>	SLOVAKIA	<input type="checkbox"/>
SLOVENIA	<input type="checkbox"/>	SPAIN	<input type="checkbox"/>	SWEDEN	<input type="checkbox"/>
UNITED KINGDOM	<input checked="" type="checkbox"/>				

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

Yes No Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

Yes No Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

Yes No Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

Yes No Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable Molnupiravir

D.3.2 Product code where applicable

D.3.3 ATC codes, if officially registered

D.3.4 Pharmaceutical form (use standard terms)

D.3.4.1 Is this a specific paediatric formulation? Yes No Not Answered

D.3.5 Maximum duration of treatment of a subject according to the protocol 5 days

D.3.6 Dose allowed

D.3.6.1 First dose for first-in-human clinical trial	
D.3.6.1 Specify per day or total:	<input type="radio"/> per day <input type="radio"/> total <input type="radio"/> Not Answered
D.3.6.1 Specify total dose (number and unit)	
D.3.6.1 Route of administration (relevant to the first dose):	
D.3.6.2 Maximum dose allowed	8000 mg
D.3.6.2 Specify per day or total:	<input type="radio"/> per day <input checked="" type="radio"/> total <input type="radio"/> Not Answered
D.3.6.2 Specify total dose (number and unit)	8000 mg milligram(s)
D.3.6.2 Route of administration (relevant to the maximum dose): Oral use	

D.3.7 Routes of administration for this IMP

Oral use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1

Name of active substance (INN or proposed INN if available): Molnupiravir

CAS number:

Current sponsor code:

Other descriptive name:

Full Molecular formula

Chemical/biological description of the Active Substance

Strength

Concentration unit: mg milligram(s)

Concentration type: equal

Concentration number (only use both fields for range): 200

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? Yes No Not Answered

Of biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) Yes No Not Answered

Is this a:

- Advanced Therapy IMP (ATIMP) ⁽¹⁾ Yes No Not Answered
- Combination product that includes a device, but does not involve an Advanced Therapy Yes No Not Answered
- Radiopharmaceutical medicinal product? Yes No Not Answered
- Immunological medicinal product (e.g. vaccine, allergen, immune serum)? Yes No Not Answered
- Plasma derived medicinal product? Yes No Not Answered
- Extractive medicinal product? Yes No Not Answered
- Recombinant medicinal product? Yes No Not Answered
- Medicinal product containing genetically modified organisms? Yes No Not Answered
- Herbal medicinal product? Yes No Not Answered
- Homeopathic medicinal product? Yes No Not Answered
- Another type of medicinal product? Yes No Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Molnupiravir is a prodrug that is metabolised to the ribonucleoside analogue N-hydroxycytidine (NHC) which distributes into cells where it is phosphorylated to form the pharmacologically active ribonucleoside triphosphate (NHC-TP). NHC-TP acts by a mechanism known as viral error catastrophe. NHC-TP incorporation into viral RNA by the viral RNA polymerase, results in an accumulation of errors in the viral genome leading to inhibition of replication.

Is it an IMP to be used in a first-in-human clinical trial? Yes No Not Answered

^(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

^(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

⁽⁴⁾ As defined in Article 2(1)(b) of Regulation 1394/2007/EC

⁽⁶⁾ Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D1. Indicate which of the following is described below then repeat as necessary for each:

This refers to the IMP number: **PR26**
 Investigational medicinal product category:
 Test IMP

D2. Status of the IMP *If the IMP has a marketing authorisation in the Member State concerned by this application but the trade name and marketing authorisation holder are not fixed in the protocol, go to section D.2.2*

D2-1. Does the IMP to be used in the trial have a marketing authorisation?

Yes No Not Answered

D2-2. Situations where an IMP to be used in the CT has a MA in the MS concerned, but the protocol allows that any brand of the IMP with a MA in that MS be administered to the trial subjects and it is not possible to clearly identify the IMP(s) in advance of the trial start

In the protocol, is treatment defined only by active substance?
 Yes No Not Answered

If 'Yes', give active substance in D.3.8 or D.3.9

In the protocol, do treatment regimens allow different combinations of marketed products used according to local clinical practice at some or all investigator sites in the MS?
 Yes No Not Answered

The products to be administered as IMPs are defined as belonging to an ATC group
 Yes No Not Answered

If yes, give the ATC group of the applicable authorised codes in the ATC code field (level 3 or the level that can be defined) in D.3.1

Other :
 Yes No Not Answered

D2-3. IMPD submitted:

Full IMPD
 Yes No Not Answered

Simplified IMPD
 Yes No Not Answered

Provide justification for using simplified dossier in the covering letter

Summary of product characteristics (SmPC) only
 Yes No Not Answered

D2-4. Has the use of the IMP been previously authorised in a clinical trial conducted by the sponsor in the Community?

Yes No Not Answered

Specify which Member States:

AUSTRIA	<input type="checkbox"/>	BELGIUM	<input type="checkbox"/>	BULGARIA	<input type="checkbox"/>
CROATIA	<input type="checkbox"/>	CYPRUS	<input type="checkbox"/>	CZECH REPUBLIC	<input type="checkbox"/>

DENMARK	<input type="checkbox"/>	ESTONIA	<input type="checkbox"/>	FINLAND	<input type="checkbox"/>
FRANCE	<input type="checkbox"/>	GERMANY	<input type="checkbox"/>	GREECE	<input type="checkbox"/>
HUNGARY	<input type="checkbox"/>	ICELAND	<input type="checkbox"/>	IRELAND	<input type="checkbox"/>
ITALY	<input type="checkbox"/>	LATVIA	<input type="checkbox"/>	LIECHTENSTEIN	<input type="checkbox"/>
LITHUANIA	<input type="checkbox"/>	LUXEMBOURG	<input type="checkbox"/>	MALTA	<input type="checkbox"/>
NETHERLANDS	<input type="checkbox"/>	NORWAY	<input type="checkbox"/>	POLAND	<input type="checkbox"/>
PORTUGAL	<input type="checkbox"/>	ROMANIA	<input type="checkbox"/>	SLOVAKIA	<input type="checkbox"/>
SLOVENIA	<input type="checkbox"/>	SPAIN	<input type="checkbox"/>	SWEDEN	<input type="checkbox"/>
UNITED KINGDOM	<input checked="" type="checkbox"/>				

D2-5. Has the IMP been designated in this indication as an orphan drug in the Community?

Yes No Not Answered

D2-6. Has the IMP been the subject of scientific advice related to this clinical trial?

Yes No Not Answered

Please indicate source of advice and provide a copy in the CTA request:

From the CHMP?

Yes No Not Answered

CHMP = Committee for Medicinal Products for Human Use

From a MS competent authority?

Yes No Not Answered

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3. Description of IMP

D3-1.

D.3.1 Product name where applicable	Nirmatrelvir/ritonavir
D.3.2 Product code where applicable	
D.3.3 ATC codes, if officially registered	
D.3.4 Pharmaceutical form (use standard terms)	Film-coated tablet
D.3.4.1 Is this a specific paediatric formulation?	<input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Not Answered
D.3.5 Maximum duration of treatment of a subject according to the protocol	5 days

D.3.6 Dose allowed	
D.3.6.1 First dose for first-in-human clinical trial	
D.3.6.1 Specify per day or total:	<input type="radio"/> per day <input type="radio"/> total <input type="radio"/> Not Answered
D.3.6.1 Specify total dose (number and unit)	
D.3.6.1 Route of administration (relevant to the first dose):	
D.3.6.2 Maximum dose allowed	
	3000 mg Nirmatrelvir 1000 mg Ritonavir
D.3.6.2 Specify per day or total	<input type="radio"/> per day <input checked="" type="radio"/> total <input type="radio"/> Not Answered
D.3.6.2 Specify total dose (number and unit)	
D.3.6.2 Route of administration (relevant to the maximum dose):	

D.3.7 Routes of administration for this IMP
Oral use

This is a sub-set of questions about each IMP. To return to the list of IMPs select "See all" at the top of the page or select "Navigate". To complete further questions about this IMP select "Next".

D3-8. Active substances

Complete all fields that currently apply to this Active Substance in this Product. If you have IMPs with different concentrations of the Active Substance complete a new Sub-section D for each.

Active Substance 1	
Name of active substance (INN or proposed INN if available):	Nirmatrelvir
CAS number:	
Current sponsor code:	
Other descriptive name:	
Full Molecular formula	
Chemical/biological description of the Active Substance	
<i>Strength</i>	
Concentration unit:	mg milligram(s)
Concentration type:	equal
Concentration number (only use both fields for range):	150
Active Substance 2	
Name of active substance (INN or proposed INN if available):	Ritonavir
CAS number:	155213-67-5
Current sponsor code:	
Other descriptive name:	

Full Molecular formula	C37H48N6O5S2
Chemical/biological description of the Active Substance	
<i>Strength</i>	
Concentration unit:	mg milligram(s)
Concentration type:	equal
Concentration number (only use both fields for range):	100

D3-11. Type of IMP

Does the IMP contain an active substance:

Of chemical origin? Yes No Not AnsweredOf biological / biotechnological origin?(other than Advanced Therapy IMP (ATIMP)) Yes No Not Answered*Is this a:*Advanced Therapy IMP (ATIMP) ⁽¹⁾ Yes No Not AnsweredCombination product that includes a device, but does not involve an Advanced Therapy Yes No Not AnsweredRadiopharmaceutical medicinal product? Yes No Not AnsweredImmunological medicinal product (e.g. vaccine, allergen, immune serum)? Yes No Not AnsweredPlasma derived medicinal product? Yes No Not AnsweredExtractive medicinal product? Yes No Not AnsweredRecombinant medicinal product? Yes No Not AnsweredMedicinal product containing genetically modified organisms? Yes No Not AnsweredHerbal medicinal product? Yes No Not AnsweredHomeopathic medicinal product? Yes No Not AnsweredAnother type of medicinal product? Yes No Not Answered

Specify the mode of action for the active substance in this medicinal product

The mode of action should briefly describe the chemical, biochemical, immunological or biological means that the IMP uses to effect its pharmaceutical action. Nirmatrelvir is a 3-chymotrypsin-like protease inhibitor which inhibits cleavage of polyproteins involved in viral replication. It is co-formulated with ritonavir which inhibits its CYP3A-dependent metabolism and hence increases the plasma concentration of nirmatrelvir.

Is it an IMP to be used in a first-in-human clinical trial? Yes No Not Answered

(1,2,3,4,5) Complete sections D.4, D.5, D.6. and D.7, as applicable

(2,3) As defined in Annex 1 part IV of Directive 2001/83/EC as amended

(4) As defined in Article 2(1)(b) of Regulation 1394/2007/EC

(6) Guideline on strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products. EMEA/CHMP/SWP/28367/2007

D8. Information on placebo (if relevant; repeat as necessary)

D8. Is there a placebo:

Yes No Not Answered

D9. Sites responsible for final QP release for distribution to investigators.

D9-1. IMPs and placebos for which no responsible site needs to be identified.

This section is used to identify IMPs and placebos which:

- Have an MA in the EU **and**
- Are sourced from the EU market **and**
- Are used in the trial without modification (eg not overencapsulated) **and**
- The packaging and labeling is carried out for local use only as per article 9.2 of the Directive 2005/28/EC (GCP Directive).

If all the conditions above are met, then select below the IMPs and placebos to which this applies.

Finished IMP
PR7

Finished IMP
PR8

Finished IMP
PR16

Finished IMP
PR17

Finished IMP
PR19

Finished IMP
PR21

Finished IMP
PR22

Finished IMP
PR25

Index of Sites where the qualified person certifies batch release

In accordance with paragraph 38 of Annex 13 of Volume 4 of the Rules Governing Medicinal Products in the European Union

D9-2. Who is responsible in the Community for the certification of the finished IMP or placebo?

This section is dedicated to finished IMPs, i.e. medicinal products randomised, packaged, labelled and certified for use in the clinical trial. If there is more than one site or more than one IMP is certified, use extra pages and give each IMP its number from section D1 or D7 In the case of multiple sites indicate the product certified by each site.

RS6

Manufacturer

Name of the organisation: Fisher Clinical Services

Address Langhurst Wood Road

Town/city Horsham

Post code RH12 4QD

Country United Kingdom

Give the manufacturing authorisation number

MIA - 18693

If no authorisation, give the reasons:

Select the relevant IMP(s) and Placebo(s) from the drop down lists.

IMP
PR24

RS8

Importer

Name of the organisation: Roche Pharma AG

Address Emil Barell-Strasse 1

Town/city Grenzach-Whylen

Post code 79639

Country Germany

Give the manufacturing authorisation number

DE_BW_01_MIA_2020_0096

If no authorisation, give the reasons:

Select the relevant IMP(s) and Placebo(s) from the drop down lists.

IMP
PR23

RS9

Importer

Name of the organisation: Roche Product Limited

Address 6 Falcon Way, Shire Park

Town/city Welwyn Garden City

Post code AL7 1TW

Country	United Kingdom
Give the manufacturing authorisation number	
MIA(IMP)31	
If no authorisation, give the reasons:	
Select the relevant IMP(s) and Placebo(s) from the drop down lists.	
IMP	
PR23	

E: Design of the Trial.

E.1 Medical Condition or Disease under Investigation

E1-1. Medical condition or disease under investigation ⁽¹⁾

Specify the medical condition(s) to be investigated (free text) :
 COVID-19 (infection with SARS-CoV-2 virus) or influenza pneumonia
 Medical condition in easily understood language
 Covid-19 or flu
 Identify the therapeutic area
 Diseases [C] - Virus Diseases [C02]

(1) In the case of healthy volunteer trials, the intended indication for the product under development should be provided.

E1-2. MedDRA information ⁽²⁾

MR1	
Version	21.1
Level	PT
Classification Code	10035737
Term	Pneumonia viral
SOC	10021881 - Infections and infestations
MR2	
Version	21.1
Level	PT
Classification Code	10061982
Term	Severe acute respiratory syndrome
SOC	10021881 - Infections and infestations

(2) Applicants are encouraged to provide the MedDRA lower level term (LLT) if applicable and classification code.

E1-3. Is any of the conditions being studied a rare disease? ⁽³⁾

Yes No Not Answered

(3) Refer to "Points to consider on the calculation and reporting of the prevalence of a condition for Orphan drug designation": COM/436/01
http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/09/WC500003773.pdf

E2. Objective of the trial

E2-1. What is the principal research question/objective? Please put this in language comprehensible to a lay person.

The primary objective is to provide reliable estimates of the effect of study treatments on death within 28 days of randomisation (with subsidiary analyses of cause of death).

E2-2. What are the secondary research questions/objectives if applicable? Please put this in language comprehensible to a lay person.

The secondary objectives are to assess the effects of study treatments on duration of hospital stay and on need for (and duration of) ventilation or renal replacement therapy.

E2-3. Is there a sub-study?

Yes No Not Answered

E3. Please list the principal inclusion criteria (list the most important, max 5000 characters).

Patients are eligible for the study if all of the following are true:

- (i) Hospitalised
- (ii) Viral pneumonia
- (iii) Confirmed SARS-CoV-2 or influenza infection
- (iv) No medical history that might, in the opinion of the attending clinician, put the patient at significant risk if he/she were to participate in the trial

In addition, if the attending clinician believes that there is a specific contra-indication (see Appendix 2; section 8.2) to one of the active drug treatment arms, then the patient will not be excluded from randomisation to that arm.

E4. Please list the principal exclusion criteria (list the most important, max 5000 characters).

Participants may be excluded from receiving one or more of the possible randomised options if their medical history suggests that a treatment may be contraindicated.

Corticosteroid

Contraindications:

- Known contra-indication to short-term corticosteroid.

Endemic infections may be screened for as required by local practice. Patients in the UK with SARS-CoV-2 infection are not eligible for the low-dose dexamethasone comparison for influenza infection because of the proven benefits of dexamethasone in COVID-19.

Tocilizumab

Contraindications:

- Known hypersensitivity to tocilizumab.
 - Evidence of active TB infection
 - Clear evidence of active bacterial, fungal, viral, or other infection (besides COVID-19)
- (Note: Pregnancy and breastfeeding are not exclusion criteria.)

Anakinra

Contraindications:

- Known hypersensitivity to anakinra
- Neutrophil count $<1.5 \times 10^9$ cells/L
- Pregnancy

Empagliflozin

Contraindications:

- Type 1 diabetes mellitus (or post-pancreatectomy diabetes)
- Pregnancy and breast-feeding
- History of ketoacidosis
- Other patients with diabetes: blood ketones ≥ 1.5 mmol/L (or urine ketones $\geq 2+$ if near-patient testing for blood ketones unavailable). Such patients are eligible once their ketosis has resolved.

Cautions:

- Participants with diabetes allocated empagliflozin should have regular checks of blood ketones (or urine ketones if blood ketone testing is unavailable). Blood ketones should be checked twice daily or urine ketones daily (or if clinical concern). If blood ketones rise ≥ 1.5 mmol/L (or urine ketones $\geq 2+$), clinicians should:
 - o Ensure adequate fluid and calorific intake
 - o Consider increasing insulin dose (if on insulin)
 - o Inform local diabetes team (if available) and treat ketosis using local protocols
 - o Consider discontinuing empagliflozin until ketosis resolves
- Clinicians should consider temporarily discontinuing empagliflozin in participants with diabetes mellitus who cannot maintain oral calorific intake (until nutrition is restored)
- Clinicians should be aware of “euglycaemic ketoacidosis” which occurs with empagliflozin and should check ketones (ideally blood) if this is suspected (e.g. unexplained metabolic acidosis)
- Empagliflozin does not cause hypoglycaemia alone, but may do so in combination with insulin or insulin secretagogues. Doses of these other medications may need to be temporarily modified while the participant is taking empagliflozin
- Empagliflozin causes an osmotic diuresis so careful fluid balance assessment is required
- Empagliflozin increases the risk of mycotic genital infections (e.g. candidiasis) which are usually easily treated with topical therapy. It is unclear whether it causes Fournier’s gangrene (a very rare genital infection), but clinicians should be aware.

Baloxavir Marboxil

Contraindications:

- Weight <40 kg
- Known hypersensitivity to baloxavir marboxil or the drug product excipients
- Participants who have received baloxavir marboxil for the current influenza infection

Oseltamivir

Contraindications:

- Known hypersensitivity to oseltamivir or the drug product excipients
- Participants who have received oseltamivir for the current influenza infection

Cautions:

- Dose should be reduced in presence of renal impairment
 - o eGFR ≥ 30 mL/min/1.73m²: dose as in normal renal function (75 mg twice daily)
 - o eGFR ≥ 10 <30 mL/min/1.73m²: 75 mg once daily
 - o eGFR <10 mL/min/1.73m²: 75 mg as a single dose on day 1

Sotrovimab

Contraindications:

- Weight <40 kg (regardless of age)
- Known hypersensitivity to sotrovimab or the drug product excipients

Cautions: no dose adjustment for kidney or liver function is required.

Molnupiravir

Contraindications:

- Age <18 years
- Pregnancy or breast-feeding

- Known hypersensitivity to molnupiravir or its excipients
- Prior treatment with molnupiravir during the index illness

Cautions: no dose adjustment for kidney or liver function is required.

E5-1. What is the primary outcome measure for the study?(max 5000 characters)

All-cause mortality within 28 days of randomisation.

Timepoint(s) of evaluation of this end point (max 800 characters)

28 days after randomisation.

The protocol will usually identify a single primary end point but there may be a co-primary end point in some cases and/or a number of secondary end points.

E5-2. Secondary end point(s) (max 5000 characters)

Duration of hospitalisation

Use of ventilation

Timepoint(s) of evaluation of this end point (max 800 characters)

28 days

E6. What is the scope of the trial?

- | | | | |
|------------------|--------------------------------------|-------------------------------------|------------------------------------|
| Diagnosis | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Prophylaxis | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Therapy | <input checked="" type="radio"/> Yes | <input type="radio"/> No | <input type="radio"/> Not Answered |
| Safety | <input checked="" type="radio"/> Yes | <input type="radio"/> No | <input type="radio"/> Not Answered |
| Efficacy | <input checked="" type="radio"/> Yes | <input type="radio"/> No | <input type="radio"/> Not Answered |
| Pharmacokinetic | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Pharmacodynamic | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Bioequivalence | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Dose Response | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Pharmacogenetic | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Pharmacogenomic | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Pharmacoeconomic | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Others | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |

Specify:

E7-1. Trial type and phase ⁽¹⁾

Human pharmacology (Phase I) Yes No Not Answered

Therapeutic exploratory (Phase II) Yes No Not Answered

Therapeutic confirmatory (Phase III) Yes No Not Answered

Therapeutic use (Phase IV) Yes No Not Answered

(1) The descriptions of the trial types provided are those recommended in preference to Phases. See page 5 of Community guideline CPMP/ICH/291/95. The development of a new indication after initial approval of a medicine should be considered as a new development plan.

E8. Design of the Trial.

E8-1. Is the trial design controlled?

Yes No Not Answered

Specify:

Randomised Yes No Not Answered

Open Yes No Not Answered

Single blind Yes No Not Answered

Double blind Yes No Not Answered

Parallel group Yes No Not Answered

Cross over Yes No Not Answered

Other Yes No Not Answered

E8-2. If controlled, specify the comparator:

Other medicinal product(s) Yes No Not Answered

Placebo Yes No Not Answered

Other Yes No Not Answered

Specify the comparator

Standard care

Number of treatment arms in the trial

7

E8-3. Single site in the Member State concerned (see also section G):

Yes No Not Answered

E8-4. Multiple sites in the Member State concerned (see also section G):

Yes No Not Answered

Number of sites anticipated in Member State concerned

175

E8-5. Multiple Member States

Yes No Not Answered

Number of sites anticipated in the Community.

E8-6. Trial being conducted both within and outside the EEA

Yes No Not Answered

Trial conducted completely outside EEA

Yes No Not Answered

Specify the countries in which trial sites are planned

Vietnam

Indonesia

Nepal

Ghana

South Africa

Sri Lanka

Pakistan

Specify the number of sites anticipated outside of the EEA

20

E8-7. Will a data monitoring committee (DMC) be convened?

Yes No Not Answered

E8-8.

Definition of the end of trial, and justification in the case where it is not the last visit of the last subject undergoing the trial.

If it is the last visit of the last subject, please enter "LVLS". If it is not LVLS provide the definition.

All randomised participants are to be followed up until death, discharge from hospital or 28 days post-randomisation (whichever is sooner). Longer term follow-up will be sought through linkage to electronic healthcare records and medical databases including those held by NHS Digital, Public Health England and equivalent bodies. The end of the study is the date of the final data extraction from NHS Digital (anticipated to be 10 years after the last patient is enrolled).

E8-9. How long do you expect the study to last? ⁽¹⁾

In all countries concerned by the trial

Years: 11 Months: 6 Days: 11

In the MS concerned

Years: 11 Months: 6 Days: 11

(1) From the first inclusion until the last visit of the last subject.

E8-10. Recruitment start date

Recruitment start date in MS

19/03/2020

In any country

19/03/2020

(1) If not provided in the protocol.

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F: Population of Trial Subjects

F1. What is the age span of the trial subjects?

Less than 18 years	<input checked="" type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Not Answered	Approx no of participants: 500
Please specify the estimated number of participants planned in each age range for the whole trial:		
In Utero	<input type="radio"/> Yes <input checked="" type="radio"/> No <input type="radio"/> Not Answered	Approx no of participants: 0
Preterm newborn infants (up to gestational age less than 37 weeks)	<input checked="" type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Not Answered	Approx no of participants: 10
Newborn (0-27 days)	<input checked="" type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Not Answered	Approx no of participants: 10
Infant and toddler (28 days - 23 months)	<input checked="" type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Not Answered	Approx no of participants: 10
Children (2-11 years)	<input checked="" type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Not Answered	Approx no of participants: 240
Adolescent (12-17 years)	<input checked="" type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Not Answered	Approx no of participants: 240
Adult (18-64 years)	<input checked="" type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Not Answered	Approx no of participants: 20000
Elderly (geater than 65 years)	<input checked="" type="radio"/> Yes <input type="radio"/> No <input type="radio"/> Not Answered	Approx no of participants: 20000

The number of participants will be initial estimates. Applicants will not be required to update this information nor do they constitute an authorisation or restriction on the inclusion of these numbers of patients in the trial.

F2. What is the gender of the trial subjects?

Female Yes No Not Answered

Male Yes No Not Answered

F3. Please select the categories of the trial subjects:

Healthy volunteers Yes No Not Answered

Patients Yes No Not Answered

Specific vulnerable populations Yes No Not Answered

F4. Planned number of subjects to be included:

In the member state 50000

For a multinational trial:

In the European community: 48000

In the whole clinical trial: 50000

F5. Plans for treatment or care after a subject has ended his/her participation in the trial. *If it is different from the expected normal treatment, please specify:*

It would not be appropriate for participants to continue to receive their study treatment after the end of the trial as it is an acute treatment for an acute condition.

G1. and G2. Investigator Details

G1. National coordinating investigator (for a multicentre trial) or principal investigator (for a single centre trial)

- National coordinating investigator
- Principal investigator

Given name Peter
 Family name Horby
 Qualification (MD...) MBBS PhD FRCP
 Institution name University of Oxford
 Institution department name Nuffield Department of Medicine
 Street address New Richards Building, Old Road Campus, Headington
 Town/city Oxford
 Post Code OX3 7LG
 Country United Kingdom
 Telephone 01865 612940
 Fax
 E-mail peter.horby@ndm.ox.ac.uk

G2. Other principal Investigators (for a multicentre trial)

IN1

Given name Peter
 Family name Horby
 Qualification (MD...) MB BS 1992 University of London
 Institution name OXFORD UNIVERSITY HOSPITALS NHS FOUNDATION TRUST
 Institution department name
 Street address JOHN RADCLIFFE HOSPITAL
 Town/city HEADLEY WAY
 Post Code OX3 9DU
 Country United Kingdom
 Telephone
 Fax
 E-mail peter.horby@ndm.ox.ac.uk

For multi-centre trials where the CI is also a local PI, please list the CI as a PI at G2 (single-centre).

G3. Central Technical Facility Details

G3. Central technical facilities to be used in the conduct of the trial. *Laboratory or other technical facility, in which the measurement or assessment of the main evaluation criteria are centralised.*

Organisation

Central technical facility organisation name

Central technical facility organisation department
 Contact person Given name
 Contact person Family name
 Street address
 Town/city
 Post code
 Country
 Work Telephone
 Fax
 E-mail

Enter the details of any duties subcontracted to this central technical facility in this trial:

- | | | | |
|---|---------------------------|-------------------------------------|------------------------------------|
| Routine clinical pathology testing | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Clinical chemistry | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Clinical haematology | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Clinical microbiology | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Histopathology | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Serology / endocrinology | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Analytical chemistry | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| ECG analysis / review | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Medical image analysis/ review - X-ray, MRI, ultrasound, etc. | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Primary/ surrogate endpoint test | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |
| Other | <input type="radio"/> Yes | <input checked="" type="radio"/> No | <input type="radio"/> Not Answered |

Network organisation details

G4. Network organisation details

Organisation
 Contact person Given name
 Contact person Middle name
 Contact person Family name
 Street address
 Town/city
 PostCode
 Country
 Telephone number
 Fax number
 E-mail

Activities carried out by the network

G5. Organisations to whom the sponsor has transferred trial related duties and functions

G5. Subcontractor organisations.

Enter details of central CRO facilities supplying services for at least this Member State.

Organisation
Department
Contact person Given name
Contact person Family name
Street address
Town/city
PostCode
Country
Telephone number
Fax
E-mail

Enter the details of any duties/ functions subcontracted to this sponsor's subcontractor facility in this trial

- All tasks of the sponsor: Yes No Not Answered
- Monitoring: Yes No Not Answered
- Regulatory (e.g. preparation of applications to CA and Ethics Committee): Yes No Not Answered
- Investigator recruitment: Yes No Not Answered
- IVRS⁽¹⁾ - treatment randomisation: Yes No Not Answered
- Data management: Yes No Not Answered
- E-data capture: Yes No Not Answered
- SUSAR reporting: Yes No Not Answered
- Quality assurance auditing: Yes No Not Answered
- Statistical analysis: Yes No Not Answered
- Medical writing: Yes No Not Answered
- Other duties subcontracted: Yes No Not Answered

H: Ethics Committee

H1-1. Type of application

Please tick the Ethics Committee box and give information of the Ethics committee concerned.

Ethics committee

H2-1. Limited Name and address of ethics committee:

Organisation HRA REC Cambridge East

Work Address

PostCode

Country

Fax

H2-2. Date of submission:

12/03/2020

H2-3. Current status of Ethics Committee Opinion at the time of submission to the National Competent Authority:

To be requested Pending Given

If "Given", please specify:

Date of opinion: 16/03/2020

State opinion: Accepted Not Accepted

I: Signature Of The Applicant In The Member State

I1. I hereby confirm that /confirm on behalf of the sponsor (tick which is applicable) that:

- The information provided is complete;

- The attached documents contain an accurate account of the information available;

- the clinical trial will be conducted in accordance with the protocol;

- The clinical trial will be conducted, and SUSARs and result-related information will be reported, in accordance with the applicable legislation.

I2. Applicant of the request for the competent authority (as stated in section C.1):

Date

Signature

Print name

J: Checklist

J3. For details of the documents required for applications to the MHRA in the UK please see <http://www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Clinicaltrials/Applyingforaclinicaltrialauthorisation/Whattosend/index.htm>

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