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:

2020-000154-10

A3. Full title of the trial:

Paramedic Analgesia Comparing Ketamine and MorphiNe in trauma

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

Paramedic given pain relief comparing the use of ketamine and morphine in trauma

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

PACKMaN

A4. Sponsor's protocol:

Number: SOC.12/19-20
Version: 2.0
Date: 07/10/2020

A5-1. ISRCTN number, if available :

ISRCTN14124474

A5-2. US NCT number:

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 Warwick
Given name	Jane
Family name	Prewett
Address	Research and Impact Services, University House, University of Warwick
Town/city	Coventry
Post code	CV4 8UW
Country	United Kingdom
Telephone	02476575732
Fax	
E-mail	sponsorship@warwick.ac.uk

B2.Legal representative in the European Economic Area for the purpose of this trial
A legal representative must be appointed for a clinical trial of an investigational medicinal product if the sponsor is not established within the European Economic Area (EEA) (see article 19 of Directive 2001/20/EC). If this applies, please enclose evidence that the legal representative is established within the EEA and has accepted the role of legal representative.

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):

Name of organisation	NIHR Evaluation, Trials and Studies Coordinating Centre (NETSCC)
Country	United Kingdom

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

Name of organisation	University of Warwick Clinical Trials Unit
Functional name of contact point	Trial Manager
Street Address	WMS Clinical Trials Unit
Town/city	Coventry
Post code	CV4 7AL
Country	United Kingdom
Telephone	02476150478
Fax	
E-mail	packman@warwick.ac.uk

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: Warwick Clinical Trials Unit

Contact person Given name	Charlotte
Contact person Family name	Scomparin
Address	Gibbet Hill Campus
Town/city	Coventry
Post code	CV4 7AL
Country	United Kingdom
Telephone	02476 150478
Fax	
E-mail	packman@warwick.ac.uk

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

◉ Yes ○ No ○ Not Answered

Provide the e-mail address(es) to which it should be sent

These email addresses must have Eudralink accounts for secure password protected delivery unless you answer No to question below.

E-mail address
packman@warwick.ac.uk
m.a.smyth@warwick.ac.uk
g.d.perkins@warwick.ac.uk
s.regan@warwick.ac.uk

Do you want to receive this via password protected links?

○ Yes ◉ No ○ Not Answered

You must have a EudraLink account to receive via password protected link. If you do not know if you have a EudraLink account, answer no above and the .xml file will be transmitted by less secure e-mail link(s).

C2.Request for ethics commitee

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

.....

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

PR1 Ketamine

PR2 Morphine sulfate

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

This refers to the IMP number: **PR1**
Investigational medicinal product category:
Comparator

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	Ketamine
D.3.2 Product code where applicable	
D.3.3 ATC codes, if officially registered	N01A X03
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	Single dose

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	30mg
D.3.6.2 Specify per day or total	○ per day ◉ total ○ Not Answered
D.3.6.2 Specify total dose (number and unit)	30 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
Intraosseous 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):	Ketamine hydrochloride
CAS number:	1867-66-9
Current sponsor code:	
Other descriptive name:	
Full Molecular formula	C13H16ClNO · HCl
Chemical/biological description of the Active Substance	

Strength

Concentration unit:	mg/ml milligram(s)/millilitre
Concentration type:	equal
Concentration number (only use both fields for range):	15

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. Ketamine is an NMDA 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: **PR2**
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	Morphine sulfate
D.3.2 Product code where applicable	
D.3.3 ATC codes, if officially registered	N02AA01
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	Single dose

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	20mg
D.3.6.2 Specify per day or total	◯ per day ◉ total ◯ Not Answered
D.3.6.2 Specify total dose (number and unit)	20 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
Intraosseous 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):	Morphine sulphate
CAS number:	6211-15-0
Current sponsor code:	
Other descriptive name:	
Full Molecular formula	C34H40N2O10S
Chemical/biological description of the Active Substance	
Strength	
Concentration unit:	mg/ml milligram(s)/millilitre
Concentration type:	equal
Concentration number (only use both fields for range):	10

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. Morphine is a phenanthrene opioid receptor agonist.

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.

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.

RS1

Manufacturer

Name of the organisation:	Calderdale and Huddersfield NHS Foundation Trust trading as Huddersfield Pharmacy Specials (HPS)
Address	Acre Mills, Gate 2, School Street West, Lindley
Town/city	Huddersfield
Post code	HD3 3ET
Country	United Kingdom

Give the manufacturing authorisation number

MIA(IMP) 19055

If no authorisation, give the reasons:

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

IMP

PR1

IMP
PR2

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) :
Severe pain after traumatic injury

Medical condition in easily understood language
Severe pain after traumatic injury

Identify the therapeutic area
Diseases [C] - Injuries, poisonings, and occupational diseases [C21]

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

E1-2. MedDRA information (2)

(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.pd

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 of this trial is to determine whether paramedic administered ketamine or morphine provides more effective pain relief for patients reporting severe pain following trauma. This will be measured by using a 0-10 numeric rating scale and the Sum of Pain Intensity Difference (SPID).

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

Secondary objectives of the trial are to assess the effects of the paramedic administered ketamine and morphine on patient outcomes up to 6 months post injury. Specifically on overall pain relief and patient experience, including tolerability and longer term outcomes. We will review the resource used and cost effectiveness of each drug.

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).

- Age 16 years or over
- Patient reports a pain score ≥7/10 on a 0-10 NRS following acute traumatic injury
- Intravenous or intraosseous access obtained
- Determined by a paramedic to require IV morphine or equivalent

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

- Known or suspected pregnancy
- Unable to articulate severity of pain using the 0-10 NRS
- Lack of capacity due to a reason other than pain
- Ketamine or opioid analgesia prior to randomisation
- Known contraindication to either ketamine or morphine as per the SmPC
- Patient declines participation
- Known prisoner

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

Effectiveness of pain relief from randomisation to arrival at hospital as measured by Sum of Pain Intensity Difference (SPID) score (using a 0-10 numerical rating scale).

Timepoint(s) of evaluation of this end point (max 800 characters)
Following arrival at hospital.

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)

Effectiveness of pain relief and overall patient experience from randomisation to arrival at hospital
- Total Pain Relief (TOTPAR) score
- Time to perceptible analgesia
- Time to meaningful analgesia
- Time to peak analgesia
- Duration of analgesia
- Requirement for rescue analgesia
- Proportion of patients with a pain intensity score below 4/10 (0-10 numerical rating scale (NRS)) on arrival at hospital
- Vital signs (oxygen saturation, blood pressure, heart rate, respiration rate, Glasgow Coma Scale)
- Patient Global Impression of Change on arrival at hospital

Incidence of side effects and adverse events
- Airway: vomiting, aspiration, advanced airway management
- Respiratory: desaturation, need for ventilatory support
- Cardiovascular: arrhythmia, hypotension and hypertension
- Neurologic: sedation, excitatory movements, adverse behavioural reactions
- Other: nausea, allergic reaction

Resource use
- Ambulance job cycle time (scene arrival to arrival at hospital)
- Number of ambulance resources (technicians, paramedics, doctors and vehicles) in attendance
- Cumulative IMP doses administered
- CT scan use
- Hospital or ICU admission
- Length of stay ED, ICU, Hospital

Longer term outcomes
- Chronic pain using BPI-SF at 3 & 6 months from randomisation
- Health-related quality of life EQ-5D-5L and CSRI at 3 and 6 months from randomisation
- Cost-effectiveness expressed in terms of incremental cost per quality-adjusted life year (QALY) gained using EQ-5D 5L and CSRI (at 3 and 6 months post randomisation)

Timepoint(s) of evaluation of this end point (max 800 characters)
After the 6 month follow up.

E6. What is the scope of the trial?

Diagnosis	○ Yes	◉ No	○ Not Answered
Prophylaxis	○ Yes	◉ No	○ Not Answered
Therapy	◉ Yes	○ No	○ Not Answered
Safety	○ Yes	◉ No	○ Not Answered
Efficacy	○ Yes	◉ No	○ Not Answered
Pharmacokinetic	○ Yes	◉ No	○ Not Answered
Pharmacodynamic	○ Yes	◉ No	○ Not Answered
Bioequivalence	○ Yes	◉ No	○ Not Answered
Dose Response	○ Yes	◉ No	○ Not Answered
Pharmacogenetic	○ Yes	◉ No	○ Not Answered
Pharmacogenomic	○ Yes	◉ No	○ Not Answered
Pharmacoeconomic	○ Yes	◉ No	○ Not Answered
Others	○ Yes	◉ No	○ 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

Number of treatment arms in the trial

2

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

2

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

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.

End of collection of secondary outcome data.

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

In all countries concerned by the trial
Years: 1 Months: 9 Days: 31

In the MS concerned
Years: 1 Months: 9 Days: 31

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

E8-10. Recruitment start date

Recruitment start date in MS
01/11/2020
In any country
01/11/2020

(1) If not provided in the protocol.

F: Population of Trial Subjects

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

Less than 18 years	◉ Yes ○ No ○ Not Answered	Approx no of participants: 100

Please specify the estimated number of participants planned in each age range for the whole trial:

In Utero	○ Yes ◉ No ○ Not Answered	Approx no of participants: 0
Preterm newborn infants (up to gestational age less than 37 weeks)	○ Yes ◉ No ○ Not Answered	Approx no of participants: 0
Newborn (0-27 days)	○ Yes ◉ No ○ Not Answered	Approx no of participants: 0
Infant and toddler (28 days - 23 months)	○ Yes ◉ No ○ Not Answered	Approx no of participants: 0
Children (2-11 years)	○ Yes ◉ No ○ Not Answered	Approx no of participants: 0
Adolescent (12-17 years)	◉ Yes ○ No ○ Not Answered	Approx no of participants: 100
Adult (18-64 years)	◉ Yes ○ No ○ Not Answered	Approx no of participants: 246
Elderly (geater than 65 years)	◉ Yes ○ No ○ Not Answered	Approx no of participants: 100

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
Women of childbearing potential not using contraception	○ Yes ◉ No ○ Not Answered
Women of child bearing potential using contraception	○ Yes ◉ No ○ Not Answered
Pregnant women	○ Yes ◉ No ○ Not Answered
Nursing women	○ Yes ◉ No ○ Not Answered
Emergency situations	◉ Yes ○ No ○ Not Answered
Subjects incapable of giving consent personally	◉ Yes ○ No ○ Not Answered

If yes, please specify:
Participants will lack the capacity to consent prior to the IMP being administered due to severe pain.

Others	○ Yes ◉ No ○ Not Answered

F4. Planned number of subjects to be included:

In the member state 446

For a multinational trial:

In the European community: 446

In the whole clinical trial: 446

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:***

Morphine is currently used routinely in this patient population, ketamine is available to prehospital doctors and specialist paramedics already. If the use of ketamine is found to be beneficial then we hope the use of ketamine would become more widespread.

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	Perkins
Family name	Gavin
Qualification (MD...)	MB ChB, MD, FRCP, FFICM, FIMC RCS(Ed)
Institution name	University of Warwick
Institution department name	Clinical Trials Unit
Street address	Gibbet Hill Campus
Town/city	Coventry
Post Code	CV4 7AL
Country	
Telephone	
Fax	
E-mail	g.d.perkins@warwick.ac.uk

G2. Other principal Investigators *(for a multicentre trial)*

IN1

Given name	Alison
Family name	Walker
Qualification (MD...)	
Institution name	WEST MIDLANDS AMBULANCE SERVICE UNIVERSITY NHS FOUNDATION TRUST
Institution department name	
Street address	WATERFRONT BUSINESS PARK
Town/city	WATERFRONT WAY
Post Code	DY5 1LX
Country	United Kingdom
Telephone	
Fax	
E-mail	alison.walker@wmas.nhs.uk

IN2

Given name	Julian
Family name	Mark
Qualification (MD...)	
Institution name	YORKSHIRE AMBULANCE SERVICE NHS TRUST
Institution department name	
Street address	SPRINGHILL 2,
Town/city	WAKEFIELD 41 INDUSTRIAL ESTATE
Post Code	WF2 0XQ
Country	United Kingdom
Telephone	

Fax	
E-mail	j.mark@nhs.net

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	○ Yes ◉ No ○ Not Answered
Clinical chemistry	○ Yes ◉ No ○ Not Answered
Clinical haematology	○ Yes ◉ No ○ Not Answered
Clinical microbiology	○ Yes ◉ No ○ Not Answered
Histopathology	○ Yes ◉ No ○ Not Answered
Serology / endocrinology	○ Yes ◉ No ○ Not Answered
Analytical chemistry	○ Yes ◉ No ○ Not Answered
ECG analysis / review	○ Yes ◉ No ○ Not Answered
Medical image analysis/ review - X-ray, MRI, ultrasound, etc.	○ Yes ◉ No ○ Not Answered
Primary/ surrogate endpoint test	○ Yes ◉ No ○ Not Answered
Other	○ Yes ◉ No ○ 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	ModePharma Ltd
Department	
Contact person Given name	Oliver
Contact person Family name	Gupta
Street address	114 Barnfield Wood Road
Town/city	Beckenham
PostCode	BR3 6SX
Country	United Kingdom
Telephone number	0207 0432 442
Fax	
E-mail	ogupta@modepharma.com

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

If yes to others, please specify:

Project management of trial IMPs

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	West of Scotland REC 1
Work Address	Ward 11, Dykebar Hospital Grahamston Road, Paisley
PostCode	PA2 7DE
Country	United Kingdom
Fax	

H2-2. Date of submission:

17/08/2020

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: 01/09/2020
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:

- [x] The information provided is complete;
- [x] The attached documents contain an accurate account of the information available;
- [x] the clinical trial will be conducted in accordance with the protocol;
- [x] 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):

This section was signed electronically by Mrs Jane Prewett on 30/10/2020 16:58.

Job Title/Post:	Head of Research Governance and Deputy Director Research & Impact Services
Organisation:	University of Warwick
Email:	sponsorship@warwick.ac.uk

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***