journey to change

NHS
Tees, Esk and Wear Valleys
NHS Foundation Trust

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Ketamine Protocol for treatment of severe resistant depression

Ref: PHARM-0138-v2

Status: Approved
Document type: Protocol
Overarching policy: Medicines Overarching Framework

Contents

1 Introduction

Ketamine is a drug commonly used as a sedative and analgesic in emergency medicine, as well as a general anaesthetic.

Ketamine is also a novel treatment for depression which is slowly gaining momentum as an alternative to other mainstream treatments. Its mechanism of action is different from existing treatments and it has demonstrated efficacy in helping people with depression where conventional first line treatments have not proved to be fully effective.

An analogue of Ketamine (EsKetamine) has been approved by FDA in the USA for treatment of depression; the same (as intranasal) also been licensed to be used in the UK, but is not recommended by NICE (Recommendations | Esketamine nasal spray for treatment-resistant depression | Guidance | NICE). The Royal College of Psychiatrists have also issued a position statement on ketamine to treat depression.

1.1 Clinical Governance

Clinical governance of the ketamine protocol is being led by the Consultant Psychiatrist Lead for Ketamine, the lead Consultant Anaesthetist and the ECT (Electroconvulsive Therapy)/Ketamine Team Manager. The governance will be via exception reporting to the DTV&F governance system which the ECT/Ketamine Manager will link into. Any issues requiring escalation will be reported to the Drug & Therapeutics (D&T) Committee (medicines-related issues).

In addition, the consultant psychiatrist is part of a peer group for Ketamine Consultant leaders from across the UK who are linked into the Red Kite Research Group in Oxford led by Dr Rupert McShane. This comprises regular webinars to share documentation and exchange experience from this consortium, peer meetings are facilitated by the lead consultant's admin support. The aim is to have shared patient information documentation and agreed protocols across multiple sites so that clinical data can be shared and compiled with the Red Kite project.

1.2 Our Journey to Change

This procedure supports Our Journey to Change as set out in the Medicines Overarching Framework.

2 Purpose

Following this protocol will help the Trust to:

- Provide a safe ketamine service
- Ensure full compliance with the Trust Guidelines for Unlicensed and off label use of medicines
- Ensure full compliance with the Medicines Overarching Framework
- Ensure full compliance with the Consent to Examination or Treatment Policy

As the use of ketamine for the treatment of severe resistant depression is relatively new, this protocol will be subject to change as new information becomes available. Proposed changes will be reviewed by the Drug & Therapeutics committee.

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2.1 Objectives

This document aims to provide clinical guidance to ensure safe administration of ketamine (sub anaesthetic dosage) for treatment of depression.

3 Who this procedure applies to

- This protocol applies to persons aged 18 years of age and above who are receiving services from our Trust and have been referred for ketamine treatment by their treating teams.
- The treatment is currently only administered at the Ryedale Suite, Roseberry Park, Middlesbrough; though it may be expanded to other sites after due consideration of facilities and governance processes. This would require an application by local team supported by existing Trust ketamine team in the form of a paper to Trust Drug & Therapeutic Committee

4 Related documents

Guidelines for Unlicensed and Off-Label Use of medicines
Medicines Overarching Framework
Royal College Statement on ketamine to treat depression

Information for carers – please see appendix 2

5 Intravenous Ketamine (sub anaesthetic dose) as a treatment option

5.1 Indications

Patients must

- Currently be suffering from depression.
- Have tried at least 3 different types of antidepressants for at least 6 weeks each at an adequate treatment dose.
- Have tried at least one type of psychological treatment, e.g., CBT, CAT, Mindfulness. In addition, they have either received or been considered for ECT and/or augmentation strategies to antidepressant treatment.
- Be referred to the service by their treating psychiatrist.
- Be able to travel safely for treatment and assessment appointments.
- Be willing and able to complete regular questionnaires.
- Be able to understand the nature and purpose of the treatment, its benefits and possible side effects and give informed consent for this treatment.

These patients would be very much considered Tertiary Service patients and may continue to exhibit a high level of functional impairment with subjective distress with or without suicidal risk.

The abuse potential of ketamine is widely recognised, clinicians should be fully aware when considering suitability of the patient for treatment.

5.2 Contraindications

- Patient does not give consent
- Patient lacks capacity
- Current or recent history of psychosis
- Significant and untreated cardiovascular disease, Thyroid disease, Glaucoma, Raised Intracranial pressure, Epilepsy
- Are pregnant, breast feeding, undergoing IVF or are trying to conceive
- History of drug or medication induced manic episodes
- Cannot abstain from alcohol for at least three days

NOTE: treatment where one of the aspects above are present would subject to MDT discussion and Anaesthetist approval on a case-by-case basis

5.3 Frequency of treatment

The clinic will use a modified version of the protocol reported in Biological Psychiatry 2010; 67(2):139-45 using a weekly regime within the Ketamine clinic with a maximum of 6 sessions for the acute phase of treatment. Then this will continue at an extended time frame for maintenance., e.g., weekly, fortnightly etc. The frequency may be modified in consultation with the patient as per clinical needs.

Response rates in controlled trials have ranged from 25% to 85% at 24 hours post infusion and from 14% to 70% at 72 hours post infusion. The mean time to relapse after the acute phase at the end of the trial was 19 days. A weekly assessment is proposed with a planned further infusion fortnightly extended to 3 weekly depending on response.

6 Obtaining consent

Before starting the first treatment obtaining informed consent is the responsibility of the lead Consultant Psychiatrist for Ketamine or the nominated deputy & will follow guidance detailed in the Guidelines for Unlicensed and off- label use of medicines (key themes).

6.1 Recording consent

Capacity and consent assessment will be recorded via MCA1 form and in the electronic care record or by an entry in the electronic care record and a signature on a paper consent form.

During the consent process patients must confirm that they will have access to a responsible adult with them for 24 hours post treatment. For patients who return to an inpatient ward the ward, staff to ensure that they remain in care for this period. For patients who live alone with no post-treatment support available at home, CMHT to propose alternative arrangements which may include support and monitoring from colleagues from Crisis team, local authority or other organisations.

Verbal consent will be reconfirmed by ketamine team prior to each treatment.

6.2 Advice to patients

Cautionary advice should be given where relevant; pains may be felt due to uterine contractions, depending on the stage of their menstrual cycle when treatment is administered.

Patients **must** also be advised:

- They must not drive or operate machinery for 24 hours.
- They should not sign legal documents for 24 hours post treatment.
- That they should not consume alcohol or use illicit drugs or be left in charge of minors for 24 hours post treatment.
- That there may be other patients of different genders in the department during treatment however a single bay will be allocated to the patient and a member of staff will be present in the room (not necessarily always in the bay) during their treatment.

6.3 Patient Information

Patient information leaflets must be supplied to the patient during the consent process a record of which must be made in the electronic care record. Generic patient information leaflet about unlicensed and off–label use of medicines is available to support discussions with patients and carers.

6.4 Patient escort

Patients coming for Ketamine treatment must be escorted to and from the clinic. This may be a carer or family member or member of the community mental health team (CMHT) this is determined by the patient's history, presenting behaviour and level of risk which must be taken into consideration. This must be documented in the patients electronic care records and must be reviewed in line with the Care Programme Approach and Standard Care (CPA) policy.

7 Prescribing Ketamine

- This will be the responsibility of the Anaesthetist in consultation with the Ketamine supervising Consultant Psychiatrist.
- Ketamine will be prescribed on the inpatient medication prescription and administration chart.
- Ketamine will be used as a single sub-anaesthetic intravenous dose at 500 micrograms per kilogram given over 40 minutes with continuous vital sign monitoring; the dose can be altered according to response and tolerability (treatment often aims to achieve slight dissociative effects as a marker of adequate dose).

8 Treatment process

When	What	Who
Pre-treatment	Physical assessment: • A pregnancy test **must** be performed where relevant.	Referring team
Pre-treatment	• A full physical examination must be undertaken, and results made available to the Anaesthetist recorded on the electronic care record. • Blood tests –FBC, U&Es, LFTs • ECG, if clinically indicated.	Delegated member of staff
Pre-treatment	Rating scales: • Depression scale (MADRS) • Bladder screening tool (ISCI & ISPI)	Delegated member of staff
Day before treatment	Contact the patient to confirm appointment time.	Delegated member of staff
Day of treatment	Fasting requirements: • Food - patient must refrain from consuming food for 4 hours prior to their appointment. • Fluids - clear fluids may be taken up to 2 hours prior to attending.	Patient
Day of treatment	• Verbally reconfirm consent • Remain with the patient during the treatment • Weigh patient and record on electronic care record	Delegated member of staff
Day of treatment	Review pre-treatment physical assessment and confirm whether anything has changed since last treatment e.g. attended GP or A & E Department	Anaesthetist
Day of treatment	Complete screening tools – see above.	Delegated member of staff

Administration of Treatment	Cannulation & setting up of the syringe driver and ketamine dose calculation. • **Dose:** 500 micrograms per kg • **Product:** ketamine injection 10 mg/ml (Ketalar) • **Diluent:** sodium chloride 0.9% • **Recommended concentration for IV infusion:** 1 mg/ml • **Recommended infusion rate/method:** over 40 minutes by syringe driver.	Anaesthetist
Administration of Treatment	Record the patients BP, TPR and SP02 before and after administration as clinically indicated (not frequently during administration as this may interfere with the desired dissociative phase)	Delegated member of staff

If the patient becomes distressed the process should be reviewed. The Anaesthetist will decide if the dose should be reduced (usually 400 micrograms per kg).

The Anaesthetist must remain in the department until treatment is finished.

When	What	Who
Post-treatment	The patient will be observed for 1 hour post treatment and have observations recorded every 30 minutes post infusion until clinically satisfactory values are obtained.	Medic / ketamine clinic staff
Post-treatment	MADRS will be performed	Medic / ketamine clinic staff
Post-treatment	The patient will be offered a light snack and drink.	Ketamine clinic staff
Discharge from the Ryedale suite	Discharge will be agreed when vital signs are stable	Anaesthetist/medic/nursing staff
Discharge from the Ryedale suite	The patient and responsible adult collecting the patient will receive advice following the administration of an anaesthetic agent. For people who live alone and cannot be supported by a carer for the rest of	Ketamine clinic staff

	the day, the CMHT should decide to contact the patient later in the day to confirm their well-being.	
Discharge from the Ryedale suite	If patient is returning to an inpatient unit revert to pre-treatment observation and monitoring status.	Inpatient staff

9 Delivering same sex accommodation

- The patient will attend the department wearing their own loose-fitting clothes.
- Screens will always be used to ensure patients privacy and dignity while receiving treatment.
- The patient will be accompanied by a member of staff during their treatment.
- The referring consultant will alert the ketamine Clinic team if there any vulnerabilities which would trigger a traumatic response or memory which the team must consider when planning treatment sessions.

10 Side effects

The following side effects may occur:

- Abdominal discomfort due to increased uterine tone in women.
- High dissociation – normalises within minutes if infusion is halted.
- BP rise and tachycardia return to normal soon after infusion.

The above can be managed with Diazepam/Midazolam/Lorazepam (benzodiazepines).

- Occasional low BP & premature ventricle beats can occur, usually normalise soon after stopping infusion. Termination of treatment is not required.

11 Patient reported side effects

- Abnormal sensations
- Weakness
- Fatigue
- Headaches

12 Monitoring

When	What	Who
During ketamine infusions	The patients mental state and risks will be monitored on a regular basis	Care Coordinator/Lead Professional
After final infusion	A final review will be offered by the Ketamine Team	Ketamine Lead Consultant Psychiatrist or delegated member of staff

13 Termination of treatment

Will be considered if there is no response to the number of agreed treatments or if there develops a consistent nonresponse for 3 consecutive treatments.

Non-compliance by patient with Ketamine treatment protocol.

14 Definitions

All definitions noted in document

15 How this procedure will be implemented

- This procedure will be published on the Trust's intranet and external website.
- Line managers will disseminate this procedure to all applicable Trust employees that are involved in the ketamine service.

15.1 Training needs analysis

No training needs identified. A small cohort of staff manage this process.

16 How the implementation of this procedure will be monitored

No planned audit

17 References

Oxford Health Ketamine Service

Royal College Statement on ketamine to treat depression

18 Document control (external)

To be recorded on the policy register by Policy Coordinator

Required information type	Information
Date of approval	27 May 2023
Next review date	27 May 2026
This document replaces	PHARM-0138-v1 Ketamine protocol for treatment of severe resistant depression
This document was approved by	Drug & Therapeutics Committee
This document was approved	27 May 2023
This document was ratified by	n/a
This document was ratified	n/a
An equality analysis was completed on this policy on	Generic Pharmacy Equality analysis applies
Document type	Public
FOI Clause (Private documents only)	n/a

Change record

Version	Date	Amendment details	Status
1	18 July 2019	New document	Superseded
2	25 May 2023	Full review of document, changes: • Language updated throughout to reflect organisational changes • References added for process of future service expansion • Minor updates throughout document.	Approved

Appendix 1 – Approval checklist

To be completed by lead and attached to any document which guides practice when submitted to the appropriate committee/group for consideration and approval.

	Title of document being reviewed:	Yes/No/ Not applicable	Comments
1.	**Title**		
	Is the title clear and unambiguous?	Y	
	Is it clear whether the document is a guideline, policy, protocol or standard?	Y	
2.	**Rationale**		
	Are reasons for development of the document stated?	Y	
3.	**Development Process**		
	Are people involved in the development identified?	Y	
	Has relevant expertise has been sought/used?	Y	
	Is there evidence of consultation with stakeholders and users?	Y	
	Have any related documents or documents that are impacted by this change been identified and updated?	Y	
4.	**Content**		
	Is the objective of the document clear?	Y	
	Is the target population clear and unambiguous?	Y	
	Are the intended outcomes described?	Y	
	Are the statements clear and unambiguous?	Y	
5.	**Evidence Base**		
	Is the type of evidence to support the document identified explicitly?	Y	
	Are key references cited?	Y	
	Are supporting documents referenced?	Y	
6.	**Training**		
	Have training needs been considered?	Y	
	Are training needs included in the document?	n/a	

	Title of document being reviewed:	Yes/No/ Not applicable	Comments
7.	**Implementation and monitoring**		
	Does the document identify how it will be implemented and monitored?	n/a	
8.	**Equality analysis**		
	Has an equality analysis been completed for the document?	n/a	See Medicines overarching framework
	Have Equality and Diversity reviewed and approved the equality analysis?	N/A	
9.	**Approval**		
	Does the document identify which committee/group will approve it?	Y	
10.	**Publication**		
	Has the document been reviewed for harm?	Y	
	Does the document identify whether it is private or public?	Y	
	If private, does the document identify which clause of the Freedom of Information Act 2000 applies?	N/A	

Appendix 2 – Ketamine Clinic - Important information for carers

Please see over page

Ketamine Clinic - Important information for carers

We ask patients coming for Ketamine treatment to arrange for a responsible adult to escort them to their appointment and accompany them home. Patients should not travel home on public transport. Please note If the patient is going home they should ideally have a responsible adult with them for 24 hours

Attending the appointment

When you bring a relative or friend for Ketamine treatment you should report to the reception in Dalesway, Roseberry Park. Parking is available on site. Visitors must sign in at reception and a member of reception staff will advise the Ketamine clinic staff of your arrival.
A member of the Ketamine clinic staff will greet you and answer any queries which you may have. You will not be able to remain with the person while they have their treatment. Staff will show you to an area where you can wait. A coffee shop is available on site.

The person you are accompanying will go through to the treatment room.

After treatment

A member of staff will contact you when the patient's treatment is complete. This can take up to two hours. You will then be able to join them in the clinic.
Initially they may still feel a little strange; however, this will pass before they are allowed to leave the clinic. Before the patient is discharged a member of staff will confirm the post discharge requirements with you.

- If the patient is going home they should ideally have a responsible adult with them for 24 hours
- The patient must not drive or operate machinery for 24 hours
- The patient must not sign any legal documents for 24 hours
- The patient must not consume alcohol/ use illicit drugs for 24 hours
- The patient must not be responsible for looking after dependents for 24 hours after receiving treatment.

You will be asked to sign an outpatient discharge form confirming the above instructions.

After treatment people often feel tired. We encourage them to do very little for the rest of the day. They may have a headache and can take paracetamol as normal for this.

They may describe their experience to you. Sometimes treatments can be an emotional experience of release for some people and they can initially feel overwhelmed.

If you have concerns:
If you are worried about your friend or relative, you should speak to the team in clinic about any concerns you have. They can be contacted Monday-Friday between 9.00am and 4.00pm 01642 838133. Outside of these times please contact the patients care coordinator or GP.