CARer-ADministration of as-needed subcutaneous medication for breakthrough symptoms in home-based dying patients: the CARiAD open pilot RCT

Supplementary File 2: HCP materials

CARer-ADministration of as-needed subcutaneous medication for breakthrough symptoms in home-based dying patients: the CARiAD open pilot RCT

Risk assessment (RA) tool

Risk Assessment for Inclusion of Dyad

This document aims to:

- support healthcare professional decision making on whether a dyad should be approached to participate in the CARiAD trial
- monitor for risk occurrences in dyads who are already participating.

For completion by:

- the healthcare professional responsible for approaching the dyad
- healthcare professionals involved in ongoing care

Answer **Yes (Y)** or **No (N)** to each question. If the answer to any of the statements is **NO**, the dyad are not suitable for inclusion in the CARiAD study and should not be approached to take part or should be withdrawn from the study.

The initial risk assessment should be completed on the patient and available carers. Following confirmation from the patient of who they would like to act as a carer in the study, the risk assessment should be confirmed using the box provided.

If the dyad do not fulfil the initial risk assessment or decide not to take part, the risk assessment should be destroyed and the reason for exclusion or decline noted on the screening log.

If the dyad fulfil the initial risk assessment and agree to take part in the study, this form should be kept in the handheld patient notes. Risk should be reassessed at regular intervals and if the circumstances change.

Upon completion of or withdrawal from the study, completed risk assessments should be returned to the study team.

If the dyad are to be withdrawn from the study or there are any concerns regarding dyad inclusion, please contact the CARiAD team.

CARiAD Trial Manager: [redacted]

CARiAD Trial Administrator: [redacted]

Risk Assessment for Inclusion of Dyad

	Initial check	Confirm throughout study		
Patient and carer are aged 18 or over				
Patient has no known allergies to usually prescribed anticipatory medications. Patients with an allergy may be recruited if a suitable alternative medication can be prescribed				
Patient and carer are able and willing to access available healthcare support systems e.g. out of hours services				
Carer is not confused, disorientated or forgetful				
Carer has no significant vision problems				
Carer has sufficient literacy skills to understand and complete necessary documentation				
Carer has sufficient dexterity to prepare and give subcutaneous injections				
Carer is engaged with healthcare team, understands the importance of medications and is able to understand information relating to them				
No known relational issues between carer and patient which may contraindicate carer administration of medications				
No known issues of substance misuse in immediate circle of family and/or friends				
There is a suitable place for medications to be stored				
Initial risk assessment confirmed on identification of carer?				
Date				
Print name				
Signed				
Name of carer assessed				

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Information for prescribers (intervention group only)

Information for prescribers (for patients in the intervention arm)

The CARiAD trial is about **carer-administration** of **subcutaneous (SC) as-needed** medication for **four common symptoms** in the last days of life. This leaflet does not intend to suggest changes to your usual way of anticipatory prescribing (e.g. drug choice, dosing), instead, it explains additional and specific considerations pertaining to prescribing for patients in the CARiAD trial. Usual procedures for drug storage and disposal apply.

It does not cover

- oral as-needed medication,
- the administration of medication via continuous SC infusion (CSCI, e.g. syringe driver or pump), or
- as-needed SC medication for any other indication (including breathlessness, seizures, or massive terminal haemorrhage). For these, please follow existing advice and procedure.

Safety considerations for the Intervention arm:

- **A relative/carer will only be allowed to administer a maximum of 3 SC doses of medication for the same indication in any 24 hour period**. If a symptom is not controlled, it will trigger healthcare professional (HCP) review through the usual mechanisms and might result in a change of prescription. If 3 doses have been given by the carer, all further doses in any 24 hour cycle must be given by a HCP (i.e. reverting to usual care mechanisms). Any patient receiving carer-administered SC medication will be reviewed by a HCP on a daily basis.
- **A HCP must not change the prescription** (e.g. increase the dose or frequency of administration) **by discussion with the carer over the telephone** – prescriptions can only be changed after direct (face-2-face) assessment. **A carer must not exceed the prescribed frequency of administration**.
- To reduce the risk of error, n**o dose range or dose steps should be prescribed** (e.g. '2.5 to 5mg', or '2.5 or 5mg'), instead the prescriber should choose one dose to prescribe and be willing to review the prescription at regular intervals and increase the dose if appropriate.
- **Be aware of dose volumes to ensure ease of drawing up for carers.** This may mean you either prescribe a full ampoule per dose, or suggest a ampoule size that is easy for the carer to draw up or waste in part. Unless diamorphine is specifically indicated (usually because of the use of higher doses), please avoid its use as the carer will need to reconstitute it. A quick guide of Diamorphine: Morphine conversion can be found at the end of this document.
- Though it is usual practice to prescribe as-needed SC medication for all 4 common symptoms, **you are under no obligation to prescribe for all these indications** if you deem it not appropriate (including in terms of number of injections available to the carer to give) in specific cases. It may therefore be the case that not all SC as-needed drugs are prescribed for the carer to give.
- **The carer will be provided with detailed written information for each drug**, including the name, dose, indication, the exact volume required from a ampoule for the prescribed dose (especially if it is not a full ampoule), likely undesirable effects, the time before a repeat dose is permitted and the maximum number of injections per

24 hours. There is space in the Carer Diary to record this to provide at-a-glance information for the carer, and the District Nurses, after having trained the carer, will complete this section of the Carer Diary. (The information in the Carer Diary is not intended to act as a prescription, so, as a prescriber, you will still need to complete the usual prescription chart for HCP use. Prescribing suggestions are provided in the table below.)

Usually, the assessment of effect of as-needed medication will occur after about 1 hour post-administration. If at any time (even if this is within this one hour window) the carer feels a symptom is worsening despite appropriate as-needed medication, or it is not lessening at all in that time, they should inform their HCP team without delay. The call is likely to trigger the need for a direct (face-2-face) assessment to rule out any new or reversible causes for the symptom.

In line with nationally accepted practice for anticipatory prescribing and existing local guidance in the CARiAD recruitment areas, and taking into account the above safety considerations, the as-needed SC medication(s), doses and maximum frequency of administration for each of these indications are:

<table>
<tr><th>Symptoms</th><th>Medication classes and licensing</th><th>Prescribing suggestions</th></tr>
<tr><td rowspan="2">Pain</td><td>▪ A strong opioid e.g. morphine (first line) or oxycodone (second line)</td><td>▪ One sixth of the 24 hour background dose of strong opioid PRN 4-hourly
▪ If not on background strong opioids, consider a starting dose of morphine 2.5 or 5mg PRN 4 hourly</td></tr>
<tr><td colspan="2">A carer, after careful consideration by the HCP team, could be advised that, if the prescribed dose of opioid has not taken effect after one hour, they can give one further dose and then inform their HCP team that this has happened. After this ‘second’ dose, the carer would not be allowed to give any further opioid for pain for another 4 hours.</td></tr>
<tr><td>Agitation/restlessness</td><td>▪ Benzodiazepines (midazolam) or antipsychotics</td><td>▪ e.g. starting dose of Midazolam 2.5 or 5 mg PRN 4-hourly</td></tr>
<tr><td></td><td colspan="2">▪ A carer, after careful consideration by the HCP team, could be advised that, if the prescribed dose of midazolam has not taken effect after one hour, they can give one further dose and then inform their HCP team that this has happened. (The HCP may wish to consider the use of antipsychotics at this point.) After this ‘second’ dose, the carer would not be allowed to give any further midazolam for any other indication for another 4 hours.</td></tr>
<tr><td>Nausea and vomiting</td><td>▪ Any anti-emetic deemed appropriate for the likely cause</td><td>▪ e.g. Cyclizine 50 mg PRN 8-hourly (usual maximum dose in 24 hours = 150mg), or
▪ Levomepromazine 6.25 mg PRN 4 hourly (usual maximum dose in 24 hours = 25mg)</td></tr>
<tr><td>Noisy respiratory secretions</td><td>▪ Antimuscarinics</td><td>▪ e.g. Hyoscine hydrobromide 400 mcg PRN 4 hourly, or
▪ Glycopyrronium 200 mcg PRN 4 hourly</td></tr>
</table>

Using morphine (rather than diamorphine) as first line: Diamorphine SC: Morphine SC is 2:3, thus for quick reference:

- 5mg of Diamorphine SC = 7.5mg of Morphine SC
- 10mg of Diamorphine SC = 15mg of Morphine SC
- 15mg of Diamorphine SC = 22.5mg of Morphine SC
- 20mg of Diamorphine SC = 30mg of Morphine SC
- 30mg of Diamorphine SC = 45mg of Morphine SC

Daily checklist for District Nurses

CARiAD Daily Checklist for District Nurses – Patients in the Intervention Arm

- Carer diary
  - Remind carers that the diary must be completed for each breakthrough symptom
  - Ensure that any medications given are transcribed to the All Wales Care Decisions paperwork and noted as “carer administered”
  - Remind carers to complete the QOLLTI-F questionnaire every 48 hrs from the first time they have noted a breakthrough symptom
  - Check that medication instruction table in carer diary is up-to-date and that any dose changes have been explained to the carer.

- As per usual practice, check that drug stocks tally.

- Check Saf-T-Intima.

- If there has been a change in the mental capacity of the patient since the last visit, please contact the trial manager.

- Report any Serious Adverse Events to the trial manager.

- If the patient or carer wish to withdraw from the study, or if a patient consultee advises the patient would want to withdraw from the study, please contact the trial manager. Ensure that the carer diary is collected and that the carer understands they should not administer subcutaneous medication for breakthrough symptoms following their withdrawal from the study. Management of breakthrough symptoms should revert to the usual care pathway.

Following the patient’s death, please contact the trial manager and collect the carer diary.

CARiAD Trial Manager

[redacted]

CARiAD Daily Checklist for District Nurses – Patients in the Control Arm

- Carer diary
  - Remind carers that the diary must be completed for each breakthrough symptom
  - Remind carers to complete the QOLLTI-F questionnaire every 48 hrs from the first time they have noted a breakthrough symptom

- As per usual practice, check that drug stocks tally.

- If there has been a change in the mental capacity of the patient since the last visit, please contact the trial manager.

- Report any Serious Adverse Events to the trial manager

- If the patient or carer wish to withdraw from the study, or if a patient consultee advises the patient would want to withdraw from the study, please contact the trial manager. Ensure that the carer diary is collected.

Following the patient's death, please contact the trial manager and collect the carer diary.

CARiAD Trial Manager

[redacted]

Adverse event (AE) record

CARiAD Adverse Event Record – Participant Number __ __ __ __

What is an "adverse event?"

An adverse event is any untoward medical occurrence in a trial participant, including occurrences that are not necessarily caused by or related to the trial. This might include things like a sore mouth or a nosebleed. Severity relates to the intensity of the specific event. It may be severe but of relatively minor medical significance. You can record all adverse events on this form.

What is a "serious adverse event?"

A serious adverse event is one that

1) results in death or is life-threatening
2) requires inpatient hospitalisation (or prolongation of an existing hospitalisation)
3) results in significant disability or incapacity

As CARiAD is a study in patients who are terminally ill, all adverse events should be considered in the context of the expected decline of the participant. It is expected that death will be a frequent outcome, but it may not be considered serious if it is a natural conclusion to a patient's terminal illness. If you are in any doubt about whether an event is serious, please report it to the principal investigator (PI) who will determine seriousness.

Other medical events may also be considered serious if they jeopardise the participant or require an intervention to prevent one of the listed consequences. **All serious events should be reported to the PI for your area using the CARiAD SAE reporting form within 24 hours of becoming aware of the event.**

What is a "related event?"

Other events may occur that are related to the trial, but do not have a serious outcome. For example, the cannula for carer administration could become blocked but did not result in a serious event. As CARiAD is a feasibility study we would like to know about all events that could be related to participation in the study, so **please report these to the PI within 24 hours using the SAE reporting form.** Examples of related events include

1) appropriateness of administration
2) dose errors
3) side effects of anticipatory medications
4) drug stocks which do not tally
5) carer distress or other carer event.

Participant Number __ __ __ __

Adverse event	Start date	End date	Severity 1=Mild 2=Moderate 3=Severe	Action taken	Outcome	Serious or related? If yes, please complete SAE form	Date reported to PI	Withdrawn due to event?	Person recording AE (please sign)

Serious Adverse Event Reporting Form

CARiAD Serious Adverse Event Reporting Form

Participant ID number __ __ __ __

Part A – to be completed by the person who becomes aware of the serious adverse event

Please indicate if this is:

- ☐ Initial report
- ☐ Follow up report
- ☐ Final report

Please return to PI within 24 hours of becoming aware of the event. Any change of condition or other follow-up information should be provided as soon as it is available or at least within 24 hours of the information becoming available. Events should be followed up until the event has resolved or a final outcome has been reached.

Adverse event identified by:	
Date identified:	
Date (and duration, if applicable) of adverse event:	
Who experienced the event? E.g. carer, patient, both	
Details of adverse event: e.g. location, type of event, was trial participation a factor? Please attach any relevant reports relating to the event	
How did you become aware of this event?	
Please categorise the event by ticking **all** appropriate boxes:	☐ Death Please include date of death __/__/___ ☐ Life threatening

	☐ Hospitalisation or prolongation of existing hospitalisation Please include number of days _____ ☐ Persistent or significant disability or incapacity ☐ Related to participation in the trial ☐ Otherwise considered medically significant (please give detail below)
Any action taken:	
Outcome:	
Date principal investigator notified:	

When you have completed the form, please send a copy to the principal investigator and trial manager and retain a copy for your records.

CARiAD Trial Manager:

[redacted]

CARiAD Principal Investigators

Betsi Cadwaladr University Health Board

[redacted]

Cardiff & Vale University Health Board

[redacted]

Gloucestershire Care Services

[redacted]

Part B – to be completed by the Principal Investigator

Please return a copy to Trial Manager or CI and retain a copy for the trial site file.

All serious events should be reported to the Trial Manager or CI within 24 hours.

In your opinion, is the adverse event assessed as serious, according to the CARiAD protocol?	
In your opinion, did the adverse event arise as a result of participation in the CARiAD study? (Please tick one)	☐ Not related ☐ Probably unrelated ☐ Possibly related ☐ Probably related ☐ Definitely related
Please add any further comments regarding the adverse event:	
Action taken:	
What was the outcome of the event? (Please tick one)	☐ Recovered ☐ Recovered with sequelae ☐ Ongoing ☐ Fatal
Name of PI:	
Signature:	
Date:	

When you have completed the form, please send a copy to the trial manager and chief investigators and retain a copy for your records.

CARiAD Trial Manager: [redacted]

Co-chief investigators:

[redacted]

[redacted]

Competency Checklist

CARiAD - Carer Competency Checklist

To be completed by the healthcare professional (HCP) after training the carer to administer as-needed subcutaneous medication as part of the CARiAD trial and to confirm ongoing competency throughout their time in the trial.

The carer must fulfil all of the competencies below before being allowed to administer as-needed subcutaneous medications without HCP supervision.

	Initials of HCP	Initials of HCP	Initials of HCP
Is aware of the symptoms of pain, restlessness/anxiety, nausea/ vomiting and noisy breathing and which medications to use for each of these symptoms			
Understands why it is necessary to wash and dry hands			
Is able to assemble equipment into a clean container			
Is able to attach a needle to a syringe			
Can reconstitute drugs if required			
Is able to draw up medication from an ampoule into a syringe			
Is able to ensure correct volume required for prescribed dose is in the syringe (either by drawing up a part ampoule or wasting)			
Is able to give an injection into the cannula by either: • No needle technique, or • Blunt needle technique			
Understands how to check the injection site for redness, tenderness, swelling or leakage and what to do if this occurs			
Is able to record accurately the medication that was given and understands the importance of completing all associated study paperwork			
Is aware of how many as-needed doses can be administered of each drug in 24 hours			
Is able to safely store medications and needles and dispose of ampoules, used needles and unused medication appropriately			
Has contact numbers of appropriate healthcare team contacts and knows when to use these			
Understands the importance of contacting the healthcare team immediately if an error is made with medications or unusual symptoms develop			
Date			
Signed (HCP)			
Print name (HCP)			