Specialist Palliative Care
Audit and Guidelines Group

SPAGG

Coversheet for Specialist Palliative Audit and Guideline Group Agreed Documentation

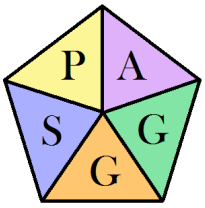
This sheet is to accompany all documentation agreed by SPAGG. This will assist maintenance of the guidelines as well as demonstrating the governance process undertaken prior to members seeking local approval in their areas of work.

Document Title	**Guidelines for the use of Naloxone in Adult Palliative Care Patient**
Document Date	March 2017
Document Purpose and Intended Audience	To provide guidance to generalist / specialist healthcare professionals in the management of opioid toxicity within the palliative care setting
Authors	L. Seager (revised and updated original pan-birmingham cancer network document)
References	Please see Document
Consultation Process	L.Seager reviewed and updated Guidelines Subsequently reviewed and endorsed by SPAGG

ENDORSED BY GOVERNANCE COMMITTEE

Review Date (must be within three years)	March 2020
Approval Signatures: SPAGG chair SPAGG deputy chair SPAGG secretary	L.Seager C.Radcliffe M.Blaber
Date Approved by SPAGG:	01 /03 /2017
Date submitted to Area Prescribing Committee:	

ENDORSED BY GOVERNANCE COMMITTEE



Specialist Palliative Care
Audit and Guidelines Group

Guidelines for the Use of Naloxone in Palliative Care in Adult Patients

Version History

Version	Date	Summary of Change/Process
0.1	17/12/08	Draft guideline discussed at Specialist Palliative Care Audit and Guidelines Sub Group (SPAGG)
0.2	18/03/09	Amended draft re-discussed
0.3	15/06/09	Received comments from Professor Ferner and circulated document to SPAGG for discussion at meeting on 17.6.09
0.4	19/08/09	Approved at SPAGG meeting pending minor changes
0.4	25/08/09	Endorsed at Governance Committee Sub Group subject to minor amendment and clarification of 6.1
1.0	28/09/09	Amendments made following Governance Committee Sub Group
1.1	20/12/11	Prepared for discussion by Supportive and Palliative Care Network Site Specific Group
1.2	17/01/12	Author identified at NSSG 16/1/12 template updated and sent to Trisha Castanheira for review
1.3	February 2012	With updating by Trisha Castanheira
1.4	February 2012	With comments by Anna Lock and Lara Barnish
1.5	March 2012	Updated by Trisha Castanheira and forwarded to the NSSG for comments
1.6	March 2012	With Lara Barnish comments for Trisha Castanheira and Network Site Specific Group
2.0	May 2012	Reviewed and endorsed by Guidelines Sub Group and prepared for uploading on to website
3.0	March 2017	Guideline reviewed by Louise Seager and Michelle Aslett. Changes made based on comments from the group. Endorsed by Specialist Palliative Care Audit and Guidelines Group

ENDORSED BY GOVERNANCE COMMITTEE

Changes between Version 1 and 2

1. Guideline background
2. Guideline statements
3. Diagnosis and treatment of opioid induced respiratory depression
4. Monitoring after first naloxone administration
5. Patient information and counselling
6. Clinical trials

Changes between Version 2 and 3

1. Guideline background
2. Section 4.2
3. Addition of section 5 reversal of buprenorphine-induced respiratory depression
4. References

1. Scope of the guideline

1.1. This guideline provides information about the use of naloxone, an opioid antagonist in the palliative patient who is receiving prescribed opioid medication in the clinical setting.

1.2. It is **not** intended to cover the management of acute opioid overdose

1.3. It does not cover administration in the patient's home environment

1.4. Advice on treatment with continuous naloxone is outside the scope of this guideline.

2. Guideline background

2.1. This guideline was initially produced in response to the National Patient Safety Agency recommendation (May 2006) that naloxone is available in all clinical locations where morphine and diamorphine injections are administered or stored.[1] Subsequent patient safety alerts NHS/PSA/W/2014/016 [2] and NHS/PSA/Re/2015/009 [3] recommended that naloxone must be given with great caution to patients who have received longer-term opioid/opiate treatment for pain control or who are physically dependent on opioids/opiates. It acknowledges that the BNF doses recommended for opioid/opiate overdose may not be appropriate for the management of opioid/opiate induced respiratory depression and sedation in those receiving palliative care and in

chronic opioid/opiate use.

2.2. This guidance on the use of naloxone for overdose of prescribed opioids in palliative care patients has been developed to address this. They are based on information in PCF 5 Palliative Care Formulary accessed via www.palliativedrugs.com on 01/07/2016

Guideline statements

3. General principles

3.1. Naloxone should only be used in palliative care in those circumstances where a clinician suspects opioid-induced toxicity.

3.2. Naloxone is not indicated for:

- patients on opioids who are dying as a natural result of their disease progression
- symptoms induced by non- opioids e.g. barbiturates, benzodiazepines
- opioid induced drowsiness and/or delirium which is not life threatening

3.3. It is important, in the management of patients in pain, that the signs of advanced progressive disease are not confused with those of opioid overdosage, leading to inappropriate use of naloxone.

3.4. Patients on regular opioids for pain and symptom control are physically dependent; naloxone given in too large a dose or too quickly can cause an acute withdrawal reaction and an abrupt return of pain that is difficult to control.

3.5. Patients who are taking opioids and have recently received another intervention e.g. Radiotherapy or nerve block are at risk of opioid toxicity

3.6. Naloxone's antagonism of buprenorphine is less complete because of the latter's high receptor affinity, see section 5 for reversal of buprenorphine-induced respiratory depression.

4. Diagnosis and treatment of opioid induced respiratory depression

4.1. If respiratory rate ≥ 8 breaths/min and the patient is easily rousable and not cyanosed, adopt a policy of 'wait and see'; consider reducing or omitting the next regular dose of morphine or reducing rate of/discontinuing continuous parenteral administration

4.2 Administer high flow oxygen via face mask, if the patient is hypoxic

4.3 If respiratory rate < 8 breaths/min, and the patient is comatose/unconscious and/or cyanosed[4,5]

- Stop opioid administration
- Dilute naloxone 400 mcg (1 ampoule) to 8ml with 0.9% sodium chloride for injection to give a 50mcg/ml solution
- Initially administer 100-200mcg (2ml of diluted naloxone) intravenous (IV) as a slow bolus then flush the cannula with 0.9% sodium chloride
- Administer 100 mcg (2ml) IV every 2 minutes until the patient's respiratory status is satisfactory
- Flush the cannula with 0.9% sodium chloride after each bolus injection
- Further boluses may be necessary because naloxone is shorter acting than morphine (and other opioids)
- The aim is for slow, paced administration of the drug to avoid a surge of pain from complete antagonism of opioid
- Wait until there has been a sustained improvement in consciousness before restarting a lower dose of opioid, it may be preferable to switch the type of opioid
- If there is little or no response consider other causes (e.g. other sedatives)

4.3 If repeated naloxone doses are required, start a continuous intravenous infusion of naloxone:[6]

- add 1mg of naloxone (2.5ml of 400 mcg/ml naloxone injection) to 100ml

0.9% sodium chloride to give a concentration of 10 mcg/ml

- calculate the dose requirement per hour by totalling the naloxone bolus doses and dividing by the time period over which all the doses have been given
- start the IV infusion of naloxone at **half** this calculated rate
- adjust the naloxone infusion rate to keep the respiratory rate above 8 (do not titrate to the level of consciousness)
- continue to monitor the patient closely
- continue the infusion until the patients condition has stabilised
- additional IV boluses may need to be given using naloxone diluted in sodium chloride 0.9% as above

5. **Buprenorphine**

Due to very strong receptor affinity (reflected in its high relative potency with morphine), naloxone in standard doses does not reverse the effects of buprenorphine and higher doses must be used, see table below

Reversal of buprenorphine-induced respiratory depression	
1	Discontinue buprenorphine (stop CSCI/CIVI, remove TD patch).
2	Give oxygen by mask.
3	Give IV naloxone *2mg* stat over 90seconds
4	Commence naloxone *4mg/hour* by CIVI.
5	Continue CIVI until the patient's condition is satisfactory (probably <90min).
6	Monitor the patient frequently for the next 24h, and restart CIVI if respiratory depression recurs.
7	If the patient's condition remains satisfactory, restart buprenorphine at a reduced dose, e.g. half the previous dose.

6. Other management issues

6.1 Intra-venous is the preferred route of administration for naloxone, but can be given intra-muscularly or sub-cutaneously if venous cannulation is not possible (If using IM/SC route, be aware that onset of action will be slower, approx 2-5 minutes, though duration of action may be more prolonged).

ENDORSED BY GOVERNANCE COMMITTEE

6.2 Administer high flow oxygen via face mask, if the patient is hypoxic.

7. Monitoring after first Naloxone administration

7.1 Naloxone has a much shorter half life than morphine. There is a risk that opioid toxicity will recur as the naloxone wears off and the opioid is still active. Respiratory rate and oxygen saturation should be monitored closely until stable. The length of this period of monitoring will be dependant on the half life of the opioid causing toxicity. The half life of morphine and some other opioids is prolonged in renal failure and other metabolic disturbance.

7.2 It may be appropriate to transfer the patient to a facility where naloxone infusion and monitoring can be initiated. This course of action should be considered if respiratory depression continues to recur despite repeated administration of naloxone (as above).

8. Patient information and counselling

8.1. To comply with the NICE Guidance for use of opioids in palliative care, all patients, and (with their consent) their partners will be given access to appropriate written information during their investigation and treatment, and on diagnosis will be given the opportunity to discuss their management with a clinical nurse specialist who is a member of the relevant MDT. The patient should have a method of access to the specialist palliative care team at all times.

8.2. Access to psychological support will be available if required. All patients should undergo an holistic needs assessment and onward referral as required.

9. Monitoring of the guideline

Adherence to the Network guidelines may from time to time be formally monitored.

ENDORSED BY GOVERNANCE COMMITTEE

Author of Version 1

Dr Debbie Talbot, Specialist Registrar, St Giles Hospice

Author of Version 2

Trisha Castanheira, Head of Nursing, Birmingham St Mary's Hospice

Author of Version 3

Michelle Aslett, Specialist Clinical Pharmacist, Marie Curie, Solihull
Louise Seager, Specialist Clinical Pharmacist, John Taylor Hospice, Birmingham

References

1. National Patient Safety Agency. Ensuring safer practice with high dose ampoules of diamorphine and morphine. Issued- 25th May 06. Available at: www.npsa.nhs.uk/nrls/alerts-and-directives/notices/morphine-diamorphine/ Accessed November 2008
2. Patient Safety Alert. Stage One: Warning. Risk of distress and death from inappropriate doses of naloxone in patients on long-term opioid/opiate treatment. NHS/PSA/W/2014/016, 20/11/2014. Available via https://www.england.nhs.uk/wp-content/uploads/2014/11/psa-inappropriate-doses-naloxone.pdf
3. Patient Safety Alert. Stage Two: Resources. Support to minimise the risk of distress and death from inappropriate doses of naloxone. NHS/PSA/Re/2015/009, 26/10/2015. Available via https://www.england.nhs.uk/patientsafety/wp-content/uploads/sites/32/2015/10/psa-naloxone-stage2.pdf
4. Twycross R. Wilcock A. et al. Palliative Care Formulary 5. Available via: www.palliativedrugs.com . Accessed February 2017.
5. UKMI Medicines Q&A. What naloxone doses should be used in adults to reverse urgently the effects of opioids or opiates? June 2015. Available via file:///C:/Users/louise.seager/Downloads/QA227_3_Naloxone_final_Oct2015%20(5).pdf
6. Scottish Palliative Care Guidelines – Naloxone monograph. 04/05/2014. Review date 04/05/2017. Available via

ENDORSED BY GOVERNANCE COMMITTEE

http://www.palliativecareguidelines.scot.nhs.uk/media/1216/scottish-palliative-care-guideline-naloxone.pdf

ENDORSED BY GOVERNANCE COMMITTEE