Gateshead Council Public Health;

Substance misuse pathway for the provision of take-home Naloxone.

1.0 Background

1.1 Drug related deaths (DRDs)

This briefing relates to the introduction of 'take home' Naloxone for opiate related overdose in Gateshead. The September 2015 Office of National Statistics *Deaths related to drug poisoning* update showed a 17% rise in the drug misuse mortality rate in 2014 (from 2012) to 39.9 deaths per million population – the highest ever recorded. Of these deaths, those involving heroin and/or morphine increased by almost two-thirds between 2012 and 2014 [1].

The North East had the highest mortality rate for the second year running; 69.3 deaths per million population, compared to England average of 33.5 deaths per million. Gateshead had the fifth highest rate in the North East (out of 12 local authorities) at 56.6 per million population [2]. The annual review of DRDs in Gateshead shows that the majority were linked to opiates along with other complex factors.

In 2012, the Advisory Council on the Misuse of Drugs (ACMD) released a report entitled 'Consideration of Naloxone'. One of the key recommendations from this report is that Naloxone should be made more widely available to tackle the high numbers of fatal opioid overdoses in the UK [3]. Similarly, the World Health Organisation also recommended that access to Naloxone and training in its use should be made available to both people who use opioids and people who are likely to witness an opioid overdose [4]. In 2015, Public Health England issued updated advice for local authorities and local partners to promote the wider availability of Naloxone to reduce overdose deaths from heroin and similar drugs [5].

Naloxone Action Group England (NAG England) has produced a list of key facts on Naloxone [6]: "10 important facts on naloxone for commissioners and providers.

- Take home naloxone reduces death due to opioid overdose
- Issuing naloxone doesn't encourage heroin use

- Having naloxone and the relevant training encourages people to phone an ambulance
- Naloxone can be administered by the public while awaiting the arrival of professional assistance
- Naloxone is unlikely to harm others even if used by mistake
- Issuing naloxone to people who are no longer using opioids (for example, leaving rehab) is a protective action
- Risk of opioid overdose and what can be done to mitigate this risk is a matter of concern for anyone involved with the welfare of people who use opioids
- The training is quick and simple to deliver
- The cost is minimal, especially when compared to the clear benefits
- This isn't just a new, 'trendy' drug treatment intervention"

More information on the above statements is available on the Naloxone Action Group England website [6].

1.2 Naloxone

Naloxone is a prescription only medication used for the complete or partial reversal of respiratory depression induced by natural and synthetic opioids, including methadone, diamorphine (diacetylmorphine (INN)) and certain other opioids such as dextropropoxyphene and certain mixed agonist/antagonist analgesics: nalbuphine and pentazocine [7].

There are several licensed preparations available from different manufacturers and in different strengths. However, **Prenoxad® Injection is the only presentation of naloxone currently licensed for emergency use in the community – in the home or other non-medical setting by appropriate individuals for the complete or partial reversal of respiratory depression induced by opioids [7].**

An abbreviated Summary of Product Characteristics (SPC) is included as Appendix 1. For the full Summary of Product Characteristics, please see the Electronic Medicines Compendium: https://www.medicines.org.uk/emc/medicine/27616.

Dosage for Adults: 400 micrograms or 0.4ml of Prenoxad® Injection solution by intramuscular injection into the outer thigh or muscles of the upper arm as part of the resuscitation intervention. The dose of 0.4ml can be repeated every 2-3 minutes in subsequent resuscitation cycles until the contents of a syringe are used up.
N.B. The duration of action of certain opioids can outlast that of an IV bolus of Naloxone, e.g. dextropropoxyphene, dihydrocodeine and methadone. In situations where one of these opioids is known or suspected it is recommended that an infusion of Naloxone be used to produce sustained antagonism to the opioid without repeated injection [7].

Children: The Prenoxad® Injection presentation is **not** intended to be used for children in the home setting other than by an appropriately trained healthcare professional. In the event of a child being given or taking an opioid inappropriately an ambulance should be called and resuscitation started if required [7].

The most common side effects of Naloxone administration are dizziness, headache, ventricular tachycardia, hypertension, nausea and vomiting [7]. Furthermore, rapid opiate withdrawal facilitated by Naloxone may induce nausea, vomiting and sweating. In a small number of patients there has been the risk of cardiac problems and death [8].

Prenoxad® comes in a pre-filled syringe for injection, ready for use, with 5 pre-marked doses of 400mcg to be administered as an intramuscular injection. It is packaged in a small yellow box, designed to act as a sharps box after use. The box also contains 2 hypodermic needles and instructions on use. It should be stored at room temperature and has a shelf life of 3 years. It is to be administered as part of a resuscitation intervention in suspected overdose, alongside the ambulance service call out, providing a valuable intervention in this situation, in addition to basic life support. A comprehensive training package for both prescribers and recipients of Prenoxad® is thus required, see section 3.0.

1.3 Legislation

Naloxone remains a prescription only medicine, however, in 2005 it was added to the list of injectable medicines that may be legally used by anyone for the purpose of saving a life in an emergency [9]. Subsequently, in October 2015, new legislation also came into force that enables naloxone to be supplied to individuals by drug services without prescription, as a parenteral drug (similar to adrenaline) for saving a life in an emergency [5].

Following the change in legislation, it can now be supplied by substance misuse services, without prescription (or Patient Group Directive) to:

- someone who is using or has previously used opiates (illicit or prescribed) and is at potential risk of overdose
- a carer, family member or friend liable to be on hand in case of overdose
- a named individual in a hostel (or other facility where drug users gather and might be at risk of overdose), which could be a manager or other staff

There is no need for the usual Prescription Only Medicine requirements, just a requirement that the supply is suitably recorded [5]. The provision of Naloxone should also be accompanied by appropriate training in overdose prevention and management.

2.0 Gateshead Take-Home Naloxone pathway

A pathway has been developed for the distribution of Take-Home (TH) Naloxone kits in Gateshead, as the licensed preparation Prenoxad® (Figure 1).

Gateshead Evolve will be the sole distributors of TH Naloxone kits in Gateshead. To date, Gateshead Evolve staff, i.e. keyworkers, recovery champions and recovery mentors have received training to enable them to be competent to give out TH Naloxone kits in addition to providing the approved client training, to ‘at risk’ clients, carers of ‘at risk’ individuals, named hostel workers and named housing workers when appropriate.

The ‘At risk’ group includes clients:

- taking prescribed opioids
- using opiates intravenously
- accessing the needle exchange service
- on release from prison and history of / current substance misuse
- Hospital discharge, following an opiate overdose.

A steering group has been established within Gateshead Evolve to promote and support the uptake of TH Naloxone kits in the locality. The distribution of TH Naloxone kits to at risk

groups is to be run as a 3 year pilot, commencing February 2016. Data regarding the number of kits supplied, used, lost, confiscated and expired will be collected by Gateshead Evolve throughout the 3 years pilot. Activity reports and governance issues will be shared regularly with Gateshead Council Public Health.

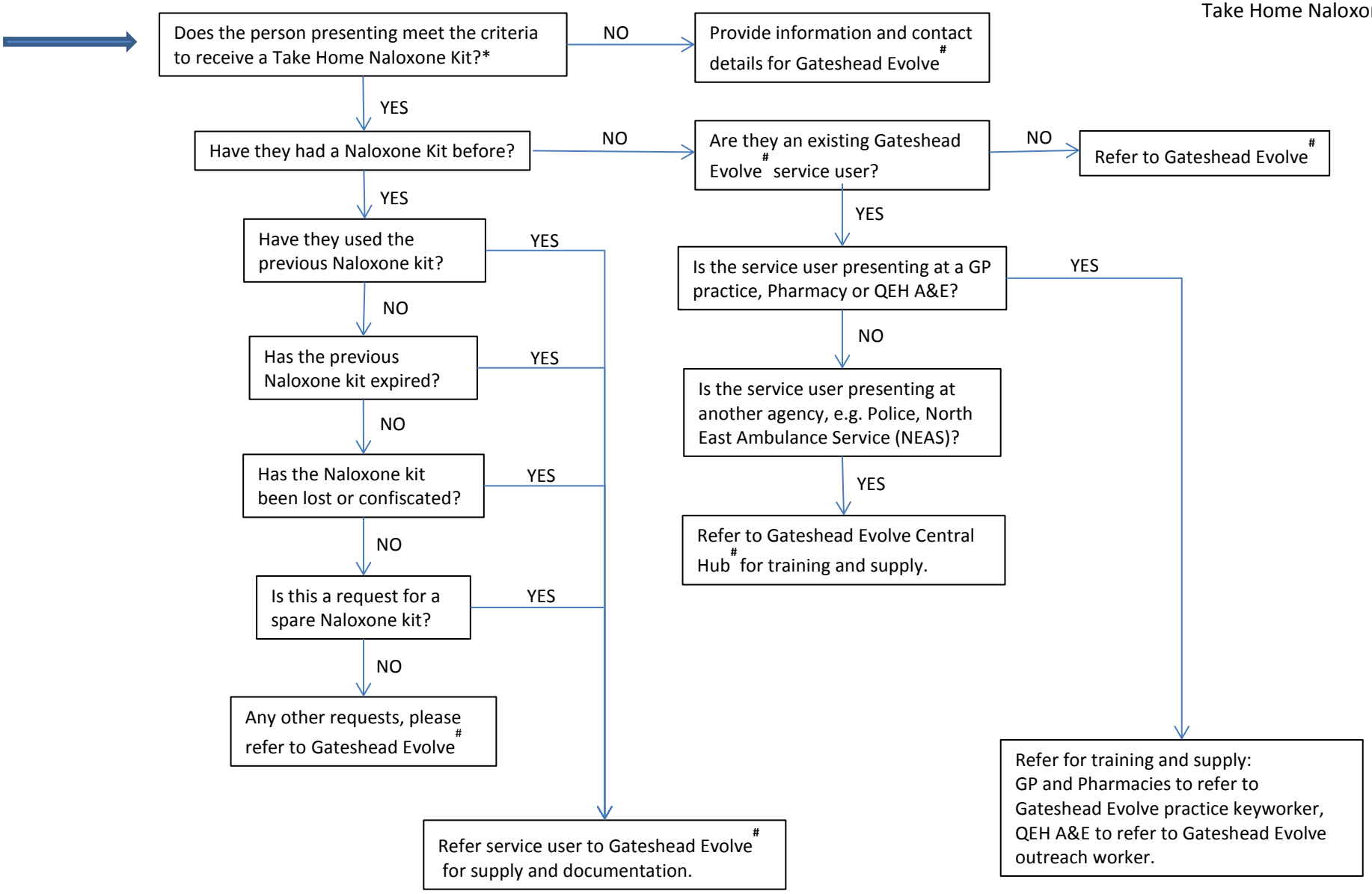
The desired outcome from this pilot is to demonstrate a reduction in DRDs in Gateshead caused by opioids. The effect on DRDs will therefore be analysed as part of the evaluation of the effectiveness of the pilot.

Currently, each General practitioner (GP) practice in Gateshead providing a Substance misuse service, has an aligned practice keyworker from Gateshead Evolve, attending the practice weekly. As illustrated in the pathway, both GPs and pharmacies would be expected to refer directly to the associated practice keyworker, rather than centrally in to the Gateshead Evolve Hub. However, that support is accessible if required.
Similarly, there is an outreach worker from Gateshead Evolve who attends Queen Elizabeth Hospital (QEH) Accident and Emergency (A&E) on a weekly basis. The outreach worker is the preferred point of contact for QEH accessing the pathway.

GPs and Pharmacies

Within the scope of this pilot, it is not expected that the supply of TH Naloxone kits will take place through the provision of an FP10 prescription from the GP. The funding arrangements for the pathway **do not** include reimbursement for kits issued by means other than from the Gateshead Evolve stock obtained for the pilot.

Figure 1. Take Home Naloxone Pathway



* Inclusion criteria: Prescribed opioids, Using opiates (i.e. Intra-venous), Accessing needle exchange services, Prison release, Hospital discharge following overdose, Carer of substance misuser, Named hostel worker, Named housing worker.

Gateshead Evolve Central Hub: 0191 594 7821

3.0 Training

Gateshead Evolve will be responsible for ensuring they provide the accredited training to clients, prior to receipt of a TH Naloxone kit. However, it would be beneficial for partner agencies (GPs, carers, hostels and supported accommodation, pharmacies, police, A&E) to access awareness raising training on this pathway and Naloxone. Several training and awareness raising events have already been delivered between October 2015 and March 2016, by Gateshead Evolve .

It is further **recommended** that all those involved in the provision of the substance misuse service in Gateshead should access the free eLearning 'Naloxone Saves Lives', produced by Substance Misuse Management in General Practice (SMMGP) and endorsed by the Centre for Postgraduate Pharmacy Education (CPPE).

This is available at: http://www.smmgp-elearning.org.uk/. The learning should take a maximum of 1 hour to complete and a certificate of completion is available at the end of the programme.

Furthermore, Martindale Pharma provides information and educational support materials for Prenoxad® (TH Naloxone kit) at www.prenoxadinjection.com. There are separate sections of the website to access depending on role, i.e. Healthcare professional, drug and alcohol treatment services and service user.

4.0 Useful contacts

Gateshead Evolve Central Hub: 0191 594 7821

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5.0 References

[1] Office for National Statistics. (2015). Statistical Bulletin: Deaths related to drug poisoning in England and Wales: 2014 Registrations. http://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsrelatedtodrugpoisoninginenglandandwales/2015-09-03. *Accessed 3/5/16.*

[2] Office for National Statistics. (2016). Drug Misuse deaths by local authority. http://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/datasets/drugmisusedeathsbylocalauthority. *Accessed 3/5/16.*

[3] Advisory Council on the Misuse of Drugs. (2012). Consideration of Naloxone. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/119120/consideration-of-naloxone.pdf. *Accessed 3/5/16.*

[4] World Health Organization. (2014). Community management of opioid overdose. http://www.who.int/substance_abuse/publications/management_opioid_overdose/en/. *Accessed 3/5/16.*

[5] Public Health England. (2015). Take home Naloxone for opioid overdose in people who use drugs. *http://www.nta.nhs.uk/uploads/phetake-homenaloxoneforopioidoverdosefeb2015rev.pdf. Accessed 3/5/16.*

[6] Naloxone Action Group England. NAG England's Key Facts – 10 important facts on naloxone for commissioners and providers. https://nagengland.wordpress.com/key-documents/. *Accessed 10/5/16*.

[7] Martindale Pharmaceuticals Ltd. (2013). SPC. Prenoxad® 1mg/ml Injection. https://www.medicines.org.uk/emc/medicine/27616. *Accessed 3/5/16.*

[8] NHS England. (2014). Patient Safety Alert. Stage One: Warning. Risk of distress and death from inappropriate doses of Naloxone in patients on long-term opiate/opioid treatment. https://www.england.nhs.uk/wp-content/uploads/2014/11/psa-inappropriate-doses-naloxone.pdf. *Accessed 3/5/16.*

[9] The Medicines for Human Use (Prescribing) (Miscellaneous Amendments) Order 2005. http://www.legislation.gov.uk/uksi/2005/1507/pdfs/uksi_20051507_en.pdf. *Accessed 3/5/16.*

[10] Martindale Pharma. (2013). Prescribing information for Prenoxad ® 1mg/ml injection. http://www.prenoxadinjection.com/downloads/prescribers_guide.pdf. *Accessed 11/5/16.*

6.0 Abbreviations

Abbreviation	Definitions
ACMD	Advisory Council on the Misuse of Drugs
A&E	Accident and Emergency
CPPE	Centre for Postgraduate Pharmacy Education
DRD	Drug Related Deaths
GP	General practitioner
NAG England	Naloxone Action Group England
NEAS	North East Ambulance Service
QEH	Queen Elizabeth Hospital
SMMGP	Substance Misuse Management in General Practice
SPC	Summary of Product Characteristics
TH	Take-Home

Appendix 1: Prescribing information for Prenoxad® 1mg/ml Injection, extracted from Martindale Pharma [10] http://www.prenoxadinjection.com/downloads/prescribers_guide.pdf

Prescribing Information for Prenoxad 1mg/ml Injection

Please refer to Summary of Product Characteristics before prescribing.
Presentation: A 2ml pre-filled syringe containing Naloxone Hydrochloride 1mg/ml.
Indications: Prenoxad Injection is intended for emergency use in the home or other non-medical setting by appropriate individuals or in a health facility setting for the complete or partial reversal of respiratory depression induced by natural and synthetic opioids, including methadone, diamorphine (diacetylmorphine (INN)) and certain other opioids such as dextropropoxyphene and certain mixed agonist/ antagonist analgesics: nalbuphine and pentazocine. Prenoxad Injection should be carried by persons at risk of such events. It may also be used for the diagnosis of suspected acute opioid overdose.
Dosage and Administration: Prenoxad Injection may only be made available once the prescriber has assessed the suitability and competence of a client or representative to administer Naloxone in the appropriate circumstances. Prenoxad Injection is for administration by intramuscular injection.
Adults and the Elderly. Opioid overdosage (known or suspected). For Use by individuals in the community.
In patients where breathing does not appear to be normal: In patients where breathing does not appear to be normal administration of Prenoxad Injection should be preceded by calling emergency services and requesting an ambulance. Following this, 30 chest compressions and if possible 2 rescue breaths (Basic Life Support SINGLE CYCLE) should be given; 0.4ml Prenoxad Injection solution should then be administered by intramuscular injection into the outer thigh muscle or muscles of the upper arm, through clothing if necessary. A further 3 cycles of chest compressions and rescue breaths should then be given followed by administration of 0.4ml Prenoxad Injection. Three cycles of chest compression and rescue breaths should take approximately 2 minutes. This should be repeated until an ambulance arrives or the patient begins breathing normally / regains consciousness. The patient when breathing normally or has regained consciousness should be placed in the recovery position (lying on their side, mouth open pointing towards the ground) and observed continuously.
In patients where breathing is normal but the patient is unrousable or suspected to be unconscious: The patient should be placed in the recovery position. 0.4ml Prenoxad Injection solution should be administered by intramuscular injection into the outer thigh muscle or muscles of the upper arm, through clothing if necessary, and an ambulance should be called. 0.4ml Prenoxad Injection solution should then be administered every 2-3 minutes and continued until the ambulance arrives and or the patient regains consciousness.
Children and Neonates: The Prenoxad Injection presentation is not intended to be used for children in the home setting other than by an appropriately trained healthcare professional.
Contra-Indications: Known hypersensitivity to Naloxone or any of the ingredients.
Warnings and Precautions: Prenoxad Injection is intended as an emergency treatment and the patient should be advised to seek medical help immediately. It should be administered cautiously to patients who have received large doses of opioids or to those physically dependent on opioids since too rapid reversal of opioid effects by Prenoxad may precipitate an acute withdrawal syndrome in such patients. Patients who have responded satisfactorily to Prenoxad should be kept under medical observation for at least 2 hours. Repeated doses of Prenoxad may be necessary since the duration of action of some opioids may exceed that of Prenoxad. Use with caution in patients with pre-existing cardiac, hepatic or renal disease and in those receiving medications with potential adverse cardiovascular effects e.g. hypotension, ventricular tachycardia or fibrillation and pulmonary oedema. Caution should be exercised and patients monitored when Prenoxad Injection is administered to this patients with renal insufficiency/failure or liver disease.
Interactions: Administer cautiously to opioid dependent patients including newborns of mother's dependant or those suspected of having received large doses and observe for signs of acute withdrawal.
Pregnancy and Lactation: Prenoxad should be used with caution in pregnancy. The neonate must also be monitored for signs of opioid withdrawal. Naloxone may be administered during the second stage of labour to correct any respiratory depression due opioid analgesics. It is not known whether Naloxone is excreted in human milk therefore use with caution in breastfeeding mothers.
Undesirable Effects: Common side effects include nausea, vomiting, dizziness, headache, ventricular tachycardia, hypotension and hypertension.
Less common side effects: Tremor, sweating, arrhythmia, bradycardia, diarrhoea, dry mouth, hyperventilation, inflammation. Seizure tension, allergic reactions, anaphylactic shock, fibrillation, cardiac arrest, erythema multiforme, fever, dyspnoea, runny nose, sneezing and yawning. Piloerection, weakness, shivering.
Product Licence Number: PL 12064/0125
Product Licence Holder: Aurum Pharmaceuticals Ltd, Bampton Road, Harold Hill, Romford, Essex RM3 8UG
Basic NHS Price: £18.00
Legal Category: POM.
Date of Preparation: April 2013
For more details contact: Aurum Pharmaceuticals Hubert Road, Brentwood, Essex CM14 4LZ
01277 266600

Adverse events should be reported.
Reporting forms and information can be found at www.mhra.gov.uk/yellowcard.
Adverse events should also be reported to Martindale Pharma Tel. 01277 266600
Fax 01708 382739
e-mail drugsafety@martindalepharma.co.uk

REFERENCES
1. Prenoxad Injection Summary of Product Characteristics (SmPC)

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Date of preparation: April 2013 Job code: CRIT/04/2013/119