A clinical audit to determine whether intravenous naloxone is prescribed and administered according to Trust guidelines in adult patients at Western Sussex Hospital NHS Foundation Trust

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Abstract

Title

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Introduction

NHS England issued a patient safety alert in 2014 regarding concerns with inappropriate doses of naloxone administered in patients on long-term opioid treatment. Rapid reversal of opioid analgesia can lead to intense pain and distress and acute withdrawal syndrome resulting in hypertension, cardiac arrhythmias, pulmonary oedema and cardiac arrest. Recommendations given in the alert stated that naloxone should be given with caution to certain patient groups in respiratory depression. The report also highlighted that doses given in the British National Formulary for acute opioid overdose may not be appropriate for the management of respiratory depression in those receiving palliative care and chronic opioid use.

An audit carried out in 2015 at Western Sussex Hospital Foundation Trust (WSHFT), showed poor compliance with these recommendations. Subsequently, a guideline was created for naloxone dosing together with changes to EPMA (electronic prescribing and medicines administration) prescribing protocols.

Aim

To assess if naloxone is prescribed and administered at Western Sussex Hospital Foundation Trust in accordance with Trust guidelines for opioid-induced respiratory depression.

Method

Data was collected from all adult wards in Medicine and Surgery using electronic records from June 2019 to January 2020. Doses were recorded from all patients that were administered naloxone in this time period together with respiratory rate and AVPU scores to identify respiratory depression. Data was then audited against the Trust guideline.

Results

31 patients were prescribed and given 54 doses of naloxone;

All patients had an AVPU score and respiratory rate recorded 24 hours prior to naloxone; however, no patients were found to be in respiratory depression, the same as in 2015.

Had all patients been in respiratory depression, then 36/54 (66%) doses given, could be considered to be correctly dosed and similarly 13/31 (42%) of all initial doses administered.

Conclusion
Naloxone prescribing was found not to follow trust guidance despite changes to guidelines in 2015 as all patients failed to meet the respiratory depression criteria. Further changes are therefore required including a review of the naloxone pathway, EPMA prescribing support as well as education on naloxone use for healthcare professionals. An additional re-audit after implementation is recommended.

Introduction

Patient safety alert

In 2014, a patient safety alert was issued by NHS England drawing attention to the safety implications of inappropriate doses of naloxone being administered to patients on long-term opiate/opioid treatment.

It identified that caution should be taken to prevent the rapid reversal of opioids by naloxone. Rapid reversal can lead to intense pain and distress, and acute withdrawal syndrome. This can lead to hypertension, cardiac arrhythmias, pulmonary oedema and cardiac arrest. Caution should also be used when prescribing and administering naloxone to a patient with pre-existing heart disease although the risks of higher doses are not well documented.

The alert highlighted that doses in the BNF may differ further from those found in other product literature. The difference in dosing schedules could therefore result in inappropriate doses of naloxone being given.

Respiratory depression

Naloxone should not be primarily used to restore a normal level of consciousness in a patient who has been administered an opioid, but one who presents with respiratory depression.

Respiratory depression is a breathing dysfunction characterised by ineffective respiration resulting to reduced depth and rate of breathing.

The absence of a standard definition however and lack of clarity in assessment methods for opioid-induced respiratory depression is one of the main barriers that may limit diagnosis and management.

Naloxone is commonly found to be given where there is a possibility of opiate toxicity, often resulting in its overuse.

Trust Guidance 2015-20

A clinical audit was carried out at Western Sussex Hospital Foundation Trust (WSHFT) in 2015 to identify if recommendations from the alert were followed in conjunction with guidance from the Trust's Pain team on naloxone dosing and administration.

Trust guidance on naloxone dosing varied with different definitions of respiratory depression. The Electronic Prescribing and Administration System (EPMA) also gave differing prescribing options creating uncertainty for prescribers.

The Trust's guidance on the management of opioid-induced respiratory depression expressed a respiratory rate less than 8 and an AVPU scale of P or U.

An AVPU scale is a system adapted for the measurement of a level of consciousness. This shows if the patient is alert (A), has a response to verbal stimulation (V), to pain stimulation (P) or if the patient is completely unresponsive (U).

Audit data was collected against these criteria and results were subsequently poor. 92% had their respiratory rate and AVPU score recorded before naloxone was given, but these patients were found not to be in respiratory depression and thus failed to follow Trust and NHS England guidance.

As a result of this clinical audit, recommendations were made, and a pathway for naloxone administration was drawn (see appendix 1) together with changes on EPMA. Dosing protocols were developed based on the indication/patient group.

It was thus necessary to conduct another clinical audit to evaluate the adherence by prescribers when prescribing naloxone following these new Trust guidelines.

Aim

To assess if naloxone is prescribed and administered at Western Sussex Hospital Foundation Trust in accordance with Trust guidelines for opioid-induced respiratory depression.

Objectives

1. To identify at least 20 patients that have been prescribed naloxone and compare current prescribing of naloxone with Trust guidelines (Appendix 1)

2. To make suitable recommendations and feedback to clinical staff who prescribe or administer naloxone based on the results of the audit.

Audit standards

1. 100% of patients prescribed and administered naloxone should be confirmed to have respiratory depression defined as "respiratory rate less than eight breaths per minute and an AVPU score of P or U".

2. 100% of patients that are confirmed to have respiratory depression should be given the correct dose of naloxone following the Trust guidelines.

Methodology

Audit data was collected retrospectively for a period of 6months between July 2019 and January 2020 from adult medical and surgical wards across the two sites of the Trust (St Richards and Worthing hospital).

Patients' electronic drug charts from previous care episodes were viewed; this was used to ascertain when naloxone was prescribed and administered. Naloxone infusion prescriptions were excluded. Prescriptions were also used to check if the patient had been given any opioid 24hours prior to naloxone being administered.

In addition, patients' drug histories were viewed to identify any long term opioid use or recent use prior to admission. Observational report systems (Patient track) were used to find patients' respiratory rate and AVPU score at the point of or shortly prior to naloxone being given.

The Evolve system was used to review any medical notes for any management decisions around prescribing and the need for naloxone.

Patients were classed as:

a) **palliative care** if they were known to be for end of life/palliative treatment associated with terminal disease and on regular or recently started opioid therapy

b) **acute opioid overdose** if opioids had been taken or initiated in the previous few days either in primary care or secondary care. This may have been pre-operative/hospital treatment, intentional overdose/suicide attempt or unintentional patient overdose.

c) **opioid naïve** where no opioid was found to have been given in the past 24hrs

d) **chronic opioid users,** known to be using opioids long term in the community or

e) **post operative opioid treatment**

and audited according to Trust guidelines. These outline 3 dose regimen pathways:

- 400micrograms initially for emergency acute overdose,
- 100micrograms for chronic or post-operative patients and
- 20micrograms for palliative care patients until the patient no longer experiences respiratory depression.

Patients who were classified as acute opioid overdose but not requiring emergency treatment (e.g. from intentional large overdoses) were considered to require 100microgram doses and audited against this standard.

Results

- Primary data analysis revealed that 39 patients were prescribed naloxone.
- 8 patients were excluded for varying reasons including lack of information.
- Twelve of the 31 patients received multiple doses resulting in a total of 54 doses of naloxone being given.

- 19 patients (61%) were given naloxone at Worthing hospital and 12 (39%) patients were given naloxone at St. Richard's hospital.
- Data shows that 21 patients fell within Medicine & 10 within Surgery.
- Naloxone was most frequently prescribed on the emergency floor admission areas.

Opioid Naïve

2 out of 31 patients given naloxone were found to be opioid naïve ie they were not taking any opioids before coming into hospital nor were known to be given any opioid 24 hours prior to naloxone. Both patients were seriously ill. One had atrial fibrillation and possible sepsis. The other patient had received intravenous oxycodone 2 days before. Both patients deteriorated and died soon after naloxone administration.

Palliative Care

4 patients were found to have known metastases, a chest tumour, a new cancer diagnosis and pancreatic cancer. The first 2 were not known to have opioids prior to admission but had been receiving Oramorph during admission and one was later made for end of life care. The new cancer diagnosis patient also received Oramorph before requiring naloxone. The pancreatic cancer patient was thought to be opioid toxic on admission to hospital and after several naloxone doses was made for end of life care too.

Post operative overdose

9 patients received naloxone post-operatively despite all being alert.

Chronic opioid users

4 patients were found to be chronic opioid users – patients taking opioids before admission into the hospital.

Acute Opioid Overdose

12 patients were thought to be opioid toxic due to acute usage.

4 cases were intentional prior to arrival at hospital through use of excess tramadol, cocaine, morphine or oxycodone.

One patient had been given Oramorph for dyspnoea and then naloxone to help relieve the 'patient's family about their concerns of morphine causing wheeze and breathlessness.'

4 patients had recently fallen. Three of these had opioids started in hospital resulting in drowsiness and one later was deemed for end of life care. The other patient was said to often be drowsy.

One patient had 3 days of opioid during admission before deteriorating suddenly and following naloxone, died a few hours later.

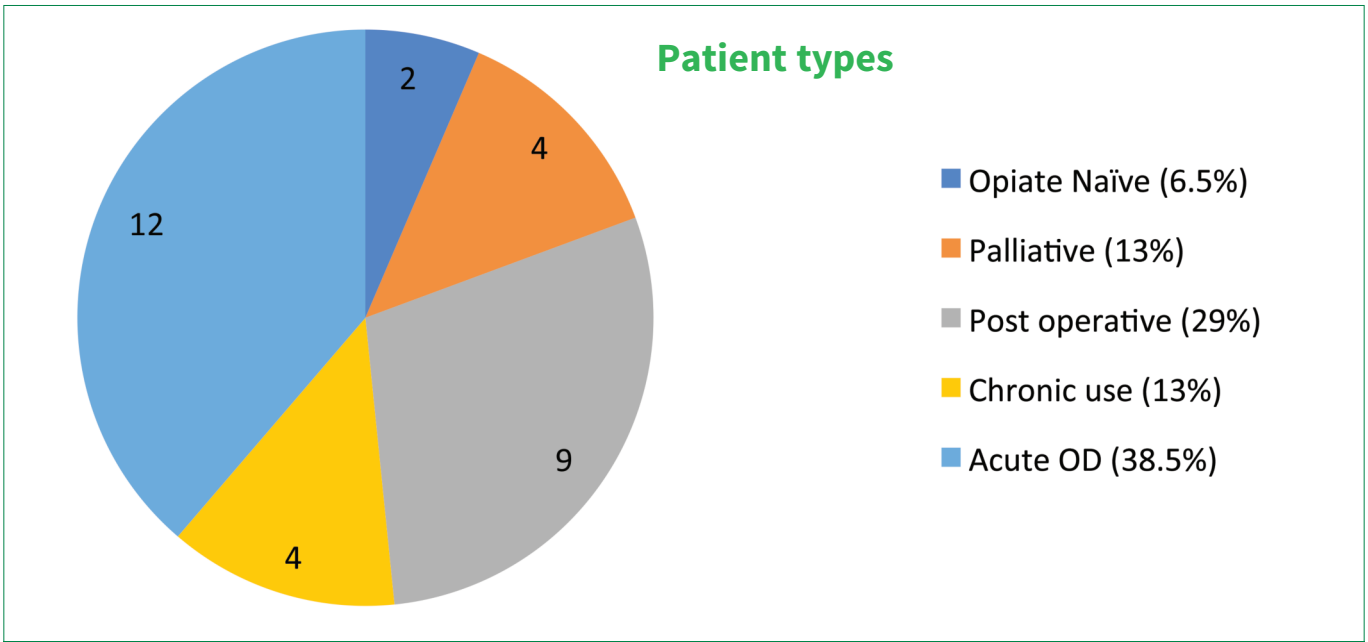

Figure 1. Patient types

The remaining two patients had received opioids, one pre operatively for a hip dislocation and the other for pain after a recent toe amputation.

Naloxone dosing

A range of doses were prescribed across the 54 doses administered in total, from 20micrograms to 800micrograms, the most frequent being 100microgram (Fig 2).

Respiratory depression

- All 31 patients had their respiratory rate and AVPU score recorded within 24 hours of naloxone being given.
- None of these patients however were confirmed cases of respiratory depression according to Trust guidelines (respiratory rate <8 breath per minute and an AVPU score of U or P).
- 11 doses were given where the AVPU score was U or P but the respiratory rate did not meet the criteria.
- Similarly, 3 patients had a respiratory rate of less than 8 but all were alert.

Discussion

31 patients who received naloxone across the two hospital sites were audited in 2019 compared to 26 in 2015. 61% of patients were given naloxone at Worthing hospital, which was in contrast to 2015, where more patients received naloxone at St Richards (63%). Naloxone was seen to be prescribed most frequently on the emergency floors (28%), a large area where patients are admitted, but again, this was significantly less than in 2015 where it constituted 46% of all ward administrations. None of these differences could be explained.

Oxycodone and morphine were the most commonly implicated opioids due to their prevalence of prescribing.

Patient Type & Dosing (see fig 3)

A number of patient types were identified, the majority receiving naloxone for acute opioid overdose, either from intentional overdose or recent hospital initiation resulting in drowsiness opioid overdose, either from intentional overdose or recent hospital initiation resulting in drowsiness.

Patient groups could not reliably be compared to 2015 due to different classifications by the author.

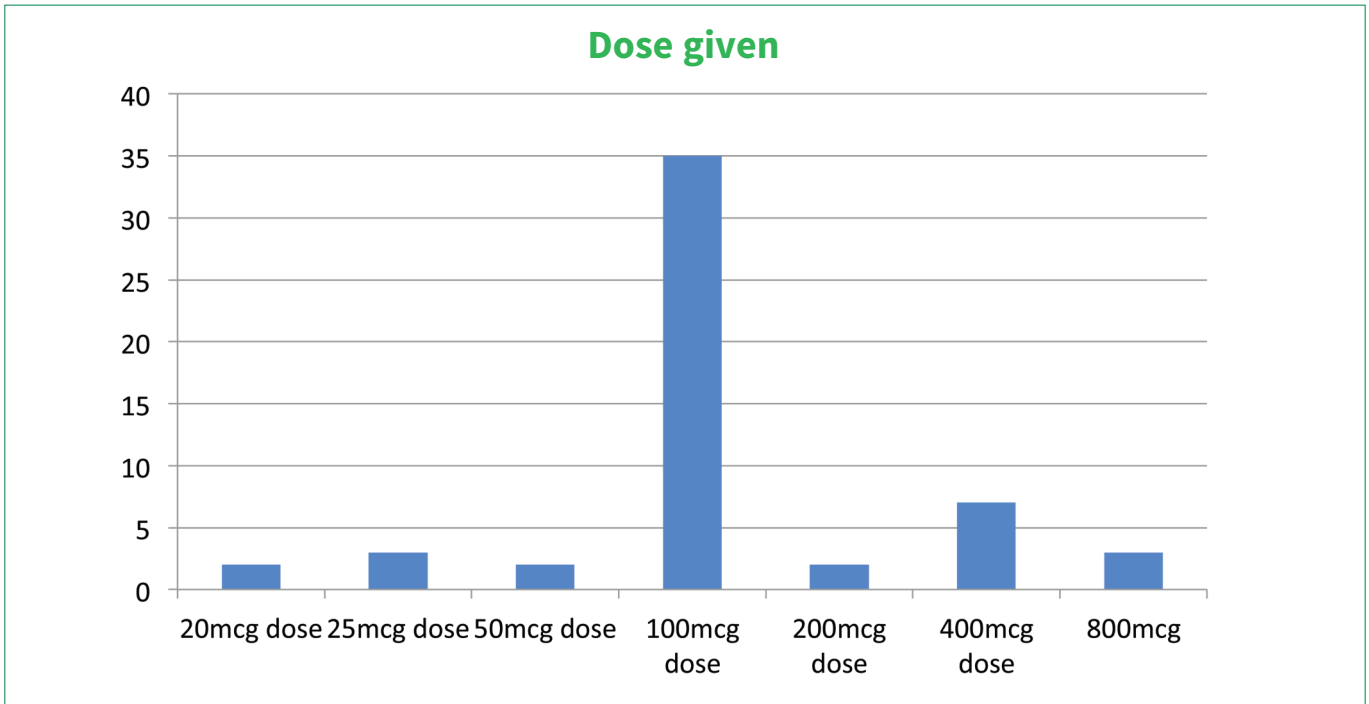

Figure 2. Patient types

The Trust guideline created to support staff initiating naloxone outlines 3 dosing regimens depending on the indication:

- 20mcg for palliative care patients,
- 100mcg for patients not requiring full reversal eg post-operative respiratory depression or chronic opioid users and
- 400mcg initial starting dose for acute overdose.

For audit purposes, the category for acute overdose included patients who had acutely overdosed intentionally prior to admission, as well as those that were thought to be opioid toxic during admission of newly prescribed opioids. The former patients were deemed to require 400mcg doses for emergency reversal but the latter were classified as requiring the 100mcg dose in discussion with the Lead Clinical Nurse Specialist Inpatient Pain Service

A further category was added for audit purposes of those patients that were opioid naïve where no opioid had been given in the previous 24 hours either in hospital or pre-admission. Two such patients were found to have received naloxone where an opioid hadn't been given. The two patients were seriously ill and died shortly after receiving naloxone at 400mcg and 20mcg. It may be that their symptoms were misidentified as possible opioid toxicity instead of the process of dying. It was unclear why such a variance of doses was prescribed.

Similarly, two of the 4 palliative care patients received 400mcg doses but were significantly ill and were deemed for end of life care soon after, which may not have been recognised earlier. The 100mcg dose given in the remaining two patients did not follow Trust guidelines either.

The majority of the 9 post-operative patients received the appropriate 100mcg dose of naloxone. Of the 3 patients who didn't, one was subsequently found to be receiving naloxone for itching due to a reaction from fentanyl PCA. This is an unlicensed indication but was advised by the Lead Clinical Nurse Specialist for Inpatient Pain Service where doses of 20-25mcg are suggested. It was unclear from the medical notes as to why a small dose of naloxone was given to the other 2 post- op patients.

Patient type	Initial Dose given	Number of doses	Dose appropriate
Opioid naive	400mcg	1	N
	20mcg	1	N
Palliative care	400mcg	2	N
	100mcg	2	N
Post operative	100mcg	6	Y
	25mcg	2	N
	20mcg	1	N
Chronic opioid use	100mcg	4	Y
Acute opioid overdose			
- intentional	200mcg	2	N
	400mcg	1	Y
	100mcg	1	N
- unintentional	50mcg	1	N
	100mcg	6	Y
	400mcg	1	N

Figure 3. Breakdown of initial naloxone dose by patient type

4 chronic opioid users were identified. One overdose was said to be accidental and another stated that painkiller use was 'getting out of control'. One case was thought to be due to mixed opioid and benzodiazepine overdose. All were given an appropriate 100mcg dose of naloxone.

Of the 12 patients who were thought be suffering from acute opioid overdose, 4 were intentional overdoses taken prior to admission. Only one was given the appropriate 400mcg dose, the others received 100mcg or 200mcg.

It is interesting to note that a number of elderly patients requiring opioids having suffered a fall and sometimes a fracture, required naloxone. Opioid usage may need to be considered more carefully for such elderly patients and those given opiates post operatively. Inappropriate naloxone use was also seen, where it was given for a family's concern and where also there had been little change in a patient's drowsy status.

Of the initial doses given for the 31 patients, dosing was considered appropriate for 13 (42%). Of all subsequent 54 doses administered, 36 (66%) doses would be considered appropriate.

Despite only 1 patient out of 26 in 2015 receiving an appropriate naloxone dose, due to changes in the guideline from 2015 the appropriateness of dosing cannot be compared directly.

Respiratory depression

The Trust guidelines for prescribing naloxone define respiratory depression as a respiratory rate of less than 8 with an AVPU score of P or U since there is no universal definition.

No patient was found to be in respiratory depression and as such Trust guidelines were not followed and failed to meet the audit standard set. This was similar to the first audit in 2015 audit where only 1/25 patients were found to be in respiratory depression.

It was evident that doctors were not recording AVPU scores in medical notes when deciding on whether naloxone was appropriate and that this was recorded by nursing staff prior to and after administration. Prescribing decisions were made on clinical signs and symptoms such as drowsiness, respiratory rate, pupil dilation and other factors. In one instance, medical staff initiated naloxone to allay the concerns of the family for a patient who was given Oramorph for dyspnoea associated with end stage COPD. A further dose of Oramorph was given 5 hours after the naloxone. Similarly in many other patients, further doses of opioids were given within hours or even minutes of naloxone being given, underlying the inappropriateness and misunderstanding of its use.

It could be understood that many patients on opioids as part of their medical condition might look drowsy. Clinicians may perhaps consider naloxone a safe drug and thus prescribe it in the belief it poses little harm to a patient if given where it is unclear there is opioid toxicity or true respiratory depression. Some patients were not only drowsy but very sick and approaching the end of life. A lack of recognition of the dying phase may be a factor when trying to diagnose opioid related respiratory depression.

Similarly, doctors may not be familiar in using the AVPU score in the diagnosis of respiratory depression and use other markers/symptoms.

Limitations

Sample size is small and may not reflect all practice.

There are several limitations to this audit when compiling data obtained from medical records through retrospective review. These include incomplete or missing data and difficulty in verification and interpretation of documented information. Where there were limited notes, sensible assumptions were made from the prescription.

Only naloxone administration recorded on EPMA was used for the purposes of the audit. As such, doses of naloxone or opioids that had been documented as given on paper prescriptions in A&E or in theatres may not have been fully captured. Patients considered opioid naïve may have been given an opioid e.g by paramedics en route to hospital. Similarly, it was not clear if a patient had taken an opioid prior to admission or if a GP had provided an opioid prior to admission.

Differences in the AVPU score and respiratory rate may have occurred from that recorded on

Patientrack shortly before naloxone administration and that noted by medical staff on reviewing the patient beforehand. The clinical picture of the patient therefore may be different to that documented retrospectively and there may have been instances where the naloxone was warranted. Similarly, the time in which naloxone was recorded as given may not be entirely accurate and may not correlate with the observations on Patientrack accurately.

Categorisation of patients was subject to the author's discretion based on the data available.

Conclusion

Naloxone was found to be given inappropriately in all patients identified, showing no improvement in management following changes to guidelines in 2015. Further changes are required to improve management of opioid toxicity related respiratory depression.

Recommendations

- Discuss findings with clinicians to identify improvements for action
- Review the current guidelines with the Lead Clinical Nurse Specialist Inpatient Pain Service. Introduce a new sedation score with S 0-3 replacing the AVPU scale and consider emphasis on assessment of respiratory depression and sedation.
- Review and make the algorithm visible at the point of prescribing to guide decision making with clear definitions of respiratory depression. Incorporate into EPMA.
- Educational sessions on naloxone prescribing for prescribers and nurses administering naloxone, with focus on the Emergency Floor ward, highlighting the importance of respiratory depression being diagnosed and confirmed before naloxone administration.
- Education on safe use of opioids to reduce need for naloxone.
- Re-audit annually to track progress on previous audit recommendations.
- Sharing of the audit results via appropriate forums

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Declaration of interests

The author has no interests to declare.

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Naloxone Hydrochloride Administration Pathway for Adults

Give oxygen and if appropriate lay patient in recovery position

Where RR is <8/min, patient is barely rousable/uconscious and or cyanosed

**STOP administrations of ALL opioids -
including PCA, syringe driver with opioids, epidural infusions with opioids
and remove any opioid transdermal patches in situ**

Emergency treatment of accute opiod overdose	Reversal of opioid respiratory depression and sedation where full reversal is not desirable e.g. post op; chronic opiate users	**Palliative care patients established on opioids**
Administer 400 microgram naloxone IV Give antiemetic	Administer 100 microgram naloxone IV Give antiemetic	Administer 20 microgram naloxone IV Give antiemetic
If no response after 1 min administer 800 microgram Repeat if no response after 1 min	If no response after 2 min administer 100 microgram naloxone IV Can be repeated every 2 min. to max. dose of 400 microgram till resp. rate is >8/min & sedation score is A or V	If no response after 2 min administer 20 microgram naloxone IV every 2 min till satisfactory respiratory status max. 400 microgram in total
If no response after 1 min administer 2mg (4mg may be required) **Max dose 10mg**		

**In any patient who does not respond a senior doctor
must consider alternative diagnosis/causes**

**Preparation available = 400 microgram/mL injections (ready diluted).
To prepare 100 micrograms - dilute 1mL of 400 microgram/mL with 3mL sodium chloride 0.9%.
Gives a solution of 100 microgram/mL.
To prepare 20 micrograms - dilute 1mL of 400 microgram/mL with 9mL sodium chloride to
gives a solution of 40 microgram/mL.**

Appendix 1