

Draft Human Medicines (Amendments Relating to Naloxone and Transfer of Functions)

Regulations 2024: Additional information from the Department for Health and Social Care

Cost/benefit analysis

Q1: What is the unit cost of Naloxone and how many extra units do you foresee being issued per year for these purposes?

A1. Naloxone is currently available for use in the community in two forms: intra-muscular injection ('injectable') and intra-nasal spray ('nasal'). There are three formulations with market authorisations in the UK for community/lay use:

- Ethypharm's Prenoxad, intramuscular (IM) injection, usual price is £18. Each pre-filled syringe contains 5 x 0.4mg doses of naloxone, a total of 2mg.
 - Napp's Nyxoid intranasal (IN) spray, usual price is £26. Each pack contains 2 applicators each with a single dose of 1.8mg naloxone, roughly equivalent to 0.4mg IM in the first 10 minutes (but reaching a higher plasma concentration thereafter, closer in equivalence to 0.8mg IM).
 - Accord's Naloxone 1.26mg Nasal Spray, usual price is £25. Each pack contains 2 applicators, with a lower dose of 1.26mg naloxone in each but also considered to be broadly equivalent to 0.4mg IM initially and 0.8mg in the longer term.
2. We do anticipate some increase in demand for naloxone as a result of these legislative changes, however the scale of this is currently unknown. These changes are enabling only, meaning it will be a choice for individuals or organisations to decide whether they

want to use this power and give out naloxone; which will be based on local need and also whether we start to see an increase in the use and harms associated with synthetic opiates. This makes it very difficult to predict uptake and therefore we are unable to provide a robust estimate of the increased demand for naloxone, but are engaging with the market to ensure that any changes in demand can be met.

Local authorities are responsible for commissioning drug treatment services as part of their public health responsibilities, and they provide funding for naloxone supplied through drug treatment services based on their assessment of local need. Although local authority public health will want to support wider provision of naloxone, their resources are limited and additional services and organisations that want to provide take-home naloxone may need to pay for it through their own funding streams.

In the 2021 consultation '*Expanding access to naloxone*'¹ we asked, "if you represent any of the following services or individuals, do you think it is likely that they would keep a stock of and supply naloxone if the regulations were changed such that they were eligible to do so?". Figure 1 shows the responses of those who reported that they did represent the services and individuals listed.

¹ ['Expanding access to naloxone'](#)

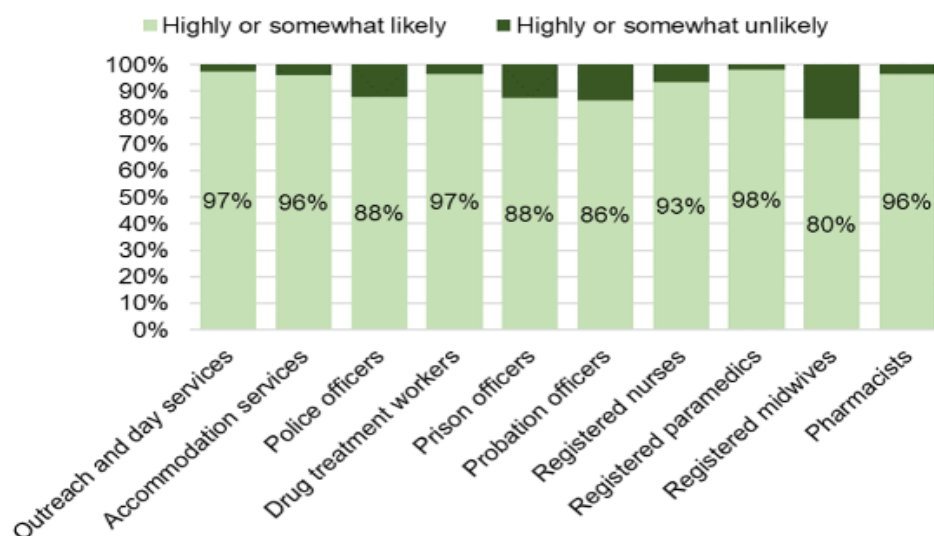


Figure 1. Perceived likelihood that each service or profession would keep a stock of naloxone and supply it if regulations were changed.

The situation in the UK is also evolving and there are additional factors impacting current demand for naloxone:

- Current rate of opioid poisoning deaths, which average 40 a week in England.²
- Rate of supply needed to prevent deaths in this “business-as-usual” situation (Bird et al. recommends a rate of 9-20x opiate deaths).
- An increased need for naloxone supply and additional doses occasioned by the impact of more potent synthetic opioids:
 - o in heroin and largely restricted to dependent heroin users

² [Deaths related to drug poisoning in England and Wales - Office for National Statistics \(ons.gov.uk\)](https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/deaths/articles/deathsrelatedtdrugpoisoninginenglandandwales/2017)

- o in other drugs and spreading into non-dependent drug using populations
- An increased demand as more public bodies and services are supporting and adopting naloxone carriage/supply, including police, prisons, ambulances, EDs, etc.
- Rates of product replacement due to:
 - o use (in the event of overdose)
 - o loss/damage
 - o expiry

Q2: What is the shelf-life of the medicine - especially if carried around in say a Police Car rather than being properly stored in a medical facility - how much is likely to be wasted if it is distributed on a contingency basis?

A2: The three naloxone formulations for community/lay use in the U.K have a shelf-life of around 3 years after which they should be replaced. There are no special storage requirements and testing on naloxone subjected to extreme conditions has found minimal degradation even over extended periods of time.

Training on the use of available naloxone is already very well established in most parts of the country alongside naloxone provision. As part of the proposed legislative changes, we will require that new services and professionals supplying naloxone, other than armed forces personnel, meet specific training requirements, including understanding appropriate practice around storing naloxone, and ensuring they can properly support an individual being supplied

with naloxone, including how to store and administer the medicine. This will limit any potential wastage of naloxone products and ensure safe usage.

Q3: How many overdose deaths are there per year - how many extra might this enabling provision prevent?

A3: There were 4,907 deaths related to drug poisoning registered in England and Wales in 2022; this is the highest number since records began in 1993. The rate of drug-poisoning deaths has increased every year since 2012 and was 81.5% higher in 2022 than it was in 2012.³

In 2022, opioids were involved in 73% of drug-misuse deaths in England and 60% of drug-misuse deaths in Wales,⁴ 82% of drug misuse deaths in Scotland⁵ and 60% of drug-related deaths in Northern Ireland⁶ – This is a total of approximately 3000 opioid-related deaths across the UK. We are also currently monitoring the emerging threat posed by highly potent synthetic opioids, such as nitazenes, which are leading to increased deaths in the UK.

It is expected that by increasing the number of services that can buy and stock naloxone, and therefore increasing the number of people who have access to naloxone, lives will be saved. However, we are unable to provide an accurate figure of extra overdose deaths prevented because there are a number of assumptions made in estimating the

³ [Deaths related to drug poisoning in England and Wales - Office for National Statistics \(ons.gov.uk\)](https://ons.gov.uk/deaths/articles/deaths-related-to-drug-poisoning-in-england-and-wales)

⁴ *Ib id*

⁵ [Drug-related Deaths in Scotland in 2022 - Report \(nrsotland.gov.uk\)](https://nrsotland.gov.uk/drug-related-deaths-in-scotland-in-2022-report)

⁶ [Drug-Related and Drug Misuse Deaths 2012-2022 | Northern Ireland Statistics and Research Agency \(nisra.gov.uk\)](https://nisra.gov.uk/drug-related-and-drug-misuse-deaths-2012-2022)

impact. These assumptions are subject to large levels of uncertainty due to the different possible scenarios for what the threat could look like and how much Naloxone would be distributed and administered as a result.

Wider case for making the antidote so widely available

Q4: Are there any risks from taking naloxone - you state it is currently a prescription only medicine - why?

A4: Naloxone is already widely accepted and used across the UK and worldwide. It is not addictive and only has an effect if the individual has taken opioids.

Naloxone is a World Health Organization (WHO) recommended medicine and its efficacy has been proven in several published studies and pilots. Naloxone has been found to have high efficacy in reversing overdoses even when administered by a layperson (75-100%).⁷ A systematic review to assess the effectiveness of take-home naloxone (THN) selected nine studies for inclusion in a Bradford Hill analysis. Evidence extracted from non-randomised studies showed that there was a link between THN and a reduction in opioid-related overdose mortality and indicated a low frequency of adverse events (Mc Donald and Strang, 2016).

The WHO has published that 'Naloxone has virtually no effect in people who have not taken opioids'.⁸ It may have some side effects such as confusion if the overdose is reversed too sharply, and there are some cardiac or respiratory related risks, although

⁷ [A systematic review of community opioid overdose prevention and naloxone distribution programs - PubMed \(nih.gov\)](#)

⁸ [Opioid overdose \(who.int\)](#)

evidence is that the frequency of adverse events relating to the administering of naloxone is very low (<1%).

Several countries (for example, Australia, Canada, and Italy), as well as some US states, have introduced naloxone as over-the-counter medication and have also started proactive distribution in communities.

In England, injectable medicines are automatically prescription only (POM) (paragraph 1(a)). Most medicines will however have their classification determined by the licensing authority and the presumption is they will be classified as POMs, unless and until manufacturers/suppliers apply, with supporting safety data, for a change in categorisation. In the case of a product such as nasal naloxone, this can be a costly process and to date the market has not generated sufficient income for it to be a worthwhile prospect. Discussions are underway with suppliers and MHRA to see if a move away from POM status would be feasible.

Q5: Are there any risks from administering Naloxone? Are charity workers likely to be sued if they do it wrong? Will they be covered by appropriate indemnity insurance?

A5: Naloxone is already widely accepted and used across the UK and worldwide. As these legislative changes are enabling only, it will be a choice for individuals or organisations to decide whether they want to use this power to carry naloxone and give out naloxone.

There is some risk of naloxone bringing about withdrawal symptoms, which can cause confusion and aggression from the person who was treated with naloxone. This could

pose some risk to the person administering the naloxone. Specifically for injectable naloxone, there is risk of accidental needle stick injuries if handled incorrectly.

DHSC will update operational guidance on the provision of naloxone when the regulations have come into force. The guidance will include information on safe usage of naloxone and outline that upon entering into these arrangements, it is for service providers/public bodies to see if their public liability insurance covers this.

It is important to note that naloxone can already be administered by anyone in an emergency situation, including charity workers; these changes will enable more services to give it out to individuals for future use, and does not change current rules around administration directly, although we hope it will significantly increase the likelihood of naloxone being available to administer by people such as charity workers.

In principle, therefore, as a necessary corollary to that, there will also be an increase of the number of occasions when things might go wrong, leading to two broad types of potential breaches of legal duties owed in “rescuer” contexts: firstly, breaches of duties owed to the “rescuer”, which in this instance is the person administering the naloxone, and to whom duties may be owed either by the person who has overdosed or someone else, e.g. the rescuer’s employer; and secondly breaches of duties owed to the person being “rescued”, principally to the person who as overdosed but also potentially to someone else, for example family members.

However, even though there is likely to be an increased number of occasions on which two potential areas of liability arise, we consider it very unlikely that legal activity in this

area will increase in any significant way, and in particular that there will be that a significant increase in rescuers being sued. Firstly, even when used by a layperson, naloxone is relatively speaking very safe. Secondly, the training that will be put in place will be our principal method of preventing things going wrong. Thirdly we understand that the courts are reluctant to hold rescuers liable where they have acted in a way that in all the circumstances is reasonable. Adding these three factors together, we think the package of measures we have put in place should ensure that and so the likelihood of charity workers being sued for administering naloxone remains very low and should not add in a significant way to the background legal risk that they take on in performing their wider roles.

Q6: How would you respond to the suggestion that by providing a widely available antidote you are encouraging addicts to overdose?

A6: Research indicates that naloxone does not lead to more drug use or riskier drug use. We are not aware of any significant body of evidence that indicates naloxone provision encourages increased drug use or overdose. In fact, some studies have shown that naloxone results in decreased drug use (Seal et al., 2005; Wagner et al., 2010).

Naloxone is already widely accepted and used across the UK and worldwide; the potential to reduce harm and save lives is far greater than any risk of encouraging increased risk-taking that could lead to overdose. It can be argued that it is not useful to focus on the harms of drug use when compared with an opportunity to intervene and potentially save lives (Bazazi et al., 2010).

Naloxone is an important harm reduction measure for those who are at risk of opioid overdose, but 'should be viewed as a crucial intervention as part of an adequately funded treatment and support system'.⁹ Treating drug dependence and promoting recovery is our main objective, which is why DHSC is also working to improve the quality and capacity of the drug treatment and recovery system. However, drug use can continue despite prevention and treatment efforts, and naloxone is crucial in reducing the morbidity and mortality associated with drug use.¹⁰ There are also additional benefits of naloxone around engaging with drug users and empowering family members and carers.¹¹

Having an opioid overdose reversed by naloxone is a negative, and sometimes unpleasant, experience as Naloxone can cause opioid withdrawal symptoms.

Additional Points:

- Naloxone is already widely used and available in the UK, being supplied for take-home use through drug and alcohol treatment services. These proposed changes to legislation aim to streamline existing supply arrangements and give a broad range of services and professionals (other than drug treatment services) the power to hand out supplies to others on a take-home basis for future use in an emergency.
- One of the main drivers for this work is the rise in synthetic opioids in the UK's illicit drug market. We want as many people as possible to be able to access naloxone

⁹ [ACMD review of the UK naloxone implementation \(accessible\) - GOV.UK \(www.gov.uk\)](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/444444/ACMD_review_of_the_UK_naloxone_implementation_accessible.pdf)

¹⁰ [Preventing Opiate Overdose Deaths: Examining Objections to Take-Home Naloxone - PMC \(nih.gov\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC444444/)

¹¹ [Advisory Council on the Misuse of Drugs - Naloxone Consideration Report May 2012 \(publishing.service.gov.uk\)](https://publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/444444/Advisory_Council_on_the_Misuse_of_Drugs_-_Naloxone_Consideration_Report_May_2012.pdf)

if/when they may need it as this will allow better national response and preparedness if we see something like the rise in fentanyl in America.

- There is strong support from stakeholders to amend current legislation on naloxone, including, The Association of Directors of Public Health, Community Pharmacy England and London Mayor's Office for Policing and Crime (MOPAC). Whilst we recognise quantitative data is limited on the potential to save lives, the widespread support from stakeholders on our proposals demonstrates the perceived real-life benefits of these changes.

Additional evidence:

- Despite some of the efforts to make naloxone widely available, findings from research by Carre and Ali (2019) highlight that this has still not been achieved in England. Nationally, the estimated coverage of THN among people who use opioids was as low as 16% in 2017-18. The study also found in 58% of cases local authorities THN was not available to clients accessing community pharmacies, including those providing opioid substitution treatments and needle syringe programmes.
- Opioid-related deaths have generally continued to rise, and achieving widespread availability of naloxone across the UK will help reduce this. A study published in 2018 also indicated, based on Bradford Hill criteria, that there is an association between reduced deaths from overdose and the implementation of THN programmes (Olsen, et al, 2018).
- Drug deaths are considered avoidable deaths - The mortality rate for drug-related deaths has continued to increase in England and Wales. In England, the ASMR for

alcohol-related and drug-related deaths was 25.9 per 100,000 people in 2022, compared with 21.3 in 2019. In Wales, the ASMR for alcohol-related and drug-related deaths was 30.2 per 100,000 people in 2022, compared with 24.2 in 2019.

- In comparison, COVID-19 is also classified as an avoidable death – In 2021 the ASMR for COVID-19 was 42.1 deaths per 100,000 people in England and 38.5 deaths per 100,000 people in Wales.
- The WHO published [guidelines for community management of opioid overdose](#) which strongly recommended that, ‘people likely to witness an opioid overdose should have access to naloxone and be instructed in its administration to enable them to use it for the emergency management of suspected opioid overdose’. It reported that a number of programmes around the world have shown that providing naloxone to people likely to witness an opioid overdose, in combination with training on the use of naloxone and on the resuscitation of people following an opioid overdose, could substantially reduce the number of deaths resulting from opioid overdose. The WHO notes that this is particularly relevant for people with opioid use disorders and leaving prison, as they have very high rates of opioid overdose during the first four weeks after release.
- A study which assessed the effectiveness of Scotland’s THN policy, the authors utilised a pre-post design to compare data from 2006-10 with a period post-implementation (2011-13) of the Scottish naloxone programme in January 2011. The study determined the proportion of overdose-related deaths which, in the four weeks before, had been either released from prison or discharged from hospital.

Results showed a statistically significant decrease of 3.5% in the numbers of opioid related deaths in the post-release period when comparing the periods 2006-10 and 2011-13. Applying Bradford Hill's criteria for causality, in 2016 Bird et al. found a 36% decrease in Scotland (Bird et al, 2016)

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