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Naloxone for Opioid Overdose

Intranasal or intramuscular?

What programmes and policymakers in Eastern Europe and Central Asia should consider

Both routes save lives. The best policy gets acceptable, affordable naloxone into the hands of people most likely to witness an overdose - before it happens.

Key messages

01 **There is no universally 'best' formulation.** Intranasal and intramuscular naloxone can both reverse opioid overdose. Performance depends on the specific product, dose, responder and setting - so policy should compare real products, not routes in the abstract.

02 **Ready-to-use nasal naloxone can remove important barriers.** It requires no needle, preparation or injection skills and may be easier for relatives, friends and other inexperienced responders. Intramuscular naloxone remains effective, familiar to many peers and usually less expensive.

03 **Dose matters.** The immediate objective is to restore adequate breathing, not necessarily complete awakening. Higher naloxone exposure can precipitate severe withdrawal; sufficient repeat doses should be available when breathing remains dangerously suppressed.

04 **There is no single community preference.** Some people prioritise simplicity and comfort; others value familiarity and more incremental dosing. Programmes should offer choice where feasible and involve people who use drugs in product selection, training and evaluation.

05 **Availability is not the same as access.** Registration or hospital procurement does not mean naloxone is carried by people likely to witness an overdose. Take-home and peer-to-peer distribution are the decisive steps for community coverage.

06 **A new formulation should expand access, not shrink it.** Introducing a higher-cost nasal product should not displace affordable injectable naloxone if the result is fewer kits, fewer doses or fewer people reached.

Why this question matters now

Naloxone is a life-saving opioid antagonist that can rapidly reverse the respiratory depression caused by opioid overdose. The World Health Organization (WHO) recommends that people likely to witness an overdose - including people who use opioids, peers, family members and friends - should have access to naloxone and training in its use. WHO recognises both intramuscular and intranasal administration and advises selecting the route according to the available formulation, responder skills, setting and local context.[1]

This approach moves overdose response beyond ambulances and hospitals. Take-home naloxone (THN) programmes place the medicine directly with people who may need to use it, and peer-to-peer models extend distribution through the networks in which overdoses occur.[2,3,15,16]

The EECA region has already shown that community distribution can work at scale. The UNODC-WHO Stop Overdose Safely (S-O-S) project in Kazakhstan, Kyrgyzstan, Tajikistan and Ukraine demonstrated both high use of naloxone by trained witnesses and high reported survival in witnessed events.[4,17]

14,000+	about 40,000	89.1%	98.3%
potential witnesses trained	naloxone ampoules distributed	used naloxone when witnessing an overdose	reported survival in the most recent event

S-O-S project in Kazakhstan, Kyrgyzstan, Tajikistan and Ukraine. Sources: [4,17].

Ready-to-use nasal sprays create a genuine opportunity to reach people who are unwilling or unable to inject. But convenience is only one dimension of good policy. Dose, speed of response, withdrawal, cost, product supply, population coverage and community preference all matter. This framing is consistent with the EHRA Strategy 2025-2029, which identifies access to naloxone as a

regional advocacy priority and emphasises evidence-based services and community participation.[5,6]

> **Central policy question:** Which mix of products will maximise timely use, community coverage, choice and dignity - rather than which route appears most modern?

How to read the evidence

Comparisons between 'nasal' and 'injectable' naloxone can mislead unless three distinctions are kept clear:

- **Route is not product.** Older studies often used injectable naloxone solution sprayed into the nose through an atomiser. These larger-volume, lower-concentration preparations are not equivalent to modern, highly concentrated, ready-to-use nasal sprays.[1,7]
- **Dose and concentration matter.** Two products using the same route may perform differently. Evidence from one dose or device should not be generalised to every intranasal or intramuscular product.
- **Nominal milligrams are not directly comparable across routes.** Nasal absorption differs from intramuscular absorption. A nasal device containing more milligrams is not automatically 'stronger' in clinical effect than a lower-milligram injection.

The evidence base is heterogeneous. Direct trials test particular products in supervised or ambulance settings, and comparative evidence from community responders is limited. The findings support context-specific product decisions, not a universal ranking of routes.[7-9,14]

Intranasal and intramuscular naloxone at a glance

Consideration	Ready-to-use intranasal (IN)	Intramuscular (IM)
Can reverse opioid overdose	Yes	Yes
Product presentation	Ready-to-use, single-use nasal device	Ampoule, vial or pre-filled syringe, depending on product
Needle and preparation	No needle; little or no assembly	Needle required; ampoules or vials may require preparation
Responder skills	May be easier for people with little injection experience	Requires training and willingness to inject; familiar to many peer responders
Response in comparative trials	Effective, but some tested products needed rescue doses more often	Faster in some head-to-head trials of specific products and doses
Dosing	Fixed dose per device	Some presentations allow more incremental administration
Repeat doses	May be needed and should be available	May be needed and should be available
Withdrawal	Possible; risk relates importantly to total naloxone exposure	Possible; risk relates importantly to total naloxone exposure
Needlestick or ampoule injury	None	Possible
Cost and coverage	Often costs more per dose; local prices and programme design matter	Generic products are usually cheaper and may support wider coverage
Community preference	Preferred by many people for simplicity and comfort	Preferred by some experienced responders for familiarity and dose control

Note: comparisons apply to specific products and doses, not to the route in the abstract. Nominal milligram doses should not be compared directly across routes. Sources: [1,7-9,14].

What does the comparative evidence show?

Both routes work, but product performance differs

An EU Drugs Agency (EUDA) evidence summary found similar overall reversal success for intranasal and intramuscular/intravenous naloxone in a meta-analysis, while rescue dosing was more frequent after intranasal administration. EUDA also distinguishes higher-concentration intranasal products, which performed similarly to intramuscular naloxone at equivalent doses, from lower-concentration nasal formulations, which were less effective.[7]

Head-to-head trials reinforce the need to name the product and dose. In an Australian randomised trial, 0.8 mg naloxone delivered intramuscularly restored breathing faster and required rescue naloxone less often than the same 0.8 mg delivered intranasally; the intranasal route was effective but less efficient at that dose and concentration.[8]

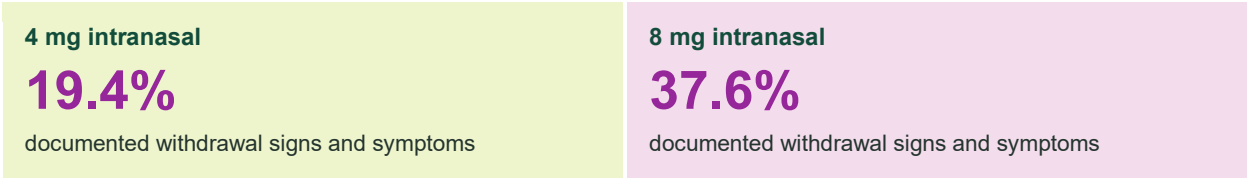
In a Norwegian double-blind randomised trial, a commercial 1.4 mg/0.1 mL nasal spray was compared with 0.8 mg intramuscular naloxone. Adequate spontaneous breathing within ten minutes after one dose was restored in 79.6% of participants receiving intranasal naloxone and 97.2% receiving intramuscular naloxone; additional naloxone was more often needed in the intranasal group. Even so, one nasal dose restored breathing in about four of five events.[9]

These studies do not show that intramuscular naloxone is always the better programme choice. A ready-to-use nasal device may be administered sooner or more confidently by a person who would hesitate to inject. Real-world effectiveness includes whether a product is carried, accepted and used correctly under pressure.

Dose matters: restore breathing and avoid unnecessary harm

Naloxone can abruptly displace opioids from receptors and precipitate acute withdrawal in a person with physical dependence. Symptoms may include nausea, vomiting, sweating, agitation, anxiety and pain. Withdrawal can follow either route; the risk relates importantly to total systemic naloxone exposure and the speed of receptor displacement.[1,10]

A New York State field comparison of 8 mg and 4 mg intranasal naloxone found no significant difference in survival or the average number of doses administered, but documented withdrawal signs and symptoms were substantially more frequent with the higher-dose product.[10]



No significant difference in survival or average number of doses; observational law-enforcement study of two specific nasal products. Source: [10].

This observational study involved law-enforcement responses and two specific nasal products; it does not establish one optimal dose for every overdose. It does challenge the assumption that a higher initial dose is inherently better.

The emergence of fentanyl and other highly potent synthetic opioids requires preparedness, including enough naloxone for repeat administration. A 2024 review incorporating the perspectives of people who use drugs concluded that most reported fentanyl overdoses could be reversed with standard intramuscular or intranasal naloxone, sometimes with repeat doses, and cautioned against routinely replacing standard products with higher-dose formulations.[11]

> **Compassionate response:** Use enough naloxone to restore adequate breathing, repeat it when breathing remains dangerously suppressed, monitor the person, and avoid unnecessary exposure once the clinical objective has been achieved. Survival and the experience of the person being revived both matter.[1,12]

Community perspectives: choice is part of access

There is no single 'community preference'. People weigh ease, speed, safety, comfort, familiarity, dose control, cost and the circumstances in which an overdose occurs. The responder and the person experiencing the overdose may also value different things.

An international qualitative study of people who use opioids in the United States and Australia found that most participants preferred intranasal naloxone, principally because of ease, speed, safety and comfort. People with experience of injections were generally more comfortable with intramuscular products. The authors recommended offering a choice of device where possible and asking people what they prefer and why.[13]

Canadian guidance, developed with substantial community expertise, conditionally recommends that THN programmes offer both formulations. Participants valued the ease of nasal products, while some experienced overdose responders preferred intramuscular naloxone for familiarity and the ability to titrate the dose. The same guidance noted that, in its Canadian environmental scan, intranasal naloxone cost programmes about ten times as much as an equivalent intramuscular formulation at the time of data collection - a context-specific figure that should not be transferred directly to EECA prices.[14]

EuroNPUD similarly reports that some drug-user activists prefer pre-filled injectable naloxone because it can support more incremental revival and may reduce severe withdrawal, while also recognising the role of nasal products. INPUD and EuroNPUD both emphasise that peers are often first at the scene and that peer distribution can reach networks missed by treatment or conventional services.[15,16]

Two perspectives that policy must hold together

- **For the responder:** Is the product available, easy to carry, simple to use and possible to administer confidently under pressure?
- **For the person experiencing overdose:** Does it restore breathing effectively while avoiding unnecessary withdrawal, distress and disrespect?

A formulation that is clinically effective but not carried or used is not fully accessible. A low-cost product that reaches many people can still leave gaps if some potential responders will not inject. Acceptability is therefore a core dimension of access alongside availability, affordability and quality.[5]

EECA policy and access reality

Having naloxone in the health system is not the same as having it in the community

Naloxone access across EECA is highly uneven. A binary question - 'Is naloxone available?' - hides several distinct stages. A medicine may be registered, procured for hospitals or ambulances, supplied through harm reduction services, issued as take-home naloxone, or redistributed by peers. Progress at one stage does not guarantee progress at the next.

From registration to community saturation

Availability at an earlier stage does not guarantee community access at the next.

The S-O-S project proved that community provision is feasible at scale in four regional countries.[4,17] Yet demonstration projects have not automatically become sustained nationwide systems. Harm Reduction International's 2024 mapping recorded operational peer-distribution programmes in Georgia, Kyrgyzstan and Tajikistan, but not in Armenia, Azerbaijan, Belarus, Kazakhstan, Moldova, Ukraine or Uzbekistan. HRI's 2023 update had identified Moldova as starting peer distribution, illustrating that programme status can change and that country-level verification remains essential.[18,19]

Take-home naloxone is also documented in Moldova and Ukraine; a civil-society submission describes availability in community and prison settings in Moldova.[18,25] The broader pattern, however, remains one of limited and uneven reach.

Medical supply is not proof of community possession. Ukraine continues to procure injectable naloxone through public institutions, including 0.4 mg/mL solution for injection in a 2026 procurement. Moldova's 2026 central procurement similarly included thousands of 0.4 mg/mL ampoules, and Azerbaijan's regulated medicines pricing system lists injectable naloxone products.[20-22] These records confirm supply in parts of the health system, not whether naloxone is carried by people present at an overdose.

Ukraine shows how regulation can remove one barrier: national rules allow pharmacies and pharmacy points to dispense up to 2 mg of naloxone without a prescription.[23] Ukrainian first-aid guidance recognises both intramuscular and intranasal administration.[24] However, a protocol that describes spraying naloxone solution into the nose may refer to atomised injectable solution; it should not be treated as evidence that a licensed, ready-to-use nasal product is marketed.

Ready-to-use nasal products: evidence remains limited in the assessed countries

The desk review for this brief did not identify a licensed ready-to-use intranasal naloxone product in publicly available national sources for ten countries: Armenia, Azerbaijan, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Moldova, Tajikistan, Ukraine and Uzbekistan. This should not be read as definitive evidence of absence. Some registries are incomplete, difficult to search or not transparent online. The finding is best understood as an evidence gap: injectable naloxone appears to remain dominant, while the registration and availability of purpose-designed nasal products are poorly documented.

A nasal spray can remove the practical barrier of giving an injection. It cannot by itself remove prescription rules, restrictive procurement, limits on NGO distribution, weak financing, stigma, policing risks or policies that prevent peers from carrying and redistributing naloxone. If a new product remains confined to ambulances or hospitals, the technology changes but community access does not.

> **Test for every reform:** Will this decision put naloxone into the hands of more people likely to witness an overdose - in sufficient quantities and in a form they will use?

Policy priorities for EECA

1. **Make possession and distribution straightforward.** Remove unnecessary prescription, legal and administrative barriers. Explicitly authorise take-home provision by pharmacies, harm reduction services and community organisations, and enable peer-to-peer distribution without fear of sanction.
2. **Institutionalise community coverage.** Move successful pilots into sustained national and local programmes with reliable domestic financing, low-threshold access, replenishment after use and specific provision for prisons and release settings.
3. **Protect choice and coverage in procurement.** Where feasible, offer both ready-to-use intranasal and intramuscular products. Where budgets do not permit both, involve people who use drugs and peer responders in choosing the product and assess the effect on the total number of people, kits and repeat doses reached.
4. **Procure products, not labels.** Compare the actual concentration, dose, device, evidence, shelf life, storage needs, training requirements, unit cost and supply security. Do not infer clinical performance from the route or nominal milligram dose alone.
5. **Ensure enough naloxone and practical training.** Provide sufficient repeat doses and training that covers recognition of respiratory depression, airway and breathing support, product use, reassessment, repeat administration when needed, observation and compassionate post-overdose care, consistent with national guidance.[1,14]
6. **Share decision-making with communities.** Include people who use drugs as paid partners in formulation selection, procurement, training design, peer distribution, monitoring and programme governance. Community involvement is a quality requirement, not a consultation after decisions are made.
7. **Measure access, not warehouse stock.** Track who receives and carries naloxone, geographic and population coverage, replenishment, actual use, repeat dosing, successful breathing restoration, withdrawal and other adverse experiences, acceptability, and barriers reported by people who use drugs.

Conclusion

Naloxone policy should not become a contest between a 'modern' nasal spray and a 'traditional' injection. Both routes can save lives, and each has advantages and limitations. Ready-to-use intranasal naloxone can make response easier for people who are uncomfortable with injections. Intramuscular naloxone remains effective, affordable and preferred by some experienced responders. Dose, withdrawal, usability, cost and the experience of the person being revived all matter.

For EECA, the central challenge is broader than formulation. Naloxone may exist in a medical system without being routinely available to people who use drugs, peers and families. Moving from an ampoule to a nasal spray will not by itself create take-home access, peer distribution, sustainable financing or community trust.

The introduction of ready-to-use intranasal naloxone should expand the range of overdose-response options - not withdraw affordable injectable naloxone or reduce the number of people reached. The strongest system is the one that achieves community saturation: naloxone is easy to obtain, affordable, carried where overdoses occur, available in sufficient quantities, and provided in formulations people are willing and able to use.

The goal is access, choice, coverage and community control.

About this brief

This policy brief synthesises WHO and EUDA guidance, comparative studies, community-informed recommendations, regional harm reduction mapping and publicly available national regulatory and procurement sources. The regional desk review covered Armenia, Azerbaijan, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Moldova, Tajikistan, Ukraine and Uzbekistan. Online registries and procurement portals differ in completeness and accessibility; country findings should therefore be verified with national authorities and community organisations before procurement or regulatory decisions are finalised.

This is a policy analysis, not a clinical dosing protocol. Overdose response should follow applicable national guidance and include immediate attention to airway and breathing, naloxone administration, reassessment, repeat dosing when needed and observation until recovery.[1]

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