Naloxone Rescue: Recommendations for Use

Naloxone Rescue [Naloxone HCl Nasal Spray (Narcan®, Kloxxado®) and Injection (Zimhi®)] for the VA Opioid Overdose Education and Naloxone Distribution (OEND) Program

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VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. Local adjudication should be used until updated guidance and/or CFU are developed by the National PBM. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. The drug Product Information should be consulted for detailed prescribing information.

BACKGROUND [1-9]

Naloxone is a safe and effective opioid antagonist that works predominantly at mu-opioid receptors and less so at kappa- and delta-opioid receptors. Its safety is due to its specificity; its only action is to reverse opioid mediated effects, which include respiratory depression, central nervous system depression and hypotension. Naloxone does not reverse the effects of alcohol, benzodiazepines or other central nervous system depressants. Naloxone is a highly effective intervention for reversing opioid overdoses and has been used for this purpose by emergency departments and emergency services personnel in the U.S. and abroad for decades.

In 1996, community-based programs such as syringe exchange and other harm reduction programs for people who inject drugs began to offer naloxone and other opioid overdose educational services to drug users, their families and friends, health care providers, substance use disorder treatment programs and other service providers (e.g., homeless shelters). Opioid overdose education and naloxone distribution (OEND) programs aim to ensure that individuals who are likely to require intervention are educated and trained about overdose prevention, recognition and naloxone administration. Many OEND programs target people most likely to be present during an opioid overdose (e.g., family and peers), thereby improving chances of immediate resuscitative intervention and naloxone administration.

As observations emerged that OEND programs might prevent numerous opioid-related overdose deaths, the support for OEND programs grew in the U.S. and abroad. The World Health Organization recommends naloxone as an essential intervention to prevent overdose. The Centers for Disease Control and the Global Fund to Fight AIDS, Tuberculosis, and Malaria both support naloxone distribution to drug users. The United Nations, American Medical Association (AMA), American Public Health Association (APHA), and the U.K. Advisory Council on the Misuse of Drugs (ACMD) support opioid overdose education and training and provision of naloxone to prevent opioid overdose, especially among high-risk populations such as illicit drug users. Moreover, in 2010, Scotland became the first country to implement a national naloxone program. Currently, naloxone is available in pharmacies without prescription in Australia, Canada, Italy, the United Kingdom of Great Britain and Northern Ireland, and Ukraine. In response to public health concerns about opioid overdose, in 2013 the Substance Abuse and Mental Health Services Administration (SAMHSA) released an Opioid Overdose Prevention Toolkit (Revised in 2018). This toolkit suggests that patients on long-term opioid therapy or who are at risk for overdose (e.g., completing abstinence programs) may benefit from education and access to naloxone rescue. The 2017 VA/DOD Clinical Practice Guideline for Opioid Therapy for Chronic Pain also recommends the prescribing of naloxone rescue and accompanying education as one of the proposed risk mitigation strategies (https://www.healthquality.va.gov/guidelines/Pain/cot/). In April 2018, the Surgeon General also released an Advisory on Naloxone and Opioid Overdose emphasizing the importance of naloxone and the need to increase its availability and targeted distribution (https://www.hhs.gov/surgeongeneral/priorities/opioids-and-addiction/naloxone-advisory/index.html). In July, 2020 the U.S. Food and Drug Administration announced it is requiring that labeling for opioid pain medicine and medicine to treat opioid use disorder (OUD) be updated to recommend that as a routine part of prescribing these medicines, health care professionals should discuss the availability of naloxone with patients and caregivers, both when beginning and renewing treatment.

The VA has had an increasing concern about the risk for opioid-related adverse events among Veteran patients and fully endorses efforts designed to minimize risk. The **VA Opioid Overdose Education and Naloxone Distribution (OEND) Program** is a risk mitigation initiative that aims to decrease opioid-related overdose morbidity and mortality among VA patients. Educational resources geared towards opioid overdose prevention, recognition of opioid overdose and rescue response and data resources to identify candidates for OEND are available on PBM Academic Detailing Service's OEND campaign page (https://dvagov.sharepoint.com/sites/vhaacademicdetailing/sitepages/oend.aspx). Implementation resources to support the development of new OEND programs are available on the VA OEND SharePoint (https://dvagov.sharepoint.com/sites/VACOMentalHealth/OEND/default.aspx). Naloxone rescue medications have been made available via the VA National Formulary process. VA providers should consider providing OEND to Veterans who are at significant risk of opioid overdose. Decisions to provide OEND can be assisted through use of tools designed toidentify such patients by estimating individual patient risk for overdose.

Naloxone rescue product utilization and rates of opioid overdose and mortality are tracked nationally in VA to evaluate the OEND program's performance. VA policy requires clinicians to document overdoses, including opioid overdoses, in the medical record utilizing a standardized note template (e.g., Suicide Behavior and Overdose Report) and clinicians are also encouraged to use the ICD-10 codes described in this document when appropriate. The PBM, MAP, and VPEs, in collaboration with the VA OEND National Support and Development Work Group, prepared the following recommendations to provide standardized guidance on the issuance of naloxone rescue under the VA OEND program.

In an effort to reduce the incidence of overdose among the veteran population, Congress, in two separate statutes, has required that VA must exempt from co-payment (1) opioid antagonists furnished under chapter 17 to a veteran who is at high risk for overdose of a specific medication or substance in order to reverse the effect of such an overdose, and (2) education on the use of opioid antagonists to reverse the effects of overdoses of specific medications or substances. See Pub. L. 114-198, sec. 915 (July 22, 2016) and Pub. L. 114-223, sec. 243 (Sept. 29, 2016). These provisions were effective upon enactment and have already been implemented. These changes have been codified in the Code of Federal Regulations (https://www.federalregister.gov/documents/2021/09/20/2021-20196/elimination-of-copayment-for-opioid-antagonists-and-education-on-use-of-opioid-antagonists) with an explanation of how VA would identify a veteran at high risk for overdose under the new provisions. This rule adds an explanation of how VA identifies a veteran at high risk for overdose under the new provisions.

Naloxone nasal spray is available in 4mg/0.1ml and 8mg/0.1ml formulations. The FDA granted approval of Naloxone HCL Injection 5 mg/0.5ml on October 15, 2021 through the 505(b)(2) approval pathway. A new drug application submitted through this pathway may rely on the FDA's finding that a previously approved drug is safe and effective or on published literature to support the safety and/or effectiveness of the proposed product if such reliance is scientifically justified. In this case, the manufacturer submitted a 505(b)(2) application that relied, in part, on the FDA's finding of safety and effectiveness for naloxone hydrochloride (NARCAN injection) to support approval. The applicant demonstrated that reliance on the FDA's finding of safety and effectiveness for Narcan was scientifically justified and provided pharmacokinetic data for the 8mg nasal spray to establish the drug's safety and efficacy for its approved use. The C_{max} and AUC of the 8mg NS is slightly greater than twice that of the 4mg NS (see Table).

RECOMMENDATIONS AND INFORMATION FOR OFFERING NALOXONE RESCUE

The nasal spray formulations of naloxone are our preferred products; however, the naloxone 5 mg/0.5ml Injection is available for those patients who have a contraindication to or are unable to use the preferred nasal product (e.g., allergy, anatomic nasal obstruction).

Assess the risk of opioid-related adverse events***. Discuss*** the provision of naloxone rescue as an opioid risk mitigation option with patients and/or family/caregivers. ***Offer*** naloxone rescue to Veterans prescribed or using opioids who are at increased risk for opioid overdose or whose provider deems, based on their clinical judgment, that the Veteran has an indication for ready naloxone availability. ***Educate*** patients and caregivers on opioid overdose prevention, recognition, and response, including the proper use and storage of naloxone rescue medications. ***Document*** OEND-related discussions and overdoses in patients' medical records, including reversal events with VA naloxone rescue medications, using nationally recommended and standardized documentation tools (see *Computerized Patient Record System Products* section).

The Risk Index for Overdose or Serious Opioid-induced Respiratory Depression (RIOSORD) is a practical and relatively simple and brief risk assessment instrument that has been automated by VA to assess a patient's baseline risk. Another automated tool is the VA Stratification Tool for Opioid Risk Mitigation (STORM) which helps identify patients – including patients prescribed opioids – who are at risk for adverse events such as drug overdose or suicide. The Opioid Therapy Risk Report (OTRR) and the Current Opioid Misuse Measure (COMM)™ are also useful tools (see Overdose Risk Assessment and Opioid Risk Mitigation, pages 6-11).

Examples of Candidates for Naloxone Rescue include *but are not limited to*:

Veterans with:

- History of previous opioid overdose †
- An opioid use disorder or substance use disorder diagnosis (including individuals receiving treatment, such as medications for opioid use disorder or inpatient, residential, or outpatient treatment, or attending support groups) †
- History of prescription opioid misuse or injection opioid use †
- Use of non-prescribed drugs (e.g., heroin, cocaine, methamphetamine or other stimulants) which could be contaminated with potent opioids like illicitly manufactured fentanyl †
- Prescribed or using opioids, or have an opioid use history, and who are at increased risk for opioid overdose as determined by provider
- Whose provider deems, based on their clinical judgment, that the Veteran may benefit from ready availability of an opioid antagonist
- Chronic hepatitis, cirrhosis, alcohol use disorder, sleep apnea or pulmonary disease and taking opioids
- Household or community access to opioids who are at increased risk for overdose (e.g., psychiatric disorder or high risk for suicide)
- Predicted high risk for overdose based on standardized assessments or predictive models (e.g., Risk Index for Overdose or Serious Opioid-induced Respiratory Depression [RIOSORD], Stratification Tool for Opioid Risk Mitigation [STORM])
- An extended-release or long-acting opioid prescription
- An opioid prescription of ≥ 50 mg morphine equivalents per day
- Concurrent use of central nervous system depressant, such as benzodiazepine, non-benzodiazepine sedative hypnotic

(e.g., zolpidem), skeletal muscle relaxant, or alcohol
- Homeless or unstably housed
- Veterans who receive VA or non-VA care in these situations:
    - HIV education / prevention program (which may provide care to people who inject drugs)
    - Syringe service program
    - Emergency departments (e.g., for opioid poisoning / overdose or intoxication)
    - Primary health care (e.g., for follow-up of recent opioid poisoning / overdose or intoxication)
    - Inpatient residential care or community-based treatment for homeless Veterans taking an opioid

NOTE: Veterans in the above examples may be at-risk even after a period of abstinence from opioids (e.g., due to treatment, detoxification, incarceration) because loss of tolerance can increase the risk for an overdose. High risk patients that have gone through a period of abstinence may be candidates for the 8mg nasal spray where physical dependence and the chances for precipitated withdrawal are low.

[†] These patients may be candidates for the 8mg naloxone nasal spray. Providers should exercise clinical judgment when prescribing the 8mg naloxone nasal spray, currently there are no clinical trials to help guide its place in therapy and identify the most appropriate candidates for its use. The higher C_{max} and $AUC_{0\text{-}inf}$ achieved with the 8mg nasal spray may provide a better opioid overdose reversal response in select patients, e.g. those who OD on the stronger fentanyl synthetic analogues or patients who required multiple 4mg doses in prior revival attempts, but these higher levels may also potentially increase the risk for precipitated withdrawal when compared to the 4mg nasal spray (See *Precipitated Opioid Withdrawal* section below). The use of the 8mg nasal spray should be based on a shared patient-provider decision process, e.g., if biggest concern is that the naloxone dose won't be enough, the patient-provider may agree on the 8mg dose; if biggest concern is for withdrawal symptoms, the 4mg dose may be used.

Individuals in hospice/palliative care are likely NOT appropriate candidates for naloxone rescue. The signs and symptoms of life-threatening opioid overdose overlap with and may be mistaken for the common signs and symptoms of the dying process. A family member may erroneously administer naloxone to a Veteran approaching death, causing opioid reversal, withdrawal symptoms, pain and suffering. Family members of Veterans in hospice programs who receive OEND training should simultaneously receive education about the overlap in signs and symptoms with the dying process. While OEND is not routinely used in patients who have comfort-oriented goals receiving opioids to reduce suffering toward the end of life (e.g., hospice patients), OEND should be considered for those seeking or under palliative care with clinical consideration including (but not necessarily limited to) the patient's clinical conditions (including medical, mental health, and substance use disorder comorbidities), prognosis, goals of care, opioid dose andprior opioid history.

Tramadol. Clinicians may not routinely consider the use of naloxone to manage tramadol overdose because of the risks of inducing seizures and questionable efficacy.[10] Tramadol's affinity for the mu receptor is 6,000-fold less than morphine and is equivalent to dextromethorphan.[11,12] Pharmacological evidence that suggest a non-opioid mechanism of action for tramadol and low mu receptor affinity include a lack of naloxone reversibility of its analgesic effect and a lack of significant naloxone-induced withdrawal.[11] A retrospective cohort study analyzed single medication tapentadol and tramadol exposures, from June 2009 to December 2011, that were reported to the National Poison Data System of the American Association of Poison Control Centers.[10] Of the 8,566 reported cases for tramadol exposure, only 6.3% (n = 540) received naloxone. Increased risk for seizure induction, questionable efficacy, and unwarranted need were proposed explanations for the low use. While most low risk patients on single agent tramadol may not warrant a naloxone prescription, high risk patients including those with opioid use disorders, substance use disorders, prior history of overdose, history of positive urine drug screens, and prescription opioid misuse are candidates for naloxone. It is recommended to provide patients prescribed tramadol with broad opioid overdose education to ensure that if they have other opioids available to them (e.g., previous prescriptions) they are aware of risks associated with using those opioids and ways to mitigate risk and prevent an opioid overdose. Naloxone administration may also increase the risk of seizure when administered in the context of a tramadol overdose.[13]

VA STAFF EDUCATIONAL, INFORMATIONAL, AND IMPLEMENTATION RESOURCES (also see *Patient Education and Patient Education Resources*).

- Educational and data resources are available to all VA staff via VA Academic Detailing Service's OEND campaign page. The link to the SharePoint is: https://dvagov.sharepoint.com/sites/vhaacademicdetailing/sitepages/oend.aspx
- Implementation resources to support the development of new OEND programs and links to past VA OEND Monthly Community of Practice Call presentations are available on the VA OEND SharePoint. The link to the SharePoint is: https://dvagov.sharepoint.com/sites/VACOMentalHealth/oend/default.aspx.
- Implementation resources for the Suicide Behavior and Overdose Report (SBOR) National Note Template, including FAQs, user guides, and staff-specific guidance documents, are available at this SharePoint link: https://dvagov.sharepoint.com/sites/VACOMentalHealth/SitePages/Safety-Planning-%26-Suicidal-Behavior-Reporting.aspx.
- VHA Rapid Naloxone Initiative resources—including toolkits for VA Police Naloxone and select Automated External Defibrillator (AED) Cabinet Naloxone—are available at this SharePoint link: http://vaww.ncps.med.va.gov/Initiatives/Med/naloxone/index.html**.** VA facility availability of naloxone rescue (similar to that of AEDs) may increase access and reduce opioid overdose response time, particularly at sites without crash cart availability.
- **TMS trainings:**
  - Opioid Overdose Education and Naloxone Distribution (OEND) Training (TMS items 27440 and 27441). VA health professionals who work with patients on opioids or with patients at risk for opioid overdose may choose to take this hour-long knowledge-based course to integrate OEND into clinical practice. Target audience participants may include but are not limited to doctors, dentists, pharmacists, nurses, nursing assistants, social workers, counselors, psychologists, occupational therapists and healthcare executives. This is TMS item number 27440 (Pharmacists and other clinicians) and is accredited for ACCME, ACCME-NP, APA, ANCC, ADA, AOTA, ASWB, NBCC, and ACPE (for Pharmacy Technicians it is TMS item 27441, accredited for ACPE-T).
  - How to Use Naloxone Nasal Spray (Narcan®; TMS item 37795). Brief training on how to use the nasal spray. Created in part to support implementation of VHA's Rapid Naloxone Initiative.
  - Suicide Behavior and Overdose Report (SBOR) (TMS item 45626). Training on reporting suicide behaviors and overdose events using national standardized note templates in the EHR. Target audience participants may include but are not limited to Suicide Prevention Coordinators and suicide prevention teams, VA medical center staff members, and Veterans Integrated Service Network (VISN) leaders.

PATIENT EDUCATION AND PATIENT EDUCATION RESOURCES

- Discuss naloxone rescue as an opioid harm reduction/risk mitigation option with patients and/or family/caregivers.
- Emphasize opioid overdose prevention and explain that naloxone combined with overdose education complement, but donot replace, safe and responsible opioid use. NOTE: Any opioid dose can be risky (even a small dose) and can increase risk for overdose. There is also risk when using non-prescribed drugs (e.g., heroin, cocaine, methamphetamine or other stimulants) which could be contaminated with potent opioids like illicitly manufactured fentanyl.
- Educate and train the patient on the proper use, storage, administration and disposal of naloxone rescue products.
- Emphasize the importance of being familiar with naloxone administration technique before an emergency arises.
- Advise the patient about the importance of friends, family members, partners, and caregivers being educated and trained on the proper use, potential harms and limitations of naloxone treatment.
- Patient education resources also include the following (VA resources can be ordered through the VA National Repository):
  - VA OEND Patient Education Brochures (available at https://dvagov.sharepoint.com/sites/vhaacademicdetailing/sitepages/oend.aspx
- VA OEND Videos:
  - Introduction to Naloxone for People with Opioid Use Disorders: https://youtu.be/-qYXZDzo3cA
  - Introduction to Naloxone for People Taking Prescribed Opioids: https://youtu.be/NFzhz-PCzPc
  - How to Use the VA Naloxone Nasal Spray: https://youtu.be/0w-us7fQE3s
  - How to Use the VA Intramuscular Naloxone Kit https://www.youtube.com/watch?v=lg1LEw-PeTE
- SAMHSA Opioid Overdose Prevention Toolkit: Contains safety advice for patients and resources for family members. https://store.samhsa.gov/product/Opioid-Overdose-Prevention-Toolkit/SMA18-4742
- Prescribe to Prevent: Patient resources and videos demonstrating overdose recognition and response, including naloxone administration. http://prescribetoprevent.org/video/
- It is highly encouraged to also educate and train at least one patient-authorized acquaintance (i.e., one who is likely to witness an opioid overdose such as a friend, family member, partner or caregiver).

PRESCRIBING AND AVAILABILITY OF NALOXONE RESCUE

- The nasal preparations of naloxone are the preferred national formulary products; however, the naloxone IM kit and IM injection are available and on the national formulary for those patients who have a contraindication to the preferred nasal products.
- A prescription is required to provide patients with naloxone rescue.
- Each prescription order contains 2 dose units of naloxone.
- Patient refusal of an offer for naloxone should be documented.
- Prescriptions should be marked with at least one refill; this will ensure that the prescription remains active for 365 days. Naloxone prescription and refill discussion should ascertain that the patient has naloxone on hand, readily available and with good expiration dating, as well as any treatment and educational needs the patient may have around naloxone that a caregiver or significant other may have.

The Naloxone Nasal Sprays are the preferred product given their favorable pharmacokinetic profile which should provide better outcomes for those exposed to higher potency, longer acting opioids and to partial agonists and mixed agonist-antagonist opioids.

Contraindications to intranasal naloxone can include nasal septal abnormalities, nasal trauma, epistaxis, excessive nasal mucus, and intranasal damage caused by the use of cocaine and other substances. Relative contraindications to intranasal naloxone: severe hypotension and the recent use of vasoconstrictors (which may prevent adequate absorption).[14]

Use requests to renew naloxone rescue prescriptions as opportunities to determine the circumstances (e.g., product was used for overdose, lost, confiscated, expired, etc.) and to identify whether any changes to the patient's treatment plan may be needed to improve patient safety (e.g., assessment for opioid use disorder (OUD); medications for OUD; increased level of care if the patient is struggling with recovery).

Also use the discussion as an opportunity to engage the patient, re-assess risk-benefits, provide re-education about overdoses, review *Safe and Responsible Use of Opioids for Chronic Pain* (as applicable), consider other opioid risk mitigation strategies (patient-centered risk mitigation strategies are included in the Stratification Tool for Opioid Risk Mitigation (STORM)), and modify treatment plans.

Programs serving Veterans that are not on VA campuses but would like to equip residents and staff with naloxone should be instructed to work with VA staff (e.g., social work liaisons) to ensure that all at-risk VA patients are prescribed naloxone. Program staff are encouraged to work with community-based programs, SAMHSA Opioid State Targeted Response (STR)/State Overdose Response (SOR) grant administrators/ programs, community-based pharmacies, and/or pharmaceutical companies to identify strategies for equipping non-VA staff/programs with naloxone. Programs serving high risk patients are encouraged to budget for naloxone as they would other lifesaving equipment (e.g., fire extinguishers).

COMPUTERIZED PATIENT RECORD SYSTEM (CPRS) PRODUCTS

To support implementation of OEND, VHA has developed and released several CPRS products to the field. These products include the *Naloxone Prescribing* progress note, *Offer Naloxone Prescription* clinical reminder, and two naloxone Clinical Reminder Order Checks (CROCs). To facilitate the integration of the RFU guidance into the ordering process, a sample naloxone order menu has been developed. The order menu includes quick orders that align with the RFU (e.g., 1 refill, 1 day supply) and dosing considerations to ensure the appropriate naloxone product is ordered. Please see https://tinyurl.com/NaloxoneEducationalPPT for additional information including screenshots for the CPRS products, order menu and quick orders (POC: Elizabeth.Oliva@va.gov). VHA has also standardized documentation of overdose events (see next section).

DOCUMENTATION OF OVERDOSE EVENTS

Clinicians are required to document overdose events in CPRS using a standardized VA national note template (e.g., Suicide Behavior and Overdose Report [SBOR]). The SBOR template was developed by the Office of Mental Health and Suicide Prevention in conjunction with other stakeholders. It is designed to standardize, streamline, and enhance both the process of suicide behavior and overdose reporting as well as naloxone use and adverse effect reporting. Standardized documentation is specifically designed to improve post-overdose care, facilitate national tracking of overdose events, and assist with evaluating OEND program performance. The SBOR should be used to report all accidental or intentional overdoses involving the patient, regardless of whether naloxone was administered. The national Naloxone Use Note should be used instead of the SBOR when the patient's naloxone was used on someone other than the patient.

To facilitate correct documentation of opioid overdose events, we recommend the following **ICD-10-CM** codes.

Begin with DIAGNOSTIC CATEGORY T40, followed by a:

- 3 digit EXTERNAL CAUSE code, followed by a
- 7th character DESCRIBING ENCOUNTER

Because DIAGNOSTIC CATEGORY T40 denotes "*Poisoning by, adverse effect of and underdosing of narcotics and psychodysleptics (hallucinogens)"* broadly, it is important to use one of the opioid-related 3-digit EXTERNAL CAUSE codes to allow documentation of the specific agent involved (if known) and whether the event was unintentional, intentional, an assault, undetermined, or due to an adverse effect. The 7th character DESCRIBING ENCOUNTER are suffix letters A or D (initial or subsequent encounter, respectively) or S (sequela; a complication or condition arising from the overdose event). See the Table below for opioid-related 3-digit external cause codes to be tracked nationally.

Table 1. Three-digit external cause codes (added to T40 Diagnostic category) for documentation/tracking of opioid poisonings/overdoses

Poisoning by:	Accidental (unintentional)	Intentional self-harm	Assault	Undetermined	Adverse effect
Opium	T40.0X1	T40.0X2	T40.0X3	T40.0X4	T40.0X5
Heroin	T40.1X1	T40.1X2	T40.1X3	T40.1X4	N/A
Other opioids	T40.2X1	T40.2X2	T40.2X3	T40.2X4	T40.2X5
Methadone	T40.3X1	T40.3X2	T40.3X3	T40.3X4	T40.3X5
Other synthetic narcotics	T40.4X1	T40.4X2	T40.4X3	T40.4X4	T40.4X5
Unspecified narcotics	T40.601	T40.602	T40.603	T40.604	T40.605
Other narcotics	T40.691	T40.692	T40.693	T40.694	T40.695

EFFICACY AND SAFETY OF NALOXONE [14-21]

Efficacy: Naloxone produces virtually no pharmacologic effects in patients not taking opioids. Onset of action is less than 2 minutes when naloxone is administered intravenously (IV) to adults. IV has a faster onset than intranasal (IN) administration when time from dose administration to clinical response is measured, but there is no time difference when measuring the time from patient contact to clinical response due to the time required to establish an IV access. Time to clinical response is similar for IM and IN routes when a concentration of at least 2mg/ml is utilized for nasal administration.

Safety: Naloxone has a low risk of side effects; the most common stem from opioid withdrawal in persons who have a physical dependence.

Precipitated Opioid Withdrawal: In individuals with a physical dependence on opioids, precipitation of withdrawal occurs in a dose-related manner: the higher the dose of naloxone, the longer and more severe the withdrawal syndrome may be. Route of naloxone administration is an additional factor in incidence and severity of withdrawal symptoms; for example, IV push administration of naloxone can provide rapid and relatively higher exposure compared to routes that require drug absorption. Lastly, the dose of opioid taken and its affinity for the mu receptor will also influence potential for naloxone-precipitated withdrawal.

Withdrawal symptoms may start within minutes of naloxone administration but typically dissipate within an hour due to the metabolic clearance rate of naloxone relative to that of the offending opioid. Opioid withdrawal symptoms include: body aches, diarrhea, tachycardia, fever, runny nose, sneezing, piloerection, sweating, yawning, nausea or vomiting, nervousness, restlessness or irritability, aggressiveness/agitation/combativeness, shivering, trembling, abdominal cramps, weakness and increased blood pressure. Abrupt postoperative reversal of opioid depression may result in adverse CV effects including tachycardia, hypotension, hypertension, seizures, ventricular tachycardia and fibrillation, pulmonary edema, and cardiac arrest. Death, coma, and encephalopathy have been reported as sequelae of these events. These events have primarily occurred in patients who had pre-existing CV disorders or received other drugs that may have similar CV effects. Monitor these patients closely in an appropriate healthcare setting after use of naloxone hydrochloride. Withdrawal symptoms are often a necessary part of reversal of an opioid overdose; while they may be distressing to the patient and may complicate clinical management, they are generally not life threatening and represent a superior outcome to an overdose death.

IV naloxone may be titrated to minimize withdrawal symptoms; however, titration is not recommended when naloxone is administered via the IM or IN routes.

Recurrence of Respiratory Depression: Opioids with long durations due to formulation design (e.g., extended-release tablets, capsules or patches) or inherently slow systemic clearance (e.g., buprenorphine, levorphanol and methadone) may outlast the duration of effects of naloxone. Naloxone formulated for rescue use in the community has a half-life of 74 to 125 minutes (see Table 2). The duration of naloxone effect is dependent on the route of administration; being longer with IN or IM than IV. Duration of IN naloxone effect is not well described but plasma concentrations following 4mg IN have exceeded those obtained with 0.4mg IM at 1 hour and at 6 hours.

The maximum volume for effective nasal drug administration is 0.1 to 0.2µL per nares. Delivery of a greater volume results in pharyngeal pooling, swallowing, and inactivation of drug in the gastrointestinal tract.[19] Non-response rates of between 9 and 26% have been reported in association with the 2mg dose of nasal naloxone (which were typically given in volumes that exceeded 1ml).[20] While the exact incidence of recurrent respiratory depression after bystander administration of naloxone is unknown, in the Massachusetts community-based OEND program experience, 52% of bystanders used 2 or more doses of IN naloxone.[21]

Rare, Life-Threatening Injuries Post-Naloxone Administration have been reported but these adverse effects (pulmonary edema, arrhythmias, hypertension, cardiac arrest) are more likely to be related to the excessive opioid dose, co-consumed drugs (e.g., cocaine), hypoxia, or pre-existing cardiac disease rather than to naloxone.

Table 2: NALOXONE (NARCAN®) NASAL SPRAY AND IM (GENERIC) KIT [22-23]

All products are FDA-approved forms of naloxone that the FDA states can be considered as options for community distribution. The Nasal Spray was specifically designed for layperson use, e.g., product labeling includes instructions for layperson use, and is ready-to- use with no assembly required.	**Nasal Spray (4 mg) (Preferred Naloxone Formulation)**	**Nasal Spray (8 mg)**	**Injectable IM (0.4mg) generic**	**Injection (5 mg/0.5ml)**
				
Trade name	Narcan	Kloxxado	Not applicable	Zimhi
Strength	4 mg/0.1ml	8 mg/0.1ml	IM: 0.4 mg/ml	5 mg/0.5ml
Total volume of kit/package	8 mg/0.2 ml	16 mg/0.2 ml	IM: 0.8 mg/2ml	10 mg/1ml
Assembly	None required	None required	IM: Remove cap from naloxone vial, uncover needle; insert thru rubber plug of upside down vial. Pull back on plunger to1ml.	None required
Dosing [a]	Spray 0.1ml into one nostril; repeat with second device into other nostril after 2-3 minutes if no/minimal response or until medical assistance arrives	Spray 0.1ml into one nostril; repeat with second device into other nostril after 2-3 minutes if no/minimal response or until medical assistance arrives	IM: Inject 1ml (0.4mg) at 90^0 angle into large muscle (upper arm, thigh, outer buttock). Give another dose if no reaction or if breathing stops again	Administer the initial dose intramuscularly or subcutaneously into the anterolateral aspect of the thigh, through clothing if necessary, and repeat after 2-3 minutes if no or minimal response until medical assistance arrives
Administration. Instruct the patient or caregiver to read the *Instructions for Use* at the time they receive a prescription for naloxone.	1. Place the patient on their back 2. Hold the nasal spray with your thumb on the bottom of the plunger and your first and middle fingers on either side of the nozzle 3. Gently insert the tip of the nozzle into **one nostril** until your fingers on either side of the nozzle are against the bottom of the	1. Place the patient on their back 2. Hold the nasal spray with your thumb on the bottom of the plunger and your first and middle fingers on either side of the nozzle 3. Gently insert the tip of the nozzle into **one nostril** until your fingers on either side of the nozzle are against the bottom of the	1. Place the patient on their back 2. Remove cap from naloxone vial and uncover the needle 3. Insert needle through rubber plug with vial upside down 4. Pull back on plunger and pull down to 1 ml 5. Inject 1 ml of naloxone at a 90^o angle into a large	1. Place the patient on their back 2. Remove the needle cap 3. Inject into outer thigh and push the plunger all the way down until it clicks and hold for 2 seconds 4. After use, slide the safety guard over the needle. Put the used syringe into the blue case and close the case.

	person's nose. 4. Press the plunger firmly to give the dose of naloxone 5. Remove the nasal spray from the nostril after giving the dose 6. Get emergency medical help (call 911) 7. If required use a new nasal spray to give another dose in the other nostril 8. If the person is breathing normally, turn the patient on their side (recovery position) after giving naloxone	person's nose. 4. Press the plunger firmly to give the dose of naloxone 5. Remove the nasal spray from the nostril after giving the dose 6. Get emergency medical help (call 911) 7. If required use a new nasal spray to give another dose in the other nostril 8. If the person is breathing normally, turn the patient on their side (recovery position) after giving naloxone	muscle (upper arm/thigh or outer buttocks) 6. Get emergency medical help (call 911) 7. If required, use a second dose of naloxone 8. If the patient is breathing normally, turn the patient on their side (recovery position) after giving naloxone	5. Get emergency medical help (call 911) 6. If required, give an additional dose using a new prefilled syringe. 7. If the person is breathing normally, turn the patient on their side (recovery position) after giving naloxone
Pharmacokinetics ▪ ***Dose/route*** ▪ ***$T_{1/2}$ (h)*** ▪ ***T_{max} (h)*** ▪ ***C_{max} (ng/ml)*** ▪ ***$AUC_{0\text{-}inf}$ (ng·h/ml)*** ▪ ***Bioavailability (%)[c]***	4 mg IN[b] 2.08 0.50 4.83 7.95 44.2%	8mg IN 1.76-2.69 0.25 12.3-12.8 16.7-19.0 41.6-47.0%	0.4mg IM 1.24 0.38 0.88 1.76 100%	5mg IM/SQ 1.50 0.25 17.2 26.6 100%
Usability	Successful use of the 4mg NS was observed in 90.5% of users without training.[d] All forms are FDA approved options for community distribution and use by individuals with or without medical training to stop or reverse the effects of an opioid overdose.[23]			Usability study reported a 100% successful completion of all steps needed to use the device among untrained adolescents.[26]
Storage requirements [f]	Store at 59-77ºF; excursions permitted from 39-104ºF. Do not freeze. Protect from light.	Store at 68-77ºF; excursions permitted from 41-104ºF. Do not freeze. Protect from light.	Store at 59-86^{0}F. NOTE: fragile (glass)	Store at controlled room temperature 20°C to 25°C (68°F to 77°F), excursions between 15° and 30° (59° and 86° F) are allowed. Do not refrigerate. Protect from light, extreme heat, and freezing.
Disposal of Used or Expired Product	Dispose of the used nasal spray in a place that is away from children.	Dispose of the used nasal spray in a place that is away from children.	Dispose of the used syringe in a biohazard sharps container	Give used syringe, contained in the blue case, to the healthcare provider for inspection and proper disposal. IM: Biohazard sharps container

[a]Response = return of spontaneous respirations to rate ≥ 10 breaths/minute. [b]All values listed for naloxone spray 4mg are geometric mean values, T_{max} reported as median. [c]Relative bioavailability listed for naloxone NS and Injection is relative to IM-administered product.[d]Successful use = correct performance of two critical tasks 1) insertion of the nozzle of the spray applicator into the nostril and 2) correct use of the plunger to release dose of naloxone into the nose (reference 20). [e]Usability[23]. [f]All naloxone products should be stored away from light and not subjected to freezing.

OVERDOSE RISK ASSESSMENT AND OPIOID RISK MITIGATION IN VETERANS

Opioid Overdose Education and Naloxone Distribution (OEND) is an important risk mitigation strategy for clinicians to incorporate into their practice to save Veteran lives. Risk assessment tools are available in VA—and have been automated and integrated into VA clinical decision support tools (e.g., dashboards, reports) available to clinical staff with appropriate permissions to aid the clinical care

teams in identifying patients who may benefit from this life saving intervention. Risk assessment tools identified below along with the integrated data management risk tools such as OTTR and STORM will not identify every patient appropriate to offer OEND as a risk mitigation strategy, therefore it's critical that providers make an assessment at the point of care to consider OEND when overdose risk is identified as part of the clinical interview and assessment process in addition to population management approaches using the risk assessment tools. In addition, currently there is no recommendation regarding prescribing the 8mg nasal spray based on STORM, OTRR, COMM, or RIOSORD data.

RIOSORD – Risk Index for Overdose or Serious Opioid-Induced Respiratory Depression [24]

Zedler et al. (2015) performed a retrospective, case-controlled analysis of health care information drawn from a VA database which included 1,877,841 patients that had received an opioid between Oct 1, 2010 and Sept 30, 2012. Of these, 817 patients were determined to have had an overdose or episode of serious opioid-induced respiratory depression (OSORD). Ten controls (total n = 8,170) were selected for each case of OSORD. Items for the risk index were selected from model variables that were statistically significantly associated with OSORD. Each item was assigned a point value and point values were totaled to give scores. Modeling of risk index scores produced risk classes that predicted probabilities of OSORD. The intent was to develop a practical and relatively simple and brief risk assessment instrument that could be utilized in a busy community health care setting before prescribing opioids to assess a patient's baseline risk of OSORD.

Fifteen items most highly associated with OSORD were retained for calculation of the risk index (Table 3). Table 4 (next page) displays the risk classes and predicted probabilities from the case-controlled analysis.

Table 3: RIOSORD questions.

RIOSORD (Risk Index for Overdose or Serious Opioid-Induced Respiratory Depression) Questions	Points for 'Yes" Response
In the past 6 months, has the patient had a healthcare visit (outpatient, inpatient or ED) involving any of the following health conditions?	
Opioid dependence?	15
Chronic hepatitis or cirrhosis?	9
Bipolar disorder or schizophrenia?	7
Chronic pulmonary disease (e.g. emphysema, chronic bronchitis, asthma, peumoconiosis, asbestosis?	5
Chronic kidney disease with clinically significant renal impairment?	4
An active traumatic injury, excluding burns (e.g., fracture, dislocation, contusion, laceration, wound)?	3
Sleep apnea?	
Does the patient consume	
An extended-release or long-acting (ER/LA) formulation of any prescription opioid? (e.g., OxyContin, Oramorph-SR, methadone, fentanyl patch)	9
Methadone? (Methadone is a long-acting formulation so also check "ER/LA formulation" [9 points]	9
Oxycodone? If it has an ER/LA formulation [e.g., OxyContin] also check "ER/LA formulation" [9 points]	3
A prescription antidepressant? (e.g. fluoxetine, citalopram, venlafaxine, amitriptyline)	7
A prescription benzodiazepine? (e.g., diazepam, alprazolam)	4
Is the patients current maximum prescribed opioid dose:	
≥ 100 mg morphine equivalents per day?	16
50 to < 100 mg morphine equivalents per day?	9
20 to < 50 mg morphine equivalents per day?	5
In the past 6 months, has the patient:	
Had one or more emergency department (ED) visits?	11
Been hospitalized for one or more days?	8
Total Point score (maximum 115)	

Adapted from Zedler et al. Pain Medicine 2015; 16: 1566-79

The RIOSORD risk index has been validated in both US Veterans and in the general population.[25] RIOSORD scoring has been automated by VA and integrated into clinical decision support tools that are available to VA staff with appropriate permissions (e.g., OEND Patient Risk Dashboard and Stratification Tool for Opioid Risk Mitigation, see below).

The research that resulted in development of RIOSORD was funded by kaléo, Inc., Richmond, VA, manufacturer of the Evzio® naloxone HCL auto-injector, now discontinued. Kaleo also reviewed and commented on the study methods utilized.

Table 4: RIOSORD: Risk classes and predicted probabilities

			Overdose or Serious Opioid-Induced Respiratory Depression (All patients, n = 8,987)	
Risk class	**Risk Index score (Points)**	**All Patients (n = 8,987), n (%)**	**Average Predicted Probability (95% CI)**	**Observed Incidence**
1	0-24	7,133 (79.4)	0.03 (0.03, 0.03)	0.03
2	25-32	780 (8.7)	0.14 (0.14, 0.15)	0.14
3	33-37	306 (4.5)	0.24 (0.25, 0.24)	0.23
4	38-42	238 (2.7)	0.34 (0.34, 0.35)	0.37
5	43-46	133 (1.5)	0.46 (0.45, 0.46)	0.51
6	47-49	77 (0.9)	0.55 (0.54, 0.55)	0.55
7	50-54	101 (1.1)	0.64 (0.64, 0.65)	0.60
8	55-59	87 (1.0)	0.76 (0.75, 0.76)	0.79
9	60-66	73 (0.8)	0.85 (0.84, 0.85)	0.75
10	≥ 67	59 (0.7)	0.94 (0.93, 0.95)	0.86
Model performance: C-statistic = 0.88		Hosmer-Lemeshow goodness-of-fit statistic = 10.8 (p > 0.05		

Adapted from Zedler et al. Pain Medicine 2015; 16: 1566-79

VA NOTE: Average predicted probabilities are not population-based (based on case-control study matching 817 cases with OSORD to 10 controls).

Academic Detailing Service (ADS) OEND Data Resources

The ADS provides OEND data resources that identify overdose risk factors and calculate the RIOSORD score for patients at risk for opioid overdose. These resources are available to VA staff nationally. All VA employees have access to view the summary level data presented on the OEND Patient Risk Dashboard; patient-level data are available to staff with PHI/PII access granted at the facility level.

The OEND Patient Risk Dashboard provides summary data available at the National, VISN, Facility, and Provider levels and has the ability to drill down to the OEND At Risk Patient report. The patient report displays the RIOSORD score, Opioid-Induced Respiratory Depression (OIRD) % Risk, STORM Risk (see below), diagnoses relevant to increased overdose risk, upcoming appointments and other related information. The report allows an authorized user to identify and filter a group of patients by risk factor(s), provider(s), RIOSORD Risk Class, and upcoming appointment. It also gives the ability to drill down into additional information about the patient, including a list of upcoming appointments, details for the RIOSORD calculation, and benzodiazepine and opioid fill and dose history over the previous year.

Each of the OEND data resources is available from the ADS SharePoint Site:

ADS Dashboards and Reports Site - https://dvagov.sharepoint.com/sites/vhaacademicdetailing/SitePages/Data-Resources.aspx
OEND Patient Risk Dashboard - https://vaww.pbi.cdw.va.gov/PBIRS/Pages/ReportViewer.aspx?/GPE/PBM_AD/SSRS/OEND/OENDDashboard
OEND At Risk Patient Report - https://vaww.pbi.cdw.va.gov/PBIRS/Pages/ReportViewer.aspx?/GPE/PBM_AD/SSRS/OEND/OENDPatientReport

STORM – Stratification Tool for Opioid Risk Mitigation

STORM is a clinical decision support tool that utilizes a VA-developed predictive model that estimates the likelihood of drug overdose or suicide-related events in patients receiving opioid prescriptions from VA. A description of the development and applications of STORM has been peer-reviewed and is available through *Psychological Services.*[26, 27]

A multivariate mixed effects logistic regression model was formulated to predict the occurrence of an overdose- or suicide-related event (overdose/suicide) using secondary data from VA national administrative databases. Each model participant had at least one outpatient opioid analgesic prescription during FY2010; participants were followed for one year (FY2011) to identify any overdose/suicide-related events. The predictor variables were derived from FY2010 data and addressed the following domains: (a) Demographics; (b) Previous Overdose/Suicide and Treatment Risk Indicators; (c) Prescriptions; (d) Substance Use and Mental Health Disorder diagnoses; and (e) Medical Co-morbidities. The outcome variable of overdose/suicide related events came from FY2011 data. This predictive model greatly improves identification of patients receiving opioid prescriptions at risk of adverse events; once identified, STORM provides a tailored list of risk mitigation strategies, including non-pharmacological pain modalities, for providers to consider that could help to reduce risk and address risk factors.

Variables included in the risk model were selected based on published literature, the VA/DoD Clinical Practice Guideline for the Management of Opioid Therapy for Chronic Pain (2010), and recommendations from the VA National Pain Workgroup. STORM, including definitions for the predictor variables, may be viewed in detail at this link:

https://vaww.pbi.cdw.va.gov/PBIRS/Pages/ReportViewer.aspx?/RVS/OMHSP_PERC/SSRS/Production/CDS/STORM/ORM_Summary Report

STORM estimates ***Specific Risk,*** defined as risk for suicide-related event or opioid, sedative, acetaminophen, or other drug (e.g., stimulants) poisoning or overdose. Risk groups are defined by magnitude of risk scores and classified into "Very High", "High", "Medium", and "Low" risk groups.

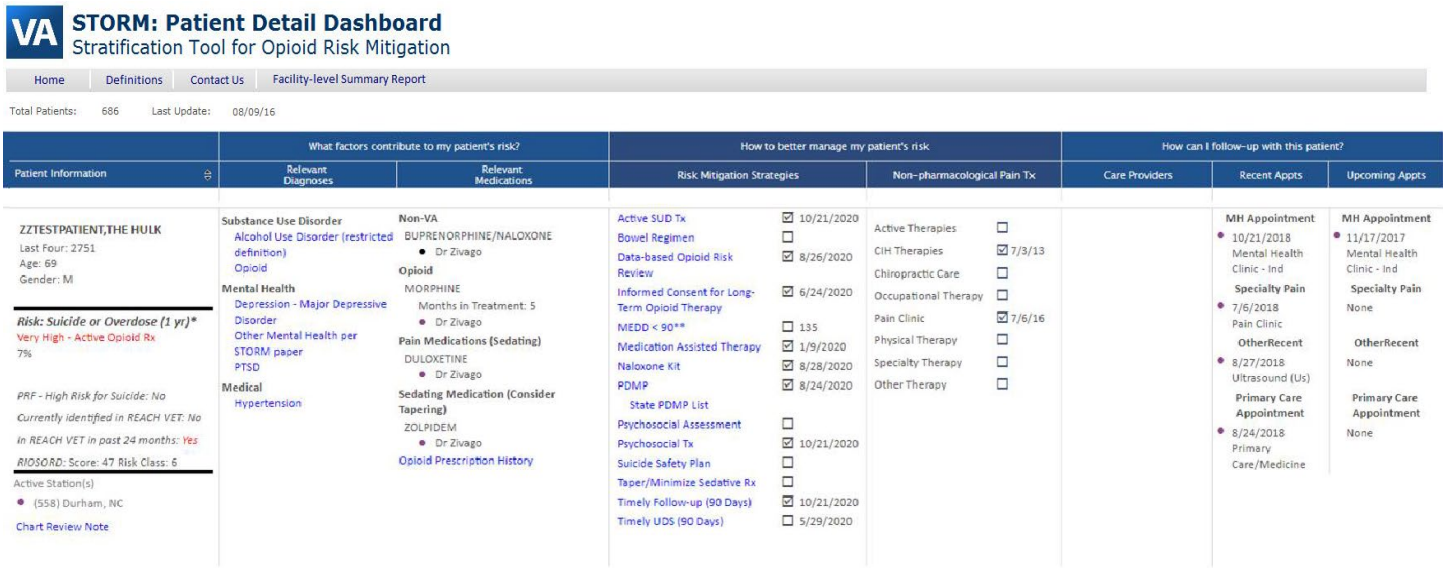
In addition to providing an estimate of specific or overall risk score, STORM also:

- Provides patient-specific information on key clinical factors that elevate risk per the model
- Provides a tailored list of risk mitigation strategies for consideration, with tracking of current use of the strategy
- Provides information on key providers and appointments to facilitate communication and care coordination between mental health and primary care teams, and the opioid prescriber
- Provides tracking of non-pharmacological treatments for pain
- Includes hypothetical risk report that estimates patient risk when considering initiating opioid therapy

STORM provides risk scores and risk mitigation strategies for patients with an active outpatient prescription order for any opioid analgesic and hypothetical risk scores for all patients through the ORM_PatientLookup - Report Viewer (va.gov), data utilized in STORM is updated nightly. RIOSORD risk classes and scores have been integrated into STORM and the predictive risk model will be updated annually and/or as data become available.

STORM is available to VA staff nationally. All VA employees have access to view the summary level data presented on the STORM dashboard; STORM patient-level data are available to staff with SSN access granted at the facility level. Link to STORM homepage: https://dvagov.sharepoint.com/sites/VHAPERC/Reports/SitePages/STORM_home.aspx

Figure 1: STORM patient report showing estimated risk score, RIOSORD risk class and score, diagnoses and medications relevant to increased risk, risk mitigation strategies and other related information. The report allows an authorized user to identify and filter a group of patients by risk mitigation strategies, opioid prescriber, and risk score.



OTRR- Opioid Therapy Risk Report

The Opioid Therapy Risk Report (OTRR) is a patient-focused, actionable and provider-specific report that is available to Primary Care Providers (PCP), Primary Care Managers, Primary Care Administrators and Chiefs of Staff, Patient Aligned Care Teams, Clinical Pharmacists, Pain Clinic and Specialty Care clinicians caring for patients on opioid therapy and Behavioral Health Interdisciplinary Program (BHIP) Team Members. Users must have real SSN authorization to view.

Data are gathered across VA and updated daily (data freshness is indicated by the 'As of' date) so that the most recent information is available, regardless of where care was delivered. Data presented includes documented diagnoses that influence patient risk, such as PTSD, Substance Use Disorder (SUD) and Obstructive Sleep Apnea (OSA) as well as the most recent patient interaction with health providers such as Last PCP visit date, Last Pain Clinic visit date and last Mental Health visit date. Dates and status of the signed iMedConsent™ for Opioid Therapy are included. The Patient Details page contains results from the latest Urine Drug Test (UDT), Patient Pain Scores as well as patient Opioid and Benzodiazepine medication history tables listing the prescriber, dispensing location, strength, number of days supply and Morphine Equivalents.

OTRR can be accessed through several avenues; a commonly used route by Primary Care Practitioners is via CPRS → Tools → Primary Care Almanac → Opioid Therapy Risk Report → Patient List. Another method to access: http://vssc.med.va.gov/ then click "Primary Care" under "Clinical Care", then "Primary Care management" then "Opioid Therapy Risk Report". VA Academic Detailing Services' Data Resources page lists the following OTRR links as well: **PCP** | **Patient**.

Figure 2 contains an example of an OTRR Patient Detail Report. The upper right corner contains several links to useful sites or resources; including: Data Definitions, VA OEND, State PDMP Resources, VHA Pain Management, and a link to the 2017 VA/DoD Clinical Practice Guidelines for Chronic Opioid Therapy.

Figure 2: Example of OTRR Patient Detail Report. A detailed description of the information contained can be found in the following text.

Opioid Therapy Risk Report
Patient Details

Current As Of: 10/30/2020

Double Asterisk identifies values evaluated for the past two years.

PDMP Resources | OEND Resources
Data Definitions | 2017 CPG
VSSC Help Desk | VHA Pain Mgt Site
Excel-Ready Multi-Select for Analysis

To Print: Use toolbar located just above report title, click the Export icon select PDF, then Print

[redacted]

SSN:	DOB:	Age:	Gender:
[redacted]	[redacted]	[redacted]	[redacted]

Last 30 days Avg Morph Equiv	RIOSORD Score	/Class	/ Prob	LTOT OSI	Active Opioid Rx	Active Benzo Rx	Any Opioid in Past Year	Tramadol Only
! 107	51	7	64%	✓	✓	!	✓	✓

UDT Screen Date**	Consent Date	Last PDMP	Naloxone Date	DEP**	SMI**	OMD**	PTSD**	SUD**	SUD Visit**	OSA**	Pain Visit	PalCare**	PalCare Visit	CA Pain**	SeriousCKD**
[redacted]	[redacted]	[redacted]	[redacted]	✓	✓	✓		✓			[redacted]				

Agonist Tx	Last Op Sub Visit	Dispense Date	Naloxone Product Dispensed	OT Consent Date	iMed User	iMedConsentnu Location
		[redacted]	NALOXONE HCL 4MG/SPRAY SOLN,SPRAY,NASAL	[redacted]	✓	[redacted]

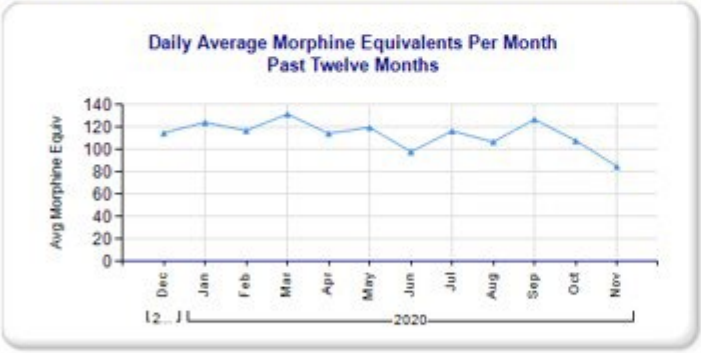
Last PDMP Check	Days Post Ck	PDMP Location	PDMP Entered By	PDMP Signed By	PDMP Source Clinic
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Last PC Visit **	Location	Team	PCP Name	Next Appt Date	Next Appointment Clinic
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Last MH Visit**	Mental Health Team Location	Mental Health Team	Mental Health Team Provider & Role
[redacted]	No MH Team Assignment Found		

Most Recent Urine Drug Test: [redacted]

Sta6a	AMPHET	BARB	BENZO	CANNAB	COCAINE	CODIENE	ETHANOL	HYDROCODO	HYDROMORPH	METHADONE	MORPHINE	OPIATE	OXY
[redacted]	Negative mAbs		Positive mAbs	Negative mAbs	Negative mAbs					Positive mAbs		Negative mAbs	



Opioid History Past Twelve Months

Release Date	VA Product	Strength	Days Supply	Daily Morphine Equivalent
Prescriber: [redacted]				
[redacted]	TRAMADOL HCL 50MG TAB	50.00	30	30
[redacted]	OXYCODONE HCL 5MG TAB	5.00	28	75
[redacted]	TRAMADOL HCL 50MG TAB	50.00	30	30
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Benzodiazepine History Past Twelve Months

Release Date	VA Product	Strength	Days Supply
Prescriber: [redacted]			
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	ALPRAZOLAM 0.5MG TAB	0.50	30
Prescriber: [redacted]			
[redacted]	[redacted]	[redacted]	[redacted]
Prescriber: [redacted]			
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]

Upper banner: Patient name, SSN, date of birth, age, gender, Last 30 days average morphine equivalents, RIOSORD Score, LTOT OSI, Active Opioid Rx, Active Benzo Rx, Any Opioid in Past Year, Tramadol Only. Also see DATA DEFINITIONS.

1st line: Urine drug screen test screen date, Consent date. last PDMP, Naloxone date, documented diagnosis that increase patient risk (depression (DEP), serious mental illness (SMI), other mental disorder (OMD), PTSD. substance use disorder (SUD, obstructive sleep apnea (OSA)), SUD visit, Pain visit, palliative care (PalCare), PalCare visit, cancer pain (CA), serious chronic kidney disease (CKD).
2nd line: Agonist treatment, last OP Sub visit, dispensed date, naloxone product dispensed, OT consent date, iMed User, iMed consent location
3rd line: Last PDMP Check, Days past check, PDMP locaton, PDMP entered by, PDMP signed by, Source clinic
4th line: Last PCP visit, PCP Location, PCP Team, PCP Name, Next appointment date, Next appointment clinic
5th line: Last MH visit, MH Team Location, MH Team, MH Team Provider and Role
6th line: Most Recent Urine Drug Test: amphetamine, barbiturates, benzodiazepines, cannabis, cocaine, codeine, ethanol, hydrocodone, hydromorphone, methadone, morphine, opiates, oxycodone
7th line graphs: average morphine equivalent daily dose, by month for past 12 months; pain scores past 12 months
8th line tables: opioid history past 12 months; benzodiazepine history past 12 months.

COMM™ - Current Opioid Misuse Measure [28]

The Current Opioid Misuse Measure (COMM)™ is a validated, 17-question easy-to-administer patient self-assessment that can be completed in less than 10 minutes. Completion of the COMM™ helps clinicians identify whether and to what extent a patient currently on long-term opioid therapy may be exhibiting aberrant behaviors associated with misuse of opioid medications; in addition, it can be utilized to develop or justify treatment strategies such as the level of monitoring planned for a patient or referral to a specialty pain clinic.

The assessment questions focus on six key issues:

- Signs and symptoms of intoxication
- Emotional volatility
- Evidence of poor response to medications
- Addiction
- Healthcare use patterns
- Problematic medication behavior

Each question asks the relative frequency of a thought or behavior over the last 30 days. Responses are recorded from 0 = “never” to 4 = “very often”. A score ≥ 9 is considered a positive indicator that misuse of medication is likely occurring.

COMM™ was developed with a grant from the National Institutes of Health and an educational grant from Endo Pharmaceuticals.

REGULATION OF NALOXONE AND COMMUNITY MEDICO-LEGAL RISK

Naloxone is available without a prescription in most states in the U.S.; however, some States still require a prescription in order to obtainthe medication.

In general, the risk of civil liability for a layperson who administers naloxone in an overdose is very low; a recent review found no case where a layperson was sued for using naloxone in an emergency.[29] Almost every state provides laypeople who provide medical assistance to another person in an emergency with some civil liability protection. In addition, most states have enacted laws that provide specific immunity to people who administer naloxone in the event of an overdose. The particulars of this protection vary between states.

For additional information and to review state specific legislation surrounding naloxone, including Good Samaritan laws, refer to the following links: http://prescribetoprevent.org/
http://www.pdaps.org/datasets/laws-regulating-administration-of-naloxone-1501695139
http://phlr.org/product/naloxone-community-opioid-overdose-reversal

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