Evzio® (naloxone hydrochloride auto-injection) and Narcan® (naloxone hydrochloride nasal spray) Quantity Limit Criteria Program Summary

This program applies to Commercial, GenPlus, NetResults A series, NetResults F series and Health Insurance Marketplace formularies.

OBJECTIVE

The intent of the Evzio and Narcan quantity limit criteria is to appropriately select patients for therapy according to product labeling and/or clinical guidelines and/or clinical studies. Additional doses of Evzio or Narcan will be approved when the patient has experienced an overdose and sought emergency medical care after previous administration. If the patient has a diagnosis of substance abuse, dependence, or addiction they must be receiving addiction counseling services. Only enough doses for one overdose event will be approved. Requests for Evzio and Narcan will be reviewed when patient-specific documentation is provided.

TARGET DRUGS

Evzio® (naloxone)
Narcan® (naloxone)

PROGRAM QUANTITY LIMIT

Brand (generic)	GPI	Multisource Code	Quantity Limit
Evzio (naloxone)			
0.4 mg/0.4 mL auto-injector	9340002010D530	M, N, O, or Y	1 package (2 auto-injectors) per 365 days
Narcan (naloxone)			
4 mg/0.1 mL nasal spray	93400020100920	M, N, O, or Y	1 package (2 nasal sprays) per 365 days

QUANTITY LIMIT CRITERIA FOR APPROVAL

Evzio or Narcan will be approved when ALL of the following are met:

1. The patient experienced an overdose that required administration of the requested agent
   AND
2. Emergency medical care was sought after administration of the requested agent
   AND
3. If the diagnosis is substance abuse, dependence and/or addiction, the patient is receiving addiction counseling services
   AND
4. The current prescription contains sufficient doses to manage ONE overdose event

Length of Approval: 1 time/1 package

This pharmacy policy is not an authorization, certification, explanation of benefits or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member's plan in effect as of the date services are rendered. All pharmacy policies are based on (i) information in FDA approved package inserts (and black box warning, alerts, or other information disseminated by the FDA as applicable); (ii) research of current medical and pharmacy literature; and/or (iii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

The purpose of Blue Cross and Blue Shield of Alabama's pharmacy policies are to provide a guide to coverage. Pharmacy policies are not

intended to dictate to physicians how to practice medicine. Physicians should exercise their medical judgment in providing the care they feel is most appropriate for their patients.

Neither this policy, nor the successful adjudication of a pharmacy claim, is guarantee of payment.

FDA APPROVED INDICATIONS AND DOSAGE[5,6]

Evzio:

For the emergency treatment known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression. Evzio is intended for immediate administration as emergency therapy in settings where opioids may be present. Evzio is not a substitute for emergency medical care.

Dosing: the recommended dose is 0.4 mg/mL intramuscular or subcutaneous injection. Additional doses may be given every 2 to 3 minutes until emergency medical assistance arrives.

Narcan:

For the emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression.

Dosing: the recommended dose is 4 mg/ 0.1 mL administered into one nostril. Additional doses may be given every 2 to 3 minutes until emergency medical assistance arrives.

CLINICAL RATIONALE

Naloxone has been an established antidote for opioid overdose for decades, with primary use among emergency department personnel and first responders (paramedics). Naloxone is accepted as the standard of care for treating opioid overdoses and is recommended by the Office of the U.S. Attorney General and the World Health Organization for this indication.[1,2]

Efficacy

Prescribing information for naloxone does not include clinical trial data supporting efficacy of naloxone. However, naloxone has been accepted as the standard of care for treating opioid overdoses and is recommended by the Office of the U.S. Attorney General and the World Health Organization for this indication.[2]

Naloxone is a potent and competitive antagonist of the μ-opioid receptor. It acts rapidly to reverse centrally mediated respiratory depression as a result of opioid overdose, whether intentional or unintentional. It has been an established antidote for opioid overdose for decades, with primary use among emergency room personnel and first responders such as paramedics. Naloxone is approved for IV, IM, and SC administration.[1]

Alternative, off-label routes of administration, including endotracheal, sublingual, inhaled, and intranasal (IN) administration, have allowed health care providers to care for overdose patients in emergent scenarios without IV access. Needle-free routes of administration have afforded several advantages to both patients and health care providers (e.g., avoidance of HIV and hepatitis transmission with needle sticks). A multitude of states have started outpatient naloxone dispensing to curb opioid overdose-related deaths.[1]

According to the FDA, naloxone has been increasingly used (off-label) by non-health care professionals, including family, friends and other caregivers. A number of jurisdictions across the US have begun providing naloxone to patients, and providing instruction for its use to the patients' family, friends and/or caregivers. However, as the products are only available in glass vials and ampules, they are distributed with syringes and needles for manual injection, or with syringes and atomizers for nasal administration.[3]

Safety

Naloxone injection may be administered intravenously (IV), intramuscularly (IM), or subcutaneously (SC). The most rapid onset of action is achieved by IV administration and it is recommended in emergency situations. Since the duration of action of some opioids may exceed that of naloxone, the patient should be kept under continued surveillance. Repeated doses of naloxone should be administered, as necessary. For adult opioid overdose (known or

suspected), an initial dose of 0.4 mg to 2 mg of naloxone may be administered IV. If the desired degree of counteraction and improvement in respiratory functions is not obtained, it may be repeated at 2 to 3 minute intervals. If no response is observed after 10 mg of naloxone have been administered, the diagnosis of opioid induced or partial opioid induced toxicity should be questioned. If an IV route of administration is not available, naloxone may be administered IM or SC in divided doses. If necessary, naloxone injection can be diluted with sterile water for injection.[4]

Naloxone auto-injector: Upon actuation, the auto injector automatically inserts the needle IM or SC to deliver 0.4 mg naloxone injection, and then retracts the needle fully into its housing. The initial dose for adult or pediatric patients is given into the anterolateral aspect of the thigh, through clothing if necessary, and then emergency medical assistance should be summoned. In adults and pediatric patients age >1, administer according to instructions. In patients age <1, the thigh muscle should be pinched while administering naloxone. Requirement for repeat doses depends upon amount, type, and route of administration of opioid being antagonized. If the desired response is not obtained after 2 or 3 minutes, another dose may be given. If still no response and additional doses are available, may administer every 2 to 3 minutes until emergency medical assistance arrives.[5]

Patients with pre-existing cardiac disease or those on medications with potential adverse cardiovascular effects should be monitored in an appropriate healthcare setting. In neonates, opioid withdrawal may be life-threatening if not properly treated. Adverse reactions due to naloxone in the post-operative setting include: hypotension, hypertension, ventricular tachycardia, fibrillation, dyspnea, pulmonary edema, and cardiac arrest. Death, coma, and encephalopathy have been reported as sequelae of these events. Excessive doses of naloxone in post-operative patients have resulted in significant reversal of analgesia and caused agitation. Abrupt reversal of opioid effects in persons physically dependent on opioids has precipitated opioid withdrawal. [5]

According to the FDA, a key risk is failure to obtain adequate medical follow-up, which is critical following initial overdose reversal. That risk has been addressed by inclusion of visual and audio instructions for the person administering the drug; instructions include noting need for emergency medical care immediately after administration of naloxone. Risk of death due to overdose clearly outweighs risks of precipitated withdrawal. [3]

REFERENCES

1. Ann Pharmacother. 2014:48(5):601-606.
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3. FDA. CDER. NDA 205787. Summary Review. Evzio (naloxone auto-injection). April 4, 2014. Accessed 10/20/2014 at: http://www.accessdata.fda.gov/drugsatfda_docs/nda/2014/205787Orig1s000SumR.pdf
4. Naloxone injection prescribing information. Hospira. January, 2007.
5. Evzio prescribing information. Kaleo Inc. April, 2014.
6. Narcan prescribing information. Adapt Pharma, Inc. November, 2015. http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/208411lbl.pdf