

Clinical Policy: Neonatal Abstinence Syndrome Guidelines

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[Revision Log](#)

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Description

Maternal drug use and intrauterine exposure of the fetus during pregnancy can lead to drug withdrawal in the infant after delivery. Clinically important neonatal withdrawal most commonly results from intrauterine opioid exposure. The constellation of withdrawal symptoms related to opioid drug use is known as neonatal abstinence syndrome (NAS). Signs of withdrawal will develop in 55 - 94% of neonates exposed to opioids in utero. Maternal use of central nervous system depressants (e.g., benzodiazepines, barbiturates and alcohol) and other drugs also results in signs of neonatal symptoms/withdrawal in exposed infants.

Typical signs of withdrawal from specific drugs occur based on the half-lives of elimination of the drug. Maternal use of multiple drugs during pregnancy will also have an impact on the onset and severity of NAS. In general though, if one week has elapsed between the last maternal opioid use and delivery, the incidence of NAS is relatively low. Table 1 below lists common drugs abused along with the typical onset of NAS symptoms.

Table 1. Common Drug NAS Symptom Onset

| Drug | Typical onset |
|------------------------|--|
| Heroin | Within 24 hrs with delay up to 5-7 days or later |
| Methadone | 24-72 hrs with delay up to 5-7 days later |
| Morphine & Hydrocodone | Within 3 days |
| Buprenorphine | Within 40 hrs |
| Ethanol | 3-12 hrs |
| Barbiturate | 4-7 days with delay up to 14 days |
| Diazepam | 12 days |
| Chlordiazepoxide | 21 days |

Policy/Criteria

- I. It is the policy of health plans affiliated with Centene Corporation[®] that the management of neonatal abstinence syndrome is **medically necessary** at the indicated level of care for the following circumstances:
 - A. Asymptomatic infants at risk for NAS
 1. Infants at risk for NAS due to maternal drug history are appropriate in Transitional level or level 1 nursery for 4 to 7 days for observation, depending on the drugs used during pregnancy (see Table 1 above).
 - B. Symptomatic infants
 1. Symptomatic infants should be managed using the appropriate nationally recognized clinical decision support tools.
 2. Once the infant is weaned to a 6 hour dosing interval, home-based withdrawal therapy may be considered if no more than 2 scores are ≥ 8 or 1 score is > 10 in the prior 48

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hours and all of the following discharge criteria are met. The home environment, caregiver, and support team must be taken into consideration.

C. Discharge Criteria

Prior to discharge home with home health, the following must be met:

1. Infant is clinically stable and meets all of the following criteria:
 - a. Infant is taking oral feeds and gaining weight satisfactorily; *and*
 - b. Infant is physiologically stable with normal vital signs including blood pressure; *and*
 - c. Infant is showing neurobehavioral recovery evidenced by reaching full alert state, responding to social stimuli, and consolable with appropriate measures
2. Home situation is assessed and deemed adequate
3. Parent or caretaker is agreeable with the plan of care
4. Appropriate transportation is available for follow up appointments
5. Home care services are arranged for nursing assessments
6. The responsible physician (neonatologist, primary care pediatrician) and back-up health care facility (NICU, community hospital) should be clarified to the family and home care agency prior to discharge

II. It is the policy of health plans affiliated with Centene Corporation[®] that if the infant is clinically stable but remains in the nursery due to social issues, these days are considered **not medically necessary** unless there is a benefit coverage requiring such days.

Background

The diagnosis and management of NAS is briefly described below. The presentation of NAS is widely variable in the onset of symptoms and types and severity of clinical manifestations. Universal screening and subsequent close observation of high risk neonates is essential for timely diagnosis and treatment of the neonate.

A. Screening – the following screening steps should be taken

1. Universal screening for maternal drug abuse
2. Maternal toxicology testing in known or suspected cases of NAS based on any of the following characteristics: (note – legal implications of testing and need for consent from the mother may vary among states)
 - a. Known history of maternal substance abuse
 - b. Maternal engagement in high risk behaviors,
 - c. Disclosure of recent substance abuse
 - d. Acting in an intoxicated manner on admission or during office visits
 - e. Previous unexplained late fetal demise, repeated spontaneous abortion
 - f. Precipitous labor, placental abruption, hypertensive episodes, severe mood swings
 - g. Cerebrovascular accidents, myocardial infarction
3. Newborn urine and/or meconium screening can be performed for recent substance abuse.
 - a. False-negatives may occur more commonly with urine testing due to urinary excretion of most drugs being relatively short.
 - b. Meconium screening yields false-negatives less frequently than urine screening; however results are not typically available for days to weeks.
 - c. Umbilical cord tissues samples may become a more viable screening tool in infants suspected of in utero exposure.

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B. Observation/Assessment

1. Infants at risk for NAS should be observed in the neonatal nursery for signs of consistent withdraw. The modified Finnegan's Neonatal Abstinence Scoring Tool is the predominant assessment tool used in the United States for quantifying the severity of neonatal withdrawal signs.
2. Timing and severity of withdrawal symptoms depends upon the maternal drug(s) used and last time of use. Duration of neonatal nursery observation should be dependent on the half-life of the drug based on maternal drug use history.
 - a. For example, maternal use of a drug with a short half-life of 4 hours (e.g. hydrocodone) indicates an infant may be safely discharged if there are no signs of withdrawal by 3 days of age.
 - b. Maternal use of a drug with a prolonged half-life (e.g. methadone) indicates an infant should be observed for a minimum of 5 to 7 days.

C. Diagnosis

1. Withdrawal symptoms such as seizures, fever, irritability, and poor feeding can all be signs of other conditions. Appropriate assessment and diagnostic tests are necessitated to differentiate NAS from other diagnoses.
2. Clinical diagnosis is made based on maternal history of drug use and neonatal screening, observation, and assessment findings.

D. Treatment

1. Nonpharmacologic
 - a. Infants showing early signs of withdrawal should have treatment directed at minimizing environmental stimuli. This includes placing the infant in a dark, quiet environment, careful positioning and comfort techniques such as swaddling, responding early to an infant's signals, and frequent small feedings of calorically dense formula or fortified breast milk.
 - b. Careful observation for signs of fever, dehydration or weight loss.
 - c. Ensure adequate sleep and caloric intake.
 - d. Additional supportive care such as IV fluids, electrolyte replacement and gavage feedings may be indicated to stabilize the infant in the acute phase and obviate the need for pharmacologic intervention.
 - e. Breast feeding has been associated with less severe NAS and should be encouraged in mothers who are adherent to a supervised drug treatment program.
2. Pharmacologic
 - a. Pharmacologic therapy should be reserved for the infants with moderate to severe signs of NAS, and to relieve complications of such, when nonpharmacologic support is ineffective. Drug withdrawal may be life-threatening, but it is ultimately a self-limited process and unnecessary pharmacologic treatment prolongs exposure to harmful drugs. Studies have only shown clear benefits of pharmacologic therapy for the short-term amelioration of clinical signs of NAS. Long term benefits or harm have not been clearly studied.
 - b. The optimal screening score for the initiation of pharmacologic therapy is not clearly defined. However, pharmacologic therapy is generally started for the neonate who has 3 or more consecutive scores above 8 or 2 scores of 11 or greater despite adequate supportive care.
 - c. Indications for pharmacologic therapy include:

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- i. Seizures
 - ii. Poor feeding with failure to gain weight
 - iii. Inability to sleep despite nonpharmacologic treatment
 - iv. Fever unrelated to another source
 - v. Significant diarrhea and/or vomiting resulting in weight loss or hypovolemia
- d. When nonpharmacologic treatment fails, the recommended first drug of choice is an opioid, either morphine or methadone. The second drug of choice is phenobarbital if the opiate does not control symptoms. Paregoric and diazepam are no longer recommended.
- e. The general course of opioid therapy is determined by the response of the infant based on abstinence scoring. If the infant remains symptomatic based on abstinence scoring, an increased dose is indicated. Once the infant responds to therapy with a decrease in scoring and weight gain is established, weaning of the medication can begin. Metabolic demands need to be considered as part of the weaning process. The rate of wean is dependent on the infant's clinical status with use of the abstinence score facilitating this process.
- f. Weaning may occur every 24 to 48 hours for infants on single drug regimens and no more frequently than every 48 hours for infants on multiple drug regimens or those who have recently failed a wean. The use of clinical judgment in the management of pharmacotherapy is vital.

Prematurity

Preterm infants have been found to be at lower risk of drug withdrawal with less severe and/or prolonged courses of NAS. Several possible causes of this effect include relation to developmental immaturity of the CNS in preterm infants, lower total drug exposure, less fat depots of the drug, or possibly that the severity of NAS is more difficult to determine in preterm infants due to scoring tools being developed for full-term infants.

Opioids

The clinical presentation of NAS is dependent on multiple variables, including opioid used; maternal drug use history; maternal, placental and infant metabolism; and other factors. Because opioid receptors focus in the central nervous system (CNS) and gastrointestinal (GI) tract, the majority of NAS symptoms reflect CNS irritability, autonomic over-reactivity, and GI tract dysfunction. Excess stimuli and hunger exacerbate the perceived severity of NAS.

Cocaine and other CNS stimulants

Neurobehavioral symptoms from intrauterine exposure to CNS stimulants such as cocaine and amphetamine frequently occur on the second or third day postnatal. Symptoms include irritability, hyperactivity, tremors, high-pitched cry, and excessive sucking. However, since cocaine and its metabolites can be detected in the neonatal urine for up to 7 days postnatal, symptoms may reflect drug effect rather than withdrawal. Pharmacological treatment of infants with neurobehavioral symptoms due to intrauterine cocaine exposure has not been carefully evaluated, thus no standard of care exists.

Selective serotonin reuptake inhibitors

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Selective serotonin reuptake inhibitors (SSRIs) are the most common class of anti-depressants used to treat depression in the general population and during pregnancy. Studies have linked third trimester use of SSRIs to a group of symptoms including continuous crying, irritability, jitteriness, and/or restlessness, shivering, fever, tremors, hypertonia or rigidity, tachypnea or respiratory distress, feeding difficulty, sleep disturbance, hypoglycemia, and seizures. Onset of these symptoms generally begins several hours to several days after birth and subsides within 1 to 2 weeks. It is not clear if these symptoms are a reflection of serotonin syndrome or SSRI withdrawal. Clinicians should arrange for early follow up after hospital discharge for infants at risk from the effects of SSRI exposure in utero.

| Reviews, Revisions, and Approvals | Date | Approval Date |
|--|-------|---------------|
| Policy created; reviewed by Neonatologist | 10/13 | 10/13 |
| Changed Policy/Criteria from Episode Days to Asymptomatic and Symptomatic infants criteria Updated criteria for symptomatic infants to refer to decision support tool criteria Updated Asymptomatic infants criteria to allow for observation in nursery according to maternal drug history Reviewed by Neonatologist | 10/14 | 10/14 |
| Converted into new template Clarified language in Policy/Criteria section I.B.2 Added short explanative paragraph at beginning of Background section | 10/15 | 10/15 |
| References reviewed and updated. Reviewed by neonatologist. | 09/16 | 10/16 |
| Changed minimum days of observation to 4 in 1.A, to reflect the half-life of common drugs contributing to NAS. References reviewed and updated. | 10/17 | 10/17 |

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Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

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Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at <http://www.cms.gov> for additional information.

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