

Clinical Policy: Neonatal Abstinence Syndrome Guidelines

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See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

Maternal use of certain prescription medications and non-prescribed substances with intrauterine exposure of the fetus during pregnancy can lead to withdrawal symptoms in the infant after delivery. Clinically important neonatal withdrawal syndromes most commonly result from intrauterine opioid exposure (both prescribed and illicit use). However, maternal use of central nervous system depressants (e.g., benzodiazepines, barbiturates, and alcohol), selective serotonin reuptake inhibitors (SSRIs)/serotonin norepinephrine reuptake inhibitors (SNRIs) and other substances also result in signs of neonatal symptoms/withdrawal in exposed infants.^{15,20}

Neonatal opioid withdrawal syndrome (NOWS) describes opioid-only withdrawal symptoms, while neonatal abstinence syndrome (NAS) refers to neonatal withdrawal from in utero exposure to opioid and nonopioid substances. Neonatal adaptation syndrome describes symptoms in neonates exposed to SSRI/SNRIs.^{15,20} The term NAS will be used here for exposures related to opioids and/or other substances.

Current best practices for pregnant individuals with opiate-use disorders includes treatment with buprenorphine or methadone throughout pregnancy. Pregnant individuals who are prescribed methadone or buprenorphine should continue to take them and not stop them prior to delivery.¹⁷ Signs of opioid withdrawal will develop in 55 to 94% of neonates exposed to opioids in utero.⁴ Fetal methadone exposure results in a 60 to 80% risk of NAS.²³ Typical signs of withdrawal from specific drugs occur based on the half-lives of elimination of the drug.¹⁵ Maternal use of multiple drugs during pregnancy will also have an impact on the onset and severity of NAS. In general, if one week has elapsed between the last maternal opioid use and delivery, the incidence of NAS is relatively low.⁴

Table 1 below lists common prescription, recreational, and illicit substances along with the typical onset of NAS symptoms.

Table 1. Typical NAS Symptom Onset⁴

Drug	Typical onset
Barbiturate	4 to 7 days with delay up to 14 days
Buprenorphine	Within 40 hours
Chlordiazepoxide	21 days
Cocaine	48 to 72 hours
Diazepam	Hours to weeks, up to 12 days
Ethanol/Alcohol	3 to 12 hours
Heroin	Within 24 hours with delay up to 5 to 7 days or later

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Methadone	24 to 72 hours with delay up to 5 to 7 days or later
Morphine & Hydrocodone	Within 3 days
SSRIs/SNRIs	Hours to days

Policy/Criteria

- I. It is the policy of health plans affiliated with Centene Corporation® that the management of neonatal abstinence syndrome (NAS) is **medically necessary** at the indicated level of care for the following circumstances:
- A. Asymptomatic infants at risk for NAS due to maternal prescription or substance use exposure are appropriate in one of the following:
1. Transitional level or level I nursery for four to seven days for observation, with duration of observation for symptoms dependent on the substances/medications used during pregnancy (see Table 1 above);
 2. Level II nursery for four to seven days for assessment and treatment, with duration of treatment dependent on the substances/medications used during pregnancy (see Table 1 above);
- Note: Infants may be assessed and managed utilizing either the modified Finnegan Neonatal Abstinence Scoring Tool (FNAST) or the Eat, Sleep, Console (ESC) approach.
- B. Level of care for symptomatic infants should be managed using the appropriate nationally recognized clinical decision support tools if assessed and treated per modified Finnegan scoring or by ESC.

Note: For opioid-exposed infants, the dosing interval for morphine should be no longer than every four hours to avoid subtherapeutic levels prior to the next dose. **Home-based withdrawal therapy** for opioid-exposed infants may be considered if no more than two modified Finnegan scores are ≥ 8 or one score is > 10 in the prior 48 hours, and all of the discharge criteria in section I.C. are met. Supports available in the home environment and caregiver abilities and needs must be taken into consideration.

If treated with pharmacologic therapy for opioid-exposed infants using ESC, discharge should be consistent with ESC recommendations.

C. Discharge Criteria

Prior to discharge home with home health, all of 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;³
 - b. Infant is physiologically stable with normal vital signs including blood pressure;³
2. Infant is showing neurobehavioral recovery evidenced by reaching full alert state, responding to social stimuli, and being consoled with appropriate measures with no significant clinical signs of withdrawal for 24 to 48 hours after applicable pharmacologic therapy;³
3. Home situation is assessed and deemed adequate;

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4. Parent(s) or caregiver(s) have received education regarding NAS and routine infant care and demonstrate understanding of and agreement with the plan of care;
5. Appropriate transportation is available for follow up appointments;
6. Home care services are arranged for nursing assessments;
7. The responsible physician (neonatologist, primary care pediatrician, or family medicine provider) and back-up health care facility (NICU, community hospital) should be confirmed with the family and home care agency prior to discharge;
8. Follow up appointment with the primary care pediatrician or family medicine provider is scheduled prior to discharge.

Note: It is recommended that an infant with opioid exposure should be seen by his or her provider within 48 hours of discharge to monitor for signs of withdrawal.²²

- 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 presentation of neonatal abstinence syndrome (NAS) is widely variable in the onset of symptoms, 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.^{15,16,20,22}

A. Screening

1. Universal screening for prescription medication use that may lead to NAS and/or maternal substance use should be discussed with the pregnant individual.
2. Maternal toxicology testing in known or suspected cases of NAS based on any of the following characteristics (note that legal implications of testing, including notification to child welfare, and need for consent from the pregnant individual may vary among states):
 - a. Known history of maternal illicit substance use
 - b. Maternal engagement in high-risk behaviors associated with substance use
 - c. Disclosure of recent substance use
 - d. Acting in an intoxicated manner on admission or during office visits
 - e. Previously unexplained late fetal demise or repeated spontaneous abortion
 - f. Precipitous labor, placental abruption, hypertensive episodes, or severe mood swings
 - g. Cerebrovascular accidents or myocardial infarction
3. Newborn urine and/or meconium screening and/or umbilical cord testing can be performed for recent substance use.
 - a. False negatives may occur more commonly with urine testing due to urinary excretion of most drugs being relatively short
 - b. False positives may also occur and should be confirmed prior to any reporting to child welfare (in states where this is required)
 - c. Meconium screening and umbilical cord testing both have a window of detection up to 20 weeks prior to delivery

B. Observation location/Assessment tool/Level of Care

1. If the hospital uses the Eat, Sleep, Console (ESC) assessment tool for infants at risk for NAS, the infant may remain in the room with the primary caregiver to provide intensive

comfort care measures and to promote caregiver bonding and breastfeeding/chestfeeding. This is considered Level II care with or without the need for medications. The infant does not have to be transferred from his/her caregiver to the neonatal intensive care unit (NICU) for Level II care to be authorized so long as the ESC assessment tool is being used and followed.

2. If the hospital uses the older modified Finnegan Neonatal Abstinence Scoring Tool (FNAST), infants at risk for NAS should be observed in the neonatal nursery for signs/symptoms of neonatal withdrawal. Level II care is appropriate under the modified FNAST if medications are given and/or if the infant is transferred to the NICU. A copy of the modified FNAST is available at <http://www.academyofneonatalnursing.org/NAS/FinneganNASTool.pdf>
3. Timing and severity of withdrawal symptoms depends upon the maternal substances(s) used and last time of use. Duration of neonatal nursery observation should be dependent on the half-life of the medication/substance based on usage/prescription history.
 - a. For example, use of a substance/medication by a birthing individual with a short half-life of four hours (e.g. hydrocodone) indicates an infant may be safely discharged if there are no concerning symptoms by three days of age.
 - b. Maternal use of a substance/medication with a prolonged half-life (e.g., methadone) indicates an infant should be observed for a minimum of five to seven days.
 - c. Polysubstance abuse and/or unknown substance use should be observed for a minimum of five to seven days.
4. Some hospitals may continue to assess using modified Finnegan scoring along with ESC scoring. However, only the scoring system used to direct care decisions should inform medical necessity for the requested level of care.

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 necessary to differentiate NAS from other diagnoses.
2. Clinical diagnosis is made based on history of substance/medication use in the birthing individual and neonatal screening, observation, and assessment findings.

D. Treatment

1. Nonpharmacologic
 - a. Infants showing early signs of withdrawal, or problems with neonatal adaptation, 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 breastfeeding/chestfeeding or formula feeding as indicated. Rooming-in (i.e., the co-location of maternal and infant care after delivery and beyond) has been shown to reduce NAS severity.
 - b. Careful observation for signs of fever, dehydration or weight loss.
 - c. Ensure adequate sleep and caloric intake.
 - d. Additional supportive care such as intravenous 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. Breastfeeding/chestfeeding, for birthing parents who are adherent to medication for opioid use disorder and not using any illicit opioids/substances, has been associated

with less severe NAS and should be encouraged in parents engaged in a supervised drug treatment program including methadone or buprenorphine.

2. Pharmacologic
 - a. Pharmacologic therapy should be reserved for the infants with severe signs of NAS and, to relieve complications of such, when nonpharmacologic support is ineffective. Pharmacologic therapy is typically not indicated for infants with poor neonatal adaptation syndrome from selective serotonin reuptake inhibitors (SSRIs)/serotonin-norepinephrine reuptake inhibitors (SNRIs). Drug withdrawal may be life-threatening, but it is ultimately a self-limited process and unnecessary pharmacologic treatment prolongs exposure to harmful substances. 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 modified Finnegan score for the initiation of pharmacologic therapy is not clearly defined. However, pharmacologic therapy is generally started for the neonate who has three or more consecutive scores above eight, or two consecutive scores averaging 12 or greater despite adequate supportive care.
 - c. The ESC method is a functional scoring approach, considering whether the infant can:
 - i. Breastfeed/chestfeed well or greater than one ounce per feed (30 ml)
 - ii. Sleep undisturbed for greater than or equal to one hour
 - iii. Be consoled within 10 minutesIf the infant is able to do these things, then the infant's NAS is being treated adequately. If not, intensive comfort care measures involving the caregiver are utilized first. After which, for infants with neonatal opioid withdrawal syndrome, opioid medication, usually morphine, can be given to lessen the withdrawal so the infant can eat, sleep, or be consoled. Once started, opioid medication, usually morphine, does not have to be continued or increased unless the infant fails to eat, sleep, or be consoled.
 - d. When nonpharmacologic treatment fails for an opioid-exposed infant, the recommended first drug of choice is an opioid, such as morphine, methadone, or buprenorphine. Clonidine and phenobarbital are second-line drugs to be used in addition to an opioid to treat NAS. Phenobarbital is an anti-seizure medicine that can help calm an infant. Clonidine is a centrally acting alpha-adrenergic receptor agonist that helps lower blood pressure and heart rate; it helps relieve neuromotor symptoms such as hypertonia, jitteriness, and agitation. Paregoric and diazepam are no longer recommended. Buprenorphine is a pharmacologic alternative to morphine and methadone; however, there are limitations related to its methods of administration.
 - 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 weaning is dependent on the infant's clinical status with use of the abstinence score facilitating this process.
 - f. The half-life of morphine in term infants (37 0/7 weeks and older) is estimated to be six to twelve hours, but this is variable and inversely related to gestational age at

- birth. As gestational age and birth weight increases, the clearance rate of morphine increases as well.²⁴ Weaning of morphine 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 weaning. Morphine may be discontinued after reaching 0.02 mg/kg/dose every three to four hours. Morphine should not be spaced out further than every three to four hours to avoid subtherapeutic levels of morphine before the next dose. Clinical judgment is vital in the management of pharmacotherapy.
- g. Weaning of clonidine may occur every 24 hours by 0.25 to 0.5 mcg/kg/dose as tolerated. Blood pressure and vital signs must be monitored every two hours for 12 hours after clonidine is completely weaned to prevent rebound hypertension or tachycardia.
 - h. Weaning of phenobarbital may occur every 48 hours by decreasing the dose by 20%. Alternatively, the infant can be discharged home on phenobarbital and be allowed to outgrow the dose within two to three weeks before stopping it.

Prematurity

Preterm infants have been found to be at lower risk of substance/medication withdrawal with less severe and/or prolonged courses of NAS. Several possible causes of this effect include relation to developmental immaturity of the central nervous system (CNS) in preterm infants, lower cumulative substance exposure, less fat deposits of the substance/medication, 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.²¹

Opioids

The clinical presentation of NAS is dependent on multiple variables, including substance/medication used; maternal prescription and substance use history; maternal, placental and infant metabolism; and other factors. Because opioid receptors focus in the 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.⁴

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 three 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.⁴

SSRIs/SNRIs

SSRIs/SNRIs are the most common classes of anti-depressants used to treat depression. Studies have linked third trimester use of SSRIs/SNRIs 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,

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and seizures. Onset of these symptoms generally begins several hours to several days after birth and subsides within one to two weeks. It is not clear if these symptoms reflect serotonin syndrome or SSRI withdrawal and is currently best described as poor neonatal adaptation. Clinicians should arrange for early follow-up after hospital discharge for infants at risk from the effects of SSRI exposure in utero. Pharmacological treatment of infants with neurobehavioral symptoms due to intrauterine SSRI/SNRI exposure is not typically indicated.⁴

Marijuana

The American College of Obstetricians and Gynecologists (ACOG) recommends pregnant individuals not use marijuana during pregnancy. Research is limited, but there are potential risks with marijuana use during pregnancy, including infants that are smaller at birth and stillbirth.¹⁹

Eat, Sleep, Console (ESC) Assessment Approach

The Finnegan Neonatal Abstinence Scoring Tool (FNAST), the most widely adopted scoring system, and modified versions of this tool are designed for use in term infants.²² Other assessment tools have been developed including the ESC assessment approach that evaluates the neonates' ability to eat, sleep, and be consoled. The ESC includes the non-pharmacologic and pharmacologic treatment of the infant and is based on infant function and comfort, rather than reducing signs and symptoms of withdrawal. This tool emphasizes maternal/caregiver involvement with a goal of reducing opioid therapy and length of birth hospitalization. The effectiveness of the ESC method has been validated by quality improvement initiatives and reviews.^{4,9,10} While the American Academy of Pediatrics does not endorse one scoring system over another, the ESC's functional assessment and family-centered treatment methodology is slowly replacing the modified FNAST for the assessment and treatment of NAS.²²

Reviews, Revisions, and Approvals	Revision Date	Approval Date
Policy created; reviewed by Neonatologist	10/13	10/13
Annual review. Description updated. Added cocaine and SSRIs, to the NAS symptom onset table. In I.B., replaced portion of note reflecting a 6-hour dosing interval with a 4-hour morphine dosing interval. Added requirement in I.C.2 discharge criteria that infant is consolable with appropriate measures 24-48 hours after the last dose of morphine prior to discharge, based on gestational age, with note about morphine half-lives applicable to a range of gestational ages. Noted in background section A.3.b regarding screening that meconium and umbilical blood reflect drug use for 20 weeks of gestation and later. Background: Changed background heading "Observation/Assessment" to "B. Observation location//Assessment tool/Level of Care," and in that section: expanded information regarding LOC for Finnegan scoring, and added section for LOC for ESC scoring; in 3.c., added that polysubstance use should correspond to observation for 5-7 days, and added note that when more than 1 scoring system is used, LOC should be determined according to the scoring system driving the care decisions. In nonpharmacologic treatment section, changed recommendation from frequent feedings of calorie dense formula or fortified breastmilk to "breastfeeding or	02/22	02/22

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formula feeding as indicated.” Added c under pharmacologic treatment regarding ESC assessment categories. Added details regarding morphine, clonidine, and phenobarbital weaning. Added additional background to “ESC Assessment Approach.” References reviewed and updated.		
Annual review. Minor rewording in description and criteria. Updated criteria I.C.7. to include family medicine provider. Added criteria I.C.8. regarding follow up appointment with the primary care pediatrician or family medicine provider scheduled prior to discharge. Background updated with no impact on criteria. References reviewed and updated.	02/23	02/23
Annual review. Updated description, criteria and background with equitable and inclusive language and no impact on criteria. References reviewed and updated. Reviewed by external specialist.	01/24	01/24
Annual review. Updated background with information on marijuana with no clinical criteria significance. References reviewed and updated.	01/25	01/25
Annual review. Description and background updated with no clinical significance. Table 1 updated. For criteria I.C.2, the corresponding note was updated with no impact on criteria. For criteria I.C.8, added “It is recommended that an infant...signs of withdrawal” as a note. References reviewed and updated.	06/25	06/25
Annual review. Description updated with no impact to criteria. Updated verbiage in Criteria I.A. for clarity. Removed use of the modified Finnegan Neonatal Abstinence Scoring Tool (FNAST) from Criteria I.A.1. Removed requirement for using the Eat, Sleep, Console (ESC) approach and added duration of treatment language in Criteria I.A.2. Added Note at the end of Criteria I.A.2. regarding assessment and management utilizing the modified FNAST or the ESC approach. Removed language regarding level II nursery in Criteria I.B. Added “with no significant clinical signs of withdrawal for 24 to 48 hours after applicable pharmacologic therapy” and removed language specific to morphine in Criteria I.C.2. Removed Note at the end of Criteria I.C.2. regarding the half-life of morphine and added this information to the Background section. Updated verbiage in Criteria I.C.4. to specify that parent(s) or caregiver(s) have received education regarding NAS and routine infant care and demonstrate understanding of and agreement with the plan of care. Background updated with no impact to criteria. Reviewed by external specialist and external specialist.	06/26	06/26

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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.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy,

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contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members/enrollees. This clinical policy is not intended to recommend treatment for members/enrollees. Members/enrollees should consult with their treating physician in connection with diagnosis and treatment decisions.

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Note: For Medicaid members/enrollees, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members/enrollees, 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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