

This treatment protocol is meant to serve as a guideline for Indiana facilities to use in developing their own pharmacologic treatment protocols and is not intended to mandate methods of care for infants diagnosed with Neonatal Abstinence Syndrome (NAS) and in need of pharmacologic treatment. *An accompanying NAS Pharmacologic Therapy Protocol Flowsheet has been developed and can be found at*



<https://www.in.gov/health/laboroflove/files/Pharmacologic-Treatment-Algorithm.pdf>

The protocol reflects current SAMHSA recommendations. There is no ‘best’ treatment protocol identified as yet for infants with NAS. The protocol outlined here has considerable clinical experience behind it and has been reviewed by a number of neonatologists, pediatricians, and a clinical pharmacologist. Its implementation, as with all clinical protocols, requires clinical judgment and experience to use successfully. It is based on conventional use of morphine (prn or scheduled dosing) along with FNASS (Finnegan) scoring. An option for use of methadone is also given for institutions that prefer it, and reasons to choose one over the other are discussed.

This pharmacologic therapy protocol is designed to be used as part of a full institutional protocol that includes identification, monitoring, and testing of infants at risk for NAS prenatally, at admission for birth, and in the newborn nursery; a full non-pharmacologic treatment and, a complete discharge planning protocol including maternal behavioral support services. All modules can be found at <https://www.in.gov/health/laboroflove/toolkits/>

Research into NAS treatment methods is currently an active area of inquiry. It is likely that new treatment methods (use of buprenorphine in infants as front-line treatment, the Eat-Sleep-Console scoring system instead of the FNASS, and so on) will change our methods of treatment over the next three to five years. While these protocols are still being studied, practitioners should carefully consider any early clinical implementation of these methods before they are fully vetted in peer-reviewed literature.

Summary: Clinical use of the NAS Pharmacologic Therapy Protocol

1. Identify an infant at risk for NAS using a formal NAS risk management algorithm.
2. Non-pharmacologic therapy and Finnegan scoring should be begun on all infants at risk for substance exposure. Non-pharmacologic therapy measures should be in place and implemented as a nursing protocol at the treating facility.
3. Identify infants with NAS. An infant is diagnosed with NAS if they have:
 - a. Signs, AND
 - b. A positive infant toxicology test OR a maternal history with either a positive verbal screen or a positive maternal toxicology test for opiates.
4. Based on clinical exam, Finnegan scoring, and clinical course an infant is assigned to one of four categories (see pp. 7-10):
 - a. Category 1. No withdrawal. Infants who are at-risk for NAS but do not develop withdrawal signs. These infants should not be coded as NAS (see p. 4 for ICD-10 coding recommendations) but as exposed infants.
 - b. Category 2. Mild withdrawal. These are at-risk infants who have signs. This group of infants will meet the formal definition of NAS above (and use ICD-10 code P96.1) but have responded to non-pharmacologic care. These infants should be monitored for progression to more severe signs that may require pharmacologic treatment.
 - c. Category 3: Moderate withdrawal. Infants who meet pharmacologic therapeutic criteria for NAS. These infants can have extended lengths of stay and may require transfer to a higher level of care.
 - d. Category 4: Severe or complex withdrawal. These are infants with NAS who have had seizure activity or failed to respond to simple single-drug pharmacologic therapy. These infants require high-dose single drug or multi-drug pharmacologic therapy and transfer to a level 3 or 4 NICU is strongly recommended.
5. Follow management recommendations for the infant's category of withdrawal. (See pp. 10-16.)

6. Regardless of category, all at-risk infants and their mothers require specialized discharge planning. Follow discharge recommendations once treatment is completed. (See p. 17.)

Executive Summary: Initial Pharmacologic Treatment Recommendations:

Opiate withdrawal or polydrug withdrawal including opiates:

- Recommended initial prn treatment:
 - Morphine 0.05 - 0.1 mg/kg/dose q3h PRN 2 consecutive NAS scores \geq 8 or any score \geq 12.
- Recommended initial scheduled treatment for more severe withdrawal:
 - Morphine 0.05 - 0.1 mg/kg/dose q3h or q4h; or
 - Methadone 0.1 mg/kg/dose q6h (in general, use q6h methadone dosing for only 24 hours; use dosing schedule from p. 13. The schedule is based on methadone pharmacokinetics and is designed to reach therapeutic levels rapidly.)
- Increase medication dose until withdrawal is controlled. (See pp. 12 - 14.)
- Wean medication dose until infant can be safely discharged. (See pp. 14 - 17.)

Non-opioid withdrawal:

- Recommended initial treatment:
 - Clonidine 1 mcg/kg/dose q6h (in the second week of life, begin at 1.5 mcg/kg/dose q6h and may consider q4h dosing if signs are severe); OR
 - Phenobarbital 2.5 mg/kg/dose q12h (a loading dose is not necessary)
- Increase medication dose until withdrawal is controlled. (See pp. 12 - 14.)
- Wean medication dose until infant can be safely discharged. (See pp. 14 - 17.)

Withdrawal with seizures:

Seizures will be difficult to control unless the withdrawal is adequately treated. Scheduled treatment with morphine or methadone should be started immediately in conjunction with treatment of seizures. (See treatment recommendations above.) Evaluation of the infant for other possible causes of seizure activity is strongly recommended as well.

- Recommended initial treatment of seizures:
 - Phenobarbital 10 to 20 mg/kg IV as the initial loading dose with a maintenance dose of 2.5 mg/kg/dose q12h. Additional seizures may be treated with 5 to 10 mg/kg IV boluses until controlled.

ICD-10 Coding for Newborn Exposure to:

Maternal use of opiates [P04.14]	Maternal use of alcohol [P04.3]
Maternal use of cocaine [P04.41]	Maternal use of tobacco [P04.2]
Maternal use of amphetamines [P04.16]	Maternal use of cannabis [P04.81]

Other maternal medication [PO4.18]

Maternal use of antidepressants [PO4.15]

Maternal use of drugs of addiction [PO4.4]

Comments on the use of the NAS Pharmacologic Therapy Protocol:

1. The following therapy recommendations are primarily designed for management of opiate withdrawal and polydrug withdrawal including opiates in infants with NAS due to in utero prescription or illicit medication exposure. ***Implementation of these recommendations, as with any generalized treatment protocol, should be tempered by clinical judgment and may require adjustment for use in individual patients.***
2. Withdrawal in infants of mothers taking medications other than opiates (benzodiazepines, SSRI/SSNI's, tobacco, caffeine, etc.) is typically neither severe nor prolonged. It can usually be managed with non-pharmacologic therapy. Finnegan scoring is often used to standardize management for these infants, though it has not been validated in non-opiate withdrawal. Therefore, clinical judgment should be used when basing management decisions in these infants on Finnegan scoring.
3. Venlafaxine (Effexor) is an SNRI that is an exception to the general rule that withdrawal from these medications is mild and self-limited. There are reports of respiratory distress, apnea, and other more severe signs with venlafaxine in addition to the more typical and milder signs normally expected with maternal antidepressant/anti-anxiety medications. Some authorities feel that other SNRI-class medications may also produce more severe neonatal withdrawal signs (similar to venlafaxine) than the SSRI-class medications and these infants should also be observed carefully.
4. Recommendations are given for pharmacologic management of severe non-opiate withdrawal should it be clinically necessary. Clinicians should be aware that these recommendations are based on limited clinical data compared to management of opiate withdrawal and polydrug withdrawal including opiates. Also, note that it is uncommon to need pharmacologic treatment for non-opiate NAS and rare to have difficulty in controlling signs with clonidine or phenobarbital. Consideration should be given in such cases to the possibility of unreported maternal opiate use, and an empiric trial of an opiate may be of benefit for severe signs.
5. Iatrogenic NAS in infants who have received extended or high-dose medications for sedation or pain control during neonatal hospitalization that are known to cause

withdrawal signs is managed differently than NAS related to maternal medication use or drug abuse during pregnancy. Management of infants with iatrogenic NAS is complex and institutions should develop their own protocols for use.

6. NAS scoring in infants on pharmacologic therapy should be continued for 48 to 72 hours after all medications are discontinued. Thus, we recommend observation of infants for 48 to 72 hours after discontinuation of pharmacotherapy.
7. Naloxone can precipitate a dangerous acute withdrawal crisis in at risk infants. The routine use of naloxone in the delivery room is no longer recommended by the AAP as part of neonatal resuscitation (NRP.) Use of naloxone for treatment of respiratory depression due to maternal pain medications at delivery in infants at risk for NAS or due to pharmacologic treatment of NAS is generally felt to be contraindicated, but little clinical data is available regarding the risk: benefit ratio. Use of naloxone in such situations clearly can be hazardous and clinicians should proceed with extreme care.
8. Most infants who are going to present with NAS will do so within the first five days. However, there are some infants whose mothers are managed with methadone (and possibly with buprenorphine) that may present as late as fourteen days of age. Providers should be aware that young infants presenting to medical attention with signs that could be explained by NAS should have that diagnosis considered. Umbilical cords can be stored at the delivery hospital for fourteen days and the cords of infants who develop signs can easily be sent for testing by contacting the delivery hospital.
9. Gabapentin (Neurontin) is a medication that is finding increased off-label use as a co-prescribed adjunct therapy in mothers treated with methadone or buprenorphine. In addition, there are reports of illicitly obtained gabapentin used in conjunction with illicit opiates; it may potentiate the 'high' from the opiate. Infants exposed to both gabapentin and opiates have been reported to have a prolonged withdrawal course with an atypical response to routine opiate treatment. There are some reports of use of gabapentin in the infants to decrease signs but information on dosing and treatment protocols in the literature is highly limited and clinicians should proceed with extreme caution.
10. Eat Sleep Console (ESC) has gained popularity in management of NAS, and certain research studies are underway nationwide. While there is no formal scoring tool, Community has developed an ESC scale that can be also used for weaning pharmacologic treatment of NAS of an infant in the NICU. For further questions on introducing this option in your NICU, you can contact [Suyog Kamatkar, MD](#).

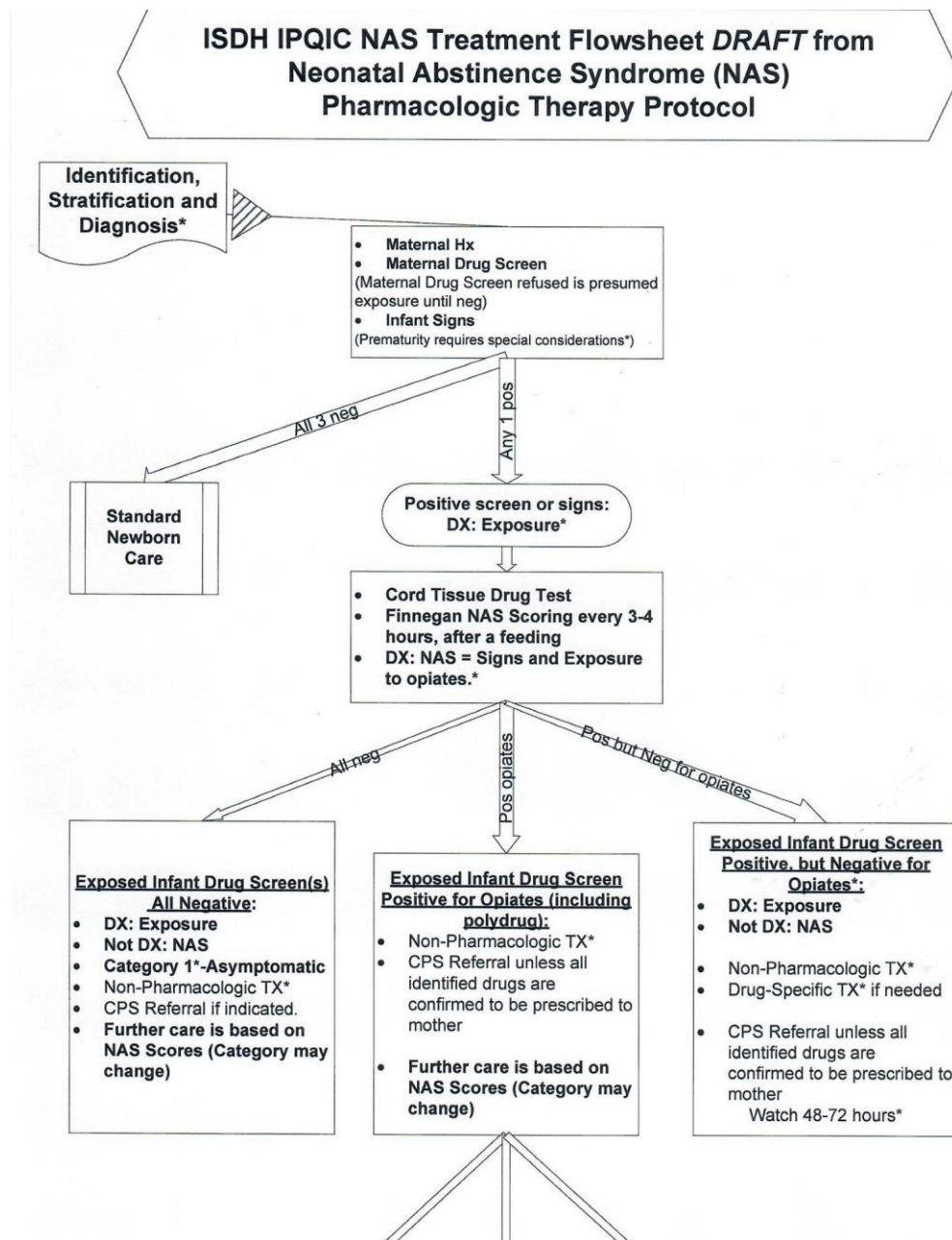
11. In certain specific populations, SL Buprenorphine is a viable option for treating NAS. If the pregnant woman was in a Subutex MAT and the fetal exposure is only to subutex, then such an infant will benefit from receiving buprenorphine for their pharmacologic management of NAS. In the right setting, this has been shown to be more effective than either methadone (1. J Wiles, J Peds 2015) or morphine (2. W Kraft, NEJM 2017). Buprenorphine solution has to be administered sublingually and will need a special formulation. CHE NICU in Indianapolis has been safely using this since 2017. For further questions on introducing this option in your NICU, you can contact [Suyog Kamatkar, MD](#).

1. *Hall ES, Isemann BT, Wexelblatt SL, et al. A Cohort Comparison of Buprenorphine versus Methadone Treatment for Neonatal Abstinence Syndrome. J Pediatr. 2016;170:39-44.e1. doi:10.1016/j.jpeds.2015.11.039*
2. *Kraft WK, Adeniyi-Jones SC, Chervoneva I, et al. Buprenorphine for the Treatment of the Neonatal Abstinence Syndrome. N Engl J Med. 2017;376(24):2341-2348. doi:10.1056/NEJMoa1614835"*

NAS Pharmacologic Therapy Protocol:

The full protocol is organized by the steps outlined in the summary above and discusses each in more detail. The protocol closes with a list of references.

Step 1: Identify an infant at risk for NAS.



The NAS risk management algorithm identifies infants at risk for NAS as infants who have a positive maternal toxicology test, have a positive maternal verbal screen, or whose mothers have refused a toxicology test. An umbilical cord drug screen should be sent for all at-risk infants.

The AAP recommends a minimum 72-hour hospitalization for at-risk infants to observe for signs of withdrawal. (SAMHSA is recommending 4 days.) Due to third party payer requirements or a parental request for discharge, however, extended monitoring beyond 48 hours may not be possible. In such cases, an early follow-up visit with the infant's PCP and close telephone follow-up by the discharging hospital are recommended. It is also recommended by the AAP that the observation period be extended to 5 to 7 days for infants with a cord drug screen positive for certain substances (but not all) or for infants at significant risk for increased withdrawal signs based on clinical judgment (for example, if the mother is taking opiates with a long half-life like methadone or buprenorphine or extended-release opiates like Oxycontin.)

Step 2: Begin non-pharmacologic therapy.

Non-pharmacologic therapy and Finnegan (FNASS) scoring should be begun on all at-risk infants. There is evidence that early implementation of non-pharmacologic therapy will reduce the number of infants going on to require pharmacologic therapy. There is also evidence that extended rooming-in by the parents with education of the parents in non-pharmacologic treatment methods may also reduce the need for pharmacologic therapy and shorten the length of stay.

Infants with mild withdrawal signs from non-opiate medications (for example, SSRI or SSNI medications used for maternal anxiety or depression disorders) frequently respond well to these care measures and require no further intervention.

Step 3: Diagnosis of NAS.

An infant is diagnosed with NAS (Neonatal abstinence syndrome: ICD-10 code P96.1) if they have:

- a. Signs, AND
- b. A positive infant toxicology test OR a maternal history with either a positive verbal screen or a positive maternal toxicology test for opiates.

NAS scoring should be performed after feedings but no less often than every four hours. NAS scoring is dependent on the clinical skills and training of staff performing the scoring. The reliability and reproducibility of the scoring results are critical to the use of the protocol. Careful attention should be paid to staff education.

Step 4: Assign withdrawal category.

Based on clinical exam, Finnegan scoring, and clinical course an infant is assigned to one of four categories. Each institution needs to evaluate their capabilities to provide the care required by each category and recognize that some infants may require transfer to a nursery or NICU providing a higher level of care depending on their treatment requirements under this protocol.

- **Category 1: No clinical withdrawal.**

Infants who are at-risk for NAS but do not develop withdrawal signs. These infants should not be coded as NAS (see p. 4 for ICD-10 coding recommendations) but as exposed infants and are at risk for NAS. These infants require a minimum of 72 hours of hospitalization for observation for withdrawal signs and many will require 5 to 7 days of hospitalization. Transfer should be considered if the birth hospital cannot provide an extended hospitalization with rooming in for the mother. These at-risk infants and their mothers will require specialized discharge planning (See step 6.)

- **Category 2: Mild neonatal abstinence syndrome.**

Infants in category 2 have mild signs of NAS from maternal opiate exposure and do not require pharmacologic therapy. These infants respond to non-pharmacologic therapy and may be cared for in a level 1 nursery. These infants may be discharged at 72 hours of age if there is no other medical indication for extended hospitalization for mother or infant and NAS scores are 7 or less. Discharge recommendations discussed below (Step 7) should be followed.

The hospitalization should be extended to 5 to 7 days with a positive cord drug screen for opiates or for infants otherwise felt to be at significant risk for increased withdrawal signs based on clinical judgment (for example, if NAS scores are slowly increasing or if the mother is taking opiates with a long half-life like methadone or buprenorphine or extended-release opiates like OxyContin.) The hospitalization may also be extended if there are concerns unable to be addressed timely regarding the family or home situation and further evaluation is required to identify a safe environment for the infant after discharge. Transfer should be considered if the birth hospital cannot provide an extended hospitalization with rooming in for the mother. These at-risk infants and their mothers will require specialized discharge planning (See step 6.)

- **Category 3: Moderate withdrawal.**

Infants in category 3 are infants with NAS who have failed to respond sufficiently to non-pharmacologic treatment. Pharmacologic treatment of NAS should be considered

for 2 consecutive Finnegan scores ≥ 8 or any single score ≥ 12 in an infant receiving non-pharmacologic therapy. Treatment should be started at once for 2 or 3 consecutive scores totaling ≥ 24 or any single score ≥ 15 .

Based on current literature, morphine or methadone should be considered for first-line pharmacologic therapy for infants of mothers using prescription or illicit opiates. While regarded as equally valid treatment options, use of morphine is simpler and does allow use of a prn dosing schedule in milder cases of NAS (where methadone does not.) Dosing advancement and subsequent weaning if higher doses are required to control signs are also more difficult with methadone unless your institution has considerable experience with its use. However, there is some evidence that use of methadone (especially using a pharmacokinetic-based regimen) may result in shorter lengths of stay. It is strongly recommended that an institution select either morphine or methadone (but not both) as their treatment of choice for NAS. There is insufficient evidence to recommend other medications such as clonidine or buprenorphine for first line therapy at this time.

Therapeutic opiates alone or in conjunction with other pharmacologic agents can cause significant apnea. Infants treated with opiate therapy may have a prolonged hospital course, may have significant gastrointestinal signs and feeding issues, and are also at increased risk of complications of NAS such as fever or seizures. Continuous cardiopulmonary monitoring is indicated for these infants, especially early in treatment while doses are being increased rapidly. The treating institution should have policies, procedures, and staff in place to permit 24/7 management of apnea or hypotensive events in these infants. Monitoring is recommended until opiates have been significantly weaned or until discharge. Consideration should be given for transfer of infants requiring pharmacologic treatment to a higher level of care if these conditions cannot be met. Recommendations for initial pharmacologic treatment, dose adjustment to control signs, and weaning from medications follow later in this protocol.

Most Category 3 infants should be hospitalized until stable for 48 to 72 hours off opioid therapy and NAS scores are 7 or less (possibly higher depending on days since delivery: “treat the baby, not the number”). Selected infants and families may be considered for early discharge with the last part of the weaning schedule performed at home. (This is likely to be the exception rather than the rule.) Discharge recommendations discussed below (Step 6) should be followed.

- **Category 4: Severe or complex withdrawal.**

These are infants with NAS who are failing standard pharmacologic therapy or any infants who have had seizure activity that is thought to be due to withdrawal. Any infant who needs high-dose opiate therapy or a second medication for adequate control of signs of NAS should also be considered a Category 4 patient. Data on combination therapy is limited and should be undertaken only by experienced clinicians.

Failure of standard pharmacologic therapy during initiation and dose advancement to control signs is defined as a daily regimen (including rescue doses) in excess of 0.2 mg/kg/dose of morphine q3h or 0.1 mg/kg/dose of methadone q6h, persistent fever on therapy with no other etiology, severe GI signs refractory to therapy, or persistent growth failure.

Failure of standard pharmacologic therapy during dose weaning is defined as intolerance to a specific dose wean after 2 or 3 attempts, as evidenced by worsening signs of withdrawal and rising Finnegan scores. Category 4 patients will benefit from care by clinicians and staff with extensive experience in managing NAS. Transfer of these infants to a level 3 or 4 NICU is strongly recommended.

Category 4 infants should be hospitalized until stable for 48 to 72 hours off therapy and NAS scores are 7 or less (possibly higher depending on days since delivery: “treat the baby, not the number”). Due to the severity of their illness, they are generally not candidates for early discharge. Discharge recommendations discussed below (Step 6) should be followed.

Step 5: Pharmacologic management recommendations.

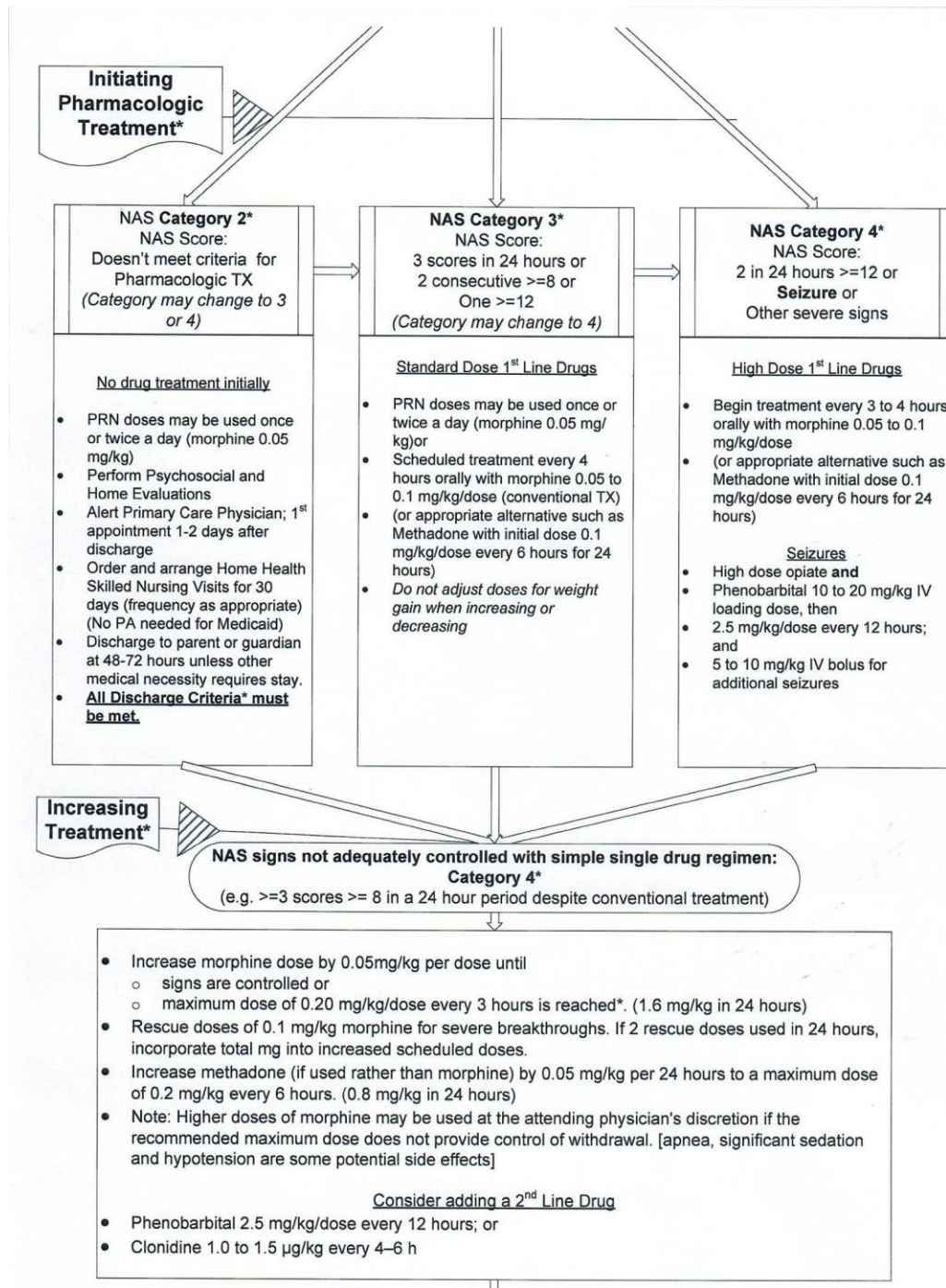
A number of management recommendations were made under the category descriptions in Step 4. Recommendations for pharmacologic management are listed below. Infants on pharmacologic therapy should receive NAS scoring every 3 to 4 hours (and every 3 hours if on q3h morphine dosing.)

Begin treatment.

The clinician should begin treatment by selecting PRN or scheduled initial treatment for NAS. This is a clinical decision that should be based on the severity of the infant’s signs, responses to any previous therapy at a referral hospital, and the medication or medications the infant was exposed to *in utero*.

Category 3 infants with NAS may be considered for initial treatment with PRN dosing of morphine if they do not present with complications (fever, seizures, or severe GI signs) indicating very severe withdrawal and may be continued on PRN therapy if they show a

good response to initial PRN morphine treatment doses. In conjunction with non-pharmacologic therapy, many Category 3 infants may be managed successfully through discharge with a PRN dosing schedule and will have a shorter course of hospitalization than infants requiring scheduled dosing. Infants started on PRN dosing schedules require careful clinical monitoring to determine if they may require a change to scheduled dosing.



Category 4 infants should always be managed with scheduled dosing of morphine or methadone.

Initial treatment for significant non-opioid withdrawal and in infants with NAS who have seizure activity is also listed below.

Notes:

- The clinician should be aware that recommendations for PRN dosing schedules are not data-driven but are drawn from extensive clinical experience; they should always be interpreted after careful consideration of the individual patient. If in any doubt, begin with scheduled dosing.
- Methadone is not recommended for use in a PRN treatment schedule and no PRN schedule is given.
- All medications below may be given orally (with the exception of the phenobarbital loading dose and bolus doses for seizure activity which should be given IV if possible and any infant actively seizing.)
 - Recommended initial PRN treatment for opioid withdrawal: Morphine 0.05 - 0.1 mg/kg/dose q3h PRN 2 consecutive NAS scores ≥ 8 or any score ≥ 12 .
 - Recommended initial scheduled treatment for opioid withdrawal:
 - Morphine 0.05 - 0.1 mg/kg/dose q3h or q4h OR Methadone 0.1 mg/kg/dose 6h (in general, use q6h methadone dosing for only 24 hours; use dosing schedule from p. 13. The schedule is based on methadone pharmacokinetics and is designed to reach therapeutic levels rapidly.)
 - Recommended initial treatment for non-opioid withdrawal:
 - Clonidine 1 mcg/kg/dose q6h (in the second week of life, begin at 1.5 mcg/kg/dose q6h and may consider q4h dosing if signs are severe); OR
 - Phenobarbital 2.5 mg/kg/dose q12h (a loading dose is not necessary)

Note: It is possible that clonidine may be more effective in this role but there is more clinical experience with phenobarbital.
- Seizures: Seizures will be difficult to control unless the withdrawal is adequately treated. Scheduled treatment with morphine or methadone should be started immediately in conjunction with treatment of seizures. (See recommendations above.) Evaluation of infant for other possible causes of seizure activity is strongly recommended as well.
 - Seizures in infants with NAS should be managed with phenobarbital as usual (10 to 20 mg/kg initial loading dose with a maintenance dose of 2.5

mg/kg/dose q12h. Additional seizures may be treated with 5 to 10 mg/kg boluses until controlled.)

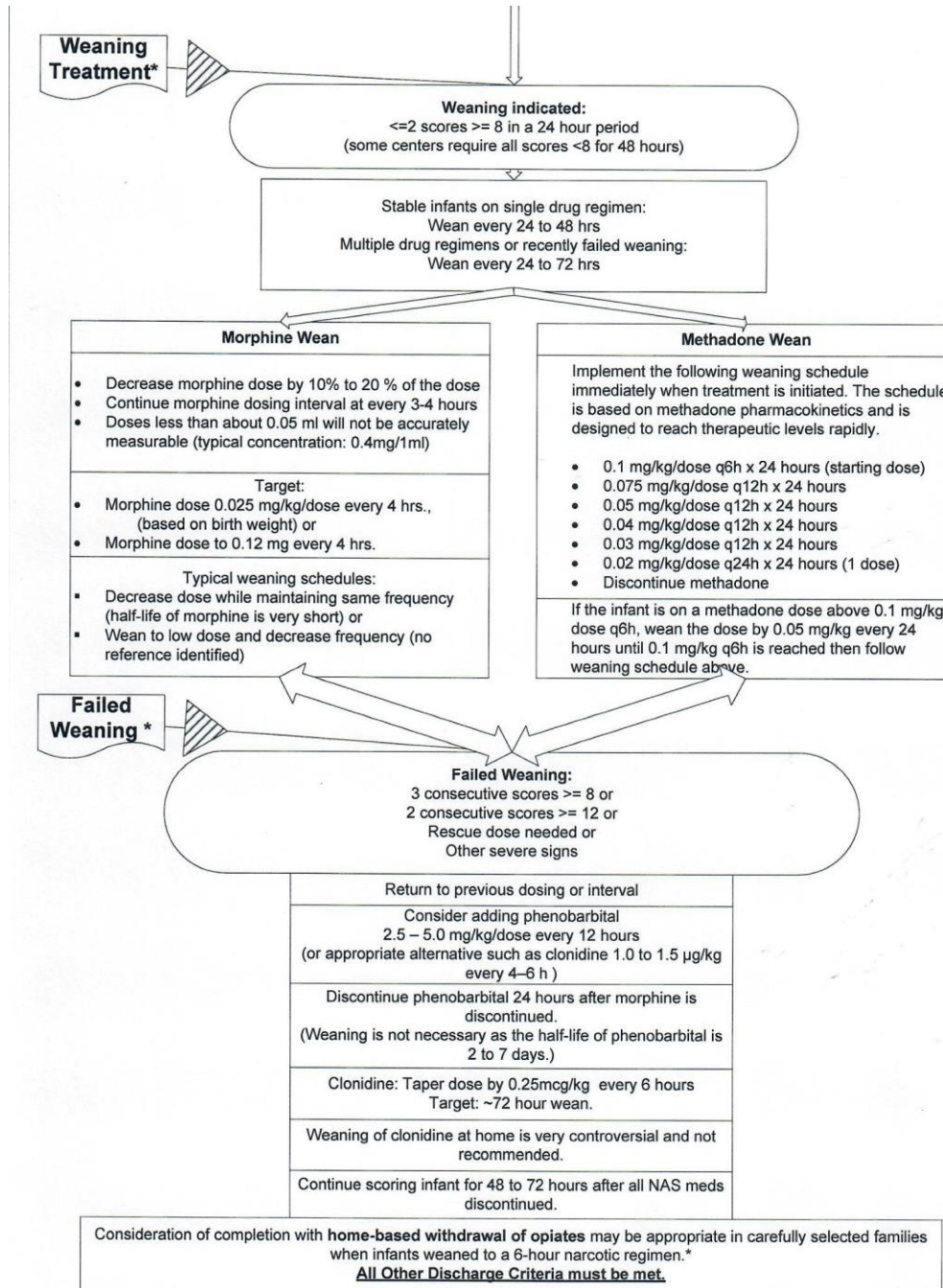
- Increase doses until signs are controlled.
- If treating with a PRN schedule:
 - If started on 0.05 mg/kg dosing, increase morphine dose to 0.1 mg/kg for repeated scores ≥ 8 . Consider starting a scheduled dosing regimen if more than 3 PRN doses are required in the first 24 hours or if 2 or more PRN doses are subsequently required on back-to-back days. If signs are controlled on a PRN schedule, move to the weaning section of the protocol after the infant is stable for 48 hours.
- If using scheduled morphine:
 - Increase morphine doses by 0.05 mg/kg/dose for 2 consecutive NAS scores ≥ 8 or any single NAS score ≥ 12 until signs are controlled. If the interval is q4h or q6h, consider decreasing interval to q3h before increasing dose.
 - Rescue doses (0.1 mg/kg/dose) may be given for severe breakthrough signs occurring in between scheduled doses. Severe breakthrough signs are defined as a total of 2 or 3 consecutive NAS scores ≥ 24 including the current score or a significant change in clinical status (seizure, disrupted sleep pattern, marked change in GI status, worsening of neurological exam, fever.)
 - If a rescue dose is required, consider increasing the current maintenance dose as well. The maintenance dose should always be increased if two rescue doses are required in a 24-hour period.
 - If the total daily dose of morphine is greater than 1.6 mg/kg/day, the infant is considered to have failed standard pharmacologic therapy and is now a Category 3 withdrawal patient. Addition of clonidine (1 mcg/kg/dose q6h) or phenobarbital (2.5 mg/kg/dose q12h) is recommended. High-dose morphine therapy may be considered but total daily doses above 1.6 mg/kg/day may produce significant sedation or hypotension in some patients and should be used with caution. A maximum total daily dose of 2.3 mg/kg/day is recommended.
- If using scheduled methadone:
 - Methadone should bring signs under control with 24 hours of initiation. See recommended dosing schedule on p. 15.
 - Rescue doses (0.1 mg/kg/dose) of morphine may be given for severe breakthrough signs occurring in between scheduled doses. Severe breakthrough signs are defined as a total of 2 or 3

consecutive NAS scores ≥ 24 including the current score or a significant change in clinical status (seizure, disrupted sleep pattern, marked change in GI status, worsening of neurological exam, fever.)

- Higher methadone doses may be considered on the second day for 2 consecutive NAS scores ≥ 8 or any single NAS score ≥ 12 until signs are controlled. The dose should be increased by no more than 0.05 mg/kg/dose in a 24-hour period; a maximum dose of 0.2 mg/kg/dose q6h is recommended. Doses above 0.1 mg/kg/dose q6h may produce significant sedation or hypotension in some patients and should be used with caution.
- As an alternative, addition of clonidine (1 mcg/kg/dose q6h) or phenobarbital (2.5 mg/kg per dose q12h) for 2 consecutive NAS scores ≥ 8 or any single NAS score ≥ 12 may be considered if signs are not controlled in an infant who has been on a methadone dose of 0.1 mg/kg/dose q6h for more than 24 hours. If the total daily dose of methadone is greater than 0.1 mg/kg q6h or if the infant requires clonidine or phenobarbital, the infant is considered to have failed standard pharmacologic therapy and is now a Category 4 withdrawal patient.
- If using clonidine or phenobarbital alone or in conjunction with an opiate:
 - Clonidine may be increased by 0.05 mcg/kg/dose every 12 to 24 hours for 2 consecutive NAS scores ≥ 8 or any single NAS score ≥ 12 . The usual required maintenance dose is 3 to 5 mcg/kg/day.
 - Phenobarbital may be managed in a similar way to its use in seizures, with 5 mg/kg boluses and small increases in the maintenance dose. There are no good guidelines for therapeutic phenobarbital levels in NAS.
 - Note: Always increase the opiate dose as the first choice in combination therapy until a maximum standard dose of the opiate is reached. After that point, use clinical judgment in selecting the medication to increase. Again, note that it is uncommon to need pharmacologic treatment for non-opiate withdrawal and rare to have difficulty in controlling signs with clonidine or phenobarbital. Consideration should be given in such cases to the possibility of unreported maternal opiate use, and an empiric trial of an opiate may be of benefit.

Wean from pharmacologic treatment when signs of NAS are controlled.

Begin weaning from pharmacologic therapy once an infant has been stable on the current dose for 48 hours without a rescue dose. (This does not apply to methadone; see below.) ***It is important to recognize that an infant will not be sign-free during the weaning process and some mildly elevated scores are to be expected.*** The need for a rescue dose is a good guideline for whether or not an infant is tolerating the scheduled wean; as always, the clinician should use their own judgment in individual patients.



In general, infants with NAS should be hospitalized until stable for 48 to 72 hours off opioid therapy and NAS scores are 7 or less (possibly higher depending on days since delivery: “treat the baby, not the number”). Selected infants and families may be considered for early discharge with the last part of the opiate weaning schedule performed at home. (This is likely to be the exception rather than the rule.) Discharge recommendations discussed below (Step 7) should be followed.

If using PRN morphine:

- Infants still on PRN dosing should be receiving no more than 1 or 2 doses daily. Most of these infants will ‘self-wean’ over a few days, gradually requiring fewer and fewer doses. Infants should be observed in the hospital for at least 72 hours after the last dose of morphine on a prn schedule before considering discharge.
- Infants who prove slow to self-wean may benefit from being changed to a scheduled morphine dose and weaned under the guidelines in that section; these infants may tolerate a faster wean than the 10 to 20% of the maximum required dose recommended in those guidelines.

Note: These are suggested guidelines; there is little available data on PRN withdrawal schedules. Use clinical judgment in individual patients.

If using scheduled morphine:

- Wean the morphine dose by 10-15% of the maximum required daily dose every 24 hours as long as rescue doses are not required in the previous 24 hours. Infants with severe initial withdrawal signs frequently will not tolerate initial weans greater than 10% and may need smaller or less frequent steps. Higher percentage dosage weaning should only be used if Finnegan scores remain very low (0-3) or near the end of the morphine wean.
- Rescue doses may be given for severe breakthrough signs occurring in between scheduled doses. Severe breakthrough signs are defined as a total of 2 or 3 consecutive NAS scores totaling ≥ 24 including the current score or a significant change in clinical status (seizure, disrupted sleep pattern, marked change in GI status, worsening of neurological exam, fever.)
- During the weaning schedule, if a rescue dose is required use a dosage equal to the current maintenance dose and do not change the maintenance dose on the following day. Also, consider skipping a weaning day for a significant worsening of the infant’s neurological exam or a marked change in feeding or sleep pattern.
- Weaning schedules commonly used include continuing a regular schedule but decreasing the dose based on the short half-life of morphine or achieving a low dose and lengthening the interval.

- Failure of standard pharmacologic therapy during dose weaning is defined as a failure to tolerate a specific dose wean after 2 or 3 attempts, as evidenced by worsening signs of withdrawal and rising Finnegan scores. Addition of clonidine (1 mcg/kg/dose q6h) or phenobarbital (2.5 mg/kg/dose q12h) may be considered to facilitate weaning. Transfer to a higher level of care may be required.

If using methadone:

- Implement the following weaning schedule immediately when treatment is initiated. The schedule is based on methadone pharmacokinetics and is designed to reach therapeutic levels rapidly.
 - 0.1 mg/kg/dose q6h x 24 hours (starting dose)
 - 0.075 mg/kg/dose q12h x 24 hours
 - 0.05 mg/kg/dose q12h x 24 hours
 - 0.04 mg/kg/dose q12h x 24 hours
 - 0.03 mg/kg/dose q12h x 24 hours
 - 0.02 mg/kg/dose q24h x 24 hours (1 dose)
- If the infant is on a methadone dose above 0.1 mg/kg/dose q6h, wean the dose by 0.05 mg/kg every 24 hours until 0.1 mg/kg q6h is reached then follow weaning schedule above.
- Rescue doses (0.1 mg/kg/dose) of morphine may be given for severe breakthrough signs occurring in between scheduled doses. Severe breakthrough signs are defined as a total of 2 or 3 consecutive NAS scores ≥ 24 including the current score or a significant change in clinical status (seizure, disrupted sleep pattern, marked change in GI status, worsening of neurological exam, fever.) Consideration should be given to holding the methadone wean for the next day.
- If a second rescue dose of morphine is needed within a 24-hour period during the weaning phase, an increase in the methadone dose to the previous day's dose and the schedule is recommended.
- Failure of standard pharmacologic therapy during dose weaning is defined as a failure to tolerate a specific dose wean after 2 or 3 attempts, as evidenced by worsening signs of withdrawal and rising Finnegan scores. Addition of clonidine (1 mcg/kg/dose q6h) or phenobarbital (2.5 mg/kg/dose q12h) may be considered to facilitate weaning. Transfer to a higher level of care may be required.
- Morphine or methadone plus clonidine:
 - Follow weaning instructions for morphine or methadone while continuing clonidine. Once off morphine or methadone for 48 hours, clonidine dose may be weaned by 25% every 48 hours until discontinued.
- Morphine or methadone plus phenobarbital:

- If phenobarbital was started as a second drug for NAS without seizure activity, follow weaning instructions for morphine or methadone while continuing phenobarbital. If the infant has not had seizures, once the infant is off morphine or methadone for 48 hours discontinue phenobarbital and allow the long half-life to wean the infant off phenobarbital. Consideration should be given to completing the phenobarbital wean after discharge.
- An infant with seizures from withdrawal who required phenobarbital during initial treatment should be able to have the phenobarbital discontinued once adequate control of other signs of withdrawal is achieved and the evaluation for other possible etiologies of the seizures is negative. The long half-life of phenobarbital will result in a slow wean for the patient and the seizures are unlikely to recur. If they do, resume phenobarbital for the treatment of the seizures and obtain a neurology consultation.

Step 6: Discharge planning.

All at-risk infants should receive specialized discharge planning (insert weblink) to include early social service evaluation of family and home situation, DCS referral as appropriate, home health nursing visits after discharge, maternal referral for behavioral support services as indicated, and other family services as indicated. Parents should be educated in neonatal signs and worsening NAS and indications to seek medical attention. An appointment for follow-up medical care for the infant within 48 to 72 hours should be scheduled prior to discharge. The future infant care provider should be involved prior to discharge, fully informed of all discharge recommendations, and should also be contacted by social services or DCS to verify that the infant has appeared at the initial follow-up appointment. Releases of information from the guardian for exchange of information of care providers with DCS may prove necessary to understand the services being provided and any restrictions that apply.

Discharge Protocol*

DISCHARGE CRITERIA:

(Discharge Planning begins at admission*)

(Please see Medical Home documents for infant and mother.*)

- Written Discharge Plan and education understood and agreed upon by all parties including PMP
- PMP appointment at 48-72 hours post-discharge confirmed and transportation and childcare for the visit addressed
- Home Health Skilled Nursing Visits arranged for first 30 days starting 24 to 48 hours post-discharge
[Home Health Care SNV,PT,OT do not need PA under Medicaid for 30 days (30 visits each discipline) if an order is in the chart at discharge]
- Mother's Medical Home and support services planning complete
- Withdrawal symptoms minimal or resolved (All NAS Scores ≤ 8 for 48 hours; perhaps higher if the infant is older)
- Caregiver education and training complete
- Outpatient non-pharmacologic and pharmacologic treatment of NAS arranged or not needed
- Breastfeeding is usually encouraged*
- Other medical issues adequately addressed
- Psychosocial and Home Evaluations completed and satisfactory
- Social Work and Child Protective Services disposition and interventions established
- Discharge planning completed

NEW ICD-10 CODES

(Changes will go into affect 10/01/2018)

- **P96.1:** Neonatal withdrawal symptoms from maternal use of drugs of addiction (NAS)
 - <https://www.icd10data.com/ICD10CM/Codes/P00-P96/P90-P96/P96-/P96.1>
- **P04.4:** Newborn (suspected to be) affected by maternal use of drugs of addiction (this code divides into two others depending on the substance- **it is not billable; use .41 or .49**)
 - <https://www.icd10data.com/ICD10CM/Codes/P00-P96/P00-P04/P04-/P04.4>
 - **P04.41:** Newborn (suspected to be) affected by maternal use of cocaine
 - <https://www.icd10data.com/ICD10CM/Codes/P00-P96/P00-P04/P04-/P04.41>
 - **P04.49:** Newborn (suspected to be) affected by maternal use of other drugs of addiction
 - <https://www.icd10data.com/ICD10CM/Codes/P00-P96/P00-P04/P04-/P04.49>
- **Q86.0:** Fetal Alcohol Syndrome (dysmorphic)
 - <https://www.icd10data.com/ICD10CM/Codes/Q00-Q99/Q80-Q89/Q86-/Q86.0>
- **P04.3:** Newborn (suspected to be) affected by maternal use of alcohol (excludes fetal alcohol syndrome)
 - <https://www.icd10data.com/ICD10CM/Codes/P00-P96/P00-P04/P04-/P04.3>

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