

# Neonatal Abstinence Syndrome and Neonates Exposed to Maternal Drug Misuse or Prescribed Medications in Pregnancy (includes anti-depressants) - Neonatal Full Clinical Guideline

*Joint Derby & Burton & Derby Maternity*

Reference no.: NIC NE 09

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## 1. INTRODUCTION & SCOPE

### *Background*

Babies born to mothers who use illicit drugs, alcohol and/or certain prescribed medications during pregnancy are at risk of problems both in the early neonatal period, and later in life. These guidelines outline the principles for the management of infants born to these mothers and provide information regarding monitoring and treatment of affected babies, as well as important social considerations in infants of maternal illicit drug/alcohol misuse. [1,2]

Mental health disorders including depression are a common occurrence with an estimated lifetime prevalence of 16.2%.[3] The most common treatment for depression is currently Selective Serotonin Reuptake Inhibitors (SSRIs), which have been linked to Neonatal Abstinence Syndrome within the infant [4] with up to 30% of exposed infants showing symptoms. The other common medications used include Serotonin and Noradrenaline Re-uptake Inhibitors (SNRI's), Tricyclic Antidepressants (TCA's) and antipsychotic medications (both 'typical and 'atypical'.) In these instances neonatal withdrawal syndrome occurs due to a sudden discontinuation of the drug being supplied to the infant after the cord has been clamped.

There is debatable evidence to suggest a link between the use of SSRI's during pregnancy and congenital malformations in the infant although the overall risk is very low;[3] some evidence suggests an association between first trimester use of some SSRIs (notably, paroxetine and fluoxetine) and congenital abnormalities that may include congenital heart defects( particularly right ventricular outflow malformations)[, omphalocele, and anencephaly.[5,6] It is therefore important for regular antenatal care for mothers on such medications, with a detailed assessment as part of the Newborn Physical Examination once the infant has delivered.

### Scope

The following substances and medications are covered by the scope of this guideline:

- **Drugs of abuse** as referenced in *Table 2*,
- **Prescribed medications** as referenced in *Table 4* including anti-depressant, antipsychotic and anti-epileptic medications/mood stabilizers.

## 2. PURPOSE AND OUTCOMES

The purpose of this policy is to rationalize and formalize the care available to infants who have been exposed in utero to illicit drugs, alcohol or high-risk prescribed medications, and to reduce the number of associated complications.

## 3. ABBREVIATIONS

AED	-	Anti-Epileptic Drugs
BBV	-	Blood Borne Viruses
CNS	-	Central Nervous System
CYPD	-	Child and Young Persons Department (Social Services)
IVDU	-	Intravenous Drug Use
NAS	-	Neonatal Abstinence Syndrome (Neonatal Withdrawal Syndrome)
NEWS	-	Neonatal Early Warning score
NICU	-	Neonatal Intensive Care Unit
NIPE	-	Newborn and Infant Physical Examination
PPHN	-	Persistent Pulmonary Hypertension of the Newborn
SGA	-	Small for Gestational Age
SNRI	-	Serotonin and Noradrenaline Reuptake Inhibitor
SSRI	-	Selective Serotonin Reuptake Inhibitor
TCA	-	Tricyclic Antidepressant

**4. Table 1: QUICK GUIDE to Maternal Prescribed Medications and Illicit Substance Misuse**

<p><b>FOR ALL BABIES:</b></p> <ul style="list-style-type: none"> <li>- Ensure NIPE within first 24h</li> <li>- Review antenatal care plan, maternal medication/substance use and detox plan             <ul style="list-style-type: none"> <li>- Review safeguarding issues and discharge plan – is a DPM needed?</li> </ul> </li> </ul>						
Drug Class	Examples	Withdrawal symptoms	Red flags /important considerations	Safe to breastfeed?	Specific management	Duration of observation
<b>Opiates</b>	Morphine/Oramorph Codeine Oxycodone	Common as per NAS symptoms		Yes <b>except codeine and oxycodone</b>	If severe may need morphine sulphate	24 hours
	Methadone	Common as per NAS symptoms	Review maternal serology (if IVDU)	Yes at lowest possible dose	If severe may need morphine sulphate	5 days minimum
	Heroin	Common as per NAS symptoms	Review maternal serology (if IVDU)  Safeguarding plan?	<b>No if active illicit drug use</b> Yes if used during pregnancy, maternal blood borne viral serology negative & drug use now controlled.	If severe may need morphine sulphate	24 hours
<b>Cannabis/cannabinoids</b>		None	Safeguarding plan?	Yes		None
<b>Stimulants</b>	Cocaine/crack cocaine	Do not withdraw but may be irritable/unsettled	<b>Possibility of intracranial lesions</b>  Review maternal serology (if IVDU)  Safeguarding plan?	<b>No</b>	CrUSS if preterm OR OFC <10 <sup>th</sup> c OR abnormal neurology OR seizures	48 hours (after last consumption)  (if not consumed in 48h pre delivery, none)
	Amphetamines Ecstasy Mamba	Non-specific	Safeguarding plan?	<b>No</b>		48 hours (after last consumption) (if not consumed in 48h pre birth, none)

<b>Antidepressants</b>						
<b>SSRI</b>	Citalopram Fluoxetine Sertraline	Poor adaptation Resp, CNS, motor, GI – within 8-48h	Possibility of PPHN	Yes <b>except doxepin</b>		24 hours minimum
<b>SNRI</b>	Venlafaxine Doxepin Mirtazapine					24 hours minimum
<b>TCA</b>	Amitriptyline Nortriptyline	CNS, resp, endocrine, metabolic disturbances within 8-48h		Yes		24 hours minimum
<b>Lithium</b>	Lithium carbonate Lithium citrate	Lethargy, hypotonia, hypothyroidism, hypoglycaemia	Possibility of cardiac defects (Ebstein anomaly) need Echo  Need glucose monitoring	<b>No</b>		48 hours minimum
<b>Antipsychotics</b> - <b>1<sup>st</sup> &amp; 2<sup>nd</sup> generation</b>	<u>1<sup>st</sup></u> : Haloperidol, Chlorpromazine, Promethazine  <u>2<sup>nd</sup></u> : Clozapine, Quetiapine, Olanzapine, Risperidone	Extrapyramidal: abnormal movements, tremor, dystonia, agitation, sedation		Yes <b>except</b> <b>clozapine</b>  (antipsychotics <i>do</i> pass into breastmilk but in small amounts)		24 hours minimum  24 hours minimum
<b>Antiepileptics</b>	Sodium valproate Phenytoin Lamotrigine Carbamazepine Topiramate	CNS depression, poor feeding, sedation, inconsolable cry	Congenital malformations (NB NIPE)  Haemorrhagic disease of newborn	<b>Check individual</b> <b>plan</b> – most <i>are</i> safe for breastfeeding	IM Vitamin K	As per individual plan (24 hours minimum)
	Perampanel	Unknown – possibly drowsiness, poor feeding, poor weight gain	<i>Unknown</i>	<b>No</b> <i>Limited evidence</i> <i>available but studies</i>	IM Vitamin K	As per individual plan (24 hours minimum)

				<i>suggest present in breastmilk</i>		
<b>Benzodiazepines</b>	Long acting: Diazepam, Clobazam Clonazepam Shorter acting: Lorazepam Temazepam	CNS depression, hypothermia, lethargy, poor feeding, respiratory depression (may be weeks after birth)	Safety net – likely to present post discharge	Yes with short acting  <b>avoid longer acting in breastfeeding</b>		Dependent on regime – see individual plan (24 hours minimum)
<b>Hypnotics</b>	Zopiclone, Zolpidem	None		Yes; <b>no data for zopiclone</b>		None
<b>Anxiolytics</b>	Propranolol	Bradycardia, hypotension, hypoglycaemia	Glucose monitoring	Yes		Until blood sugars are stable
<b>Polypharmacy</b>	Opioids Antipsychotics Gabapentin Pregabalin	Mixed	HIGH RISK WITHDRAWAL (60%)	<b>Avoid</b>		5 days

## 5. DRUGS OF ABUSE

### 5.1 Commonly abused drugs

These may include:

Table 1: Commonly abused drugs	
Opiates (heroin, methadone, oramorph, fentanyl, codeine, tramadol) Cannabis & synthetic cannabinoids Cocaine & crack cocaine Amphetamines Ecstasy/MDMA LSD (uncommon) and hallucinogenics	Ketamine (increasing use amongst young people) Benzodiazepines (temazepam, diazepam) Barbiturates (rarely) Legal highs Alcohol

### 5.2 Effects of maternal drug abuse on the fetus and newborn infant

Table 2: Effects on the fetus and newborn infant of maternal drugs of abuse [1,7,8]		
Drug	Possible Effect(s) on Fetus	Possible Effect(s) on Baby
Cannabis,	No significant harmful effects in the fetal/newborn period other than possible low birth weight due to tobacco	
LSD and magic mushrooms	No significant effect on fetus	
Alcohol	Fetal Alcohol syndrome and fetal alcohol spectrum disorders	
Amphetamines and Ecstasy	Small for dates; <b>increased risk of cleft palate and heart defects</b>	
Cocaine (crack cocaine may have less side effects than cocaine)	Small for dates; <b>increased incidence of intracranial haemorrhage and ischaemic lesions</b>	Poor feeding and difficult to settle, high-pitched cry, tremors,irritability, hyperalertness, tachypnoea, excess suck*
Opiates (heroin, methadone)	Preterm and low birth weight	<b>Withdrawal</b> (see below)
Tranquillisers including benzodiazepines (diazepam “valium”, lorazepam, clobazam, temazepam)	1st trimester use increases <b>risk of cleft palate</b> ; Preterm and low birth weight	<b>Withdrawal</b> (see below) Benzodiazepines can cause hypothermia, hyperbilirubinaemia and CNS depression
Solvent abuse	Theoretical risk of reducing oxygen supply to infant	

\*NB cocaine related symptoms tend to occur during postnatal days 2-3 and are a direct effect of cocaine rather than withdrawal.

NB. Please remember the use of multiple drugs. In utero exposure to polypharmacy along with opioids is associated with a twofold increased risk of neonatal withdrawal.

### 5.3 Signs, symptoms and timings of Neonatal Abstinence Syndrome (withdrawal)

Drug groups most likely to cause this are **opiates/opioids**, **benzodiazepines** and **prescribed psychiatric medications**.

Neonatal Abstinence Syndrome is usually non-specific in nature and does not necessarily indicate a state of withdrawal of a particular drug of dependence.

**Any of the following, if present should prompt consideration of neonatal withdrawal syndrome:**

- Sleeplessness
- Restlessness/irritability
- Hyper-reflexia
- Sneezing/nasal stuffiness
- Tachycardia
- Tachypnoea (NB respiratory depression possible with opiate intoxication)
- Vomiting
- Diarrhoea
- Fever
- Sweating
- Fist sucking
- Yawning
- Tremors/jitteriness
- Convulsions

Table 3: Timing of opiate withdrawal symptoms (taken from Kocherlakota P. "Neonatal abstinence syndrome" <i>Pediatrics</i> 2014; 134(2)e547-61)			
Drug	Onset (hours)	Frequency (%)	Duration (days)
Heroin	24-48	40-80	8-10
Methadone	48-72	13-94	30 +
Opioid prescriptions ( <i>Tramadol</i> , <i>codeine</i> , <i>oramorph</i> )	36-72	5-20	10-30

A baby is more likely to develop withdrawal syndrome if the mother has been regularly taking drugs during the later stages of her pregnancy. However even intermittent use by the mother may result in physical dependence in the fetus. A baby may show signs of withdrawal even when the mother has not recently used opiates (if more than a month since last use withdrawal is highly unlikely in the neonate).

Heroin withdrawal symptoms characteristically begin soon after birth, reaching maximum intensity after 2-4 days and fading out by 10-14 days. Methadone withdrawal is more likely to present later and to produce symptoms and signs that extend over many weeks and months. [9] (Parents should be warned of this and advised to seek medical advice if severe withdrawal symptoms develop).

Benzodiazepine withdrawal can have a delayed onset (days-weeks) and may be protracted (usually appearing after the baby has been discharged home, and not in hospital.)

## 6. PRESCRIBED MATERNAL MEDICATIONS

### 6.1 Effects of prescribed maternal medications on the newborn

<i>Table 4: Prescribed Medications Affecting the Newborn Infant</i>	
<b>a. Anti-depressants:</b>	<ul style="list-style-type: none"><li>▪ <b>SSRIs</b> (Selective Serotonin Reuptake Inhibitors) - e.g. Citalopram, Fluoxetine, Sertraline, Paroxetine</li><li>▪ <b>SNRIs</b> (Serotonin and Noradrenaline Re-uptake Inhibitors) - e.g. Venlafaxine</li><li>▪ <b>TCAs</b> (Tricyclic Antidepressants) - e.g. Amitriptyline, Lofepamine, Nortriptyline</li></ul>
<b>b. Antipsychotics</b>	<ul style="list-style-type: none"><li>▪ <b>First Generation ('Typicals')</b> - e.g. Haloperidol, Chlorpromazine, Promethazine, Flupenthixol</li><li>▪ <b>Second Generation ('Atypicals')</b> - e.g. Clozapine, Quetiapine, Olanzapine, Risperidone</li></ul>
<b>c. Anti-Epileptic Medications/ Mood stabilizers</b>	<ul style="list-style-type: none"><li>▪ Sodium Valproate, Lamotrigine, Carbamazepine, Topiramate</li><li>▪ Lithium</li><li>▪ Gabapentin, Pregabalin</li></ul>
<b>d. Other medications that may cause withdrawal syndrome</b>	<ul style="list-style-type: none"><li>▪ Diphenhydramine (<i>Benadryl</i>®, <i>Nytol</i>®)</li><li>▪ Glutethimides (<i>Doriden</i>®, <i>Elodrom</i>®, <i>Glimid</i>®)</li><li>▪ Phencyclidine (PCP)</li><li>▪ Phenothiazines (chlorpromazine, promazine, levomepromazine, prochlorperazine)</li><li>▪ Theophylline</li></ul>

### 6.2 Maternal Anti-Depressants

Anti-depressants have a wide range of uses but are usually a prescribed medication (rather than a drug of abuse). They are used to treat depression, anxiety, panic attacks, obsessive-compulsive disorder and sometimes as pain relief.

**Use of SSRIs and SNRIs during pregnancy is associated with poor neonatal adaptation.** This has been reported in approximately 30% of infants of mothers treated with SSRIs in the last trimester. The symptoms normally persist for 3 days, but can last for up to 2 weeks. Symptoms include temperature instability, feeding difficulty, jitteriness, irritability and excessive crying, sleep problems, tremors, shivering, restlessness, and less commonly, hypoglycaemia, convulsions and rigidity.[4,10] There is also an increased risk of pulmonary hypertension in these babies [11-13] Normally, the pulmonary vascular resistance falls after birth; in PPHN, this does not occur and can lead to right-to-left shunting of the blood and subsequent hypoxaemia in the infant.

There are substantial differences in term of their half-life between fluoxetine and others SSRIs. The half-life of fluoxetine and its active metabolite norfluoxetine is respectively 2 to 4 days and 7 to 15 days, more extended than other SSRIs. Symptoms in babies exposed to SSRIs usually develop within 8-48 hours postpartum and fade within 72 hours,[14,15] and in babies exposed to SNRIs usually within 8-48 hours postpartum and fade within 72 hours.

**Tricyclic anti-depressants (TCAs)** are used for mood related disorders such as depression but can also be



used for migraine, panic-disorders, recurrent headaches, neuropathic pain and in certain cases as a sleep aid. The common side effects are central nervous system, respiratory, endocrine and metabolic disturbances. The symptoms in babies can develop within 8-48 hours postpartum and fade within 72 hours. [15]

### **6.3 Maternal Antipsychotics**

As outlined in *Table 4*, there are a number of classes of medications that are used to treat psychoactive disorders, such as schizophrenia, psychoses, mania and hypomania. First and second generation anti-psychotics can both cause extra-pyramidal symptoms (e.g. abnormal movements, hypertonia, tremor, dystonia, agitation and sedation. This can be assessed for by monitoring alertness, waking for feeds and sucking response (may be poor.))[15]

### **6.4 Maternal Anti-Epileptic Medications/Mood Stabilizers**

Epilepsy is one of the most common neurological conditions in pregnancy with a prevalence of 0.5-1%7. Infants born to mothers taking anti-epileptic drugs (AEDs) are 3.5 times more likely to be small-for-gestational-age (SGA) than babies born to mothers with epilepsy who are not taking AEDs.[16]

The risk of congenital malformations in the fetus is increased in women with epilepsy taking AEDs. This risk is greatest in those taking sodium valproate or AED polytherapy.[17] Risk is lower in lamotrigine or carbamazepine monotherapy.[18] This should be taken into consideration when performing the Newborn and Infant Physical Examination (NIPE).

Rates of transfer of AEDs to the neonate across the placenta and in breast milk vary. Babies born to mothers taking AEDs can have withdrawal symptoms such as lethargy, difficulty feeding, excessive sedation, jitteriness, irritability and inconsolable crying, as well as tachypnoea and abnormalities of muscle tone. Less commonly there may be hypoglycaemia or convulsions. These symptoms are usually present within a few hours of birth, are mild and self-limiting and resolve within a few weeks, although symptoms may be severe in up to 10% of newborns. Women taking AEDs during pregnancy should have had an individual assessment antenatally for the level of post-natal monitoring required for their infant. [19] Where there are concerns about toxicity in the infant serum levels of the AEDs should be checked.[20] There is no standard duration of observation for infants exposed to AEDs in utero; this should be decided based on the AED regime taken during pregnancy.

NICE guidance is that breastfeeding is generally safe for women taking AEDs. Pharmacy can be consulted for individual cases if necessary. Mothers should be counselled on the risks and benefits of breastfeeding against the potential risks of the AED affecting the child. [21]

**AEDs and increased risk of haematological disorders in the newborn** - It is thought that taking enzyme-inducing AEDs (carbamazepine, phenytoin, phenobarbital, primidone, oxycarbazepine, topiramate and eslicarbazepine) during pregnancy can increase the risk of haemorrhagic disease of the newborn. The evidence for this is mixed but **current national guidance is that IM vitamin K should be given to all infants born to mothers taking enzyme inducing AEDs.** [19,21] This should be discussed with the mother prior to delivery.

## **7. MANAGEMENT OF NEONATAL WITHDRAWAL**

### **7.1 Antenatal care** (see Women Who Use Drugs & Alcohol in Pregnancy (S6))

Mothers who are using drug/alcohol or prescribed medications likely to cause withdrawal should be informed that their baby will require observation in hospital for a period of time dependent on the half-life of the substance likely to cause withdrawal. Initial observations will be on the postnatal ward (315) but

there is a small chance admission to NICU may be required. Mothers using drugs likely to cause withdrawal should be given the patient information on Neonatal abstinence syndrome. (Appendix A)

CYPD/safeguarding team involvement should commence in the antenatal period if indicated. A birth plan, if necessary, should be in place by 32 weeks gestation; this should be documented on Badger and in relevant obstetric/paediatric notes.

## 7.2 At Delivery

Naloxone (®Narcan) **should not** be routinely given to the infant of a mother who has been using opiates. This is because it can result in **acute withdrawal and death**. The neonatal team are not required to attend deliveries of these babies routinely as generally they don't need extra help. Observations should be undertaken for the first 2 hours of life and a Neonatal Early Warning score (NEWS) chart commenced.

## 7.3 On the postnatal ward/neonatal unit

In all cases review:

- Antenatal care plan
- Maternal medication/substance use and detox plan
- Maternal serology (if IVDU)
- Neonatal plan according to the medication used
- Safeguarding issues and discharge plan

A record of the minimum and maximum drug doses that mum has taken during her pregnancy should be noted. Sending a urine sample (minimum 1-2 ml, ideally 15-20 ml) from the baby to biochemistry for drug screening should be considered if the history is incomplete or the clinical picture atypical.

Where possible, the infant should remain with their mother unless there are other comorbidities or an immediate risk of serious medical complication, death or long-term impairment to the infant [15]. Admission to the neonatal unit or transitional care unit should be based only on clinical need.

The infant should be started on observations. Following initial observations over the first 2 hours of life, these should then be continued 4 hourly until discharge. Infants should be actively monitored for symptoms of NAS including a full assessment of alertness, feeding, muscle tone and irritability/jitteriness by a trained member of staff. [3,15] Observations should be documented on the NEWS chart and escalated as indicated. Where possible, assessment should include pulse oximetry to exclude the rare but possible complication of PPHN; any infant showing signs of respiratory distress should have pulse oximetry as standard.[11,15] **In UHDB, formalized NAS scoring charts (e.g. Rivers observations) are not used.** Use of traditional scoring systems has been associated with increased unnecessary opioid treatment of infants with NAS, and newer models of care focused on non-pharmacological interventions and parent-provided care have demonstrated reductions in length of stay and medication usage [22, 23].

If the infant presents with symptoms of respiratory distress, lethargy/irritability, poor feeding, hypothermia or temperature instability, then other conditions such as sepsis or hypoglycaemia should be considered and ruled out; it should not be assumed these symptoms are purely due to exposure to medications in utero.[15]

Required observation periods for infants exposed to different drug classes are outlined in *Table 1: Quick Guide*. As a general rule, babies who are born to mothers on prescribed medications that have stable observations after 24 hours of monitoring, normal pulse oximetry, who have established feeding well, have no other concerns and whose newborn physical exam was normal, can be discharged home after 24 hours with the NAS parental information leaflet and follow up with the community midwife the following day. This will obviously need to be assessed on a case by case basis for each individual infant and their family/social situation.[15] In certain circumstances with consultation between a senior

paediatrician (registrar or above) and Specialist Midwife, some babies may be safely discharged earlier (for example: methadone <30mg/day with no other drug use – unlikely the baby will withdraw).

If the child has symptoms of increasing drug withdrawal, then discharge must not take place and the infant must continue to be observed. If the infant has no symptoms or symptoms are mild and static, the baby may be discharged. In the case of exposure to drug with longer half-lives (e.g. methadone, benzodiazepines) the child's parents should be warned that withdrawal may present late in their child and they should be advised to seek medical advice if severe withdrawal symptoms develop. The parents should be made aware of the signs & symptoms of drug withdrawal prior to discharge.

In the presence of mild symptoms, supportive therapy only is indicated. This includes wrapping, cuddling and nursing in a quiet, dark environment. **Optimum care for babies suffering from withdrawal is supportive management provided with and by their mother, and avoidance of separation where possible.**

Specific therapy should be commenced on the observation of significant and disturbing symptoms [9,24] or the development of convulsions, and should be discussed with a senior paediatrician (either SpR, senior ANNP or Consultant.) All babies requiring specific therapy should be transferred to the neonatal unit. Where specific therapy for withdrawal is required, the child should remain in hospital for 4 days following withdrawal of treatment.

If the infant has a convulsion, other causes of fits other than drug withdrawal must be considered. These include hypoglycaemia, hypocalcaemia, hypomagnesaemia, infection, hypoxia and intraventricular haemorrhage. It is important to remember that the symptoms of neonatal abstinence syndrome may mimic those of congenital thyrotoxicosis.

It is important to review maternal blood-borne virus status. Immunize baby (hepatitis B) if appropriate i.e. if mum is injecting drugs or is Hep B or Hep C positive. Further consideration should be given in the postpartum period to child protection.

## 8. SPECIFIC THERAPY

### 8.1 Medical treatment for opiate/opioid withdrawal

This should only be started in the presence of significant and unmanageable withdrawal symptoms, or if the baby has convulsions. The aim of specific treatment is to allow sleep and feeding patterns to be as normal as possible. [24-28] The decision to start oral morphine should be made at consultant level.

First Line = Oral Morphine

#### **Morphine Oral Solution**

**Starting dose:** 40 micrograms/kg/dose every 4 hours

**Increase by steps of:** 20 micrograms/kg/dose until control is achieved

***Maximum dose 200microgram/kg/dose 4hourly.***

***RESPIRATORY RATE MUST BE CLOSELY MONITORED.***

Infants should be nursed on an apnoea monitor and have regular observations documented (4-6 hourly). When a stabilizing dose is achieved, this should be maintained for 3-5 days so that the infant sleeps well, feeds effectively and gains weight. The dose should then be gradually reduced. As a general rule,

medicines should be administered at the time of feeding in order to minimize the number of times that the baby is disturbed. If vomiting is a problem the medicines should be given 30 minutes before a feed. Pharmacological treatment should be used carefully monitoring response in symptoms closely in baby. [24-28] After 3-5 days the dose should be reduced every 24 hours if severe symptoms do not persist. Discontinue at a dose of 40 micrograms/kg/day.

Second Line = Chlorpromazine 550-750 micrograms/kg/dose QDS

If morphine fails chlorpromazine should be tried at the above dose given four times daily; this can be doubled if withdrawal is severe. Maximum dose 6mg/kg/day. Disadvantages include: a prolonged half-life making dose titration difficult; metabolites are eliminated over a period of some months with the potential for adverse effects over a considerable period of time; reduced threshold for convulsions. Hypothermia has occasionally been observed. Once stable reduce dose by not more than 2mg/kg/day on every third day.

## 8.2 Medical treatment of benzodiazepine withdrawal

First Line = Diazepam 3-6 mg/kg/day 8 hourly - please confirm with pharmacy before prescribing.

Once the infant has been stabilized then the dose should be slowly and steadily reduced over several weeks.

## 8.3 Specific management of cocaine misuse

Babies born to cocaine-using mothers are very difficult to settle and will need a lot of cuddling and touching before they will be calmed and reassured. This will involve a great deal of nursing time and the mother should be encouraged to be the main comforter to help build her self-confidence as a parent and to bond with her baby.

There is **no evidence for a cocaine-induced withdrawal syndrome**. The behaviour of cocaine-exposed infants is probably the result of CNS manifestations of fetal cocaine effect. Abnormalities in neurobehaviour have been observed to continue for up to 6- 9 months; these **do not** respond to therapeutic treatment.

*Cranial sonograms are not routinely recommended, but literature suggests CNS abnormalities, including hemorrhagic ischemic lesions may occur in some drug-exposed infants. As yet, evidence is insufficient to support a mandate for cranial sonograms in all cocaine-exposed infants. However, special consideration should be given to specific neuroimaging of cocaine-exposed preterm infants, infants whose head circumference falls below the 10th percentile on standardized fetal growth curves, and infants with abnormal neurologic signs, neurobehavioral dysfunction, or seizure activity. [29,30]*

## 9. BREAST FEEDING

Almost all drugs and chemicals are passed from maternal blood to breast milk. In general, although most recreational drugs are present in breast milk the amount is too small to cause harm to the baby. [31] In drugs of misuse there may be some effect e.g. drowsiness with opiates or tranquillizers, if the level of drugs in the milk is particularly high. Seizures have been reported in breast fed infants of mothers using cocaine or more than a small amount of alcohol.

In the majority of cases, **mothers who are using drugs, including women who are using methadone, should be encouraged to breast feed in the same way as any other mother**, providing their drug use is stable and the baby is weaned gradually. See *Table 1: Quick Guide* for specific information on breast-feeding in commonly encountered drug classes. Women should be **strongly advised not to use illicit drugs or alcohol when breast feeding** and to seek advice regarding prescribed medications. There has

been recent controversy regarding use of codeine in breastfeeding mothers following a case report of neonatal toxicity and death. Current advice remains that codeine is contraindicated in breastfeeding.

Women who are HIV positive or whose HIV status is unknown but who may have been at risk, should be informed about the risks of infecting the baby and advised against breast feeding. Hepatitis C is found in 60% of injecting drug users; Hepatitis C is not a contraindication for breast feeding and there is no effective immunization against Hepatitis C (see separate guidelines for Hep C and HIV).

Each mother should be given all the information they need to make an informed choice about breast feeding. Having made their decision, they should be fully supported by all professionals involved. They should be warned **not to suddenly stop breast feeding but to gradually tail off breast feeding**, as this may lead to acute withdrawal in their child.

## 10. **ISSUES AFFECTING DISCHARGE**

In instances of maternal illicit drug/alcohol misuse, it is important to consider the infant and mother's social situation, as mothers who have used illicit drugs and/or alcohol during pregnancy may have engaged more poorly with antenatal services and may have more chaotic lifestyles.

Referral to social care should be considered in all families where there is a history of illicit drug/alcohol misuse, and this needs to be assessed prior to discharge. [32] It is important to discuss this with parents prior to referral. Family wellbeing, safeguarding and need for support is also a pertinent consideration for infants with a maternal history of significant mental health difficulties. Referrals, where appropriate, should be made to Derby Children's Social Care either Initial Response Team or Careline by phone or online referral (or for County patients through Starting Point.)

## 11. **FOLLOW UP**

No routine follow-up is required for babies initially deemed at risk of withdrawal. If a child has seizures or neurological complications then neonatal outpatient follow-up should be arranged as discussed with the overseeing consultant.

## 12. **MONITORING COMPLIANCE AND EFFECTIVENESS**

Monitoring requirement	Numbers of babies having the appropriate observations Discharge policy followed
Monitoring method	Retrospective case note review
Report prepared by	Specialist Midwife for Substance Misuse
Monitoring report sent to:	Maternity Development & Governance Committee
Frequency of report	Annually

## 13. **REFERENCES**

1. Advisory Council on the misuse of Drugs. (2003) 'Hidden harm' report on children of drug users - GOV.UK' Available at <https://assets.publishing.service.gov.uk/media/5a756e6be5274a3edd9a4dcb/hidden-harm-full.pdf>
2. Department of Health (2004) 'Maternity Standards, National Service Framework for Children, Young People and Maternity Services.' Available at [https://assets.publishing.service.gov.uk/media/5a7b696640f0b6425d592f9d/National\\_Service](https://assets.publishing.service.gov.uk/media/5a7b696640f0b6425d592f9d/National_Service)

3. Sie, S., Wennink, J., van Driel, J., te Winkel, A., Boer, K., Casteelen, G. and van Weissenbruch, M. (2012). Maternal use of SSRIs, SNRIs and NaSSAs: practical recommendations during pregnancy and lactation. *Archives of Disease in Childhood - Fetal and Neonatal Edition*, 97(6), pp.F472-F476.
4. Jefferies, A. (2011). Selective serotonin reuptake inhibitors in pregnancy and infant outcomes. *Paediatrics & Child Health*, 16(9), pp.562-562.
5. Reefhuis, J., Devine, O., Friedman, J., Louik, C. and Honein, M. (2015). Specific SSRIs and birth defects: bayesian analysis to interpret new data in the context of previous reports. *BMJ*, p.h3190.
6. Wurst, K., Poole, C., Ephross, S. and Olshan, A. (2009). First trimester paroxetine use and the prevalence of congenital, specifically cardiac, defects: A meta-analysis of epidemiological studies. *Birth Defects Research Part A: Clinical and Molecular Teratology*, 88(3), pp.159-170.
7. BNF 88 (British National Formulary) 2024/2025 and BNFC 88 (British National Formulary for Children) 2024/2025 available at <https://bnfc.nice.org.uk>
8. ELNahas G, Thibaut F. Perinatal Psychoactive Substances Use: A Rising Perinatal Mental Health Concern. *Journal of Clinical Medicine*. 2023; 12(6):2175. <https://doi.org/10.3390/jcm12062175>
9. Kocherlakota, P. (2014). Neonatal abstinence syndrome. *Pediatrics*, 134(2), e547-e561.
10. Wang, J., & Cosci, F. (2021). Neonatal withdrawal syndrome following late in utero exposure to selective serotonin reuptake inhibitors: a systematic review and meta-analysis of observational studies. *Psychotherapy and Psychosomatics*, 90(5), 299-307.
11. Grigoriadis, S., VonderPorten, E., Mamisashvili, L., Tomlinson, G., Dennis, C., Koren, G., Steiner, M., Mousmanis, P., Cheung, A. and Ross, L. (2014). Prenatal exposure to antidepressants and persistent pulmonary hypertension of the newborn: systematic review and meta-analysis. *BMJ*, 348(jan14 7), pp.f6932-f6932
12. Ng, Q. X., Venkatanarayanan, N., Ho, C. Y. X., Sim, W. S., Lim, D. Y., & Yeo, W. S. (2019). Selective serotonin reuptake inhibitors and persistent pulmonary hypertension of the newborn: an updated meta-analysis. *Journal of women's health*, 28(3), 331-338.
13. Bérard, A., Sheehy, O., Zhao, J. P., Vinet, É., Bernatsky, S., & Abrahamowicz, M. (2017). SSRI and SNRI use during pregnancy and the risk of persistent pulmonary hypertension of the newborn. *British journal of clinical pharmacology*, 83(5), 1126-1133.
14. Levinson-Castiel, R., Merlob, P., Linder, N., Sirota, L., & Klinger, G. (2006). Neonatal abstinence syndrome after in utero exposure to selective serotonin reuptake inhibitors in term infants. *Archives of pediatrics & adolescent medicine*, 160(2), 173-176.
15. Pan-London Perinatal Mental Health: Guidance for Newborn Assessment. (2017). [pdf] London: London Neonatal Operational Delivery Network. Available at: <http://www.londonneonatalnetwork.org.uk/wp-content/uploads/2016/10/FinalNeodoc-v3.pdf> [Accessed 4 Jul. 2018].
16. Viale L, Allotey J, Cheong-See F, Arroyo-Manzano D, Mccory D, Bagary M et al.; EBM CONNECT Collaboration. Epilepsy in pregnancy and reproductive outcomes: a systematic-review and meta-analysis. *Lancet* 2015;386:1845-5
17. Meador K, Reynolds MW, Crean S, Fahrbach K, Probst C. Pregnancy Outcomes in women with epilepsy: a systematic review and meta-analysis of published pregnancy registries and cohorts. *Epilepsy Res* 2008;81:1-13
18. Tomson T, Battino D, Bonizzoni E, Craig J, Lindhout D, Sabers A, et al.; EURAP study group. Dose-dependent risk of malformations with antiepileptic drugs: an analysis of data from the EURAP epilepsy and pregnancy registry. *Lancet Neurol* 2011;10:609-17
19. RCOG Green-top guideline No 68 'Epilepsy in Pregnancy' (2016) available at

<https://www.rcog.org.uk/guidance/browse-all-guidance/green-top-guidelines/epilepsy-in-pregnancy-green-top-guideline-no-68/>

20. Davanzo R, Dal Bo S, Bua J, Copertino M, Zanelli E, Matarazzo L. Antiepileptic drugs and breastfeeding. *Italian Journal of Paediatrics* 2013:39-50
  21. NICE clinical guideline CG137 – ‘Epilepsies: diagnosis and management’ (2021) available at <https://www.nice.org.uk/guidance/cg137>
  22. Grossman, M. R., Lipshaw, M. J., Osborn, R. R., & Berkwitt, A. K. (2018). A novel approach to assessing infants with neonatal abstinence syndrome. *Hospital Pediatrics*, 8(1), 1-6.
  23. Grossman, M., & Berkwitt, A. (2019, April). Neonatal abstinence syndrome. In *Seminars in perinatology* (Vol. 43, No. 3, pp. 173-186). WB Saunders.
  24. Kassim, Z., & Greenough, A. (2006). Neonatal abstinence syndrome: Identification and management. *Current Paediatrics*, 16(3), 172-175.
  25. Jackson, L., Ting, A., McKay, S., Galea, P., Skeoch, C. A randomised controlled trial of morphine versus phenobarbitone for neonatal abstinence syndrome. *Arch Dis Child Fetal Neonatal Ed* 2004;89:F300-304
  26. Johnson, K., Gerada, C., & Greenough, A. (2003). Treatment of neonatal abstinence syndrome. *Archives of Disease in Childhood-Fetal and Neonatal Edition*, 88(1), F2-F5.
  27. Osborn, D. A., Jeffery, H. E., & Cole, M. J. (2010). Opiate treatment for opiate withdrawal in newborn infants. *Cochrane Database of Systematic Reviews*, (10).National Litigation Authority CNST Maternity Standards 2009/2010
  28. Theis, JGW et al Current management of neonatal abstinence syndrome: A critical analysis of the evidence. *Biol Neonate* 1997;71:345-356
  29. van Huis, M., van Kempen, A. A., Peelen, M., Timmers, M., Boer, K., Smit, B. J., & Van Rijn, R. R. (2009). Brain ultrasonography findings in neonates with exposure to cocaine during pregnancy. *Pediatric radiology*, 39, 232-238.
  30. Cestonaro, C., Menozzi, L., & Terranova, C. (2022). Infants of mothers with cocaine use: review of clinical and medico-legal aspects. *Children*, 9(1), 67.
  31. MacVicar, S., Humphrey, T., & Forbes-McKay, K. E. (2018). Breastfeeding and the substance-exposed mother and baby. *Birth*, 45(4), 450-458.
  32. Drugs, pregnancy and child care. A guide to professionals. Second revised ed.1995. Published by: Institute for the Study of Drug Dependency. Waterbridge house, 32-36 Loman Street, London, SE1 OEE.
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## Documentation Control

<b>Reference Number</b> NIC NE 09	<b>Version:</b> V1		<b>Status</b> Final	
<b>Version / Amendment History</b>	<b>Version</b>	<b>Date</b>	<b>Author</b>	<b>Reason</b>
	V1	Feb 2002	Directorate of Child Health/ baby Unit	New Guideline
	V2	Nov 2009	Dr N Ruggins Cons Paediatrician J. McCulloch Specialist Midwife	CNST Review
	V3	April 2012	J. McCulloch Specialist Midwife	Review and update
	V3.1	2023	Dr G Joshi	To standardise neonatal observations
	V4	March 2026	Dr Balasubramaniam – Consultant Neonatologist J.McCulloch – Specialist Midwife	Review and update
	V5	July 2024	Dr Ellen Brogan – ST7 SPIN Trainee Neonatal Medicine Dr Balasubramaniam – Consultant Neonatologist	Guideline updated and combined guideline produced (to combine Neonatal Abstinence Syndrome with Neonates exposed to Prescribed medications)
<b>Intended Recipients:</b> Paediatric Consultants Maternity staff				
<b>Training and Dissemination:</b> Cascade the information via BU newsletter and address training				
<b>Development of Guideline:</b> Dr Ellen Brogan – ST7 SPIN Trainee Neonatal Medicine Dr Balasubramaniam – Consultant Neonatologist				
<b>In Consultation with:</b> Maternity Guidelines Group Paediatric Consultants				
<b>Linked Documents:</b> (Nice guidance/Current national guidelines)				
<b>Keywords:</b> Mental Health; Anti-depressants; Prescription medication, drugs and alcohol use in pregnancy; Antipsychotics; Epilepsy; Substance Misuse; Anti-Epileptic Drugs (AEDs); Mood Stabilisers; Valproate; Valproic; Withdrawal; Antidepressants; Anti-psychotics; Substance Abuse; Drug / Alcohol Abuse; Drug / Alcohol Misuse; Antiepileptic Drugs; Anticonvulsant; Anti-convulsant; Anti-seizure.				
<b>Business Unit Sign Off</b>			<b>Group:</b> Paediatric Guidelines Group <b>Date:</b> 23/10/2024	
<b>Divisional Sign Off</b>			<b>Group:</b> Women's and Children's Clinical Governance Group <b>Date:</b> 02/12/2024	
<b>Date of Upload</b>			13/12/2024	
<b>Review Date</b>			October 2027	
<b>Contact for Review</b>			Dr Bala Subramaniam	



### **Will Social Services be informed?**

The Children and Young People's Department will only be involved in your care if you need extra help and support or if there are concerns around the safety and welfare of your baby. You **will not** be automatically referred just because you use drugs.

### **Useful Contacts:**

Women's Work

**01332 242077**

Aquarius  
(Family Drug and Alcohol Service)

**03007900265 option 2**

Phoenix Futures  
**03007900265 option 1**

Derby Family Justice Centre

**01332 256897**

### **Useful Web-sites:**

[www.talktofrank.com](http://www.talktofrank.com)  
Provides up-to-date information and advice  
about drugs and substance misuse

[www.nta.nhs.uk](http://www.nta.nhs.uk)  
National Treatment Agency for Substance  
Misuse

### **SUBSTANCE MISUSE TEAM**

**Judy McCulloch**

Specialist Midwife in Drugs & Alcohol  
[judy.mcculloch@nhs.net](mailto:judy.mcculloch@nhs.net)

**Office: 01332 786749**

**Mobile: 07799 337678**

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Smoking is not permitted anywhere in the buildings and grounds of Derby's Hospitals. For advice and support about giving up smoking please call Free Phone 0800 707 6870.

**Antenatal  
Services**

Derby Teaching Hospitals **NHS**  
NHS Foundation Trust

## **Information for Parents Neonatal Abstinence Syndrome**



*Taking pride in caring*

## WILL MY BABY HAVE WITHDRAWAL?

If you were using opiates and/or opioids (e.g. heroin, methadone, codeine, DF118, tramadol) or benzodiazepines (valium, benzo's temazepam) during your pregnancy your baby may experience withdrawal symptoms, known as Neonatal Abstinence Syndrome.

Withdrawal symptoms are rarely seen in babies born to mothers who have used stimulants (crack/cocaine/amphetamines) or have used cannabis.

Withdrawal symptoms may also be seen in babies of mothers who have been drinking heavily during pregnancy.

Symptoms usually start 24 hours after birth and may last for up to two weeks. However it has been known for withdrawal symptoms to start a few weeks after birth, especially with methadone users during pregnancy.

If the baby has shown few symptoms 4 days after birth it is unusual for withdrawal to be serious.

For this reason though you will be advised to remain in hospital with your baby for about 4 days.

Occasionally a baby may require treatment in the neonatal unit if the withdrawal symptoms are severe

## HOW WILL YOU KNOW IF YOUR BABY HAS SIGNS OF WITHDRAWAL?

Baby is difficult to settle  
High pitched crying  
Fever  
Tremor or twitching  
Difficulty in feeding  
Diarrhoea and vomiting  
Excessive weight loss or slow to gain weight  
Excessive sucking of fists  
Sneezing, stuffy nose and trouble breathing  
Fits/convulsions

## WHAT YOU CAN DO TO HELP

### SLEEPLESSNESS

Reduce noise, bright lights, patting or touching baby too much  
Soft, gentle music, singing, humming and rocking may help  
Try bathing baby in warm water  
Clean and dry nappy, watch buttocks closely for rash or skin irritation  
Feed baby on demand

### PROLONGED AND/OR HIGH-PITCHED CRYING

Hold baby close to your body  
Skin to skin contact or a baby sling may be useful.

### EXCESSIVE SUCKING OF FISTS

Cover baby's hands with mittens if skin becomes damaged  
Keep areas of damaged skin clean  
Avoid lotions/creams as the baby may suck on them

### FEVER

Remove extra covers and don't swaddle your

baby

Dress your baby in just a nappy and vest or lower the room temperature

### DIFFICULT OR POOR FEEDING

Feed small amounts often  
Feed in quiet, calm surroundings with minimal noise and disturbances  
Allow time for rest between sucking

## BREASTFEEDING

If your drug use is stable then the benefits from breast feeding for you and your baby outweigh the risk of hazards to baby. For more information on breast-feeding talk to your midwife or the Specialist Midwife in Drugs and Alcohol.

### VOMITING

Feed your baby slowly  
Clean the skin area after he/she has been sick as stomach contents contain acid which can irritate the skin.

### TREMBLING

Reduce light and noise  
Swaddle baby in a soft blanket

### FITS/CONVULSIONS

Lay your baby in a safe place making sure they can't fall or be injured.

**Call 999 immediately**

## WHEN YOUR BABY GOES HOME

### KEEP YOUR BABY SAFE

**You are advised not to sleep with your baby in a bed or on the sofa.**