

BCCNM REGISTERED MIDWIVES

# Prescribing, Ordering and Administering Controlled Substances

Standards, Limits, Conditions



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# Standards, limits and conditions of prescribing, ordering and administering controlled substances

The following standards, limits and conditions apply to the schedule of controlled substances that midwives may independently prescribe, order and administer in the community, hospital or other sites of midwifery practice. Midwives may not independently prescribe, order and administer any other controlled substance unless on the order of a medical practitioner. These standards may be amended by the British Columbia College of Nurses and Midwives (BCCNM) according to Schedule A and B of the *Midwives Regulation*.

This document outlines standards for professional behavior, conduct and clinical practice expected of a registered midwife in British Columbia when prescribing, ordering and administering controlled substances. The controlled substances are listed by name, with set limits and conditions, aligned with the midwifery scope of practice.

## GENERAL PRESCRIBING AND ORDERING STANDARDS

Midwives:

1. Prescribe and order therapeutics within their scope of practice, and in compliance with relevant federal and provincial legislation and organizational policies.
2. Are accountable for their prescribing decisions.
3. Prescribe and order therapeutics according to best evidence.
4. Before prescribing and ordering, ensure they are competent to:
  - a. establish or confirm a midwifery diagnosis for the client;
  - b. manage the treatment and care of the client; and
  - c. monitor and manage the client's response to the therapeutic.
5. When prescribing and ordering therapeutics:
  - a. consider the client's health history and other relevant factors (e.g. age, gender, lifestyle, the client's perspective);
  - b. undertake and document an appropriate clinical evaluation (e.g. physical examination, review of relevant tests, imaging and specialist reports);
  - c. obtain and document the best possible medication history for the client using PharmaNet (when access is available) and other sources;
  - d. review and document the medication history and act to address any discrepancies;

- e. ask about the client's drug allergies and ensure drug allergy information is accurate and documented;
  - f. appropriately document the therapeutic prescribed and their indication(s) in the client's medical record;
  - g. establish and document a plan for reassessment/follow-up; and
  - h. monitor and document the client's response to the therapeutic prescribed (as appropriate).
6. When prescribing, provide information to clients about:
- a. potential benefits and risks of the therapeutic;
  - b. the expected action of the therapeutic;
  - c. the duration of therapy;
  - d. specific precautions or instructions for the therapeutic;
  - e. potential side-effects and adverse effects and action to take if they occur;
  - f. potential interactions between the therapeutic and certain foods, other substances, or substances; and
  - g. recommended follow-up.
7. Complete prescriptions and orders accurately and completely, including:
- a. the date the prescription was written;
  - b. client name, address (if available), PHN (if available) and date of birth;
  - c. client weight (if required);
  - d. name, strength and dose of the controlled drug;
  - e. the quantity prescribed and quantity to be dispensed (prescriptions);
  - f. dosage instructions (i.e. frequency or interval, maximum daily dose, route of administration, duration of therapy);
  - g. their name, address, telephone number, written (not stamped) signature, and BCCNM registration number;
  - i. date of transmission, the name and fax number of the pharmacy intended to receive the transmission, and their fax number if the prescription is being faxed; and
  - j. directions to the pharmacist not to renew or alter.
8. Document all written, verbal and telephone orders accurately, contemporaneously and legibly in the client record.

9. Undertake medication reconciliation as required by the Health Authority to ensure accurate and comprehensive medication information is communicated consistently.
10. Report adverse drug reactions to the [Canada Vigilance Program](#)<sup>1</sup>.
11. Manage, document, report and disclose any medication errors.
12. Prescribe only for clients except in emergency situations when there is no other prescriber available, within scope.
13. Do not provide anyone with a blank, signed prescription.

#### PRESCRIBING AND ORDERING STANDARDS FOR CONTROLLED SUBSTANCES<sup>2</sup>

When prescribing, ordering and administering controlled substances, midwives must meet the General Prescribing and Ordering Standards above and must:

1. Have completed a BCCNM-recognized certification course on safe prescribing of opioids and benzodiazepines, such as, UBC CPD's "Opioids and Benzodiazepines: Safe Prescribing for Midwives" course. Graduates of UBC's Midwifery Education Program after May 2017 are considered certified.
2. Ensure a clinical assessment occurs in person within a timely manner prior to prescribing and ordering a controlled substance, except in cases where the client is being assessed in person by another health care provider.
3. Adhere to relevant standards, guidelines and policies established by agencies or organizations involved in the provision or control of controlled substances.
4. Prescribe the lowest possible dose and the minimum quantity to be dispensed.
5. Know, document and inform the client of the risks of co-prescribing opioid and sedative-hypnotic drugs (e.g. benzodiazepines) and limit co-prescribing whenever possible.
6. Document their advice to clients about the side effects and risks of controlled drugs and substances as applicable, and implement evidence-informed strategies for minimizing risk.
7. Document their advice to clients that they must avoid other central nervous system and respiratory depressants including alcohol, cannabis, and some over-the-counter medications.
8. Destroy expired or no-longer-needed controlled substances. This must be witnessed by another midwife, a physician, a registered nurse, nurse practitioner or a pharmacist.

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<sup>1</sup> Health Canada's surveillance program that collects and assesses reports of suspected adverse reactions to health products marketed in Canada.

<sup>2</sup> Adapted from the College of Physicians and Surgeons of British Columbia's *Practice Standard: Safe Prescribing of Opioids and Sedatives*, the College of Registered Nurses of Nova Scotia's *Nurse Practitioner Standards of Practice* and the College of Physicians and Surgeons of Alberta's *Practice Standard: Prescribing Drugs Associated with Substance Use Disorders or Substance-related Harm*.

- Unwanted supplies of these substances may also be surrendered to the pharmacist from whom they were obtained.
9. Document their review of the client's PharmaNet medication profile in the medical record (if PharmaNet is available).
  10. Document the indication and duration for which the drug is being prescribed, the goals of treatment, and the rationale for the drug's use over alternatives (if applicable)
  11. Ensure they do not prescribe refills for controlled substances.
  12. Appropriately issue prescriptions for controlled substances using regulator-approved controlled drugs and substances duplicate prescription pads<sup>3</sup>, in compliance with the College of Pharmacists of British Columbia BC's [Controlled Prescription Program](#) and [Prescription Regulations](#).
  13. Ensure that controlled drugs and substances duplicate prescription pads are safely secured when in transit or in use, and stored in a secure and locked area when not in use.
  14. Store the duplicate copy of each prescription written on controlled drugs and substances duplicate prescription pad within the client health record, not within the controlled prescription pad.
  15. Report loss, theft or misuse of a controlled drugs and substances duplicate prescription pad to BCCNM, PharmaNet Support Services, the police, and, if any client information is contained on the missing pad, the BC Privacy Commissioner.
  16. Not fax or call in prescriptions requiring use of a controlled drugs and substances duplicate prescription pad.
  17. Not prescribe controlled substances "for office use."
  18. Return controlled drugs and substances duplicate prescription pads to BCCNM if no longer practicing in BC or if non-practicing for more than 12 months.
  19. Consult with appropriate health care professionals if the client's response to the controlled drug is other than anticipated.
  20. Follow hospital protocols, record-keeping and security procedures for all prescribing, ordering, administering and disposing of controlled substances
  21. Advise clients about the dangers of taking controlled substances while performing safety-sensitive occupations, providing child or elder care, and driving.
  22. Screen for the presence or emergence of mental health disorders (particularly mood disorders) which may complicate management.

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<sup>3</sup> Regulator-approved controlled drugs and substances duplicate prescription pads are not yet available for use by midwives.

STANDARDS FOR ADMINISTERING CONTROLLED SUBSTANCES

Midwives may administer controlled substance on their own order or as ordered by a medical practitioner (physician or nurse practitioner). When doing so, they must:

1. Provide and document ongoing assessments.
2. Monitor and document the client's response to the controlled substance.
3. Communicate the client's response and change to or discontinuation of therapy to the ordering medical practitioner as appropriate.
4. Consult with the ordering medical practitioner at any point as required.

LIMITS AND CONDITIONS FOR PRESCRIBING, ORDERING AND ADMINISTERING CONTROLLED SUBSTANCES

Midwives may only prescribe, order or administer the following controlled substances within the standards set out in this document and to clients under their professional care. The entries that follow provide general information and the limits and conditions on these controlled substances approved for use in midwifery practice.

Please note that the included summaries regarding medication suitability in pregnancy and lactation are brief. Prior to counselling a client about the benefits and risks of drug therapy, please review the detailed information in the specific references provided at the end of the document.

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## Controlled substances and related medication for use in prodromal labour and the early postpartum period

### LORAZEPAM (UPDATED MAY 2019)

(Ativan®). Lorazepam is a benzodiazepine, an anti-anxiety agent and sedative which binds to benzodiazepine receptors on the postsynaptic neuron at several sites within the central nervous system.

#### Indications and clinical use

Midwives may only prescribe, order or administer Lorazepam on their own authority for:

1. therapeutic rest in prodromal labour;
2. short-term management of excessive postpartum anxiety while the midwife is arranging for consultation with a physician for further diagnosis and ongoing treatment; or
3. upon diagnosis of intrauterine fetal demise.

Lorazepam may be used to promote therapeutic rest during prodromal labour; however, due to the long half-life of 12 hours, use of analgesia may be more appropriate over Lorazepam as a first choice. Lorazepam may be used during the early postpartum period, particularly where anxiety and/or insomnia due to anxiety or transient stress are factors and non-pharmacologic measures have been ineffective. Administration under any other circumstance must be on the order of a physician.

#### Contraindications

Hypersensitivity to benzodiazepines or to any component of the formulation. Lorazepam should not be taken in conjunction with alcohol or other sedating medications. Benzodiazepines should not be used in the presence of the following medical conditions: glaucoma, liver or kidney impairment, hyperkinesias, hypoalbuminaemia, myasthenia gravis, or any type of organic brain disorder. Benzodiazepines should not be given where there is a history of substance use or dependency. Benzodiazepines are not recommended in the first trimester of pregnancy because of the potential for congenital malformations. When these drugs are taken to treat anxiety disorders, information on the risks and alternate approaches to therapy should be offered.

#### Warnings and precautions

All practitioners caring for an individual taking a benzodiazepine should be aware that long-term use can result in dependency and withdrawal symptoms when the medication is discontinued. Prolonged doses of benzodiazepines during pregnancy and/or the postpartum period may cause physical dependence with resulting withdrawal symptoms in the neonate. Before prescribing, ordering or administering a benzodiazepine to a client with a depressive, chronic psychotic, phobic or obsessive behavioral disorder or potential suicidal tendencies, consultation with a physician is required.

While benzodiazepines may be prescribed for postpartum psychosis, these medications do enter breast milk and, if used during breastfeeding, midwives should watch for possible sedation, feeding difficulties and weight loss in the neonate. Hypoglycemia and respiratory problems in the neonate may occur following exposure late in pregnancy. Elimination of benzodiazepines in the neonate following in-utero exposure can be slow. Lorazepam is considered an intermediate acting benzodiazepine with a half-life of 12 hours for adults and 30 hours, with a range of 18-73 hours for neonates.

Benzodiazepines given near delivery could cause respiratory depression and hypoglycemia in neonates. Prolonged use in gestation may cause neonatal withdrawal

Benzodiazepines have been associated with anterograde amnesia; may impair physical or mental abilities; may cause hypotension; may cause hyperactive or aggressive behavior.

Use with caution in the presence of hepatic impairment, renal impairment, respiratory disease, substance use, alcohol use, personality disorders or depression.

When taking this medication one should not operate machinery or drive a vehicle.

### **Pregnancy**

Human Data Suggest Risk in the 1<sup>st</sup> and 3<sup>rd</sup> trimesters. One report found a significant association with fetal anal atresia. When used close to delivery, respiratory depression, hypotonia, lethargy and withdrawal symptoms have been reported. The long-term effects of in utero exposure on neurobehaviour, especially when exposure occurs in the latter half of pregnancy, have not been studied but are of concern.

### **Lactation**

Category L3 - Limited Human Data - Probably Compatible

Lorazepam is one of the preferred benzodiazepines in lactation, due to its shorter half-life and lack of an active metabolite. About 3% of the dose is known to enter breastmilk. If this medication is used in lactation the lowest effective dose should be given for the shortest possible period of time. The neonate should also be monitored for signs of sedation, such as not waking up to feed at regular intervals.

### **Adverse reactions**

Benzodiazepines may cause drowsiness, blurred vision, dizziness and impaired concentration. Other potential side effects include lack of muscle coordination, nausea, constipation, visual disturbances, skin rash, and loss of bladder control. If breathing difficulties, fainting, rash or hypotension are experienced a physician should be contacted immediately.

Clinical judgement should be exercised as lorazepam does cross the placental barrier. Should labour progress more rapidly than anticipated, Flumazenil, a benzodiazepine receptor antagonist, may be

required and should be readily available for administration. Immediately after administration, physician consultation is required. (Please refer to the section on Flumazenil at the end of the benzodiazepine section.)

### **Dosage and administration**

Usual dose: 0.5-2mg SL/PO BID or TID

Insomnia: 0.5-1mg SL/PO BID or TID

Anxiety: 0.5 – 2mg SL/PO BID or TID

In prodromal labour the dose may be repeated 12 hours later if needed and labour is not yet active. No more than two consecutive doses should be given when used in labour.

In treating postpartum anxiety, the dose may be given every 12 hours for no more than 3 days or a maximum of six doses. Once postpartum treatment is initiated, physician consultation must be arranged. The sublingual tablet will dissolve in approximately 20 seconds. Wait at least 2 minutes before swallowing to allow sufficient time for absorption.

### **Prescribing/ordering**

Lorazepam may be prescribed in hospital or in the community. It does not require a controlled drugs and substances duplicate prescription pad. A prescription cannot exceed three days. No refills.

### **Onset of action**

After sublingual use: 15-30 minutes

Peak action: 2 hours

### **Half-life**

Adult - 12 hours

Neonate - 30 hours, range 18-73 hours

### **Elimination**

Urine as metabolites

## **OXAZEPAM (UPDATED MAY 2019)**

(Serax<sup>®</sup>). Oxazepam is a benzodiazepine, anti-anxiety agent and sedative which binds to benzodiazepine receptors on the postsynaptic neuron at several sites within the central nervous system.

### **Indications and clinical use**

Midwives may only prescribe, order or administer oxazepam on their own authority for:

1. therapeutic rest in prodromal labour;
2. short-term management of excessive postpartum anxiety while the midwife is arranging for consultation with a physician for further diagnosis and ongoing treatment; or
3. upon diagnosis of intrauterine fetal demise.

Oxazepam may be used for therapeutic rest during prodromal labour; it has a half-life of up to 8 hours, however use of analgesia may be more appropriate over oxazepam as a first choice.

Oxazepam may be used during the early postpartum period, particularly where anxiety or insomnia due to anxiety or transient stress are factors and non-pharmacologic measures have been ineffective. Administration under any other circumstance must be on the order of a physician.

### **Contraindications**

Hypersensitivity to benzodiazepines or to any component of the formulation. Oxazepam should not be taken in conjunction with alcohol or other sedating medications.

Benzodiazepines should not be used in the presence of the following medical conditions: glaucoma, liver or kidney impairment, hyperkinesias, hypoalbuminaemia, myasthenia gravis, or any type of organic brain disorder. Benzodiazepines should not be given where there is a history of substance use or dependency.

Benzodiazepines are not recommended in the first trimester of pregnancy because of the potential for congenital malformations. When these drugs are taken to treat anxiety disorders, information on the risks and alternate approaches to therapy should be offered.

### **Warnings and precautions**

All practitioners caring for an individual taking a benzodiazepine should be aware that long-term use can result in dependency and withdrawal symptoms when the medication is discontinued. Prolonged doses of benzodiazepines during pregnancy and/or the postpartum period may cause physical dependence with resulting withdrawal symptoms in the neonate. Before prescribing, ordering or administering a benzodiazepine to a client with a depressive, chronic psychotic, phobic or obsessive behavioral disorder or potential suicidal tendencies, consultation with a physician is required.

While a benzodiazepine may be prescribed for postpartum psychosis, these medications enter breast milk and, if used during breastfeeding, midwives should watch for possible sedation, feeding difficulties and weight loss in the neonate. Hypoglycemia and respiratory problems in the neonate may occur following exposure late in pregnancy. While elimination of benzodiazepines in the neonate following in utero exposure can be slow, oxazepam is considered a short-acting benzodiazepine (less than or equal to 12 hours) and the least lipid-soluble, so levels in breast milk tend to be low. Thus, oxazepam is considered safer during lactation than other benzodiazepines, especially if its use is short-term or intermittent.

Benzodiazepines given near delivery could cause respiratory depression and hypoglycemia in neonates. Prolonged use in gestation may cause neonatal withdrawal.

Benzodiazepines have been associated with anterograde amnesia; may impair physical or mental abilities; may cause hypotension; may cause hyperactive or aggressive behavior.

Use with caution in the presence of hepatic impairment, renal impairment, respiratory disease, substance use, alcohol use, personality disorders or depression.

When taking this medication one should not operate machinery or drive a vehicle.

### **Pregnancy**

Human Data Suggest Risk in 1<sup>st</sup> and 3<sup>rd</sup> Trimesters

Although a number of studies have reported an association with various types of congenital defects, other studies with this class of drugs have not found such associations. Denial of exposure and the concurrent exposure to other toxic drugs and substances (e.g., alcohol and smoking) may be confounding factors. Continuous use during gestation or close to delivery might result in neonatal withdrawal or a dose-related syndrome similar to that observed with diazepam.

### **Lactation**

Category L 2 - Limited Data- Probably Compatible

Oxazepam is one of the preferred benzodiazepines in lactation due to its shorter half-life and lack of an active metabolite. About 1% of the dose is known to enter breastmilk. If this medication is used in lactation the lowest effective dose should be given for the shortest possible period of time. The neonate should also be monitored for signs of sedation such as not waking up to feed at regular intervals.

### **Adverse reactions**

Benzodiazepines may cause drowsiness, blurred vision, dizziness and impaired concentration. Other potential side effects include lack of muscle coordination, nausea, constipation, visual disturbances, skin rash, and loss of bladder control. If breathing difficulties, fainting, rash or hypotension are experienced a physician should be contacted immediately.

Clinical judgement should be exercised as benzodiazepines cross the placental barrier. Should labour progress more rapidly than anticipated, Flumazenil, a benzodiazepine receptor antagonist, may be required and should be readily available for administration. Immediately after administration physician consultation is required. (Please refer to the section on Flumazenil at the end of the benzodiazepine section).

### **Dosage and administration**

Insomnia – 10-30 mg PO at bedtime

Anxiety – 10-30 mg PO TID-QID

In prodromal labour the dose may be repeated 8 or 12 hours following first dose if active labour is not yet established. No more than two consecutive doses should be given. In treating postpartum anxiety, the dose may be repeated every 8 to 12 hours in the postpartum period for no more than 3 days or a maximum of six doses. Once postpartum treatment is initiated, physician consultation must be arranged.

### **Prescribing/ordering**

Oxazepam may be prescribed in hospital or in the community. It does not require a controlled drugs and substances duplicate prescription pad. A prescription cannot exceed three days. No refills.

### **Onset of action**

Peak of action is 2-4 hours

### **Half-life**

Adult - 8 hours

Neonate - unknown

### **Elimination**

Urine as metabolites

## FLUMAZENIL (UPDATED MAY 2019)

(Anexate®, Romazicon®). Flumazenil is **not** a controlled substance but has been included here for reference purposes. Flumazenil is a benzodiazepine receptor antagonist and acts as an antidote in reversing the CNS-depressant effects of benzodiazepine compounds. Flumazenil has no effect on CNS depression from other causes such as opioids, alcohol, barbiturates or general anesthetics. Flumazenil, if required, should be readily available for administration.

### Indications for clinical use

For reversal of benzodiazepine use during procedure, or known isolated benzodiazepine overdose in those who are not taking benzodiazepines chronically.

### Contraindications

Hypersensitivity to flumazenil or benzodiazepines or to any component of the formulation.

### Warnings and precautions

Flumazenil may not reverse respiratory depression as well when longer-acting benzodiazepines have been used. There is a need to monitor in the event that respiratory depression or sedation returns. Flumazenil may not reverse amnesia. Immediately after administration physician consultation is required.

Consult physician immediately if patient takes benzodiazepines chronically but has an acute overdose – risk of seizures may occur. The indications for flumazenil in clinical use are for benzodiazepine reversal during procedure, or known isolated benzodiazepine overdose in those who are not taking benzodiazepines chronically. The number of different types of benzodiazepines does not affect efficacy of flumazenil, however flumazenil's half-life may be shorter than the benzodiazepines used and repeated doses may be necessary.

### Pregnancy

Compatible

Although an assessment of the teratogenic risk in humans cannot be made, animal data suggests the risk is low. Human-placenta transfer to the fetus is unknown, and despite the moderate plasma protein binding capacity and inactive metabolites, the very short elimination half-life will limit exposure. The indications for flumazenil are such that the benefit should outweigh the unknown fetal risk.

### Lactation

No Data- Probably Compatible

Flumazenil may be considered suitable for use in lactation as this medication has a very short half-life, however when administering this medication to a breastfeeding client for a benzodiazepine overdose, breastfeeding may need to be withheld due to the amount of benzodiazepine in milk and the potential risk of adverse effects (respiratory depression, sedation).

### **Adverse reactions**

Headache; fatigue; tremor; weakness; diaphoresis; agitation; nausea/vomiting; seizure although rare.

### **Dosage and administration**

0.1mg/ml injectable solution

IV: 0.2mg over 30 seconds

If there is inadequate response 30 seconds after the first dose, give 0.3 mg IV over 30 seconds. If inadequate response continues, repeat doses of 0.5 mg IV over 30 seconds can be given at one (1) minute intervals to a maximum cumulative dose of 3 mg.

### **Onset of action**

30-60 seconds

### **Half-life**

Adult - 4-11 minutes

Neonate – unknown

### **Elimination**

Liver

## Controlled substances and related medications for use in labour

### FENTANYL CITRATE (UPDATED MAY 2019)

Fentanyl citrate (Fentanyl) is a short-acting opioid which binds with receptors at many sites within the CNS, alters pain reception and increases the pain threshold. Fentanyl has no active metabolites and produces less sedation, nausea, and vomiting than morphine.

#### Indications and clinical use

Midwives may only prescribe, order or administer fentanyl on their own authority for the purpose of pain relief in labour *in hospital* and not for any other purpose. Administration under any other circumstance must be on the order of a physician.

#### Contraindications

Fentanyl should not be used in the presence of uncorrected hypotension or hypovolemia, liver or kidney disease, respiratory compromise (e.g. severe asthma, cystic fibrosis), allergy or prior intolerable side effects to fentanyl (hallucinations) or a known hypersensitivity to fentanyl.

Fentanyl should not be used in the presence of an atypical or abnormal fetal heart rate or in the second stage of labour.

Fentanyl should not be administered within one hour of anticipated delivery.

#### Warnings and precautions

Fentanyl should be used with caution where there is a history of difficult intubation, if more than one dose of a longer-acting narcotic has already been received in labour, for preterm labour due to increased risk of respiratory depression in the neonate, in gestational hypertension due to increased sensitivity of hemodynamic effects of fentanyl or in those with a BMI greater than 35 as fentanyl is lipophilic and can lead to latent respiratory depression.

Opioids given near delivery may cause respiratory depression in the neonate at birth. The risk increases with increased cumulative doses. Prolonged use in gestation may cause neonatal withdrawal.

Naloxone should be readily available for administration. Physician consultation immediately after administration is required if Naloxone needs to be given.

Fentanyl may cause CNS depression which may impair physical or mental abilities. Use with caution in the presence of hepatic dysfunction, renal impairment, pre-existing respiratory compromise (hypoxia and/or hypercapnia), substance use or alcohol use.

One-to-one care must be provided. Monitor post administration according to hospital protocol or monitor vital signs, including respirations, and sedation scores for 30 minutes after IV fentanyl administration, then hourly for 4 hours.

Monitor oxygen saturation for 5-minute periods if bolus dose of 2 mcg/kg or total doses greater than 200 mcg/hr are used *or* if morphine or meperidine has been administered IM in the 3 hours preceding IV fentanyl administration. A physician should be consulted if oxygen saturations fall below 94%.

### **Pregnancy**

Human Data Suggest Risk

Opioid use during organogenesis is associated with a risk of congenital birth defects. Neonatal withdrawal is a risk after long-term exposure in pregnancy.

### **Lactation**

Category L2 - Limited Data- Probably Compatible

Fentanyl is considered suitable in lactation due to its shorter half-life and lack of an active metabolite. About 3-5% of the dose is known to enter milk. If this medication is used in lactation the lowest effective dose should be given for the shortest possible period of time. The neonate should also be monitored for signs of sedation, such as not waking up to feed at regular intervals.

### **Adverse reactions**

Fentanyl may cause respiratory depression during labour and in the neonate at birth. Extra caution should be observed if fentanyl use continues for more than 5 hours or a total dose of 300 mcg has been administered. The larger the adult dose administered during labour, the greater the risk of neonatal respiratory depression. O<sub>2</sub> saturation monitoring of the neonate is advised for at least 2 hours after birth whenever greater than 250 mcg has been given. As with any narcotic, watch for aspiration, drowsiness, hypotension and/or obtunded reflexes in addition to respiratory depression.

### **Dosage and administration**

The recommended weight-based dose is 0.5 - 1 mcg/kg over 1-2 minutes waiting 5 minutes for effect and repeating every 10 minutes until satisfactory pain relief or a total maximum dose of 2 mcg/kg/hr (or 200 mcg/hr or 2-4 doses in 1 hour) has been given. Alternatively, with continuous O<sub>2</sub> saturation monitoring, doses up to 1 mcg/kg (max. 100 mcg) can be given initially with repeat dosing every 15-20 minutes to a total of 200 mcg/hr (or 2 doses). Once a total dose of 3 mcg/kg has been administered, epidural or other alternate pain relief measures should be considered.

Add 100 micrograms (2 mL ampoule) to 8 mL normal saline to obtain 10 mL solution (concentration 10 mcg/mL) and give IV.

### **Ordering**

Fentanyl citrate may only be prescribed in hospital for the specific purposes listed here following hospital protocols.

### **Onset of action**

3-5 minutes

Time to peak effect: 5-15 minutes

### **Half-life**

Adult – 2.4 hours

Neonate – 1.15 hours

## MORPHINE SULPHATE ( *UPDATED MAY 2019* )

Morphine sulphate (morphine) is an opioid. It binds to opiate receptors in the CNS, causing inhibition of pain pathways, altering perception and pain response and producing generalized CNS depression. Morphine has a similar analgesic action to Demerol® (Meperidine), but with less nausea and fewer significant side effects for the neonate.

### Indications and clinical use

Midwives may only prescribe, order and administer morphine *in hospital* on their own authority for the purpose of pain relief in non-progressive or prodromal labour and in early active labour<sup>4</sup>. Use under any other circumstance must be on the order of a physician. Morphine can be administered intramuscularly for therapeutic rest or as an analgesic for pain relief in labour.

Intramuscular (IM) morphine is often administered with dimenhydrinate (Gravol®) to counteract the side effects of nausea and vomiting. The two drugs are compatible in a syringe for only 15 minutes.

As morphine is more sedating and has a longer half-life than fentanyl, it may be a more beneficial early labour analgesic when intramuscular administration will provide longer relief, or for those who do not want IV access in labour.

### Contraindications

Hypersensitivity to morphine sulfate or any component of the formulation; alcohol use; seizure disorders.

Morphine should not be used in the presence of an atypical or abnormal fetal heart rate, in advanced labour or the second stage of labour.

### Warnings and precautions

Naloxone should be readily available for administration. Physician consultation immediately after administration is required if naloxone needs to be given.

Morphine should be used with caution in patients with a history of substance use, alcohol use or hepatic impairment, or in patients with renal impairment, pre-existing respiratory compromise (hypoxia and/or hypercapnia), seizure disorders or thyroid dysfunction.

### Monitoring

Determine cervical dilation prior to administration; generally, a nullipara should be less than 7 cm and a multipara less than 4 cm. Assess well-being prior to morphine administration, 15 minutes post administration and according to hospital protocol thereafter. Protocols in some centers allow

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<sup>4</sup> See monitoring section when IM morphine has been administered in early labour.

discharge home during early labour when IM morphine has been administered and there are no health concerns.

### Pregnancy

Human Data Suggest Risk

Opioid use during organogenesis is associated with a risk for congenital birth defects. Placental transfer is rapid. Neonatal withdrawal and potential respiratory depression is a risk with use of morphine late in pregnancy.

### Lactation

Category L3 - Limited Human Data – Probably Compatible (not the preferred narcotic in lactation)

Morphine is considered suitable for short term use in lactation; however, about 9-35% of the dose is known to enter breastmilk. This medication also has an active metabolite, thus the lowest effective dose should be given for the shortest possible period of time. The infant should also be monitored for signs of sedation such as not waking up to feed at regular intervals. If an ongoing narcotic is required postpartum consider other alternative agents such as hydromorphone.

### Adverse reactions

Morphine crosses the placental barrier and can produce depression of respiration and psychophysiological functions in the neonate. As with other opioids, morphine can depress respirations during labour and in the neonate. The larger the adult dose administered during labour, the greater the risk of neonatal respiratory depression. As with any narcotic, watch for aspiration, drowsiness, hypotension and/or obtunded reflexes in addition to respiratory depression and urinary retention.

Adult: Circulatory depression, flushing, shock, bradycardia, hypotension, drowsiness, dizziness, confusion, headache, pruritus, chest pain, hypertension, tachycardia, vasodilation, amnesia, anxiety, hallucination, nervousness, restlessness, seizure, slurred speech, rash.

### Dosage and administration

10-15mg IM every 4 hours; or

2-5mg dose IV bolus every 10 minutes prn for 1-2 hours of relief

Maximum daily dose 45 mg

Morphine has a half-life of 2-4 hours in adults and a half-life of 9 hours in neonates (or longer in premature neonates). Morphine may be used up to 4 hours prior to anticipated delivery. Most infants delivered 3 hours after a dose have been found to have no detectable levels in cord blood samples.

IM administration may be particularly appropriate for the nullipara seeking pain relief in early active first stage. Morphine should **not** be administered subcutaneously as consistency of uptake and

effectiveness cannot be determined. Morphine is often administered with dimenhydrinate (Gravol®) to counteract the side effects of nausea and vomiting.

### **Ordering**

Morphine may only be prescribed in hospital for the specific purposes listed here following hospital protocols.

### **Onset of action**

IM: 15-20 minutes

Time to peak effect: 40-50 minutes

IV: 5-10 minutes

### **Half-life**

Adult - IM: 2-4 hours

IV: 2-4 hours

Neonate – 9 hours and 18 hours metabolite

## **NALOXONE HYDROCHLORIDE (UPDATED MAY 2019)**

Naloxone hydrochloride (Narcan®) is a narcotic antagonist used to treat opioid toxicity and overdose.

Note: The American Academy of Pediatrics (AAP) no longer recommends the use of naloxone hydrochloride (naloxone) for neonatal resuscitation<sup>5</sup> at birth. There is insufficient data on the efficacy and short-term and long-term safety of naloxone to reverse respiratory depression in the neonate caused by maternal opiate exposure in labour close to the time of birth. There is also concern that naloxone is misused during resuscitation and could lead to seizures when administered to infants of opioid-dependent women. The Canadian Neonatal Resuscitation Program (NRP) Executive Committee is in agreement with this recommendation<sup>6</sup>. Refer to the most current NRP recommendations for first-line treatment of neonatal respiratory depression.

### **Indications and clinical use**

To reverse opioid toxicity.

### **Contraindications**

Previous hypersensitivity reaction to naloxone.

### **Warnings and precautions**

Naloxone is not effective in reversing respiratory depression due to any other cause than opioid toxicity. Naloxone is not recommended for use during newborn resuscitation.

### **Compatibility- pregnancy**

Compatible

No evidence of impaired fertility or fetal harm. Naloxone crosses the placenta quickly and appears in fetal blood within 2 minutes following adult dose.

### **Compatibility- lactation**

Category L3 - No Human Data – Probably Compatible

Naloxone is considered suitable for use in lactation. This medication has a very short half-life (one hour), is poorly absorbed orally and plasma levels in adults are thought to be undetectable two hours after oral doses. When administering this medication to a breastfeeding client for a narcotic overdose, breastfeeding may need to be withheld due to the amount of narcotic in milk and potential risk of adverse effects including respiratory depression and sedation.

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<sup>5</sup> [http://circ.ahajournals.org/content/122/16\\_suppl\\_2/S516#sec-61](http://circ.ahajournals.org/content/122/16_suppl_2/S516#sec-61)

<sup>6</sup> [http://www2.aap.org/nrp/docs/15535\\_NRP%20Guidelines%20Flyer\\_English\\_FINAL.pdf](http://www2.aap.org/nrp/docs/15535_NRP%20Guidelines%20Flyer_English_FINAL.pdf)

### Adverse reactions

Adverse reactions are typically related to reversing dependency and precipitating withdrawal and include abdominal cramps, diarrhea, nausea, vomiting, muscle weakness, dyspnea, respiratory depression, restlessness, irritability, cardiac arrest, fever, hypertension, hypotension and/or tachycardia.

### Dosage and administration

May be administered IV or IM routes. IM route not recommended due to slow onset of action and therapeutic effect.

Adult initial dose of naloxone for reversal of respiratory depression caused by a therapeutic dose of opioids:

- **IV:** 0.04-0.4mg, may repeat until desired response is achieved
- **IM:** 0.04-0.4mg, may repeat until desired response is achieved

Adult initial dose of naloxone cause by opioid overdose:

- **IV:** 0.4-2mg, may repeat until desired response is achieved
- **IM:** 0.4-2mg, may repeat until desired response is achieved

### Additional considerations

- consult physician following administration;
- may need to repeat doses every two to three minutes and an IV infusion may be required (midwives are unable to prescribe a naloxone IV infusion);
- additional dose(s) may be required after reversal has occurred based on the opioids half-life.

### Onset of action

- **IV:** 2 minutes
- **IM:** 2-5 minutes

### Half-life:

Adult - 0.5-1.5 hours

### Excretion

Urine as metabolites

## Controlled substances and related medications for use postpartum

### ACETAMINOPHEN WITH CODEINE (*UPDATED MAY 2019*)

(Tylenol<sup>®</sup> with Codeine No.3). An analgesic, combined opioid which peripherally blocks pain impulses as synthesis of prostaglandins in the CNS is inhibited.

Binding to opiate receptors in the CNS alters perception and response to pain which causes generalized CNS depression. Produces antipyresis and binds to opiate receptors in the CNS, altering perception and response to pain.

#### Indications and clinical use

Acetaminophen and codeine combined may be prescribed by midwives **for up to 72 hours postpartum** to relieve moderate to severe pain in the postpartum period following vaginal and/or operative delivery.

Note: a number of non-codeine-containing pain medications taken at regularly scheduled intervals in the first few days postpartum often will provide adequate pain relief without the risks or side effects of codeine exposure.

#### Contraindications

Hypersensitivity to acetaminophen, codeine, or any component found in the formulation. Contraindicated in patients with respiratory depression, bronchial asthma, hypercapnia, paralytic ileus, or known CYP2D6 ultra-metabolizers who are breastfeeding due to risk of neonatal poisoning.

#### Warnings and precautions

Due to the potential neonatal adverse effects of codeine **acetaminophen with codeine should NOT be taken during lactation**. If a pain medication is required, a different narcotic is preferred. Acetaminophen and codeine may also contain caffeine which can cause CNS and cardiovascular stimulation. Use with caution in patients with a history of peptic ulcer or GERD. May cause hepatotoxicity in the following: excessive use >4 g/day of acetaminophen-containing medications, alcohol use, pre-existing liver disease or chronic daily use.

#### Caution

Metabolism of the codeine portion is variable. Codeine must be metabolized to its active metabolite, morphine, to have a pain-relieving effect. Some people are rapid metabolizers, and may experience enhanced effect but also enhanced adverse effects such as drowsiness and sedation. Where there is a genetic predisposition to rapid metabolizing (CYP 2D6 enzyme) and increased conversion to morphine, breastfed neonates can be at significant, even life-threatening, risk. Given that an ultra-

rapid metabolizer genotype occurs in 1% in Caucasians and up to 30% in some parts of Asia and Africa, this polymorphism is clinically important. One case of neonatal death has been reported and multiple cases of neonatal apnea have occurred with the use of the medication in lactation. Exposure to acetaminophen with codeine during breastfeeding is not recommended.

Note: Some people cannot metabolize codeine to morphine, so for these people, codeine is not effective.

### **Pregnancy**

Acetaminophen – Human Data Suggest Low Risk

Codeine - Human Data Suggest Risk

There is a risk of congenital birth defects if exposure occurs during organogenesis. There is evidence of fetal and neonate toxicity if addicted to codeine or other opioids, or if high doses of these agents during the later half of pregnancy or close to delivery are consumed. Avoid in the 1<sup>st</sup> and 3<sup>rd</sup> trimesters of pregnancy.

### **Lactation**

Acetaminophen – Category L1 - Compatible

Codeine – Category L4 - Limited Data - Possibly Hazardous

Codeine is not recommended for use in lactation or the pediatric population because of its variable metabolism, via the CYP 2D6 enzyme, to its active metabolite (morphine). In addition, about 9-35% of an adult dose of morphine is known to enter breastmilk, the amount of morphine that would enter milk after codeine ingestion can be highly variable based on metabolism. There have been case reports of apnea and respiratory depression causing death with use of this medication in lactation. If ongoing narcotic is required postpartum consider other alternative agents such as hydromorphone.

### **Adverse reactions**

In greater than 10%: Dizziness, lightheadedness, sedation, nausea, vomiting, dyspnea.

In 1% to 10%: Dysphoria, pruritus, abdominal pain, constipation.

### **Dosage and administration**

Usual dose: Acetaminophen 300 mg and codeine phosphate 30 mg PO q4-6 hours

Maximum dose: Acetaminophen 4000 mg/24 hours Codeine 240 mg/24 hours and;

Dose adjustment/titration should be made according to appropriate analgesic effect as long a maximum dose is not exceeded.

### **Prescribing/ordering**

Acetaminophen with codeine no.3 may be prescribed in hospital or in the community. It does not require a controlled drugs and substances duplicate prescription pad. A prescription cannot exceed three days. No refills.

### **Onset of action**

30-60minutes

Time to peak effect: 60-90 minutes

### **Half-life**

Adult - PO: 2 hours for acetaminophen, 3 hours for codeine and 5 hours for caffeine

Neonate – 7 hours for acetaminophen, 4.5-13.3 active metabolite morphine, 72-96 hours for caffeine

### **Elimination**

In urine as metabolites

## ACETAMINOPHEN WITH OXYCODONE (*UPDATED MAY 2019*)

(Endocet<sup>®</sup>, Percocet<sup>®</sup>). An analgesic combined opioid which blocks pain perception in the cerebral cortex by binding to opiate receptors in the CNS. Binding inhibits the flow of pain sensations and peripherally blocks pain impulses as synthesis of prostaglandins in the central nervous system is inhibited. Produces antipyresis and binds to opiate receptors in the CNS, altering perception and response to pain.

### Indications and clinical use

Acetaminophen and oxycodone combined **may be prescribed by midwives for up to 72 hours postpartum to** relieve moderate to severe pain in the postpartum period following vaginal and/or operative delivery. **Midwives may only prescribe, order or administer acetaminophen with oxycodone on their own authority for the purpose of postpartum pain relief and not for any other purpose.** If a longer course of a pain medication is required, a non-narcotic medication should be prescribed upon discharge or a referral to a physician to determine if continued use of acetaminophen with oxycodone seems appropriate.

For clients with poorly controlled pain, maximum doses of non-narcotic analgesics such as acetaminophen and nonsteroidal anti-inflammatory drugs should be considered prior to prescribing this medication.

### Contraindications

Hypersensitivity to oxycodone, acetaminophen, or any component found in the formulation. Contraindicated in the presence of respiratory depression, bronchial asthma, hypercarbia, paralytic ileus.

### Warnings and precautions

May cause CNS depression, impairing mental or physical abilities. Use with caution in known G6PD deficiency. May cause hepatotoxicity in the following: with excessive use > greater than 4 g/day of acetaminophen-containing medications; alcohol use; pre-existing liver disease; or chronic daily use. History of substance use should be considered before prescribing or ordering oxycodone as it is an opioid agonist of the morphine-type and can be misused in a similar manner as other opioid agonists, legal or illicit.

### Pregnancy

Acetaminophen – Human Data Suggest Low Risk

Oxycodone- Human Data Suggest Risk

There is a risk of congenital birth defects if exposure occurs during organogenesis. Use for prolonged periods or at high doses at term can cause respiratory depression or withdrawal in the neonate.

## Lactation

Acetaminophen – Category L1 - Compatible

Oxycodone – Category L3 - Limited Data- Probably Compatible

Oxycodone is considered suitable for short-term use in lactation; about 1.5-3.5% of the dose is known to enter breastmilk. The lowest effective dose should be given for the shortest possible period of time. The neonate should also be monitored for signs of sedation, such as not waking up to feed at regular intervals. If ongoing narcotic is required postpartum consider other alternative agents such as hydromorphone.

## Adverse reactions

Allergic reaction, dizziness, light-headedness, nausea, vomiting, constipation, dysphoria, respiratory depression, sedation, skin rash.

## Dosage and administration

### Usual initial dose for mild to moderate pain:

Oxycodone: PO 2.5 mg, Acetaminophen: PO 325 mg (every 6 hours prn)

Usual initial dose for severe pain:

Oxycodone: PO 5 mg, Acetaminophen: PO 325 mg (6 hours prn)

### Maximum daily dose:

Oxycodone 20 mg/24 hours. Acetaminophen: 4000 mg/24 hours.

Doses should be given every 6 hours as needed and titrated accordingly based on appropriate analgesic effects.

The initial dose is based on the oxycodone content and the maximum daily dose is based on the acetaminophen content.

## Prescribing/ordering

Acetaminophen with oxycodone may be prescribed in hospital or in the community. If Acetaminophen with oxycodone is prescribed in the community, a controlled drugs and substances duplicate prescription pad must be used<sup>7</sup>. A prescription cannot exceed three days. No refills.

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<sup>7</sup> Regulator-approved controlled drugs and substances duplicate prescription pads are not yet available for use by midwives.

### Onset of action

10-30 minutes

Time to peak effect: 30-60 minutes

### Half-life

Adult - 2 hours for acetaminophen, ranges from 3.7 (2-4 hours) for oxycodone, 5 hours for extended release

Neonate – 7 hours for acetaminophen, 1.2-3 hours for oxycodone

*Prescribing extended-release analgesic medication is not within midwifery scope of practice. If a client has been prescribed or is currently taking an extended release prescription medication such as oxycodone or hydromorphone and requires additional pain management in labour or during the early postpartum period, a physician consultation or order is required.*

### Elimination

In urine as metabolites

## HYDROMORPHONE (*UPDATED MAY 2019*)

(Dilaudid-HP<sup>®</sup>, Dilaudid<sup>®</sup>). A potent semisynthetic narcotic analgesic which binds to opioid receptors in the CNS, inhibiting ascending pain pathways which in turn alters the response and perception of pain.

### Indications and clinical use

Hydromorphone **may be prescribed by midwives for up to 72 hours postpartum** following vaginal and/or operative delivery. It is more potent than morphine by approximately 7-10 times, but used in lower doses. **Midwives may only prescribe, order or administer hydromorphone on their own authority for the purpose of short term postpartum pain relief.** If a longer course of a pain medication is required, a non-narcotic medication should be prescribed or a referral made to a physician to determine if continued use of hydromorphone seems appropriate. Hydromorphone is the preferred drug of choice over tramadol or acetaminophen/codeine for breastfeeding clients.

For clients with poorly controlled pain, maximum doses of non-narcotic analgesics such as acetaminophen and nonsteroidal anti-inflammatory drugs should be considered prior to prescribing a single entity narcotic such as hydromorphone.

### Contraindications

Hypersensitivity to hydromorphone or any component found in the formulation. Contraindicated in patients with respiratory depression, acute or severe asthma.

### Warnings and precautions

May cause CNS depression impairing mental or physical abilities. May cause potentially life threatening respiratory depression. Use with caution in patients with a history of seizure disorder, hypovolemia, cardiovascular disease, substance use. A history of substance use should be considered before prescribing or ordering hydromorphone as it is a highly addictive morphine-type drug and can be abused in a similar manner as other opioid agonists, legal or illicit.

### Pregnancy

Human Data Suggest Risk

There is a risk of congenital birth defects if exposure occurs during organogenesis. There is a risk of neonatal withdrawal with prolonged in utero exposure. Respiratory depression in the neonate that is similar to that produced by morphine can be expected.

### Lactation

Category L3 - Limited Data- Probably Compatible (preferred narcotic in lactation)

Hydromorphone is considered the preferred narcotic in lactation. This medication does not have an active metabolite and less than 1% of the dose has been found to enter milk. The lowest effective dose should be given for the shortest possible period of time. The neonate should also be monitored for signs of sedation, such as not waking up to feed at regular intervals.

### Adverse reactions

Bradycardia, hyper/hypotension, vasodilation, tachycardia, CNS depression, confusion, dizziness, hallucinations, headache, memory impairment, mood alterations, seizure, GI disturbances.

### Dosage and administration

For moderate pain: 1-4 mg PO (immediate release) every 4-6 hours PRN

Maximum dose: 9 mg per 24 hours.

### Prescribing/ordering

Hydromorphone may be prescribed in hospital or in the community. If Hydromorphone is prescribed in the community, a controlled drugs and substances duplicate prescription pad<sup>8</sup> must be used. A prescription cannot exceed three days. No refills.

### Onset of action

Oral: 15-30 minutes; peak effect: 30-60 minutes

Extended release tablet: 6 hours; peak effect: 9 hours

### Half-life

Adult - Oral extended release: 11 hours

Oral immediate release: 2-3 hours

Time to peak: Immediate release tablet: less than  $\leq$  1 hour

Extended release tablet: 12-16 hours

Neonate - Unknown

*Prescribing extended-release analgesic medication is not within midwifery scope of practice. If a client has been prescribed or is currently taking an extended release prescription medication such as oxycodone or hydromorphone and requires additional pain management in labour or during the early postpartum period, a physician consultation or order is required.*

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<sup>8</sup> Regulator-approved controlled drugs and substances duplicate prescription pads are not yet available for use by midwives.

## ACETAMINOPHEN WITH TRAMADOL (*UPDATED MAY 2019*)

(Tramacet<sup>®</sup>) is **not** a controlled substance but has been included here because it contains Tramadol, a non-federally regulated opioid analgesic that appears to have a reduced addictive potential.

Acetaminophen and Tramadol is an analgesic, opioid combination medication. Tramadol is more potent than codeine and most closely resembles the opiates.

**Acetaminophen** component: Inhibits prostaglandin synthesis in the central nervous system and peripherally blocks pain impulse; it produces antipyresis from inhibition of the hypothalamic heat-regulating center.

**Tramadol** component: Binds to opiate receptors in the CNS causing inhibition of ascending pain pathways, altering pain perception and response to pain; also inhibits norepinephrine and serotonin uptake, and modifies ascending pain pathways.

### Indications and clinical use

Combined Acetaminophen and Tramadol **may be prescribed by midwives for up to 72 hours postpartum** to relieve acute short-term moderate to severe pain in the postpartum period following vaginal and/or operative delivery.

### Contraindications

Hypersensitivity to acetaminophen, tramadol, opioids, or any component of the formulation; opioid-dependent patients; narcotics, centrally-acting analgesics or psychotropic drugs; hepatic dysfunction.

Tramadol is contraindicated during or within 14 days following monoamine oxidase (MAO) inhibitor therapy first generation antidepressants. The MAO inhibitor antidepressants are older antidepressants, now reserved for extremely resistant cases of depression unresponsive to new agents: Isocarboxazid (Marplan<sup>®</sup>), Phenelzine (Nardil<sup>®</sup>), Tranylcypromine (Parnate<sup>®</sup>), Moclobemide (generics).

### Warnings and precautions

Acetaminophen: Do not exceed the maximum recommended dose (4000 mg = 4 g) per 24 hours. Liver toxicity has been reported following chronic abuse of acetaminophen at > 200 mg/kg/day.

Tramadol: May cause CNS depression and/or respiratory depression and may impair physical or mental abilities.

Use with caution in patients taking tranquilizers and/or antidepressants, or those with an emotional disturbance including depression; history of seizure disorder.

\*CNS depressants: Use with caution and reduce dosage when administering to patients receiving other CNS depressants.

Tramadol may enhance the neuroexcitatory and/or seizure-potentiating effect of MAO Inhibitors. Consider alternatives to combined treatment with tramadol and monoamine oxidase inhibitors due to an increased risk of serotonin syndrome and seizures.

\*Serotonin syndrome: Avoid, if possible, use with serotonergic agents such as triptans (migraine treatment), lithium, sibutramine, meperidine, dextromethorphan, St John's wort, any anti-depressant including: TCAs, MAO inhibitors (use with extreme caution; contraindicated in Canadian product labeling), SNRIs, and SSRIs (such as citalopram, sertraline, fluoxetine etc.) venlafaxine, trazodone; use caution with drugs which impair metabolism of tramadol (ie, CYP2D6 and 3A4 inhibitors); concomitant use may increase the risk of serotonin syndrome.

A history of anaphylactoid reactions to opioids may increase risks for similar reactions to tramadol.

Healthcare provider should be alert to problems of abuse, misuse, and diversion.

### **Pregnancy**

Acetaminophen – Human Data Suggest Low Risk; Compatible

Tramadol - Human Data Suggest Risk

There is a risk of congenital birth defects if exposure occurs during organogenesis. Continuous intake leads to the potential complication of neonatal withdrawal. Long term neurobehavior effects of the neonate are unknown.

### **Lactation**

Acetaminophen – Category L1 - Compatible

Tramadol – Category L3 - Limited Data - Probably Compatible

Tramadol is considered suitable for short term use in lactation as about 3% of the dose enters milk. However, the U.S. Food & Drug Administration has issued a warning against the use of Tramadol during lactation and in pediatric patients due to adverse events. This medication has an active metabolite via the CYP 2D6 enzyme, thus caution is recommended. In addition, experience with this medication is limited in the neonatal/pediatric population. If this medication is given in lactation, the lowest effective dose should be given for the shortest possible period of time. The neonate should also be monitored for signs of sedation, such as not waking up to feed at regular intervals. If ongoing narcotic is required postpartum consider other alternative agents such as hydromorphone.

### **Adverse reactions**

Acetaminophen – Diarrhea, gastric upset with overdose.

Tramadol - Sedation, respiratory depression, nausea, vomiting, constipation, pruritus, hives, angioedema, bronchospasm, toxic epidermal necrolysis, Stevens-Johnson syndrome have been reported.

Rare reactions including anaphylactoid fatalities have been reported following initial dosing. Adverse events were observed in animal studies. Tramadol has been shown to cross the human placenta when administered during labor. Postmarketing reports following tramadol use during pregnancy include neonatal seizures, withdrawal syndrome, fetal death, and stillbirth. Not recommended for intrapartum use.

### **Dosage and administration**

Tramacet<sup>®</sup> is a combination medication consisting of the following:

Acetaminophen: 325 mg plus Tramadol: 37.5 mg

Usual dose: PO1- 2 tablets every 4 to 6 hours PRN

Maximum dose: PO 8 tablets per 24 hours

Note: if 8 tablets are taken daily, this equals: acetaminophen 2600 mg/day. Maximum dose of acetaminophen is 4,000 mg/day, a top up with plain acetaminophen (4 x 325 mg or 2 x 500 mg) per 24 hours is considered safe.

May be administered with or without food.

### **Prescribing/ordering**

Acetaminophen with tramadol may be prescribed in hospital or in the community. It does not require a controlled drugs and substances duplicate prescription pad. A prescription cannot exceed three days. No refills.

### **Onset of action**

Acetaminophen: < less than 1 hour

Tramadol: 60-90 minutes.

Time to peak effect: Tramadol: 2-3 hours

### **Half-life**

Adult – Acetaminophen – 2 hours, Tramadol - 6-8 hours, 7-9 for the active metabolite

Neonate – Acetaminophen – 7 hours, Tramadol – 3.6 hours in children (no data in neonates)

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The Prescriptions Regulations synopsis of federal and provincial laws and regulations governing the distribution of drugs by prescription in British Columbia information is available at the following website: [http://library.bcpharmacists.org/6\\_Resources/6-4\\_Drug\\_Distribution/5014-Prescription\\_Regulation\\_Table.pdf](http://library.bcpharmacists.org/6_Resources/6-4_Drug_Distribution/5014-Prescription_Regulation_Table.pdf)

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