STANDARDS, LIMITS AND CONDITIONS FOR PRESCRIBING, ORDERING AND ADMINISTERING CONTROLLED SUBSTANCES

Preamble

Registered midwives in British Columbia are permitted to prescribe drugs according to the Health Professions Act - Midwives Regulations and *CMBC Standards, Limits and Conditions for Prescribing, Ordering and Administering Drugs* and *CMBC Standards, Limits and Conditions for Prescribing, Ordering and Administering Controlled Substances*

The College of Midwives of BC (CMBC) expects diligence when prescribing all drugs, including controlled substances. The midwife must maintain proper records, supply necessary information to the client regarding the proper use of the drug(s) and maintain adequate security for drug inventories as per the *College of Pharmacists Operations and Drug Scheduling Act*. The midwife must check each prescription for accuracy prior to its release to clients as a pharmacist would prior to filling a prescription.

The following are the standards for midwives to independently prescribe, order and administer controlled substances as designated under federal and provincial/territorial regulation.

Prescribing and Administering Drugs Standards

Midwifery standards of practice refer to the minimum standard of professional behavior and clinical practice expected of BC registered midwives when prescribing and administering drugs.

Midwives must have the necessary knowledge, skills and judgment to prescribe drugs from the list of designated drugs in the midwives regulations.

Midwives can prescribe drugs that are within their scope of practice.

Safety

Midwives must:

- assess the client, conduct necessary laboratory and diagnostic investigations;
- comply with relevant federal and provincial legislation;
- adhere to all relevant standards, guidelines or policies established by agencies or organizations such as public health units or blood banks involved in the provision or control of any of the authorized drugs or substances;
- provide a written, or when necessary, a telephone or verbal prescription order;
- consider whether the drug is a safe and effective treatment option for the specific client circumstances;
- provide the client and/or client representative with the necessary information about the drug prescribed such as expected therapeutic effect, potential side effects, contraindications and precautions;

- consider drug resistance, medication errors, infection control and safety when prescribing and/or administering any substance from the regulation;
- ensure that there are adequate systems in place to prevent prescription fraud;
- ensure proper reporting of drug reactions and medication errors;
- monitor client response to the drug therapy after prescribing, and continue, adjust dosage or discontinue the drug therapy as appropriate.

Record Keeping

Midwives must:

- obtain a health history and document the symptoms and/or conditions being treated;
- review and obtain a full comprehension of the drugs the client is taking;
- document in the client record, in a timely manner, all telephone or verbal prescription orders;
- provide a follow-up care plan as appropriate, and document in the client record;
- document the client's response to the drug therapy;
- ensure proper recognition and management of medication errors including documentation and reporting;
- ensure proper risk management reporting when drug reactions or medication errors occur.

Prescriptions

A prescription prepared by a midwife must include:

- full date;
- client's name;
- client's address;
- name of drug, drug strength when applicable, dose and the quantity of the prescribed drug;
- full instructions/directions for use of the prescribed drug;
- refill instructions, if any;
- printed name of the midwife prescriber with telephone number and address;
- CMBC registration number and the professional designation;
- midwife's signature;
- may not prescribe "for office use".

Midwives obtaining consults and providing inter-professional care, relating to prescriptions:

- may not delegate the act of prescribing a drug;
- must notify any relevant health care provider involved in the client's care when clinically appropriate and document this action;
- consult with appropriate health care professional if the client's response to the drug therapy is other than anticipated.

When midwives continue drug therapy initiated by another health care professional, they must:

- provide and document ongoing assessments;
- monitor and document the client's response to the drug therapy;
- communicate the client's response and change to or discontinuation of drug therapy to the initiating health care provider as appropriate;

- consult with the appropriate health care professional at any point for continuing drug therapy as appropriate.

The following are the standards for midwives to independently prescribe, order and administer controlled substances as designated under federal and provincial/territorial regulation.

Standards for Control & Prevention of Diversion or Abuse of Controlled Substances in Midwifery Practice

General Prescribing Practice
Midwives are required to follow hospital protocols, record-keeping and security procedures for all prescribing, ordering, administering or disposing of controlled substances.

Writing Prescriptions: Prescriptions must be written on regulator-approved prescription pads in a manner so that they are difficult to alter. ***Please note that while CMBC is working on this, RMs do not currently have access to duplicate prescription pads***. Prescription pads should be stored out of sight in a secure location in the office and never left unattended in a medical bag. No refills are allowed.
http://library.bcpharmacists.org/D-Legislation_Standards/D-4_Drug_Distribution/5014-Prescription_Regulation_Table.pdf

Unique Identifier Number: Midwives must use a unique identifier number when prescribing controlled substances.

Destroying Out-of-Date Drugs & Substances: Out-of-date controlled drugs and substances, or those no longer needed, must be destroyed by the midwife. This act must be witnessed by another midwife, a physician, a registered nurse, nurse practitioner or a pharmacist. Unwanted supplies of these drugs may also be surrendered to the pharmacist from whom they were obtained.

Adverse Drug Reaction: Midwives must participate in the Canadian Adverse Drug Reaction Reporting Program which includes reporting adverse reactions to vaccines.

Protection Against & Reporting of Loss or Theft: Midwives must take reasonable steps to protect controlled substance from loss or theft. Any losses or thefts must be reported to Health Canada's Office of Controlled Substance, to the CMBC, to the hospital as indicated and to a law enforcement agency.

Evidence-Informed Prescribing: Midwives must consider best-practice resources and guidelines when prescribing for clients, including when recommending complementary or alternative therapies.

Ethics: It is unethical and prohibited for a midwife to self-prescribe or administer a controlled substance or to prescribe a controlled substance to immediate family.

Demonstrating Competence: Currently practicing midwives will demonstrate their knowledge and competence to the CMBC through an approved education and assessment process prior to being authorized to independently prescribe, order and administer these

controlled substances[1]. Once prescribing, ordering and administering controlled substances is fully implemented as an entry-level competency, applicants for registration will have their knowledge and competence to independently prescribe, order and administer designated controlled substances assessed through their education program.

Prescribing Principles for Pain Relief

CMBC prescribing principles are intended to be used as a guide for midwives to ensure safe prescribing practices to all their clients.

1. Opioids prescribed by midwives are intended to be prescribed to their clients on a short-term basis and within a specific time period.
2. Treatment decisions are based on comprehensive initial and ongoing assessments and informed choice. Each assessment should include a documented history, examination, assessment and summary of the opioid treatment.
3. Always prescribe the lowest effective dosage. Medications must be tapered or discontinued if problems arise.
4. Both long and short acting opioids have the potential for abuse. Be cautious of alcohol use and/or polypharmaceutical mix of drugs, which can include opioids, sedatives, antidepressants and atypical antipsychotics. There is no evidence or assurance that this is safe or effective, and these combinations increase the risk of adverse effects.
5. Do not prescribe opioids with sedatives, particularly benzodiazepines. Use of this combination increases the risk of fatal opioid overdose.
6. Any controlled substances requiring a duplicate prescription pad may only be prescribed in hospital, as midwives do not currently have access to duplicate prescription pads. Please note that midwives can only prescribe controlled substances based on the medications listed in the *CMBC Standards, Limits and Conditions for Prescribing Controlled Substances*.
7. Prescriptions can only be written for a client's individual needs and may not be prescribed "for office use."

Note: A review of PharmaNet at the time an opioid is prescribed in order to access an updated client profile is considered best practice. At this time Registered Midwives do not have access to PharmaNet.

[1] Education (e.g. online module, workshop, course or program of study) and assessment that addresses the competencies required to prescribe narcotics and controlled drugs and/or benzodiazepines in the management of labour, birth and the postpartum period.

Standards, Limits and Conditions for Prescribing, Ordering and Administering Controlled Substances in Midwifery Practice

The standards below provide midwifery indications, routes of administration and upper dosage limits where appropriate and adverse effects and contraindications for the use of controlled substances approved for use in midwifery practice. Midwives may only prescribe, order or administer the following controlled substances within the standards set out in this document and to a client under their professional care where the drug is required for the purposes outlined below.

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.

Controlled Substances and Related Medications for Use in Prodromal Labour and in the Early Postpartum Period

Lorazepam

(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 1st and 3rd 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
0.5-2 mg SL/PO bid to tid
Insomnia - 0.5-1 mg SL/PO
Anxiety - 0.5 – 2 mg SL/PO

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.

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

Prescription:
Lorazepam may be prescribed in hospital or in the community. It does not require a duplicate prescription pad. A prescription cannot exceed three days. No refills. Please be sure to follow the guidelines on page 2 of this document.

Oxazepam

(Serax®). 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 1st and 3rd 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:
Usual dose
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.

Onset of Action:
Peak of action is 2-4 hours

Half-Life:
Adult - 8 hours
Neonate - unknown

Elimination:
Urine as metabolites

Prescription:
Oxazepam may be prescribed in hospital or in the community. It does not require a duplicate prescription pad. A prescription cannot exceed three days. No refills. Please be sure to follow the guidelines on page 2 of this document.

Flumazenil

(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:
0.1 mg/ml injectable solution
IV: 0.2 mg over 15-30 seconds

If there is no response after the initial dose, then 0.3 mg given over 15-30 sec 1 min later, if no response then again 0.5 mg IV over 15-30 sec to maximum cumulative dose of 3 mg/hr.

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

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. O2 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 O2 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.

Onset of Action:
3-5 minutes
Time to peak effect: 5-15 minutes

Half-Life:
Adult – 2.4 hours
Neonate – 1.15 hours

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

Morphine sulphate

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[2]. 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 nullipara or multipara less than 4 cm. Assess well-being prior to morphine administration, 15 minutes post administration and according to hospital protocol

[2] *See monitoring section when IM morphine has been administered in early labour.*

thereafter. Protocols in some centers allow 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 psycho-physiologic 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:
10-15 mg IM every 4 hours; or
2-5 mg 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.

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

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

Dimenhydrinate

(Gravol®) is **not** a controlled substance but has been included here for reference purposes as it is often given with morphine to counteract the side effects of nausea and vomiting.

Dimenhydrinate is categorized in a class of drugs called antihistamines. It competes with histamine for H_1-receptor sites on effector cells in the respiratory tract, gastrointestinal tract and blood vessels; blocks chemoreceptor trigger zones.

Indications and Clinical Use:
Dimenhydrinate can be administered intramuscularly as an analgesic for pain relief in labour and is often given with morphine to counteract the side effects of nausea and vomiting. While it is considered safe, dimenhydrinate may produce some sedation.

Contraindications:
Hypersensitivity or previous reactions to dimenhydrinate or any component of the formulation.

Warnings and Precautions:
Use with caution in patients with asthma, peptic ulcer or cardiac arrhythmias and thyroid dysfunction.

Pregnancy:
Compatible
Considered low risk in pregnancy, however, exposure near birth of premature infants has been associated with an increased risk of retrolental fibroplasia.

Lactation;
Category L2 - Limited Data– Probably Compatible
Dimenhydrinate is one of the preferred anti-nauseants in lactation; less than 2% of the adult dose of the active ingredient was found in milk and in multiple cases this medication was undetectable. 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:
Palpitations, hypotension, confusion, nervousness, restlessness, headache, insomnia, tingling, heaviness and weakness of hands, vertigo, dizziness, blurred vision, nasal

stuffiness, dryness of nose and throat; nausea, vomiting, diarrhea, constipation, dry mouth; tightness of chest, wheezing.

Dosage and Administration:
Usual Concentration: each ml contains 50 mg
50-100 mg PO every 4-6 hours, maximum dose 400 mg/day
25-50 mg IM or IV every 4 hours, maximum dose 100 mg every 4 hours
25 mg IV should be administered slowly over 2 minutes

Onset of Action:
IM: 20-30 minutes
IV: immediate

Half-Life:
IM: 3-6 hours
IV: 3-6 hours

Naloxone Hydrochloride

Naloxone hydrocholoride (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[3] 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[4] . 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.

[3] http://circ.ahajournals.org/content/122/16_suppl_2/S516#sec-61
[4] http://www2.aap.org/nrp/docs/15535_NRP%20Guidelines%20Flyer_English_FINAL.pdf

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.

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

Adult initial dose of naloxone cause by opioid overdose:

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

(Tylenol® 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 is used **for ≤ 72 hours** 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 1st and 3rd 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:
Acetaminophen 300 mg and codeine phosphate 30 mg;
Based on codeine (30 – 60 mg/dose) every 4-6 hours,
Maximum dose:
Codeine 240 mg/24 hours and Acetaminophen 4000 mg/24 hours;
Dose adjustment/titration should be made according to appropriate analgesic effect as long a maximum dose is not exceeded.

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

Prescription:
Acetaminophen with codeine no.3 may be prescribed in hospital or in the community. It does not require a duplicate prescription pad. A prescription cannot exceed three days. No refills. Please be sure to follow the guidelines on page 2 of this document.

Acetaminophen with Oxycodone

(Endocet®, Percocet®). 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 is used **for ≤ 72 hours** 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 in hospital 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.

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
(1-2 tablets PO every 6 hours prn)

Usual initial dose for severe pain:
Oxycodone: PO 5 mg, Acetaminophen: PO 325 mg(1tablet PO every 6 hours prn)

Doses should be given every 4-6 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.

Maximum daily dose:
Oxycodone 420 mg/24 hours. Acetaminophen: 4000 mg/24 hours.

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.

Prescription:
At this time, RMs can only prescribe Acetaminophen with oxycodone in the hospital, and do not have access to duplicate prescription pads for prescribing in the community. In general, Acetaminophen with oxycodone may be prescribed in hospital or in the community. If Acetaminophen with oxycodone is prescribed in the community, a duplicate prescription pad must be used. A prescription cannot exceed three days. No refills. Please be sure to follow the guidelines on page 2 of this document.

Elimination:
In urine as metabolites

Hydromorphone

(Dilaudid-HP®, Dilaudid®). 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 is used **for ≤ 72 hours** to relieve moderate to severe pain in the postpartum period 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.** ***At this time, RMs can only prescribe Hydromorphone in the hospital and do not have access to duplicate prescription pads.*** 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 as needed for a maximum of 72 hours
Maximum dose:
9 mg per 24 hours.

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 ≤ 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.

Prescription:
At this time, RMs can only prescribe Hydromorphone in the hospital and do not have access to duplicate prescription pads for prescribing in the community. In general, Hydromorphone may be prescribed in hospital or in the community. If Hydromorphone is prescribed in the community, a duplicate prescription pad must be used. A prescription cannot exceed three days. No refills. Please be sure to follow the guidelines on page 2 of this document.

Acetaminophen with Tramadol

(Apo-Tramadol/Acet®, Tramacet®) 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 is used **for ≤ 72 hours** 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 antidepressant drugs. The MAO inhibitor antidepressants are older antidepressants, now reserved for extremely resistant cases of depression unresponsive to new agents: Isocarboxazid (Marplan®), Phenelzine (Nardil®), Tranylcypromine (Parnate®), 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, 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® 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 as needed for pain
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.

Onset of Action:
Acetaminophen: < less than 1 hour
Tramadol: 60-90 minuntes.
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)

Prescription:
Acetaminophen with tramadol may be prescribed in hospital or in the community. It does not require a duplicate prescription pad. A prescription cannot exceed three days. No refills. Please be sure to follow the guidelines on page 2 of this document.

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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/D-Legislation_Standards/D-4_Drug_Distribution/5014-Prescription_Regulation_Table.pdf

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