OB Pharmacology Review

By: Larissa Martinez Pharm. D., RPh.

Objectives

- Review pregnancy categories and their upcoming evolution
- Discuss medication properties as they relate to pregnancy and breast feeding
- Identify common medications and doses used in acutely ill obstetric patients
- Identify certain medications to avoid during pregnancy and breast feeding
### Pregnancy Categories

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Adequate and well-controlled studies have failed to demonstrate a risk to the fetus in the first trimester of pregnancy (and there is no evidence of risk in later trimesters).</td>
</tr>
<tr>
<td>B</td>
<td>Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women.</td>
</tr>
<tr>
<td>C</td>
<td>Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.</td>
</tr>
<tr>
<td>D</td>
<td>There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.</td>
</tr>
<tr>
<td>X</td>
<td>Studies in animals or humans have demonstrated fetal abnormalities or there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience, and the risks involved in use of the drug in pregnant women clearly outweigh potential benefits.</td>
</tr>
</tbody>
</table>

### Pregnancy and Lactation Labeling Rule (PLLRR)¹

- Published December 4, 2014
- Requires that the labeling include
  - Summary of the risks of using a drug during pregnancy and lactation
  - A discussion of the data supporting that summary
  - Relevant information to help health care providers make prescribing decisions and counsel women about the use of drugs during pregnancy and lactation
New Labeling Requirements

Prescription Drug Labeling Sections 8.1 - 8.3 USE IN SPECIFIC POPULATIONS

**CURRENT LABELING**

- **8.1** Pregnancy
- **8.2** Labor and Delivery
- **8.3** Nursing Mothers

**NEW LABELING**

*effective June 30, 2015*

- **8.1** Pregnancy includes Labor and Delivery
- **8.2** Lactation includes Nursing Mothers
- **8.3** Females and Males of Reproductive Potential

Implementation Plan

<table>
<thead>
<tr>
<th>NDA’s, BLA, ESs</th>
<th>Required Submission Date of PLLR Format</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>New Applications</strong></td>
<td>Submitted on or after 6/30/2015</td>
</tr>
<tr>
<td></td>
<td>Approved 6/30/2007 - 6/29/2015 or pending on 6/30/2015</td>
</tr>
<tr>
<td></td>
<td>Applications approved prior to 6/30/2001</td>
</tr>
</tbody>
</table>
8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no studies with EMPLICITI with pregnant women to inform any drug associated risks. Animal reproduction studies have not been conducted with elotuxizumab. EMPLICITI is administered in combination with lenalidomide and dexamethasone. Lenalidomide can cause embryo-fetal harm and is contraindicated for use in pregnancy. Refer to the lenalidomide and dexamethasone prescribing information for additional information. Lenalidomide is only available through a REMS program. The background risk in the U.S. general population of major birth defects is 2% to 4% and of miscarriage is 15% to 20% of clinically recognized pregnancies.

8.2 Lactation

Risk Summary

There is no information on the presence of EMPLICITI in human milk, the effect on the breast-fed infant, or the effect on milk production. Because of the potential for serious adverse reactions in breast-fed infants from elotuxizumab administered with lenalidomide/ dexamethasone, breastfeeding is not recommended. Refer to the lenalidomide and dexamethasone prescribing information for additional information.

8.3 Females of Reproductive Potential

Pregnancy Testing

Refer to the lenalidomide labeling for pregnancy testing requirements prior to initiating treatment in females of reproductive potential.

When EMPLICITI is used with lenalidomide, there is a risk of fetal harm, including severe life-threatening human birth defects associated with lenalidomide, and the need to follow requirements regarding pregnancy avoidance, including testing.

Contraception

Refer to the lenalidomide labeling for contraception requirements prior to initiating treatment in females of reproductive potential and males.

Lenalidomide is present in the blood and semen of patients receiving the drug. Refer to the lenalidomide full prescribing information for requirements regarding contraception and the prohibitions against blood and/or sperm donation due to presence and transmission in blood and/or semen and for additional information.

For More Information Visit...

FDA U.S. Food and Drug Administration

Protecting and Promoting Your Health

Drugs

Home > Drugs > Development & Approval Process (Drugs) > Development Resources > Labeling

Pregnancy and Lactation Labeling (Drugs) Final Rule

Pregnancy Registries

Pharmacokinetic Changes During Pregnancy
### Pharmacokinetic Properties

- **Increases in volume of distribution (Vd)**
  - ↑ cardiac output
    - Maternal blood volume increases by 40-50%
    - Hydrophilic medications with low Vd are most affected
  - ↓ serum albumin → ↓ in plasma protein binding
    - Medications: digoxin, midazolam, phenytoin

- **Alterations in drug absorption**
  - Nausea/vomiting
  - Delay in gastric motility
    - Increases time to maximum concentration
  - Increases in gastric pH
    - May decrease or increase absorption pending medication properties
    - Medications: levothyroxine, iron

- **Alterations in medication clearance**
  - Renal blood flow and GFR ↑ 50% by 14 weeks
    - SrCr >0.8 may indicate underlying renal dysfunction
    - Medication: aminoglycosides, vancomycin, cefazolin, piperacillin, atenolol, digoxin, lithium, levetiracetam...
  - Cytochrome P450 liver enzymes
    - ↑ abundance and activity of CYP3A4 which increases metabolism of certain medications
      - Medications: nifedipine, carbamazepine, midazolam, lopinavir and ritonavir, various others...
## Medications used in Pre-eclampsia/Eclampsia/HELLP

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
<th>MOA</th>
<th>Onset</th>
<th>Duration</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydralazine</td>
<td>IV: 5 - 10 mg → 10 mg q 20 min</td>
<td>Direct vasodilation of arterioles</td>
<td>5-20 min</td>
<td>1 - 4 hours</td>
<td>Maternal hypotension, reflex tachycardia</td>
</tr>
<tr>
<td>Labetalol</td>
<td>IV: 20 mg → 40 mg → 80 mg q 10 min</td>
<td>α-, β1-, and β2-blocker</td>
<td>2-5 min</td>
<td>2 - 18 hours</td>
<td>Fetal bradycardia, hypoglycemia, hypotension, respiratory depression Maternal dizziness, nausea, orthostatic hypotension</td>
</tr>
<tr>
<td></td>
<td>PO: 100 - 200 mg may repeat in 30 min</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nifedipine</td>
<td>PO: 10 mg → 20 mg after 20 min</td>
<td>Ca++ channel blocker</td>
<td>20 min</td>
<td>Depends on formulation</td>
<td>↑ in perinatal asphyxia, cesarean delivery, &amp; prematurity have been described Maternal tachycardia</td>
</tr>
<tr>
<td>Nicardipine</td>
<td>IV: 2.5 – 5 mg/hr, increase by 2.5 mg q 5 - 15 min</td>
<td>Ca++ channel blocker</td>
<td>Within minutes</td>
<td>≤8 hours</td>
<td>Pulmonary edema</td>
</tr>
<tr>
<td>Nitroprusside (IV infusion)</td>
<td>Reserved for extreme emergencies and used for the shortest amount of time possible because of concerns about cyanide and thiocyanate toxicity in the mother and fetus or newborn, and increased intracranial pressure with potential worsening of cerebral edema in the mother</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Committee on Obstetric Practice. Emergent Therapy for Acute-onset, Severe Hypertension During Pregnancy and the Postpartum Period. Number 623, February 2015
# Seizure Medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
<th>MOA</th>
<th>Onset</th>
<th>Duration</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnesium³ (D)</td>
<td>IV: 4-6 gram load then 2 gram/hr</td>
<td>Poorly understood</td>
<td>IV: 30 min-2 hr</td>
<td>IM: 1 hr</td>
<td>Use &gt;5 days may cause fetal hypocalcemia, bone abnormalities, maternal hypotension, muscle weakness, respiratory depression in patients with myasthenia gravis.</td>
</tr>
<tr>
<td></td>
<td>IM: 5 g into each buttocks → 4 g q 4 hrs</td>
<td></td>
<td>IM: 1 hr</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lorazepam</td>
<td>IV/IM: 2 - 4 mg (q 10 - 15 min)</td>
<td>Enhances the inhibitory effect of GABA on neuronal excitability</td>
<td>IV: 2 min</td>
<td></td>
<td>Premature birth and low birth weight may occur; hypoglycemia and respiratory problems if given late in pregnancy; monitor for withdrawal/floppy infant syndrome.</td>
</tr>
<tr>
<td>Midazolam</td>
<td>IV/IM: 2 - 10 mg</td>
<td></td>
<td>IV: 1 - 5 min</td>
<td>&lt;2 hrs (dose dependent)</td>
<td>See above</td>
</tr>
<tr>
<td>Levetiracetam</td>
<td>IV: 500 to 1000 mg</td>
<td>Axon inhibition, modulating neurotransmitter release, inhibition calcium channels</td>
<td>IV: Peak effect within 5-15 min</td>
<td>Typically dosed q 12 hrs</td>
<td>Dizziness, somnolence Increased elimination noted during pregnancy⁴</td>
</tr>
<tr>
<td>Fosphenytoin</td>
<td>15 - 20 mg/kg may repeat 10 mg/kg after 20 min</td>
<td>Stabilizes neuronal membranes via Na ions</td>
<td>IV: ~30 min</td>
<td>Typically dosed q 8-12 hrs</td>
<td>Hypotension, somnolence, hypokalemia, nystagmus Fetal cardiac defects, dysmorphic facial features, microcephaly</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Other Uses
- Prevention and treatment of seizures in women with preeclampsia or eclampsia
- Short-term prolongation of pregnancy (up to 48 hours) to allow for the administration of antenatal corticosteroids in pregnant women who are at risk of preterm delivery within 7 days
- Fetal neuroprotection before anticipated early preterm (less than 32 weeks of gestation) delivery
- Follow clinical signs of toxicity rather than lab values
  - Renal patients are at risk for Mg accumulation
  - Reversal of toxic effects: calcium gluconate 1 gram IV
Steroids for Antenatal Use

- Given if pre-eclampsia develops between 24 to 34-36 weeks gestation or patient is at risk for pre-term delivery
  - Speeds up fetal lung development, may reduce other complications of pre-term birth
    - e.g. intraventricular hemorrhage, necrotizing enterocolitis, respiratory distress syndrome
  - Betamethasone
    - Dose: 12 mg IM q 24 hrs x 2 doses
      - Full benefit is at 48 hrs post first injection
  - Dexamethasone
    - Dose: 6 mg IM q 12 hrs x 4 doses
      - Preservative free or non-sulfite containing product should be used

Medications for Postpartum Hemorrhage/Severe Bleeding
### Uterotonic Medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
<th>MOA/Factors</th>
<th>Estimated Costs</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxytocin (Pitocin)</td>
<td>IV: 30 units/500 mL over ~1hr → 20 units/1L over ~8 hrs IM: 10 units</td>
<td>Binds smooth muscle receptors in uterus to cause increase in rhythmic contractions and increases uterine tone</td>
<td>IV: ~1 min IM: 3-5 min</td>
<td>IV: 1 hr IM: 2-3 hrs</td>
</tr>
<tr>
<td>Meprobamate</td>
<td>PR: 800 mcg</td>
<td>Prostaglandin E1, induces uterine contractions</td>
<td>IV: ~1 min IM: 3-5 min</td>
<td>IV: immediate IM: 2-5 min</td>
</tr>
<tr>
<td>Misoprostol (Cytotec)</td>
<td>IV/IM: 0.2 mg after delivery of anterior shoulder, after delivery of placenta, or during puerperium May repeat doses q 2-4 hrs as needed</td>
<td>Increases tone, rate and amplitude of contractions on the smooth muscles of the uterus, producing sustained contractions which shortens the 3rd stage of labor and reduces blood loss</td>
<td>IV: immediate IM: 2-5 min</td>
<td>IV: 45 min IM: 3 hrs</td>
</tr>
<tr>
<td>Carboprost tromethamine (Hemabate)</td>
<td>IM: 0.25 mg q 15-90 min up to 8 doses or 0.5 mg up to 3 mg or 0.5 mg intramyometrial</td>
<td>Prostaglandin F2 alpha, uterine contraction (hemostasis at the placentation site is achieved through the myometrial contractions produced by carboprost)</td>
<td>IM: 30 min time to peak</td>
<td></td>
</tr>
</tbody>
</table>

### Medications Affecting Hemostasis

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
<th>MOA/Factors replaced</th>
<th>Estimated Costs</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>NovoSeven</td>
<td>10-20 mcg/kg</td>
<td>Recombinant factor VIIa</td>
<td>5 mg vial = $9000</td>
<td>Hypo/hypertension, bradycardia, thrombosis, decreased serum fibrinogen, fever</td>
</tr>
<tr>
<td>Kcentra (C)</td>
<td>IV: 25-50 units/kg</td>
<td>4-factor complex + protein C &amp; S</td>
<td>25 unit/kg for (70 kg) = $4000</td>
<td>Hypo/hypertension, tachycardia, thrombosis, respiratory distress Note: Do not use in HIT patients</td>
</tr>
<tr>
<td>Bebulin (C)</td>
<td>IV: 25-50 units/kg</td>
<td>3-factor complex (II, IX, X)</td>
<td></td>
<td>Flushing, thrombosis, fever, paresthesia, dyspnea</td>
</tr>
<tr>
<td>RiaSTAP (C)</td>
<td>IV: 70 mg/kg if fibrinogen unknown</td>
<td>Fibrinogen concentrate</td>
<td>70 mg/kg (70 kg) = $6100</td>
<td>Fever, headache, thrombosis, dyspnea, MI</td>
</tr>
<tr>
<td>Tranexamic acid (B)</td>
<td>IV: 1000 mg</td>
<td>Inhibits fibrinolysis Displaces plasminogen from fibrin</td>
<td>1000 mg vial is ~ $50</td>
<td>Hypotension, headache, abdominal pain, thrombosis, renal cortical necrosis, vision changes</td>
</tr>
<tr>
<td>Aminocaproic acid (C)</td>
<td>IV: 4-5 g over 1 hr → 1 g/hr x ~8 hrs (NTE 30 g/24 hrs)</td>
<td>Inhibits fibrinolysis</td>
<td>5 g vial is ~ $7</td>
<td>Hypotension, bradycardia, thrombosis, abdominal pain, myalgia, glomerular capillary thrombosis, thrombocytopenia</td>
</tr>
<tr>
<td>Desmopressin (B)</td>
<td>IV: 0.3 mcg/kg over 15 minutes</td>
<td>Increases von Willebrand factor, factor VIII, &amp; t-PA contributing to ↓ APTT</td>
<td>Dose for 70 kg pt = $500</td>
<td>Low birth weight Flushing, headache, hyponatremia, rhinitis, hypo/hypertension</td>
</tr>
<tr>
<td>Phytonadione (Vitamin K) (C)</td>
<td>IV/PO: 1-10 mg</td>
<td>Promotes liver synthesis of factors II, VII, IX, X</td>
<td>10 mg IV <del>$40 10 mg PO</del>$130</td>
<td>Hypo/hypertension, pruritus, abnormal taste, dyspnea</td>
</tr>
</tbody>
</table>
### Medications Used in the ICU

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose Range</th>
<th>MOA</th>
<th>Onset</th>
<th>Duration</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fentanyl (C)</td>
<td>IV: 12.5 - 50 mcg IV infusion: 12.5 mcg/hr - 150 mcg/hr</td>
<td>Opioid receptor agonists</td>
<td>Immediate</td>
<td>30-60 min</td>
<td>Neonatal withdrawal syndrome, transient muscular rigidity, Sedation, dizziness, constipation, hyponatremia, fever, cardiac arrhythmias, hyper/hypotension, thrombocytopenia</td>
</tr>
<tr>
<td>Morphine (C)</td>
<td>IV: 1 - 4 mg IV infusion: 1 mg - 15 mg/hr</td>
<td></td>
<td>5-10 min</td>
<td>3-5 hrs</td>
<td>Neonatal withdrawal syndrome, decreased ventilatory response to CO2, at risk for SIDS, Histamine release (hypotension, flushing), constipation, hyponatremia, fever, thrombocytopenia</td>
</tr>
<tr>
<td>Hydromorphone (C)</td>
<td>IV: 0.5 - 1 mg 0.2 - 2 mg/hr</td>
<td></td>
<td>5 min; peak 10-20 min</td>
<td>3-4 hrs</td>
<td>Neonatal withdrawal syndrome, Histamine release (hypotension, flushing), bradycardia, constipation, muscle rigidity</td>
</tr>
<tr>
<td>Ketamine</td>
<td>IV: 0.1 - 0.5 mg/kg IV infusion: 0.1 - 0.5 mg/kg/hr</td>
<td>NMDA receptor antagonist</td>
<td>30 seconds</td>
<td>5-10 min</td>
<td>Neonatal depression, reduced APGAR scores reported, Uterine contractions, hyper/hypotension, brady/tachycardia, hypertonia, DI</td>
</tr>
</tbody>
</table>

- **Opioid IV conversion**
  - 100 mcg fentanyl = 10 mg morphine = 1.5 mg hydromorphone
### Sedation

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose Range</th>
<th>MOA</th>
<th>Onset</th>
<th>Duration</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propofol (B)</td>
<td>IV: 5 to ~75 mcg/kg/min</td>
<td>Agonism of GABA&lt;sub&gt;a&lt;/sub&gt; and NMDA receptor blockade</td>
<td>&lt; 1 min</td>
<td>3-10 min</td>
<td>Neonatal depression, maternal hypotension, apnea, hypertryglyceridemia</td>
</tr>
<tr>
<td>Midazolam (D)</td>
<td>IV: 1 to 20 mg/hr</td>
<td>Benzodiazepine receptor agonist</td>
<td>1-5 min</td>
<td>&lt; 2 hrs</td>
<td>Neonatal hypoglycemia, withdrawal, respiratory depression, sedation, maternal hypotension, apnea</td>
</tr>
<tr>
<td>Ketamine</td>
<td>IV: 1 to 2 mg/kg IV push or continuous infusion 0.5 to 2 mg/kg/hr</td>
<td>NMDA receptor antagonist</td>
<td>30 seconds</td>
<td>5-10 min</td>
<td>Neonatal depression, uterine contractions, plasma clearance is reduced during pregnancy, bradycardia, hypotension, hypo/hypertension, hallucinations, laryngospasm, hypersalivation</td>
</tr>
<tr>
<td>Dexmedetomidine (C)</td>
<td>0.2 to 1.5 mcg/kg/hr Titrated q 30 min</td>
<td>Selective α2-adrenoceptor agonist w/anesthetic/sedative properties</td>
<td></td>
<td></td>
<td>Uterine contractions</td>
</tr>
</tbody>
</table>

### Paralytics

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose Range</th>
<th>MOA</th>
<th>Onset</th>
<th>Recovery</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisatracurium (B)</td>
<td>IV: 0.1 mg/kg IV infusion: 2.5-3 mcg/kg/min</td>
<td>bind to acetylcholine receptors but act as competitive antagonists</td>
<td>2-5 min</td>
<td>90 min</td>
<td>Maternal bradycardia, flushing, hypotension</td>
</tr>
<tr>
<td>Rocuronium (C)</td>
<td>IV: 1 mg/kg IV infusion: 8-12 mcg/kg/min</td>
<td></td>
<td>1-4 min</td>
<td>30 min</td>
<td>Maternal tachycardia, hyper/hypotension</td>
</tr>
<tr>
<td>Vecuronium (C)</td>
<td>IV: 0.1 mg/kg IV infusion: 0.8-1.7 mcg/kg/min</td>
<td></td>
<td>2.5-5 min</td>
<td>45-60 min</td>
<td>Maternal bradycardia, flushing, rash</td>
</tr>
<tr>
<td>Succinylcholine (C)</td>
<td>IV: 1-1.5 mg/kg</td>
<td>bind &amp; activate nicotinic acetylcholine receptors → depolarization of postsynaptic membrane of striated muscle</td>
<td>&lt; 1 min</td>
<td>4-6 min</td>
<td>Tachy, bradycardia, rash, hyper/hypotension, hyperkalemia, salivation, jaw rigidity, rhabdomyolysis, malignant hyperthermia</td>
</tr>
</tbody>
</table>

- Some medications may potentiate effects of non-depolarizing neuromuscular blocking agents
  - Corticosteroids, aminoglycosides, clindamycin, polymyxins, colistin, tetracyclines
## Pressor Medications

<table>
<thead>
<tr>
<th>Medication</th>
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<th>MOA</th>
<th>Onset</th>
<th>Duration</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norepinephrine (C)</td>
<td>0.5 to 30 mcg/min</td>
<td>Stimulates β1- &amp; α-adrenergic receptors</td>
<td>Rapid</td>
<td>1-2 min</td>
<td>Vesicant Maternal bradycardia, dyspnea</td>
</tr>
<tr>
<td>Phenylephrine (C)</td>
<td>25 to 200 mcg/min</td>
<td>Direct-acting α-adrenergic agonist</td>
<td>Rapid</td>
<td>15-20 min</td>
<td>Fetal malformations in 1st trimester Vesicant Maternal reflex bradycardia, dyspnea</td>
</tr>
<tr>
<td>Epinephrine (C)</td>
<td>1 to 10 mcg/min</td>
<td>Stimulates alpha-, beta1-, and beta2-adrenergic receptors</td>
<td>Rapid</td>
<td>&lt; 1 min</td>
<td>Uterine vasoconstriction, decreased uterine blood flow, and fetal anoxia Vesicant Maternal arrhythmias, hyperglycemia, hypokalemia, dyspnea</td>
</tr>
<tr>
<td>Vasopressin (C)</td>
<td>0.03 to 0.04 unit/min</td>
<td>Direct vasoconstrictor</td>
<td>within 15 min</td>
<td>20 min</td>
<td>Tonic uterine contractions Vesicant Maternal arrhythmias, hyponatremia, abdominal cramps, thrombocytopenia, tremor</td>
</tr>
</tbody>
</table>

- For extravasation may use phentolamine, terbutaline, or nitroglycerin 2% topical ointment
Medication Transfer into Milk

- Passive diffusion from high to lower drug concentration areas
  - Maternal blood/tissue → breast milk
- Drug properties
  - Size (lower molecular weight)
  - Solubility (lipophilic > hydrophobic)
  - pH (ionization)
  - Protein binding (low > higher)

Relative Infant Dose (RID) Calculation

- RID (%) = \( \frac{\text{dose in infant (mg/kg/day)}}{\text{dose in mother (mg/kg/day)}} \times 100\% \)

- Infant dose = Average concentration milk (mg/L) x milk intake (L/Kg/d)
- Find RID in various published papers
- RID of ≥10% represents a medication dosage of concern or caution

Also consider

- \( T_{\text{max}} \) and \( t_{1/2} \) of medication
- Oral bioavailability of medication
- Postnatal age
Other Resources

- LactMed (NLM TOXNET, 2015)
    • Free access
- The Infant Risk Center from the Texas Tech University Health Sciences Center
  - [http://www.infantrisk.com](http://www.infantrisk.com)
    • Various articles, subscription available for more info
- Medications and Mothers Milk
  • Available as online subscription
- Briggs Drugs in Pregnancy and Lactation
  • Accessed through Lexicomp

Medications to Avoid
In Pregnancy...

- Medications affecting angiotensin system
  - e.g. lisinopril, losartan
- Non-steroidal anti-inflammatory medications
  - Premature closure of ductus arteriosus and oligohydramnios
- Statin medications
  - e.g. simvastatin, pravastatin
- Mineral Oil, dong quai, cohosh, turmeric, sage
  - Uterine contractions
- Methotrexate
  - Folate antimetabolite
- Dronedarone

In Breast Feeding...

- Antineoplastic agents
- Amiodarone
- Chloramphenicol
- Ergotamine
- Lithium
- Tetracyclines
- Pseudoephedrine
Question 1

- Which of the following is TRUE
  a) All medications approved after 6/30/2015 need to comply with the new PLLR format
  b) All medications must remove the Pregnancy Category (A, B, C, D, X) by 6/29/2018
  c) All medications approved prior to 6/29/2015 are required to comply with the new PLLR format
  d) A and B
  e) All of the above

Question 2

- Which of the following medications should be avoided in Pregnancy
  a) ACE inhibitors/ARBs
  b) Dronedarone
  c) NSAIDs (non-steroidal anti-inflammatory)
  d) Statin medications (i.e. simvastatin, rosvastatin)
  e) a, c, and d
  f) All of the above
References:

1. FDA Website last accessed 5/1/2016
2. Costantine, M. Physiologic and pharmacokinetic changes in pregnancy. Front Pharmacol. 2014 Apr 3;5:65
   • http://online.lexi.com/lco/action/home