

## GI Medications and Pregnancy

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## FDA Categories

- A: Controlled studies in animals and women have shown **no risk in the first trimester**, and possible fetal harm is remote.
- B: Either animal studies have not demonstrated a fetal risk but there are no controlled studies in pregnant women, or animal studies have shown an adverse effect that was not confirmed in controlled studies in women in the first trimester.
- C: No controlled studies in humans have been performed, and animal studies have shown adverse events, or studies in humans and animals not available; give if potential benefit outweighs the risk.
- D: Positive evidence of fetal risk is available, but the benefits may outweigh the risk if life-threatening or serious disease.
- X: Studies in animals or humans show fetal abnormalities; drug contraindicated

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## General Principles

- Clearly no drugs are approved for use in pregnancy
- No prospective studies, so all data is retrospective, case controlled or observational
- Informed consent is advised for any intervention
- Ob/Gyn practices vary

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### Basic Principles

- No Drug is Approved
- Pregnancy categories are a guide
- Assume no drug is safe
- Remember almost no controlled data
- Almost no prospective data
- Do NO Harm

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### Tables are to offer rapid reference

Compilation of what is known from observational data

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A 23-year-old woman in her second trimester of pregnancy is admitted for nausea, vomiting, and dehydration. Fluid repletion is not sufficient to relieve symptoms and the consult asks about which anti-emetic she can be given. Based on the literature:

1. Metoclopramide does not result in an increase in birth-related malformations or pre-term delivery compared to controls.
2. Prochlorperazine is not associated with any negative effects on birth weight nor an increase in birth defects.
3. Both A and B are correct.
4. Neither drug should be used in this patient.

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Metoclopramide is FDA pregnancy category B with no teratogenesis reported. It is low risk based on a population study. This study identified 309 women with single pregnancies who also had prescriptions for metoclopramide. Compared to controls, there were no major differences in the risk for malformations, low birth rate, or pre-term delivery. Prochlorperazine is pregnancy category C and does cross the placenta. In one study, 877 mothers had first trimester exposure and 2023 were exposed at some point in the pregnancy. There was no increase in malformations, birth weight, or IQ scores up to four years of age. As such, either would be categorized as low risk with limited or no human data in terms for recommendations for breast-feeding.

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### Metoclopramide

- Metoclopramide is FDA pregnancy category B
- Low risk based on a population study of 309 women with single pregnancies who also had prescriptions for metoclopramide.
- Compared to controls, no major differences in the risk for malformations, low birth rate, or pre-term delivery.

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### Prochlorperazine

- Prochlorperazine is pregnancy category C and does cross the placenta.
- In one study, 877 mothers had first trimester exposure and 2023 were exposed at some point in the pregnancy.
- There was no increase in malformations, birth weight, or IQ scores up to four years of age.
- As such, either would be categorized as low risk with limited or no human data in terms
- for recommendations for breast-feeding.

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A 21-year-old woman presents in the first trimester of pregnancy with severe heartburn three times a week. This is making it difficult for her to eat regularly and she is concerned about adequate nutrition for her child. Antacids are unsuccessful so you consider the following:

1. Sucralfate was superior to lifestyle and dietary modifications in control of heartburn and is of low risk because of limited likelihood of absorption.
2. All proton pump inhibitor formulations should be considered of equal efficacy and risk.
3. Proton pump inhibitors are the first choice in these patients.
4. One and two are correct

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Sucralfate, pregnancy category B, has limited absorption and therefore should be expected to have little toxicity to this patient. A trial comparing one gram sucralfate three times daily compared to dietary and lifestyle modifications showed a 90% Symptomatic remission in the treated group compared to 43% in controls,  $p < 0.05$ .

Proton pump inhibitors have a better than expected safety Profile in the pregnant patient and in general should be Considered for the most part equivalent in efficacy (no trials in pregnant patients) however, not of similar safety. Omeprazole Immediate release with sodium bicarb should probably not be Used because of the small but potential risk of alkalosis because Of the bicarbonate. This is similar to the recommendation that Sodium bicarbonate containing antacids should not be used. Proton pump inhibitors though likely safe are not the first choice.

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## Antacids

- In general safe
- Constipation/Diarrhea depending on formulation
- Avoid Bicarb for salt load
- Magnesium should be used with caution if other risks exist

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### Sucralfate

- Good choice, actual data
- Constipation in 2%
- Balance of endoscopy data (over 30 yrs old) suggests few women will have erosions
- Little down side

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### Histamine Antagonists

- Category B for most part
- Uncontrolled human data in all trimesters with no negative safety data
- Most would suggest reasonable choice if sucralfate does not work
- No efficacy studies

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### PPIs

- Most are category B, omeprazole a C
- Avoid Ome-IR with Na bicarb
- First trimester case control data (Israel) suggesting no increase in fetal abnormalities or other pregnancy issues vs controls.
- No true efficacy data

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## Prokinetics

- Metoclopramide despite major risks/black box used extensively in emesis so likely safe
- Historically never as good as PPI for GERD so no real reason to use first line for HB
- No data on any other "prokinetic"

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A 26-year-old female in her second trimester of her third pregnancy is having diarrhea that is resulting in dry mouth, tachycardia. She cannot seem to keep up with her fluids sufficiently. You are asked what else can be done to improve her diarrhea.

1. Loperamide has not been found to be associated with increased risk of congenital malformations but may be associated with smaller birth weight.
2. Diphenoxylate with atropine has not been reported to increase developmental toxicity in a small study.
3. Cholestyramine has been associated with fat soluble vitamin deficiency so should be used with caution.
4. Kaopectate should be avoided in pregnancy because of the presence of salicylates in the formulation.
5. All of the above are correct.

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One study found that loperamide was not associated with an increased risk of congenital malformations in a trial of 105 Women exposed to the drug during pregnancy. However, one in five were 200 gm smaller than infants in the control group. Diphenoxylate and atropine is teratogenic in animals (category C) However in a small study of women exposed in the first trimester, no reported evidence of developmental toxicity was seen. Cholestyramine (category C) does result in fat-soluble vitamin deficiency so may result in a coagulopathy and should be used with caution. Kaopectate (category B) historically is deemed a safe agent, however, it has been reformulated to include bismuth subsalicylate (category C) and therefore should be avoided in pregnancy. Salicylates can be absorbed and may increase mortality and/or cause neonatal hemorrhage or decreased birth weight.

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### Loperamide

- One study found that loperamide was not associated with an increased risk of congenital malformations in a trial of 105 women exposed to the drug during pregnancy.
- However, 20% were 200 gm smaller than infants in the control group.

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### Diphenoxylate and Atropine

- Diphenoxylate and atropine is teratogenic in animals (category C)
- However in a small study of women exposed in the first trimester, no reported evidence of developmental toxicity was seen.
- No controls, nor efficacy data

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### Cholestyramine

- Cholestyramine (category C) does result in fat-soluble vitamin deficiency so may result in a coagulopathy and should be used with caution.

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## Kaopectate

- Kaopectate (category B) historically is deemed a safe agent
- It has been reformulated to include bismuth subsalicylate (category C) and therefore should be avoided in pregnancy.
- Salicylates can be absorbed and may increase mortality and/or cause neonatal hemorrhage or decreased birth weight.

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A 30-year-old woman who has required three hospitalizations over the past two months for biliary colic is 10 weeks pregnant. Results of serum liver tests are normal. Ultrasonography shows multiple gallstones. When is the best time to perform cholecystectomy?

1. Immediately
2. During the second trimester
3. During the third trimester
4. Post partum

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## Pre-pregnancy Counseling

- Document the time spent with patient
- You CAN bill for a visit for this:
  - V25.09 (search under “preg”, “pre-pregnancy counseling” or “family planning”)

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### What About Men?

- Few medications GIs prescribe have a direct effect on erectile function or sperm
- Exceptions include sulfasalazine which predictably causes reversible sperm abnormalities, methotrexate that causes chromosomal damage to sperm
- Effect from 6MP/azathioprine controversial

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Your patient with inflammatory bowel disease (IBD) comes in for counseling about pregnancy. Which of the following is true regarding pregnancy and IBD?

1. Pregnancy should be deferred until she is in clinical remission.
2. Pregnancy should be deferred until she is in complete endoscopic remission.
3. Cesarean section is the preferred mode of delivery.
4. 6-MP is contraindicated in pregnancy.
5. Ulcerative colitis subjects have difficulty in conceiving.

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### Nausea and Vomiting

Drug	FDA class	Recommendations	Nursing
Dolasetron	B	No human studies	+
Domperidone	C	Unknown	?
Granisetron	B	No human studies	?
Metoclopramide	B	Low risk	-
Ondansetron	B	Low risk	+
Prochlorperazine	C	Low risk	-
Promethazine	C	Low risk	+
Trimethobenzamide	C	Low risk	+

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## GERD and Peptic Ulcer

Drug	FDA class	Pregnancy Information	Nursing
Al containing	None	Safe	+
Ca containing	None	Safe	+
Mg containing	None	Safe	+
Mg trisilicates	None	Avoid long term	+
Na bicarb	None	Not safe	+
Sucralfate	B	Safe	+

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## GERD and Peptic Ulcer

Drug	FDA class	Pregnancy Information	Nursing
Cimetidine	B	Low risk	+
Famotidine	B	Not as much data	+
Nizatidine	B	Low risk in animals	+
Ranitidine	B	Low risk	+
Esomeprazole	B	Low risk	-
Lansoprazole, Pantoprazole, Rabeprazole	B	Low risk	-
Omeprazole	C	Embryonic toxicity	-

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## Principles of Endoscopy

- Endoscopy safe if the appropriate reason for performing procedure; retrospective small study, observational data
- Monitoring fetus recommended if patient in 2<sup>nd</sup> or 3<sup>rd</sup> trimester
- Use as little sedation as possible
- Full colonoscopy rarely indicated

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Drug	FDA	Pregnancy Information	Nursing
Ampicillin	B	Safe to use	+
Diazepam	D	Midazolam preferred	-
Electricity	-	OK to use	n/a
Epinephrine	C	Avoid unless bleeding	-
Fentanyl	C	Use in low doses	+
Flumazenil	C	For benzo overdoses	+
Gentamicin	C	OK to use	+
Glucagon	B	OK for ERCP	?
Lidocaine	B	Gargle and spit	+
Meperidine	B	OK to use	+
Midazolam	D	Use in low doses	-
Naloxone	B	Severe overdose	+
Polyethylene glycol	C	No human data	?
Propofol	B	Avoid in 1 <sup>st</sup> trimester	+
Na glycol electrolyte	C	One time use	?

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## Liver Diseases

- Diseases specific to pregnancy
  - Acute fatty liver of pregnancy
  - Intrahepatic cholestasis of pregnancy
  - HELLP syndrome
- Viral hepatitis
  - Hep E seen more frequently in pregnancy
- Pregnancy uncommon in PBC

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## Liver Disease

Drug	FDA Class	Pregnancy Information	Nursing
Adefovir	C	Low risk	+
Interferon	C	Not recommended	+
Lamivudine	C	Low risk	-
B blockers	C 1 <sup>st</sup> trimester, D others	IUGR, fetal bradycardia	-
Penicillamine	D	Significant embryopathy	-
Ribavirin	X	Contraindicated	+
Trientine	C	Alternative to pen.	-
Ursodiol	B	Low risk	+

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## Liver Transplant

Drug	FDA class	Pregnancy Information	Nursing
Antithymocyte globulin	C	Low risk	?
Mycophenolate	C	Not recommended	+
OKT3	C	Probably low risk	-
Sirolimus	C	Not recommended	-
Tacrolimus	C	Use if mandated	-

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## Constipation

Drug	FDA class	Pregnancy Information	Nursing
Bisacodyl	C	Safe for short term	?
Castor oil	X	Uterine contraction and rupture	-
Docusate	C	Low risk	+
Lactulose	B	No human studies	?
Mag citrate	B	Avoid long term use	+
Mineral oil	C	Neonatal hemorrhage	-
Polyethylene glycol	C	First choice	+
Senna	C	Safe for short term	+
Tagaserod	B	Emergency NDA only	?

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## Diarrhea

Drug	FDA class	Pregnancy Information	Nursing
Alosetron	B	Restricted access	-
Cholestyramine	C	Low risk	+
Diphenoxylate/atropine	C	No human data	-
Kaopectate	C	Unsafe	+
Loperamide	B	Low risk	+

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## Inflammatory Bowel Disease

- Establish remission prior to pregnancy
- Be aggressive with controlling symptoms during pregnancy
- A C-section is not mandated in UC
- Low birth weight common outcome in CD
- Patients should be followed by high risk OB if available

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## Inflammatory Bowel Disease

Drug	FDA class	Pregnancy information	Nursing
Aza/6MP	D	Data for IBD suggests low risk	-
Balsalazide/SASP	B	Low risk	-
Biologics	B	Low risk	?
Ciprofloxacin	C	Cartilage toxicity	+
Cyclosporine	C	Low risk	-
Metronidazole	B	Risk outweighs benefit	-
Methotrexate	X	Contraindicated	-
Mesalamine	B	Low risk	+
Steroids	C	Low risk	+

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## Irritable Bowel Syndrome

Drug	FDA class	Pregnancy Information	Nursing
Amitriptyline, desipramine	C	Avoid	-
Dicyclomine	B	Possible congenital abnl	-
Hyoscyamine	C	No data	?
Imipramine, nortriptyline	D	Worse birth outcomes	-
Paroxetine	D	More birth defects	-
SSRIs	C	More AE	-
Simethicone	C	Low risk	+
Bismuth subsalicylate	C	Teratogenicity	-

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