Selection of Cardiovascular and Pulmonary Hypertension Medications in Peripartum Women

Gillian Leung, PharmD, BCCP

DISCLOSURE

- Consultant, Merck & Co., Inc.

UK HealthCare

OBJECTIVES

- Demonstrate an understanding of pharmacokinetic changes in a pregnant individual
- Assess pregnancy and lactation information on prescription drug labeling for safe prescribing of cardiovascular medications
- Plan safe and effective medication regimen for peripartum individuals

UK HealthCare

CARDIOVASCULAR (CV) DISEASE AND WOMEN

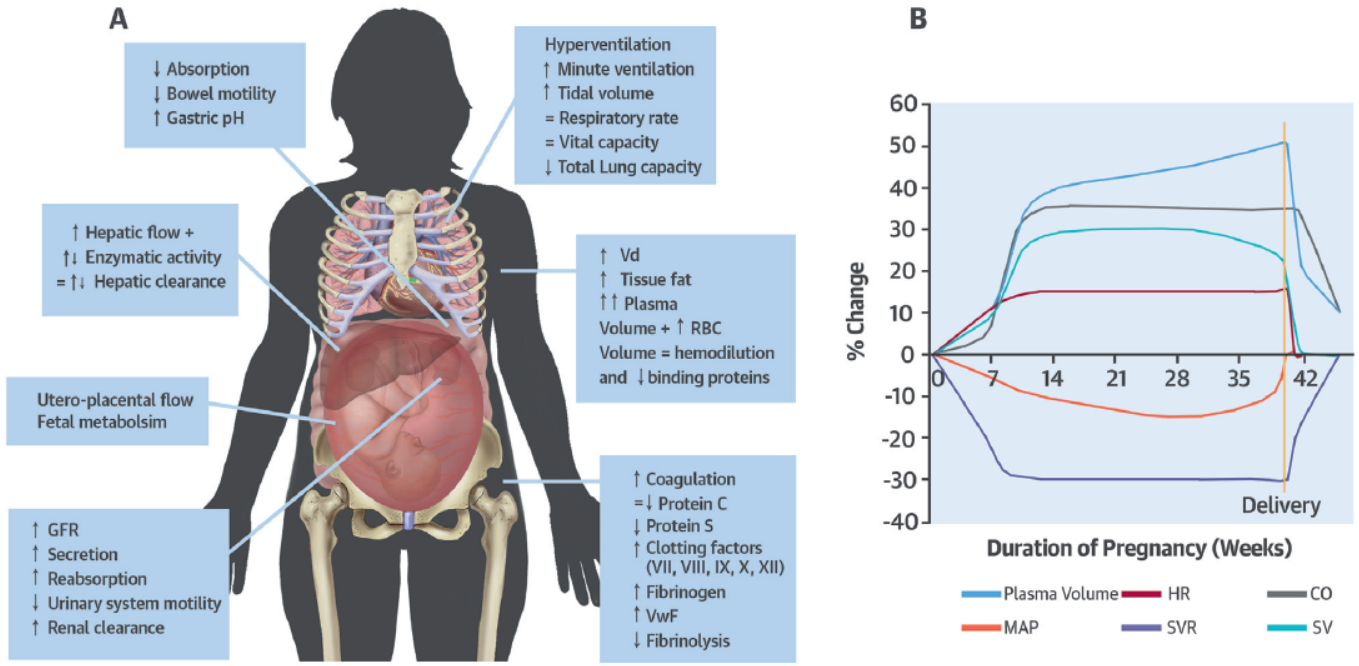
- Most common cause of indirect maternal mortality during pregnancy
- Incidence affected by individual age, CV risk factors, and history of congenital heart disease
- 64% US pregnant women receive prescription drug
- Up to 1/3 women with CVD use cardiac medications during pregnancy, increasing fetal risk
- 5% women receive “FDA Category X” drug
- General rule: Use the least number of drugs and at the lowest dose

UK HealthCare

Halpren DG, et al. J Am Coll Cardiol 2019;73:457–76.
Rakusen K. Exp Clin Cardiol 2010;15(4):e100-e103.

PHARMACOKINETIC AND HEMODYNAMIC CHANGES IN PREGNANCY

FIGURE 1 Hemodynamic and Pharmacological Changes During Pregnancy



The pharmacokinetic and hemodynamic changes throughout pregnancy. **(A)** System based pharmacokinetic changes throughout pregnancy. **(B)** hemodynamic changes diagram throughout pregnancy. CO = cardiac output; GFR = glomerular filtration rate; HR = heart rate; MAP = mean arterial pressure; RBC = red blood cell; SV = stroke volume; SVR = systemic vascular resistance; Vd = volume of distribution; VwF = Von Willebrand factor. Image in **B** adapted from Fuster V, Harrington RA, Narula J, Eapen ZJ, editors. Hurst's the Heart. 14th edition. New York, NY: McGraw Hill, 2017.

HealthCare

Halpren DG, et al. J Am Coll Cardiol 2019;73:457–76)

POTENTIAL EFFECTS ON THE PREGNANT INDIVIDUAL

Reduced GI motility and change in pH	Increased volume of distribution	Altered hepatic metabolism	Increased renal plasma flow
• Reduces absorption • Reduces bioavailability of certain drugs	• Reduces serum drug concentration • Changes half-life $Halflife = 0.693\ x\ (\frac{Vd}{CL})$ • Reduces protein binding	• Increases metabolism of drugs with high hepatic extraction ratio • Upregulates most CYP enzymes	• Increases glomerular filtration • May increase tubular function

UK HealthCare

Forinash AB, Barnes K. Pregnancy and Lactation. DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12th Edition. McGraw Hill; 2023.
Halpren DG, et al. J Am Coll Cardiol 2019;73:457–76)

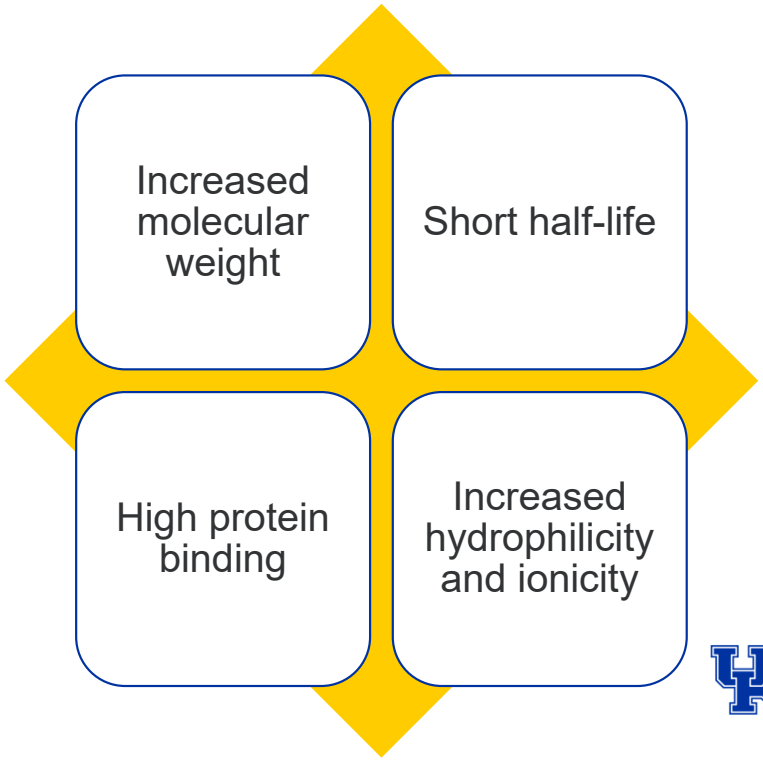
TRANSPLACENTAL MEDICATION TRANSFER

Mode of transfer

- Passive diffusion
- Active transport
- Facilitated diffusion

- Pinocytosis
- Phagocytosis

Drug properties affect medication transfer

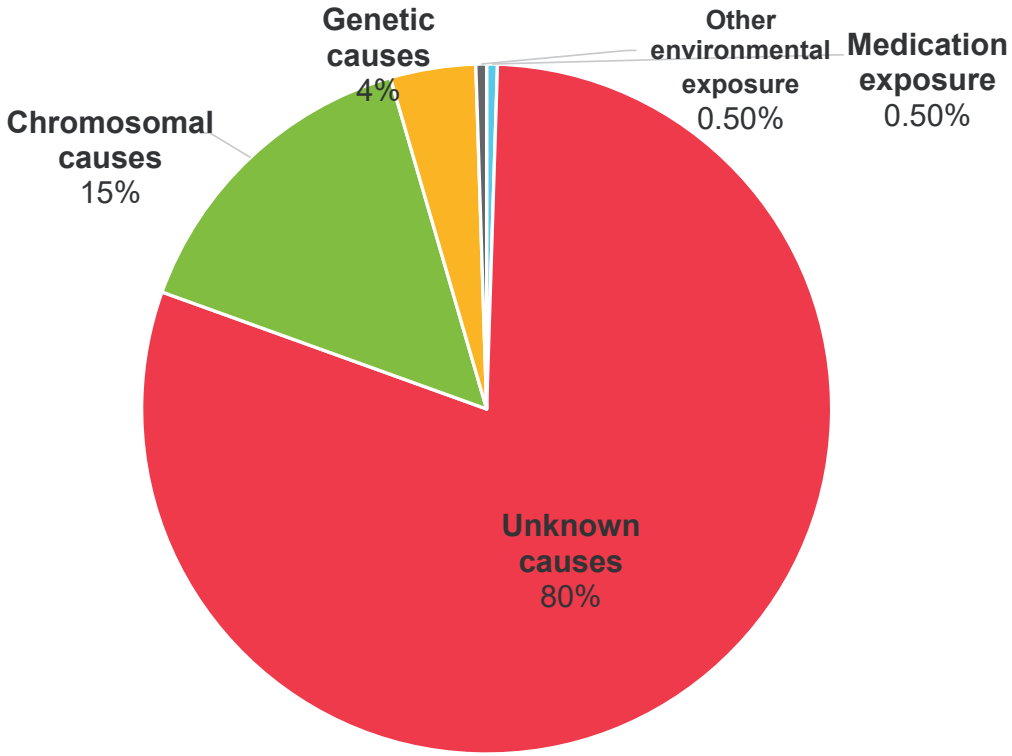


UK HealthCare

Syme MR, et al. Clin Pharmacokinet 2004; 43 (8): 487-514

CONGENITAL MALFORMATION

Background risk 3-5%

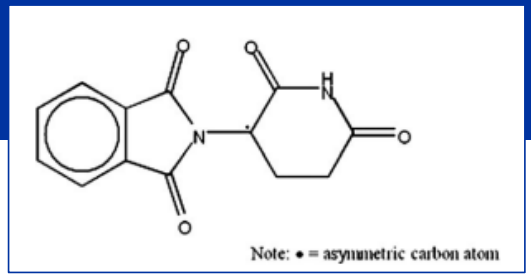


Leading Categories of Birth Defects

Birth Defects	Estimated Prevalence
Heart and circulation	1 in 115 births
Muscles and skeleton	1 in 130 births
Genital and urinary tract	1 in 135 births
Nervous system and eye	1 in 235 births
Respiratory tract	1 in 900 births
Metabolic disorders	1 in 3500 births

US Department of Health and Human Services. Food and Drug Administration. Center for Drug Evaluation and Research. Center for Biologics Evaluation and Research. Reviewer Guidance Evaluating the Risks of Drug Exposure in Human Pregnancies. April 2005.
Forinash AB, Barnes K. Pregnancy and Lactation. DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12th Edition. McGraw Hill; 2023

A TERATOGENIC DRUG EXAMPLE



1954
Thalidomide created by Chemie Grunenthal (German Rx company)

1956
First thalidomide-affected baby born in Germany

1958
Drug licensed in the UK, marketed as a wonder drug (headache, insomnia, morning sickness)

1961
Letter by Dr. William McBride published in The Lancet linking thalidomide and phocomelia

1966
FDA laid foundation for development of toxicology testing in animals

Kim JH, Scialli AR.Toxicol Sci. 2011;122(1):1-6.
Thalidomide Trust.. https://www.thalidomidetrust.org/

UK HealthCare

TOXICOLOGY: DOSE AND TIMING

"What is there that is not poison? All things are poison and nothing is without poison. Solely the dose determines that a thing is not a poison" – Paracelsus (Father of Modern Toxicology)

In reproductive toxicology, timing of exposure is critical to the development of teratogenicity.

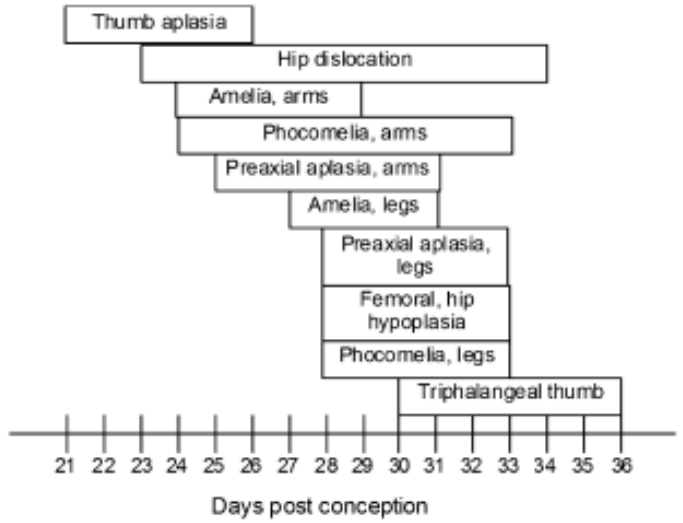
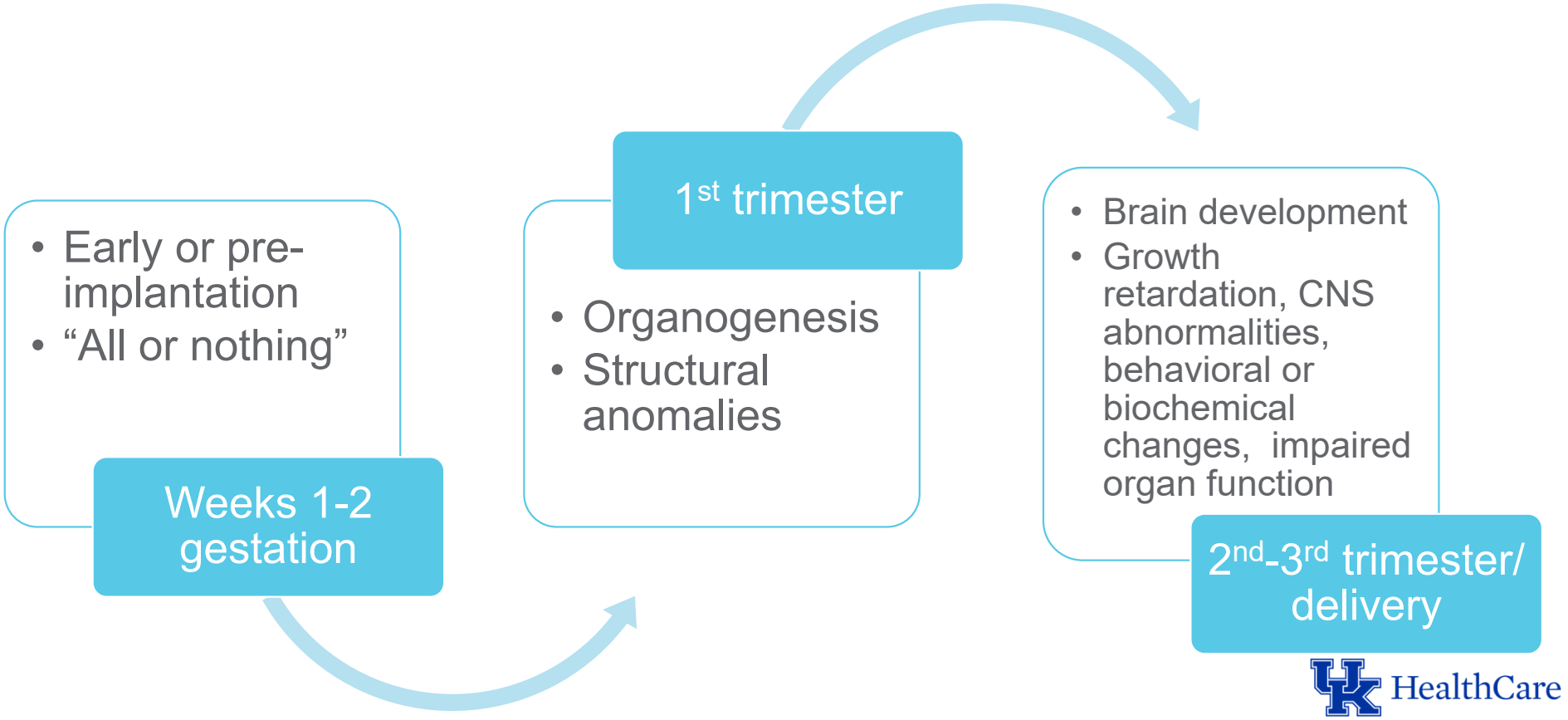


FIG. 3. Critical exposure periods for thalidomide embryopathy during human development.

Grandjean P. Basic Clin Pharmacol Toxicol. 2016;119(2):126-132.
Kim JH, Scialli AR.Toxicol Sci. 2011;122(1):1-6.

FETAL DEVELOPMENT AND TERATOGENIC EFFECTS



UK HealthCare

PREVIOUS PREGNANCY LABELING

From 1979-2015

Classification of drug teratogenicity

Category	Definition
A	Adequate, well-controlled study data in pregnant women showed no increase risk to fetus in any trimester
B	Animal studies showed no evidence of harm to fetus, no adequate data in pregnant women. Animal studies showed adverse effect, but none in adequate and well-controlled studies in pregnant women.
C	Animal studies have shown an adverse effect, however, no adequate and well-controlled studies in pregnant women; no animal studies conducted, no adequate studies in pregnant women.
D	Adequate, well-controlled or observational studies in pregnant women showed risk to fetus. Benefits of therapy may outweigh risk.
X	Adequate, well-controlled or observation studies in animals or pregnant women showed fetal abnormalities or risk. Contraindication in pregnant women

Rakusen K. Exp Clin Cardiol 2010;15(4):e100-e103

PREGNANCY AND LACTATION LABELING RULE

- Effective June 30, 2015
- Relevant information for decision-making
- Complete risk statement based on human and animal data
- Background risk in general vs. disease population
- Considerations of disease
- Animal data in context of human exposure
- Human data when available
- Explicitly states when no data are available
- Also included new category on Females and Males of Reproductive Potential
- Drugs approved after June 30, 2001 updated additional content and formatting requirements

UK HealthCare

EARLY INVOLVEMENT OF MULTI-DISCIPLINARY CARE

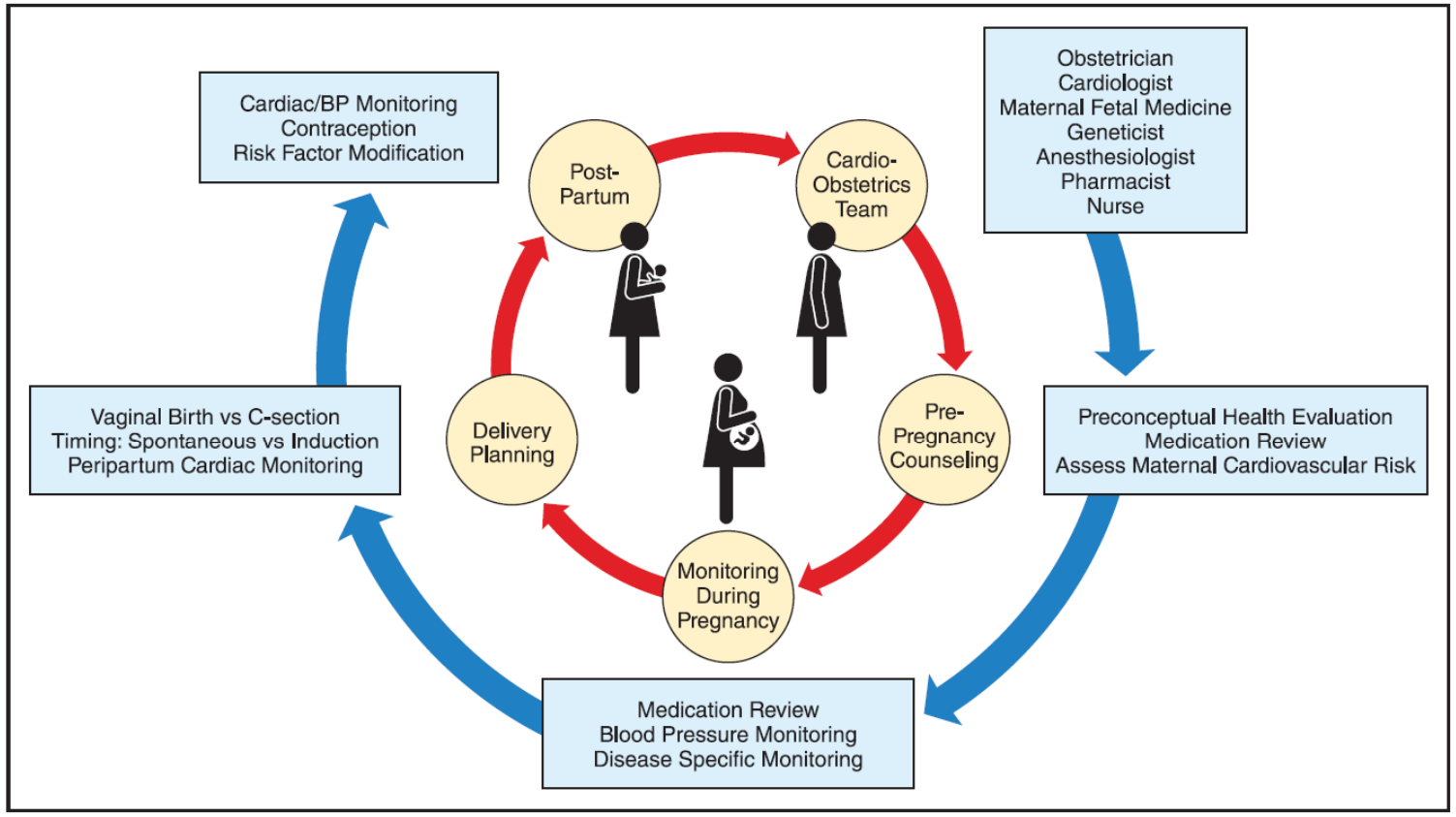


Figure 1. Cardio-obstetrics team in the management of women before pregnancy, during pregnancy, and postpartum.
BP indicates blood pressure.

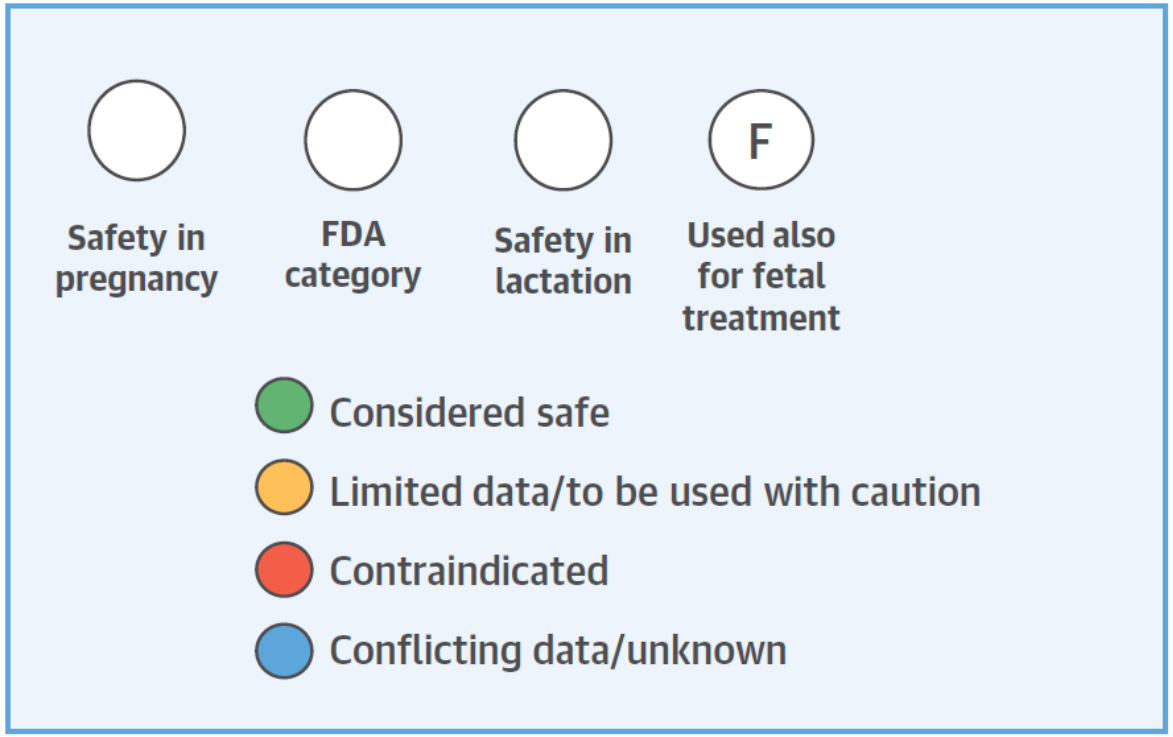
Mehta LS, et al. Circulation. 2020;141:e884–e903.

PATIENT AB

- 30-year-old female, G1P0, with history of pulmonary arterial hypertension and previous tobacco use
- Medications:
  - Ambrisentan 10 mg daily
  - Tadalafil 40 mg daily
  - Selexipag 1600 mcg twice daily
  - Furosemide 20 mg daily
  - Progesterone-only pill

UK HealthCare

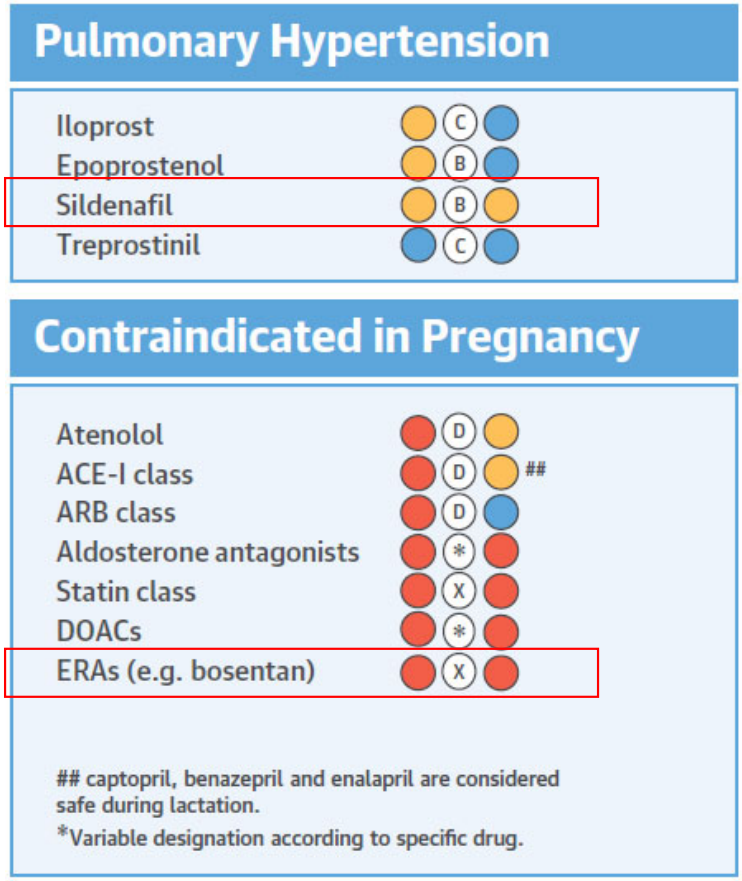
CARDIOVASCULAR MEDICATIONS IN PREGNANCY



UK HealthCare

Halpern, D.G. et al. J Am Coll Cardiol. 2019;73(4):457–76.

PATIENT AB



Halpern, D.G. et al. J Am Coll Cardiol. 2019;73(4):457–76.

Medications:

- Ambrisentan 10 mg daily
- Sildenafil 20 mg three times a day
- Selexipag 1600 mcg twice daily
- Furosemide 20 mg daily

UK HealthCare

AMBRISENTAN

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on data from animal reproduction studies, ambrisentan may cause fetal harm when administered to a pregnant woman and is contraindicated during pregnancy. There are limited data on ambrisentan use in pregnant women. In animal reproduction studies, ambrisentan was teratogenic in rats and rabbits at doses which resulted in exposures of 3.5 and 1.7 times, respectively, the human dose of 10 mg per day *[see Animal Data]*. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, advise the patient of the potential hazard to a fetus *[see Contraindications (4.1), Warnings and Precautions (5.1)]*.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal Data

Ambrisentan was teratogenic at oral dosages of ≥15 mg/kg/day (AUC 51.7 h•mcg/mL) in rats and ≥7 mg/kg/day (24.7 h•mcg/mL) in rabbits; it was not studied at lower dosages. These dosages are of 3.5 and 1.7 times, respectively, the human dose of 10 mg per day (14.8 h•mcg/mL) based on AUC. In both species, there were abnormalities of the lower jaw and hard and soft palate, malformation of the heart and great vessels, and failure of formation of the thymus and thyroid.

A preclinical study in rats has shown decreased survival of newborn pups (mid and high dosages) and effects on testicle size and fertility of pups (high dosage) following maternal treatment with ambrisentan from late gestation through weaning. The mid and high dosages were 51 x, and 170 x (on a mg/m^2 body surface area basis) the maximum oral human dose of 10 mg and an average adult body weight of 70 kg. These effects were absent at a maternal dosage 17 x the human dose based on mg/m^2.

Ambrisentan. Package insert. Actavis Pharma Inc; 2019. DailyMed. https://dailymed.nlm.nih.gov/. Accessed Sept 1, 2023.

SILDENAFIL

8.1 Pregnancy

Risk Summary

Limited published data from randomized controlled trials, case-controlled trials, and case series do not report a clear association with sildenafil and major birth defects, miscarriage, or adverse maternal or fetal outcomes when sildenafil is used during pregnancy. There are risks to the mother and fetus from untreated pulmonary arterial hypertension (see Clinical Considerations). Animal reproduction studies conducted with sildenafil showed no evidence of embryo-fetal toxicity or teratogenicity at doses up to 32-and 65-times the recommended human dose (RHD) of 20 mg three times a day in rats and rabbits, respectively (See Data).

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Clinical Considerations

Disease-Associated Maternal and/or Embryo/Fetal Risk

Pregnant women with untreated pulmonary arterial hypertension are at risk for heart failure, stroke, preterm delivery, and maternal and fetal death.

Data

Animal Data

No evidence of teratogenicity, embryotoxicity, or fetotoxicity was observed in pregnant rats or rabbits dosed with sildenafil 200 mg/kg/day during organogenesis, a level that is, on a mg/m ^{2} basis, 32-and 65-times, respectively, the recommended human dose (RHD) of 20 mg three times a day. In a rat pre-and postnatal development study, the no-observed-adverse-effect dose was 30 mg/kg/day (equivalent to 5-times the RHD on a mg/m ^{2} basis).

Sildenafil. Package insert. Advagen Pharma Ltd; 2021.

SELEXIPAG

8.1 Pregnancy

Risk Summary

There are no adequate and well-controlled studies with UPTRAVI in pregnant women. Animal reproduction studies performed with selexipag showed no clinically relevant effects on embryofetal development and survival. A slight reduction in maternal as well as in fetal body weight was observed when pregnant rats were administered selexipag during organogenesis at a dose producing an exposure to the active metabolite approximately 47 times that in humans at the maximum recommended human dose. No adverse developmental outcomes were observed with oral administration of selexipag to pregnant rabbits during organogenesis at exposures to the active metabolite up to 50 times the human exposure at the maximum recommended human dose.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2–4% and 15–20%, respectively.

Data

Animal Data

Pregnant rats were treated with selexipag using oral doses of 2, 6, and 20 mg/kg/day (up to 47 times the exposure to the active metabolite at the maximum recommended human oral dose of 1600 mcg twice daily on an area under the curve [AUC] basis) during the period of organogenesis (gestation days 7 to 17). Selexipag did not cause adverse developmental effects to the fetus in this study. A slight reduction in fetal body weight was observed in parallel with a slight reduction in maternal body weight at the high dose.

Pregnant rabbits were treated with selexipag using oral doses of 3, 10, and 30 mg/kg (up to 50 times the exposure to the active metabolite at the maximum recommended human oral dose of 1600 mcg twice daily on an AUC basis) during the period of organogenesis (gestation days 6 to 18). Selexipag did not cause adverse developmental effects to the fetus in this study.

In a pre- and post-natal development study, pregnant rats were treated with selexipag from gestation day 7 through lactation day 20 at oral doses of 2, 6, and 20 mg/kg/day (up to 35 times the exposure to the active metabolite at the maximum recommended human dose of 1600 mcg twice daily on an AUC basis). Treatment with selexipag did not cause adverse developmental effects in this study at any dose.

Sildenafil. Package insert. Actelion Pharmaceuticals US, Inc; 2023.

FUROSEMIDE

Heart Failure

Metoprolol	C
Carvedilol	C
Furosemide	C
Bumetanide	B
Dopamine	C
Dobutamine	B
Norepinephrine	C
Hydralazine	C
Nitroglycerin	C
Isosorbide dinitrate	C
Torsemide	B
Metolazone	B

Halpern, D.G. et al. J Am Coll Cardiol. 2019;73(4):457–76.

UK HealthCare

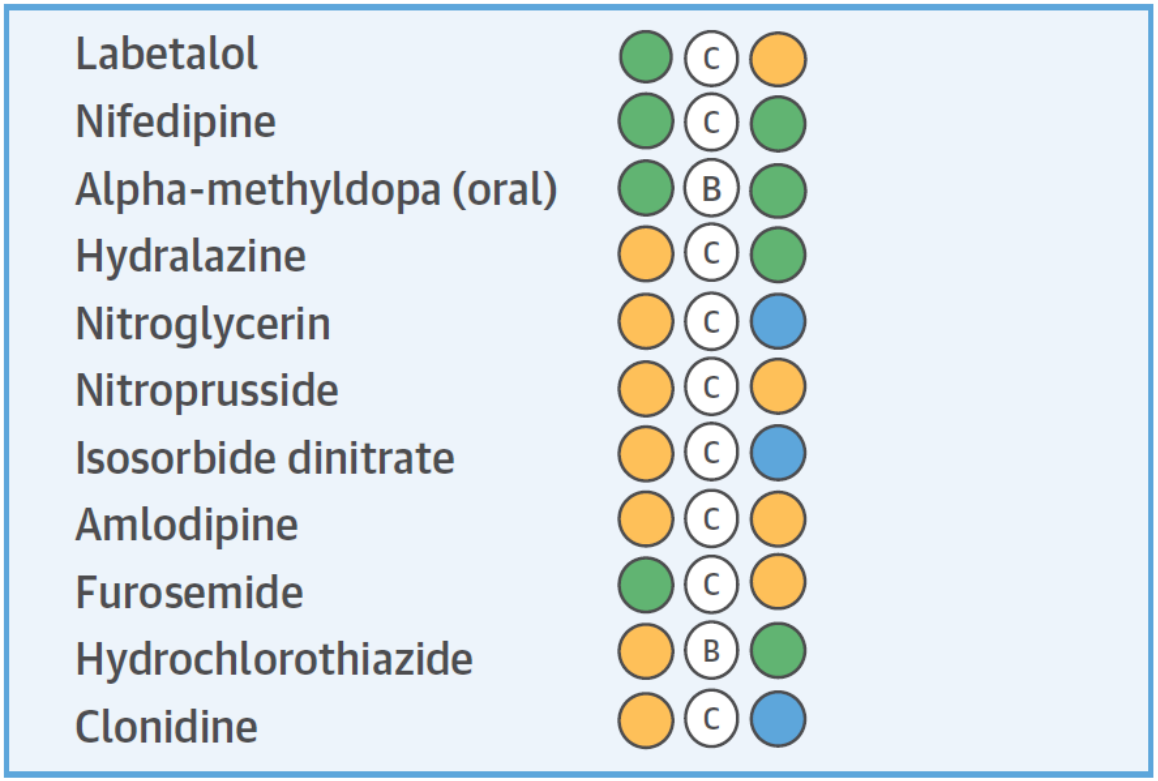
PATIENT AB

- 30-year-old female, G1P0, with history of pulmonary arterial hypertension and previous tobacco use
- Medications:
  - ~~Ambrisentan 10 mg daily~~
  - Tadalafil 40 mg daily
  - Selexipag 1600 mcg twice daily
  - Furosemide 20 mg daily
  - ~~Progesterone-only pill~~

Patient independently stopped

1. Continue tadalafil, selexipag, and furosemide
2. Refer to high-risk obstetric team for multi-disciplinary care
3. Increase surveillance of cardiovascular symptoms with frequent appointment
4. Increase frequency of echocardiogram
5. Schedule delivery with both obstetric and cardiology team at a hospital with an experienced cardiovascular team
6. Post-partum: discuss resumption of medication and lactation
7. Post-partum: discuss pregnancy and contraception

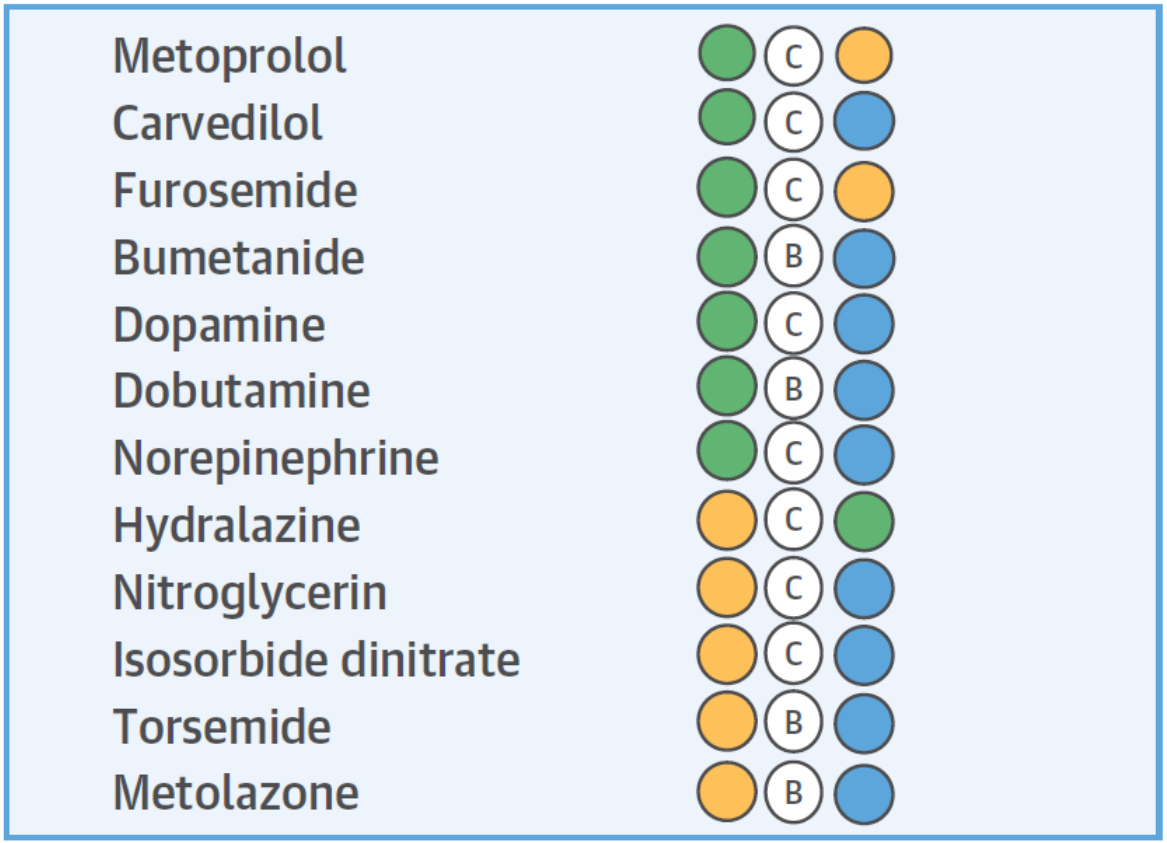
HYPERTENSION



UK HealthCare

Halpern, D.G. et al. J Am Coll Cardiol. 2019;73(4):457–76.

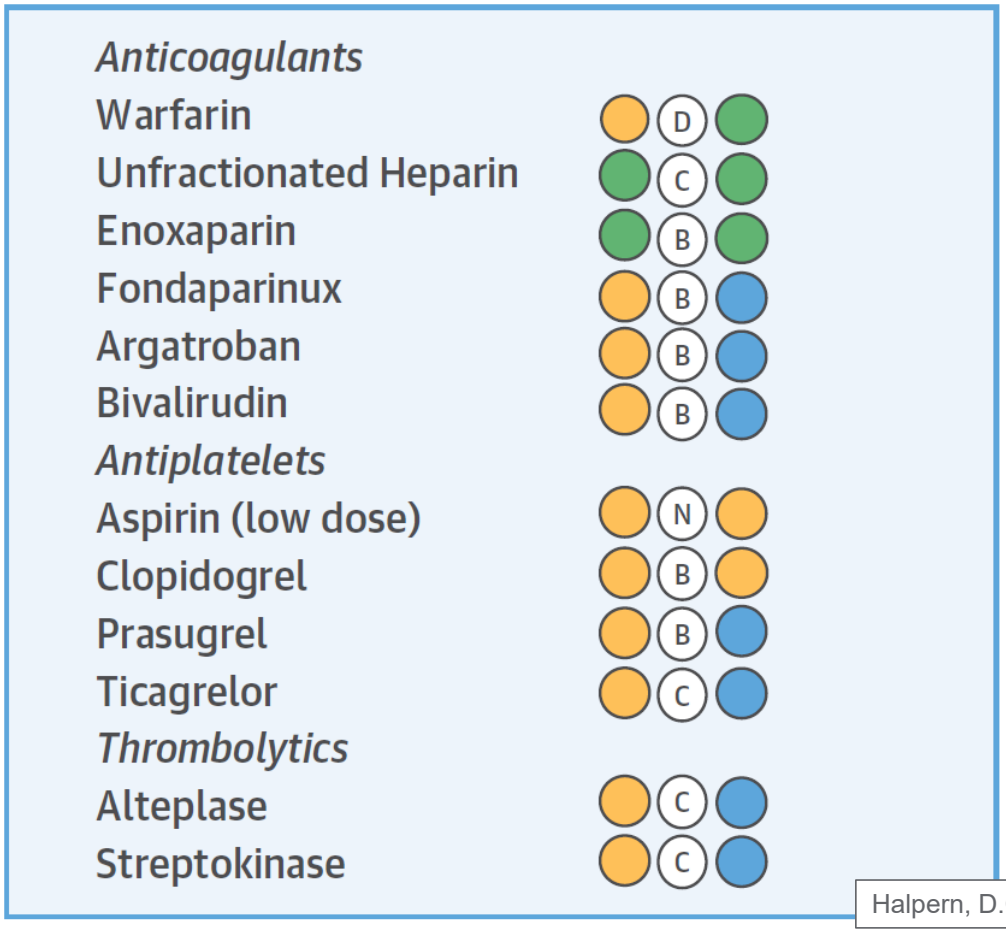
HEART FAILURE



UK HealthCare

Halpern, D.G. et al. J Am Coll Cardiol. 2019;73(4):457–76.

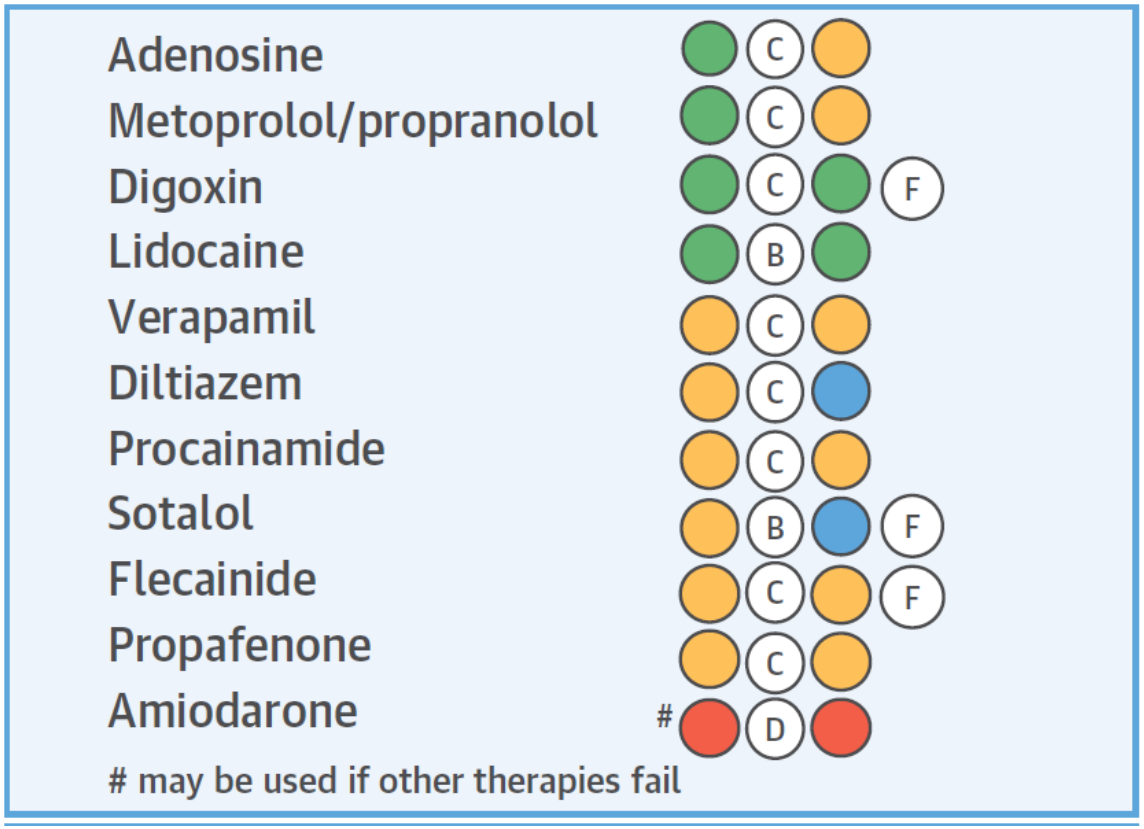
ANTICOAGULANT/ ANTIPLATELET/ THROMBOLYTIC



UK HealthCare

Halpern, D.G. et al. J Am Coll Cardiol. 2019;73(4):457–76.

ANTIARRHYTHMICS



HealthCare

Halpern, D.G. et al. J Am Coll Cardiol. 2019;73(4):457–76.

CHECKLIST

1. Discuss maternal cardiovascular risk as part of routine disease management
2. Educate on medications with high risk for fetal harm
3. Discuss effective options for contraception
4. Encourage open communication regarding family planning
5. Evaluate medication use pre-conception
6. Eliminate nonessential medications and discourage self- medication
7. Minimize exposure to harmful medication
8. Adjust medication doses to optimize health and reduce risk
9. Involve multi-disciplinary team collaboration pre-conception and during pregnancy
10. Frequently monitor CVD patients during pregnancy
11. Coordinate team-based care: determine timing and mode of delivery at a tertiary care center

UK HealthCare

APPENDIX

1. WHO Maternal Cardiovascular Risk Classifications
2. Tabular form of hemodynamic changes in pregnancy
3. Approach to Contraceptive Use in Women with cardiovascular disease
4. Properties of Various Contraceptive Options

UK HealthCare

MATERNAL CARDIOVASCULAR RISK CLASSIFICATION

Supplemental Table 2: WHO Classification of Maternal Cardiovascular Risk[15] Modified from Balci et al[16] with permission from the BMJ Publishing Group Ltd. Copyright ©2014, BMJ Publishing Group Ltd and the British Cardiovascular Society. Modified from Thorne et al[17] with permission from the BMJ Publishing Group Ltd. Copyright ©2006, BMJ Publishing Group Ltd and the British Cardiovascular Society. Reprinted from Canobbio et al.[18] Copyright ©2017 American Heart Association, Inc.

WHO Pregnancy Risk Category	Risk Description	Maternal Risk Factors
I	No detectable increase in maternal mortality and no/mild increase in morbidity risk	Uncomplicated small/mild pulmonary stenosis, PDA, mitral valve prolapse
		Successfully repaired simple lesions (ASD, VSD, PDA, anomalous pulmonary venous drainage)
		Atrial or ventricular ectopic beats, isolated
II	Small increase in maternal mortality and moderate increase in morbidity risk	If otherwise well and uncomplicated:
		Unoperated ASD, VSD
		Repaired TOF
		Most arrhythmias

UK HealthCare

Supp. Table 2 from Mehta LS, et al. Circulation. 2020;141:e884–e903.

MATERNAL CARDIOVASCULAR RISK CLASSIFICATION (CONTINUED)

WHO Pregnancy Risk Category	Risk Description	Maternal Risk Factors
II–III	Moderate increase in maternal mortality morbidity risk	Mild LV impairment
		Hypertrophic cardiomyopathy
		Native or tissue valvular disease (not considered risk category I or IV)
		Marfan syndrome without aortic dilation
		Aortic dilation <45 mm in bicuspid aortic valve aortopathy
		Repaired coarctation
III	Significantly increased maternal mortality or severe morbidity risk. Expert counseling required. In the event of pregnancy, intensive specialist cardiac and obstetric monitoring needed throughout pregnancy, childbirth, and the puerperium.	Mechanical valve
		Systemic RV
		Fontan circulation
		Cyanotic heart disease (unrepaired)
		Other complex CHD
		Aortic dilation 40–45 mm in Marfan syndrome
		Aortic dilation 45–50 mm in bicuspid aortic valve aortopathy

UK HealthCare

Supp. Table 2 from Mehta LS, et al. Circulation. 2020;141:e884–e903.

MATERNAL CARDIOVASCULAR RISK CLASSIFICATION (CONTINUED)

WHO Pregnancy Risk Category	Risk Description	Maternal Risk Factors
IV	Extremely high maternal mortality or severe morbidity risk. Pregnancy is contraindicated. In the event of pregnancy, termination should be discussed. If pregnancy continues, care should follow class III recommendations.	Pulmonary arterial hypertension (of any cause)
		Severe systemic ventricular dysfunction (LV ejection fraction <30%, NYHA class III-IV)
		Previous peripartum cardiomyopathy with any residual impairment of LV function
		Severe mitral stenosis, severe symptomatic aortic stenosis
		Aortic dilation >45 mm in Marfan syndrome
		Aortic dilation >50 mm in bicuspid aortic valve aortopathy
		Native severe coarctation

AS indicates aortic stenosis; ASD, atrial septal defect; CHD, congenital heart disease; LV, left ventricular; NYHA, New York Heart Association; PDA, patent ductus arteriosus; RV, right ventricle; TOF, tetralogy of Fallot; VSD, ventricular septal defect; and WHO, World Health Organization.

UK HealthCare

Supp. Table 2 from Mehta LS, et al. Circulation. 2020;141:e884–e903.

HEMODYNAMIC CHANGES IN PREGNANCY

Supplemental Table 1: Physiologic Changes Throughout Normal Pregnancy Compared to Pre-Pregnancy State.[13, 14]

	1st Trimester	2nd Trimester	3rd Trimester	During Labor	Early Postpartum *(<3 Months)*	Late Postpartum *(3-6 Months)*
Cardiac Output	↑	↑	↑	↑	↔	↔
Blood Pressure	↓	↓	↑	↑	↓	↔
Heart Rate	↑	↑	↑	↑	↓	↔
Systemic Vascular Resistance	↓	↓	↓	↓	↑	↔

UK HealthCare

Supp. Table 1 from Mehta LS, et al. Circulation. 2020;141:e884–e903.

APPROACH TO CONTRACEPTION USE IN WOMEN IN CARDIOVASCULAR DISEASE

Condition	Subcondition	IUD	Implant	DMPA	POP	CHC
DVT/PE	Remote, not receiving anticoagulation	R	R	R	R	U
	Acute	R	R	R	R	U
	History, receiving ≥3 mo of anticoagulation	R	R	R	R	U
	Family history (first-degree relative)	R	R	R	R	R
High blood pressure in pregnancy	History in prior pregnancy	R	R	R	R	R
Hypertension	Controlled	R	R	R	R	U
	SBP >140–159 mm Hg, DBP >90–99 mm Hg	R	R	R	R	U
	SBP >160 mm Hg, DBP >100 mm Hg	R	R	U	R	U
	Vascular disease	R	R	U	R	U
IHD	Current	Variable depending on whether IHD is present before vs after contraception. Copper IUD safe. For progesterone-IUD, implants, DMPA, and POP, risk likely outweighs benefit. CHC should be avoided.				
Multiple cardiovascular risk factors	Tobacco, diabetes mellitus, hypertension, older age, dyslipidemia	R	R	U	R	U
PPCM	Normal/mild systolic dysfunction	R	R	R	R	U
	Moderate to severe systolic dysfunction	R	R	R	R	U
Valvular heart disease	Uncomplicated	R	R	R	R	R
	Complicated*	R	R	R	R	U

CHC indicates combined hormonal contraception; CVD, cardiovascular disease; DMPA, depot medroxyprogesterone acetate; DBP, diastolic blood pressure; DVT, deep venous thrombosis; IHD, ischemic heart disease; IUD, intrauterine device; PE, pulmonary embolism; POP, progestin-only pill; PPCM, peripartum cardiomyopathy; R, reasonable (benefit outweighs risk); SBP, systolic blood pressure; and U, unreasonable (risk outweighs benefit).

*Defined as a condition that places the woman at an increased risk as a result of pregnancy.

Adapted from Curtis et al.[141]

UK HealthCare

Table 2 from Mehta LS, et al. Circulation. 2020;141:e884–e903.

PROPERTIES OF VARIOUS CONTRACEPTIVE OPTIONS

Table 2 The percentage of women who will experience an unplanned pregnancy within the first year of use of a given contraceptive method (typical and optimal usage), together with the percentage of continued use after 1 year, the risk of thrombosis and of infection associated with the method's use. Modified from[13,14]

Group	Contraceptive type	Failure (typical, %)	Failure (optimal, %)	Continued use at 1 year (%)	Thrombosis risk	Infection risk
Highly effective (<1%) Reversible	Implant	0.05	0.05	84	May be slightly increased risk	Minimal
	IUCD	0.2 (LNG)	0.2	80	No increased risk	Transient bacteraemia at insertion, increased PID
		0.8 (Copper)	0.6	78		
Highly effective (<1%) Irreversible	Vasectomy	0.15	0.1	100	No increased risk	Post-operative
	Tubal Occlusion	0.5 (abdominal, laparoscopic, or hysteroscopic)	0.5	100	No increased risk	Post-operative
Moderately effective (3–12%)	Injectable	Depo-Provera 3% Combined injectable 3%	Depo-Provera 0.3% Combined injectable 0.05%	56	Depo-provera: increased risk Combined injectable: increased risk	Minimal, but no protection from PID
	Combined oral contraceptive	8	0.3	68	Increased risk	Minimal, but no protection from PID
	Desogestrel containing progesterone-only pill	8	0.3		No increased risk	Minimal, but no protection from PID
	Patch	8	0.3	68	Increased risk	Minimal, but no protection from PID
	Ring	8	0.3	68	Increased risk	Minimal, but no protection from PID
Poorly effective (18–28%)	Male Condom	15	2	53	No increased risk	Reduced PID
	Diaphragm	16	6	57	No increased risk	Reduced PID
	Female Condom	21	5	49	No increased risk	Reduced PID
	Sponge	16–32 (nulliparous vs. parous)	9–20 (nulliparous vs. parous)	46–57 (parous vs. nulliparous)	No increased risk	No protection from PID
	Safe Period	25	3–5	51	No increased risk	No protection from PID
	Withdrawal	27	4	43	No increased risk	No protection from PID
	Spermicide	29	18	42	No increased risk	No protection from PID
No contraception		85	85			

Table 2 from Roos-Hesselink JW, et al. European Heart Journal (2015) 36, 1728–1734

Selection of Cardiovascular and Pulmonary Hypertension Medications in Peripartum Women

Gillian Leung, PharmD, BCCP