

Pregnancy and lactation in migraine

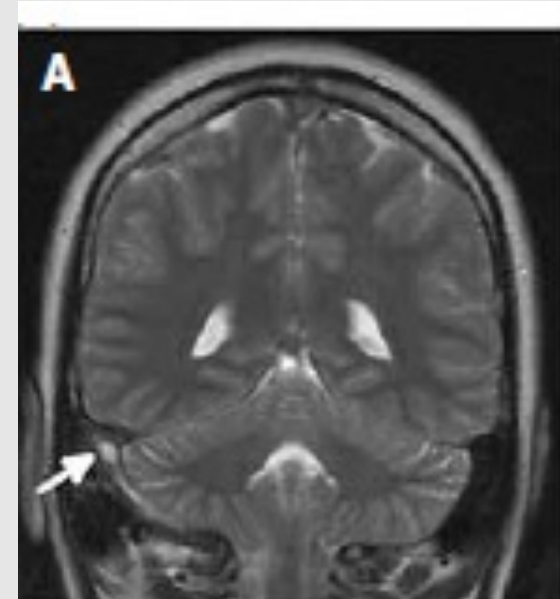
Marja-Liisa Sumelahti

Neurologist, MD, PhD

Tampere, Finland

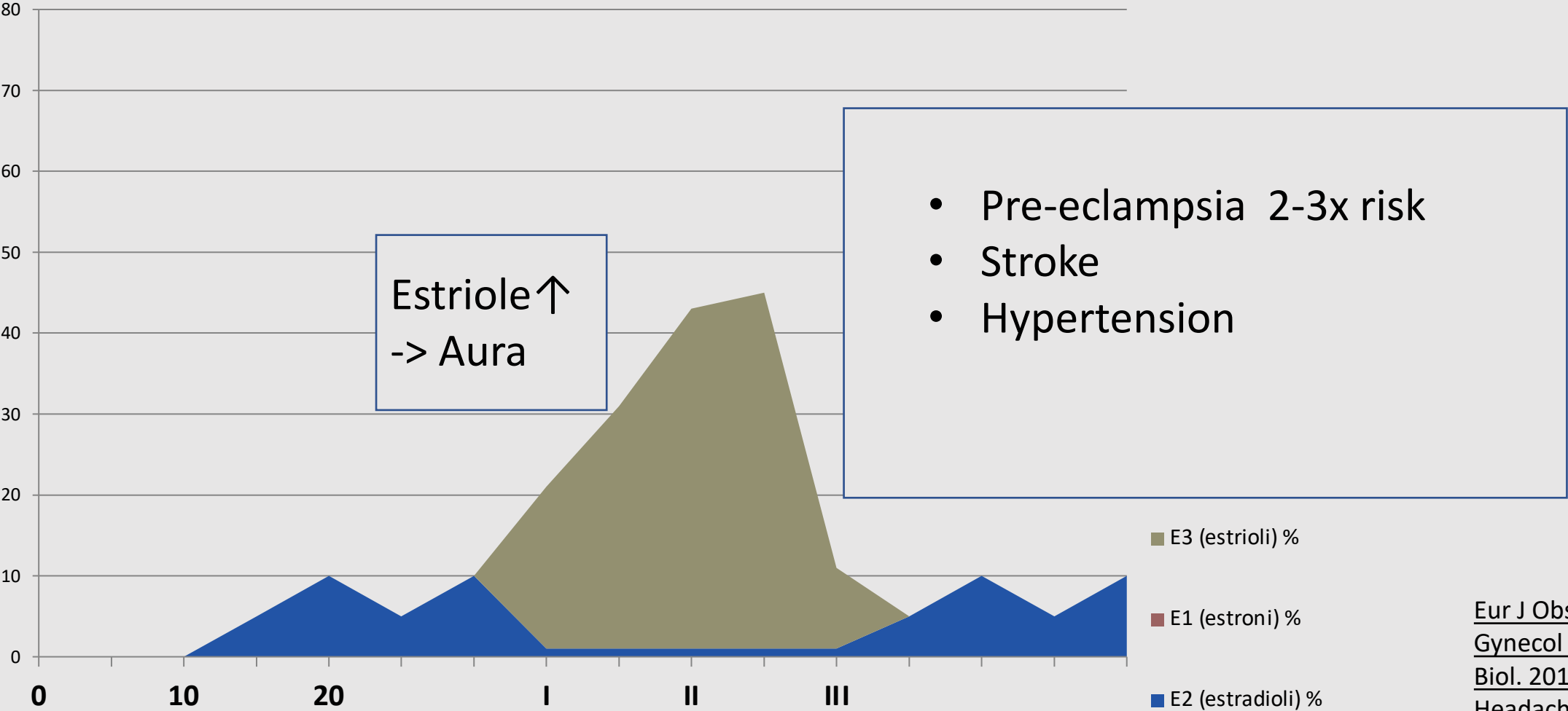
Headaches in pregnancy

- Primary headache > 50%
Migraine > 90%
- Secondary headache < 50%
 - Sinus thrombosis
 - Pre-eclampsia
 - Arterial hypertension
 - IIH (Idiopathic Intracranial Hypertension)
 - Infection
 - RCVS (postpartum), PRES
 - SAH



T2-weighted MRI: Thrombus mass in the right transverse sinus.

Risks related to migraine in pregnancy



Migraine in pregnancy

Reduction of attacks, improvement 50-75% during 2nd and 3rd trimester ^{1,2}

- Association with stable hormonal levels of estrogen
- Migraine without aura

Worsening of migraine <10%, first migraine ever 5%-10%. No change 5%-30%. ¹

Attack triggers

- Increasing hormonal levels during the 1st trimester
- Increased blood volume
- Lack of sleep
- Low blood sugar
- Stress

Counseling on optimization of lifestyle factors

Treatment: Little knowledge on safe treatments during pregnancy and lactation

1. Allais G. Is Migraine a risk factor in pregnancy. *NeuroSci*.2007 May;28(2):184-187

2. Calhoun AH. Migraine Treatment in Pregnancy and Lactation. *Curr Pain Headache Rep*. 2017 21:46:

3. Sanchez SE. Risk of placental abruption in relation to migraines and headaches, *BMC Women's Health*. 2010 Oct 26; 10:30;

4. Chen HM. Increased risk of adverse pregnancy outcomes for women with migraines.: nationwide population-based study ,*Cephalalgia*. 2010 Apr;30(4):433-8.

Alternative and other treatments

AVOID:

Feverfew, Saint John's Wort.

SAFE:

- Nondrug therapies :relaxation, sleep, massage, ice packs, biofeedback
- Acupuncture
- Non-invasive stimulation devices (transcutaneous supraorbital nerve stimulation)
- Greater occipital nerve block
- Oral prednisone or methylprednisolone

Good evidence:

Acetaminophen

Metoclopramide

Limited data:

NSAIDs, **ibuprofen** (II trimester)

CGRP mAbs

(Gepants)

Beta-blockers

Tricyclic anti-depressants

Risk to fetus:

Valproate

Topiramate

Candesartan

Ergotamine

Magnesium: risk is unclear and may be associated with fetal skeletal abnormalities

Avoid:

Ergots, ASA

Opiates



A systematic review and meta-analyses on the prevalence of pregnancy outcomes in migraine treated patients: a contribution from the IMI2 ConcePTION project

Daniel C. Dudman^{1,2,3} · Fatima Tauqeer^{4,5} · Moninder Kaur⁶ · Mary E. Ritchey² · Hu Li⁷ · Sandra Lopez-Leon¹ 

It was only possible to perform RR meta-analyses for triptans. The adjusted RR for triptan users compared the general population

major malformations	1.07, 95%CI 0.83–1.39, p 0.60
birth weight < 2500 g	1.18, 95%CI 0.94–1.48, p=0.16
gestational age < 37wk	1.49, 95%CI 0.37–6.08, p=0.58

-> No risk

TRIPTAN SAFETY IN PREGNANCY

N 4208 infants, Pregnancy outcome following prenatal exposure to triptan medications: A meta-analysis. *Headache*. 2015;55:490-501.

N 432 pregnant users, Pregnancy outcome after anti-migraine triptan use: A prospective observational cohort study. *Cephalalgia*. 2018;38:1081-1092.



A systematic review and meta-analyses on the prevalence of pregnancy outcomes in migraine treated patients: a contribution from the IMI2 ConcePTION project

Daniel C. Dudman^{1,2,3} · Fatima Tauqeer^{4,5} · Moninder Kaur⁶ · Mary E. Ritchey² · Hu Li⁷ · Sandra Lopez-Leon¹ 

Among untreated patients with migraine
0.6% (95% CI: 0–1.7%) for stillbirth
10.4% (95% CI: 8.9–12%) for gestational age < 37 weeks.

The pooled prevalence of adverse pregnancy outcomes in patients prescribed any migraine medication ranged from
0.4% (95% CI 0.2–0.7%) for stillbirth
12.0% (95% CI 7.8–16.9%) for spontaneous abortions

Drugs and Lactation Database (LactMed®)

Summary of Use during Lactation

Because of the low levels of **propranolol** in breastmilk, amounts ingested by the infant are small and would not be expected to cause any adverse effects in breastfed infants. Studies during breastfeeding have found no adverse reactions in breastfed infants clearly attributable to **propranolol**. No special precautions are required. **Propranolol** has been used successfully in cases of persistent pain of the breast during breastfeeding.[[1](#)],

Milk levels of **amitriptyline** and its metabolites are low. Immediate side effects have not been reported and a limited amount of follow-up has found no adverse effects on infant growth and development. **Amitriptyline** use during breastfeeding would usually not be expected to cause any adverse effects in breastfed infants, especially if the infant is older than 2 months. A safety scoring system finds **amitriptyline** use to be possible with caution during breastfeeding.[[1](#)] However, rare sedation has been reported in a neonate. Other agents with fewer active metabolites may be preferred when large doses are required or while nursing a newborn or preterm infant.

Drugs and Lactation Database (LactMed®)

- **Botulin A**

- Last Revision: September 21, 2020.
- *Estimated reading time: 1 minute*
- CASRN: 93384-43-1

- **Drug Levels and Effects**

- **Summary of Use during Lactation**

- No data exist on the medical use of botulin A (botulinum toxin) during breastfeeding. However, it is not detectable systemically after intramuscular use, thus excretion into breast milk is considered unlikely. Breastfeeding appears to protect infants against botulism.^[1] One infant was safely breastfed during maternal botulism and no botulinum toxin was detectable in the mother's milk or infant. Since the doses used medically are far lower than those that cause botulism, amounts ingested by the infant, if any, are expected to be small and not cause any adverse effects in breastfed infants^[2]^[3] No special precautions are required.

Fremanezumab

Last Revision: April 15, 2023.

Estimated reading time: 1 minute

CASRN: 1655501-53-3

[Go to:](#)

Drug Levels and Effects


Summary of Use during Lactation

No information is available on the clinical use of **fremanezumab** during breastfeeding.

Because **fremanezumab** is a large protein molecule with a molecular weight of about 148,000, the amount in milk is likely to be very low and absorption is unlikely because it is probably destroyed in the infant's gastrointestinal tract. Waiting for at least 2 weeks postpartum to resume therapy may minimize transfer to the infant.^[1]

Safety profile of monoclonal antibodies targeting the calcitonin gene-related peptide system in pregnancy: Updated analysis in VigiBase[®]

Roberta Nosedà¹ , Francesca Bedussi¹, Claudio Gobbi^{2,3,4}, Alessandro Ceschi^{1,3,5,6,*}  and Chiara Zecca^{2,3,*} 

Cephalalgia
2023, Vol. 43(4) 1–10
© The Author(s) 2023
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/03331024231158083
journals.sagepub.com/home/cep


VigiBaseVR, the World Health Organization (WHO) pharmacovigilance database.

Safety profile of erenumab, galcanezumab, fremanezumab and eptinezumab in pregnancy showed no consistent signals of foeto-maternal toxicity.

Table 3. Pregnancy outcomes reported with erenumab, galcanezumab, fremanezumab and eptinezumab as of 31 December 2021.

	Safety reports on erenumab, n = 89 ^{ab}	Safety reports on galcanezumab, n = 27 ^{ab}	Safety reports on fremanezumab, n = 20 ^{ab}	Safety reports on eptinezumab, n = 1 ^{ab}
Maternal outcomes	86	28	9	–
Spontaneous abortion	35	13	14	1
Foetal growth restriction	1	–	–	–
Prematurity	6	2	–	–
Birth defects	5	3	1	–
Other neonatal outcomes	13	1	–	–
Events related to lactation	1	–	–	–

^aSafety reports reporting only drug exposure were excluded from this analysis.

^bSome safety reports reported more than one pregnancy outcome.

Pregnancy is a time of substantial reduction in migraine attacks

First trimester

11% attack reduction

- Paracetamol, NSAIDs
- Metoclopramide
- Sumatriptan

Second trimester

53% attack reduction

- Paracetamol, NSAIDs
- Metoclopramide
- Sumatriptan

Third trimester

79% attack reduction

- Paracetamol, Metoclopramide
- Sumatriptan

Cephalalgia 2003;23:197-205, *Headache* 2001;41:351-6,
Headache 2000;40:20-4

Table 1 Drugs used for acute treatment of migraine during pregnancy

FDA category B

Acetaminophen

Diclofenac 3rd trimester: category D

Ibuprofen 3rd trimester: category D

Naproxen 3rd trimester: category D

Meperidine Category D if prolonged use/high doses at term

Metoclopramide

FDA category C

Aspirin 3rd trimester: category D

Indomethacin 3rd trimester: category D

Mefenamic acid 3rd trimester: category D

Codeine

Morphine

Tramadol

Prochlorperazine

Promethazine

Almotriptan

Eletriptan

Frovatriptan

Naratriptan

Rizatriptan

Sumatriptan

Zolmitriptan

Prednisolone

FDA category X

Ergotamine

Dihydroergotamine