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Human Milk and Plasma Pharmacokinetics of Single-Dose Rimegepant 75 mg in Healthy Lactating Women

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Abstract

Objective: Investigate whether rimegepant—an oral small molecule calcitonin gene-related peptide receptor antagonist for the treatment of migraine—is excreted in human milk after a single 75 mg dose and characterize its concentration–time profile in the plasma and milk of healthy lactating women to determine the relative infant dose (RID).
Methods: This open-label, single-center study enrolled healthy lactating women aged 18–40 years with a gestation of 37–42 weeks and uncomplicated delivery of a single healthy child ≥2 weeks (14 days) and ≤6 months before study drug administration. Plasma samples were collected 0, 1, 2, 4, and 8 hours postdose; human milk samples were collected at 0, 1, 2, 4, 8, 12, 16, 24, 32, and 36 hours. The milk:plasma drug concentration ratio was estimated as the ratio of the human milk:plasma areas under the curve. The RID (%) was calculated as 100 times the quotient of the body weight-normalized infant and maternal doses.
Results: Subjects ($N = 12$) were enrolled between 25 January and 15 September 2020. The mean (standard deviation [SD]) age was 29.8 (3.6) years; mean (SD) body mass index was 26.8 (4.9) kg/m^2. The mean (SD) RID of rimegepant was 0.51% (0.14). The mean (SD) body-weight normalized infant dose was 0.005 (0.001) mg/kg/day, the mean (SD) body-weight normalized maternal dose was 1.04 (0.18) mg/kg/day, and mean (SD) maternal body weight was 74.0 (13.3) kg.
Conclusion: On a weight-adjusted basis, the mean RID of rimegepant was <1% of the maternal dose.

Keywords: rimegepant, lactation, migraine, pharmacokinetics, milk, plasma

Introduction

Migraine, a chronic condition that features periodic attacks of head pain accompanied by sensitivity to light and/or sound and gastrointestinal distress,[1] affects >30 million women in the United States.[2] Among women of reproductive age (15–49 years), migraine is the most common cause of disability[3]; performance decrements ranging from mild to incapacitating have been documented in academic, professional, and social settings.[4–6] Although migraine attacks often abate or cease during pregnancy, they resume within 4 weeks of childbirth in most women who have migraine before pregnancy.[7] Because some migraine drugs are incompatible with use during lactation or have not been evaluated, concerns about infant drug exposure may delay or limit breastfeeding and lead to avoidance of migraine medications or, worse, avoidance of breastfeeding.[8]

Rimegepant is an orally administered calcitonin gene-related peptide receptor antagonist approved by the US Food and Drug Administration in 2020 for the acute treatment of migraine in adults; it received approval for the preventive treatment of episodic migraine in 2021.[9] The 75 mg dose of rimegepant has demonstrated efficacy and safety in multiple randomized, placebo-controlled clinical trials.[10–13]

Rimegepant has not previously been evaluated in lactating women. However, based on the molecular weight and

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physiochemical properties of rimegepant, we hypothesized that levels of rimegepant in human milk after a single 75 mg dose would be very low. The objective of this study was to investigate whether rimegepant is excreted in human milk after a single 75 mg dose and to determine the concentration–time profiles of rimegepant in the plasma and human milk of healthy lactating women to enable calculation of the relative infant dose (RID).

Materials and Methods

This Phase 1, single-center, open-label study assessed the excretion of a single oral dose of 75 mg rimegepant in the human milk of healthy lactating women from 2 weeks (14 days) up to 6 months postpartum at the time of study drug administration. The protocol, consent form, recruitment materials, and other written information provided to subjects were reviewed and approved by the institutional review board at the Texas Tech University Health Sciences Center (Amarillo, TX). The study was conducted in accordance with Good Clinical Practice, as defined by the International Council for Harmonisation and the United States Code of Federal Regulations, Title 21, Part 50 (21CFR50).

The study included a screening period (up to 30 days) followed by a single-dose administration of rimegepant 75 mg with 36-hour follow-up. All subjects fasted for a minimum of 8 hours and were dosed on Day 1. A light meal was administered no earlier than 2 hours after the dose to minimize possible analysis interference and variance caused by food intake just before sampling. To ensure milk production after administration, dosing did not commence until a predose milk sample had been produced by the subject.

Concomitant medications were prohibited, except acetaminophen and medications used in direct association with parturition, for the treatment of adverse events (AEs), or for treatment of noninsulin-dependent diabetes. Use of concomitant medication(s) from 1 week before dosing and throughout the study was recorded in the case report form, together with the main reason for its prescription, dose, and dosage regimen.

Eligible subjects were women aged 18–40 years who had a normal pregnancy (gestation of 37–42 weeks) without pregnancy-induced hypertension or pre-eclampsia; were amenable to disclosing pregnancy and infant history; and were willing to permit the use of pasteurized donor milk, formula, or previously pumped/stored human milk to feed the infant. Subjects also had to have delivered a single normal-term infant (cesarean section was allowed) who was able to bottle feed and established lactation from 2 weeks (14 days) up to 6 months postpartum at the time of study drug administration; be exclusively breastfeeding or pumping; and agree not to breastfeed for the 36-hour period of human milk collection after dosing with study drug.

Participants had to have a body mass index (BMI) of 18–34.9 kg/m^2 and negative serum drug screen results at screening and negative urine drug screen results at the eligibility check before dosing; a positive test for drugs used in relation to parturition was acceptable. Eligibility was also dependent on having a negative alcohol breath test at screening and at the eligibility check before dosing; being a nonsmoker or light smoker (<15 cigarettes/week in the 6 months before signing informed consent); and having a score of 0 on the Sheehan-Suicidality Tracking Scale[14] (S-STS) at screening.

Subjects also had to agree to abstain from sexual intercourse from signing of consent to the end-of-study visit (36 hours postdose) and have a negative serum b-human chorionic gonadotropin at screening and a negative urine pregnancy test at the eligibility check before dosing. Subjects could not have any clinically significant abnormality that might introduce additional risk factors or interfere with the study procedures; donate blood or plasma from the signing of consent through participation in the study; or participate in another clinical study during this study and for a minimum of 30 days after completion of participation in this study.

Subjects were excluded from participation if they had a history of breast cancer, breast surgery, breast augmentation or reduction, presence of breast implants, or clinically significant abnormalities of the breasts that might affect milk production and/or flow. They were also excluded if they had a history or current evidence of any unstable medical conditions that might expose them to undue risk of a significant AE or interfere with assessments of safety or efficacy during the course of the study.

The safety population included all subjects who received at least 1 dose of study drug. Safety outcomes included AEs; serious AEs; treatment-emergent AEs (TEAEs); AEs leading to withdrawal; laboratory assessments; liver function tests; vital signs; physical measurements; electrocardiography; concomitant medications/procedures; pregnancy testing; alcohol breath test; drug screen; and the S-STS. AEs were coded using Medical Dictionary for Regulatory Activities (version 23.1).

Vital signs were recorded at screening (Days −30 to −3), eligibility check, and at 1, 2, 4, 8, 12, 16, 24, 32, and 36 hours postdose. Height and weight were measured at screening. Body temperature, respiratory rate, blood pressure, and radial artery pulse rate were collected at predose and at 1, 2, 4, 8, 12, 16, 24, 32, and 36 hours postdose.

At screening, eligibility check, and 36 hours postdose, the following were conducted and/or administered: standard 12-lead electrocardiogram; routine physical examination, including examination of the cardiovascular, respiratory, and gastrointestinal systems with review of any other system being symptom-directed; laboratory assessments, including clinical safety laboratory tests (hematology, chemistry, and estimated glomerular filtration rate); liver function tests for aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, and bilirubin (total, direct, and indirect); urinalysis; and the S-STS.

Laboratory assessments were conducted with the subject fasted for a minimum of 8 hours, if possible. If a subject was not fasting at a given visit, the test was still performed, and the nonfasting status was documented. Drug screens were conducted in serum at screening and in urine at eligibility check. Pregnancy tests were conducted at screening (serum test), eligibility check (urine test), and 36 hours postdose (serum test). Alcohol breath tests were conducted at screening and eligibility check.

The pharmacokinetic (PK) population included all subjects with at least 1 postdose PK sample; assessments included human milk rimegepant concentrations, plasma rimegepant exposure, milk:plasma concentration ratio, and the RID.

Rimegepant PK parameters in human milk included maximum observed concentration (C_{max}), time of observed maximum concentration (T_{max}), area under the concentration–time

curve (AUC) from time zero to the last detectable concentration ($AUC_{0\text{-last}}$), AUC from time zero to infinity ($AUC_{0\text{-inf}}$), AUC from time zero to the end of the dosing interval (24 hours) (AUC_{tau}), and average concentration over the dosing interval (C_{av}). They were obtained by noncompartmental analysis (Phoenix WinNonlin version 8.1, Certara, Princeton, NJ) of observed milk rimegepant concentrations. AUC values were generated using the linear/log trapezoidal rule.

Maternal plasma rimegepant PK parameters included C_{max}, T_{max}, $AUC_{0\text{-inf}}$, and AUC_{tau}. Plasma rimegepant PK parameters for further calculations were obtained through simulations using a validated population PK model (unpublished) based on plasma concentration data from 10 previous rimegepant Phase 1 clinical studies ($N = 337$, 25% female). The structural model, which comprised 2 compartments with a transit model for oral absorption, simulated a complete predicted individual PK profile from the dose and 8-hour observed plasma PK data for each subject.

From these simulations, the PK parameters of C_{max} and T_{max} in plasma were determined, and AUC_{tau} (through 24 hours) and $AUC_{0\text{-inf}}$ in plasma were calculated. The C_{av} in human milk was calculated as $AUC_{0\text{-inf}}$ divided by 24, assuming $AUC_{0\text{-inf}}$ after a single dose represents steady-state AUC_{tau} (tau = 24 hours). Human milk and plasma concentrations below the limit of quantification were set to zero. Missing values were not imputed.

The milk:plasma concentration ratio was calculated based on the ratio of the $AUC_{0\text{-inf}}$ of human milk to the $AUC_{0\text{-inf}}$ of plasma.

The RID was calculated as 100 times the quotient of the body weight-normalized infant dose and the body weight-normalized maternal dose. The body weight-normalized infant dose was defined as the product of the milk:plasma concentration ratio, the $AUC_{0\text{-inf}}$-derived maternal C_{av}, and standardized milk consumption (150 mL/kg/day). The body weight-normalized maternal dose was defined as the quotient of the maternal dose (mg/day) and the maternal weight (kg) at screening.

Plasma samples for PK assessment were collected at predose and at 1, 2, 4, and 8 hours postdose. Human milk samples for PK assessment were collected 15–30 minutes predose and at 0, 1, 2, 4, 8, 12, 16, 24, 32, and 36 hours postdose.

Subjects washed nipples with warm water before each human milk collection time point and pumping. Milk was collected from both breasts by pumping to emptiness using an electric milk pump (12 minutes) 15–30 minutes predose (time zero). Each breast was completely emptied at 1, 2, 4, 8, 12, 16, 24, 32, and 36 hours postdose for determination of the rimegepant concentration in milk at each timepoint. Samples from both breasts were combined into a single sample. The weight and volume of the total sample for each timepoint was noted.

Frozen plasma and human milk samples were transported on dry ice to the bioanalytical facility. Analysis of rimegepant concentrations in the human milk and plasma samples was performed using validated high-performance liquid chromatographic methods appropriate to the matrix analyzed, with tandem mass spectrometry detection methods (Syneos Health, Morrisville, NC); the lower limit of quantification was 0.5 ng/mL for the plasma and human milk assays. The Watson Laboratory Information Management System (Thermo Fisher Scientific, Waltham, MA) was used at different steps of the analysis.

A sample size of 12 subjects was anticipated to be sufficient to detect quantifiable concentrations of rimegepant in human milk based on regulatory guidance and findings from previous studies with other compounds.[15,16]

Results

In total, 13 subjects were enrolled and screened; 12 received a 75 mg dose of rimegepant and completed the study (Fig. 1). Subjects had a mean (standard deviation [SD]) age of 29.8 (3.6) years, most subjects were white (83.3% [10/12]) and not Hispanic or Latino (75.0% [9/12]) as shown in Table 1. Subjects had a mean (SD) weight of 74.0 (13.3) kg and a mean (SD) BMI of 26.8 (4.9) kg/m^2. Mean (SD) postdose milk production per 24 hours was 738.0 (195.6) mL.

In addition to rimegepant, 83.3% (10/12) subjects received concomitant medications of minerals, vitamins, and/or probiotics. Two subjects (16.7%) used progestin-only oral contraceptives. One subject (8.3%) took acetaminophen to treat headache, 1 subject (8.3%) used a fluticasone and salmeterol combination inhaler to treat asthma, and 1 subject (8.3%) took levothyroxine to treat hypothyroidism.

The PK parameters for rimegepant in human milk and plasma are shown in Table 2. Both sample media showed interindividual variability of <30% on C_{max} and AUC. The geometric mean (% coefficient of variation) milk:plasma concentration ratio was 0.20 (16.2), and the median (range) was 0.20 (0.16, 0.27). The mean (SD) body-weight normalized infant dose was 0.005 (0.001) mg/kg/day; the median (range) was 0.005 (0.003, 0.007) mg/kg/day. The mean (SD) body-weight normalized maternal dose was 1.04 (0.18) mg/kg/day; the median (range) was 1.09 (0.786, 1.364). Accordingly, the mean (SD) RID was 0.51% (0.14); the median (range) RID was 0.462% (0.358, 0.773). The mean (SD) human milk concentration and plasma concentration–time curves after a single 75 mg oral dose of rimegepant are shown in Figure 2.

There were no AEs, serious AEs, TEAEs, or deaths reported; no subjects discontinued from the study due to AEs. No clinically meaningful abnormalities were observed in maternal vital signs, laboratory values, hematology results, chemistry results, or urinalysis parameters.

Discussion

Rimegepant is the only migraine medication approved for acute and preventive treatment. It is likely that the potential treatment population for rimegepant includes many postpartum breastfeeding women with migraine. This study evaluated rimegepant concentrations in plasma and human milk in lactating women and provides new information regarding use of the compound in this population.

Human milk concentrations of rimegepant were measurable in all samples taken over the 24-hour dosing period. The mean body weight-normalized infant rimegepant dose was 0.005 mg/kg/day, and the mean estimated RID was 0.51%. The study, therefore, showed that oral administration of rimegepant 75 mg to lactating women results in a <1% RID in human milk.

Administration of a single oral dose of rimegepant 75 mg to lactating women under fasting conditions was safe and well tolerated.

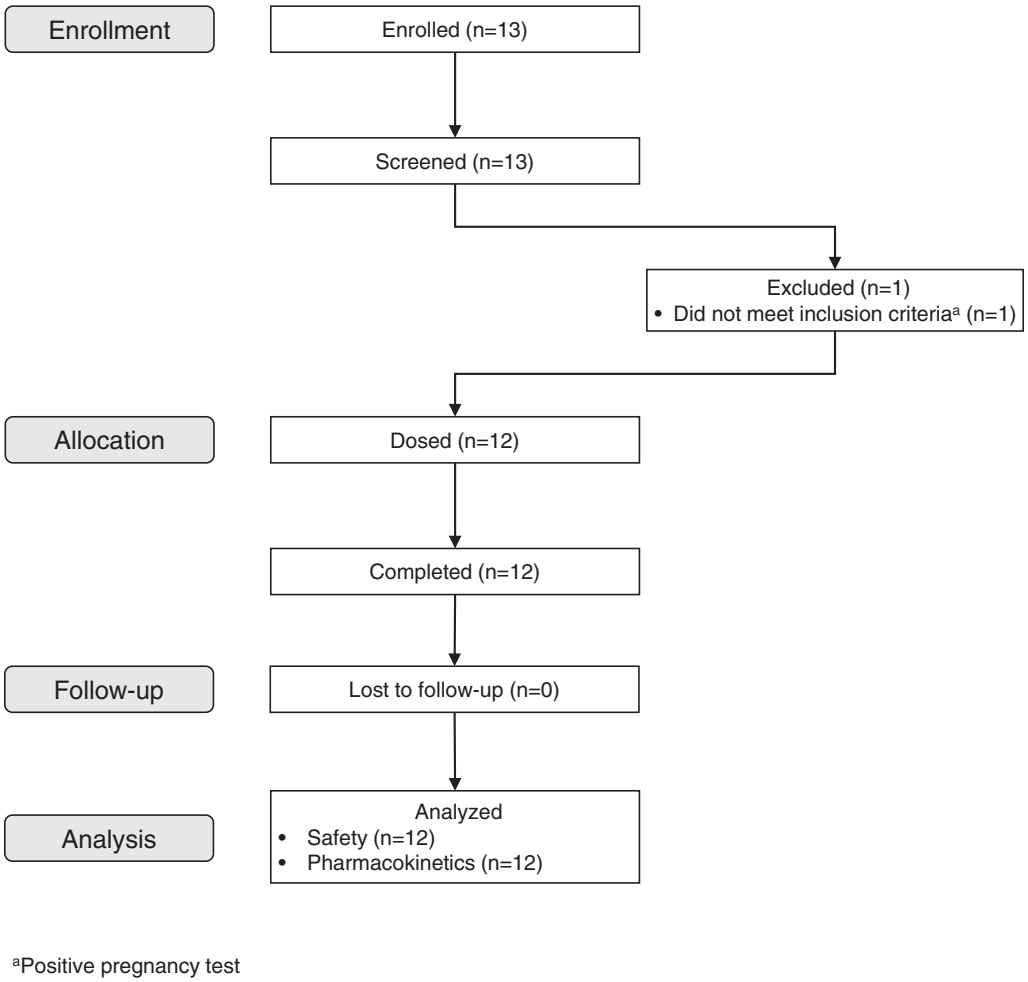

FIG. 1. Disposition of subjects.

Breastfeeding women with migraine may overestimate the risks of acute medications and avoid using prescribed treatments based on fear of harming their child.[17] This treatment pattern may be due to the long-standing paucity of information about drug safety and efficacy in pregnant and lactating women, which has been attributed to the lack of a regulatory requirement that clinical trials of new treatments enroll such

Table 1. Demographics and Baseline Characteristics

Variable	N = *12*
Age, years, mean (SD)	29.8 (3.6)
Sex, *n* (%)	
Female	12 (100.0)
Race, *n* (%)	
White	10 (83.3)
American Indian or Alaska Native	1 (8.3)
Multiple	1 (8.3)
Ethnicity, *n* (%)	
Hispanic or Latino	3 (25.0)
Not Hispanic or Latino	9 (75.0)
Weight, kg, mean (SD)	74.0 (13.3)
BMI, kg/m^2, mean (SD)	26.8 (4.9)

BMI, body mass index; SD, standard deviation.

Table 2. Summary of Pharmacokinetic Parameters After a Single 75 mg Dose of Rimegepant to Healthy Lactating Women (*N* = 12)

	Sample medium	
	Human milk	*Plasma*
$AUC_{0\text{-last}}$[a]	810.1 (22.4)	NA
$AUC_{0\text{-inf}}$[a]	816.1 (22.3)	4,039.9 (17.4)
AUC_{tau}[a]	798.0 (22.0)	3,811.9 (17.2)
C_{max}, ng/mL	169.6 (23.2)	759.2 (23.0)
C_{av}, ng/mL	34.0 (22.3)	168.3 (17.4)
T_{max}, h[b]	2.0 (1.0, 2.0)	1.4 (1.2, 1.8)
Milk:plasma concentration ratio	0.2 (16.2)	

[a]ng*h/mL.
[b]Median (range).
Data are geometric mean (% coefficient of variation) unless otherwise noted.
AUC, area under the concentration–time curve; NA, not applicable.

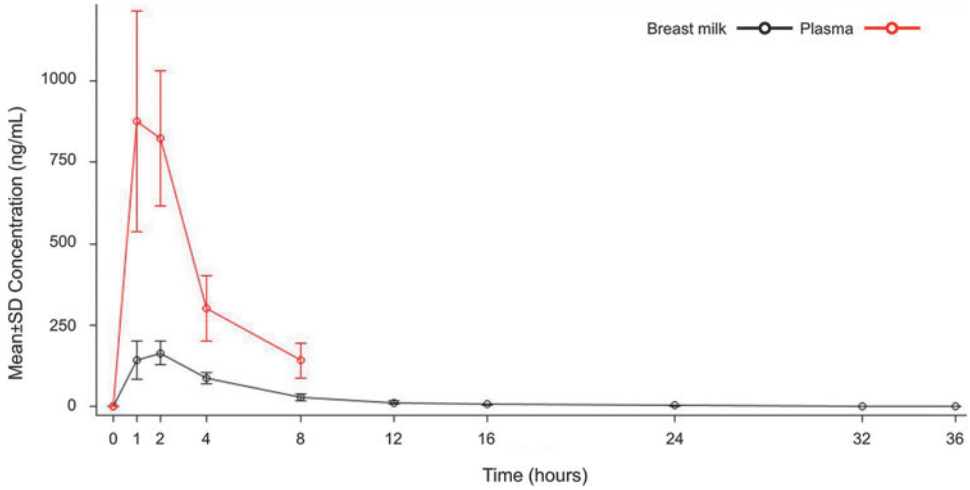

FIG. 2. Mean human milk and plasma rimegepant concentrations versus time after a 75 mg oral dose.

women, medicolegal and financial disincentives to undertake pregnancy and lactation studies, and the reluctance of pregnant and lactating women to participate in clinical trials.[18]

This suggests an unmet need for education and guidance about the appropriate use of pharmacotherapy during breastfeeding by women with migraine.[19] Although a 10% RID has been commonly cited as a safety threshold,[20] with lower percentages indicating decreased risk, no consensus has been reached, and exceptions (e.g., antineoplastic drugs) are evident. The favorable safety profile of rimegepant in adults,[9] as well as the very low RID demonstrated in this study, are reassuring. Because the treatment of migraine is a common challenge in breastfeeding women and is an important public health issue, the results of this study will help inform the safe use of rimegepant by lactating women with migraine.

This study has strengths and limitations. Strengths include its being apparently the first determination of the very limited transfer of a member of a new class of antimigraine medications, calcitonin gene-related peptide antagonists, into human milk, as well as the first evidence specific to rimegepant. Limitations include the small size of the trial population and the absence of women with migraine, which may reduce the generalizability of its findings.

Conclusion

The results of this Phase 1, single-center, open-label study assessing the PK of a single 75 mg oral dose of rimegepant in healthy lactating women demonstrate that the estimated infant exposure to maternal rimegepant from human milk is very low, and that rimegepant was safe and well tolerated by lactating women.

Data Sharing

Biohaven Pharmaceuticals will provide access to deidentified patient-level data that underlie the results in this article in response to scientifically valid research proposals. Data from this study, including the study protocol, will be made available beginning 9 months and ending 24 months after the publication of this article. Biohaven will consider requests from qualified researchers for access to the data. Biohaven will review the request using an internal committee composed of Biohaven staff who are responsible for the program, including a clinician, a statistician, and a data-sharing professional.

Biohaven will make reasonable efforts to fulfil all data requests for legitimate research purposes, but there might be instances in which retrieval or delivery of data is not feasible, such as those involving, for example, patient privacy, requirements for permissions, contractual obligations, and conflicts of interest. All those receiving access to data will be required to enter into a data use agreement provided by Biohaven, which will contain the terms under which the data will be provided.

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Authors' Contributions

T.E.B., R.C., L.K., R.B., and T.W.H. conceived and designed the study. T.E.B., R.C., and T.W.H. drafted the article. All authors were involved in the acquisition, analysis, or interpretation of data, revising the article, and in the final approval of the version to be published. The authors agree to be accountable for all aspects of the study and ensure that questions related to the accuracy or integrity of any part of the study are appropriately investigated and resolved.

Disclosure Statement

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References

1. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd ed. *Cephalalgia* 2018;38:1–211.

2. GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: A systematic analysis for the Global Burden of Disease Study 2019. *Lancet* 2020;396:1204–1222.
3. GBD 2016 Headache Collaborators. Global, regional, and national burden of migraine and tension-type headache, 1990–2016: A systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol* 2018;17:954–976.
4. Blumenfeld AM, Varon SF, Wilcox TK, et al. Disability, HRQoL and resource use among chronic and episodic migraineurs: Results from the International Burden of Migraine Study (IBMS). *Cephalalgia* 2011;31:301–315.
5. Adams AM, Serrano D, Buse DC, et al. The impact of chronic migraine: The Chronic Migraine Epidemiology and Outcomes (CaMEO) Study methods and baseline results. *Cephalalgia* 2015;35:563–578.
6. Abu Bakar N, Tanprawate S, Lambru G, et al. Quality of life in primary headache disorders: A review. *Cephalalgia* 2016;36:67–91.
7. Sances G, Granella F, Nappi RE, et al. Course of migraine during pregnancy and postpartum: A prospective study. *Cephalalgia* 2003;23:197–205.
8. Hutchinson S, Marmura MJ, Calhoun A, et al. Use of common migraine treatments in breast-feeding women: A summary of recommendations. *Headache* 2013;53:614–627.
9. NURTEC ODT (rimegepant) Orally Disintegrating Tablets. Prescribing information. Biohaven Pharmaceuticals. 2021. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/212728s006lbl.pdf (accessed November 15, 2021).
10. Marcus R, Goadsby PJ, Dodick D, et al. BMS-927711 for the acute treatment of migraine: A double-blind, randomized, placebo controlled, dose-ranging trial. *Cephalalgia* 2014;34:114–125.
11. Lipton RB, Croop R, Stock EG, et al. Rimegepant, an oral calcitonin gene-related peptide receptor antagonist, for migraine. *N Engl J Med* 2019;381:142–149.
12. Croop R, Goadsby PJ, Stock DA, et al. Efficacy, safety, and tolerability of rimegepant orally disintegrating tablet for the acute treatment of migraine: A randomised, phase 3, double-blind, placebo-controlled trial. *Lancet* 2019;394:737–745.
13. Croop R, Lipton RB, Kudrow D, et al. Oral rimegepant for preventive treatment of migraine: A phase 2/3, randomised, double-blind, placebo-controlled trial. *Lancet* 2021;397:51–60.
14. Coric V, Stock EG, Pultz J, et al. Sheehan Suicidality Tracking Scale (Sheehan-STS): Preliminary results from a multicenter clinical trial in generalized anxiety disorder. *Psychiatry (Edgmont)* 2009;6:26–31.
15. Wojnar-Horton RE, Hackett LP, Yapp P, et al. Distribution and excretion of sumatriptan in human milk. *Br J Clin Pharmacol* 1996;41:217–221.
16. US Food and Drug Administration. Center for Drug Evaluation and Research. Clinical Lactation Studies: Considerations for Study Design. Guidance for Industry. 2019. Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/clinical-lactation-studies-considerations-study-design (accessed November 15, 2021).
17. Amundsen S, Øvrebø TG, Amble NMS, et al. Risk perception, beliefs about medicines and medical adherence among pregnant and breastfeeding women with migraine: Findings from a cross-sectional study in Norway. *BMJ Open* 2019;9:e026690.
18. Caritis SN, Venkataramanan R. Obstetrical, fetal, and lactation pharmacology-a crisis that can no longer be ignored. *Am J Obstet Gynecol* 2021;225:10–20.
19. Wang J, Johnson T, Sahin L, et al. Evaluation of the safety of drugs and biological products used during lactation: Workshop summary. *Clin Pharmacol Ther* 2017;101:736–744.
20. Bennett PN. Use of the monographs on drugs. In: Drugs and Human Lactation: A Comprehensive Guide to the Content and Consequences of Drugs, Micronutrients, Radiopharmaceuticals and Environmental and Occupational Chemicals in Human Milk, 2nd ed., Bennett PN, ed. Amsterdam, The Netherlands: Elsevier, 1996, pp. 67–74.

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