A Third Way

The Headache "Rescue Room"

You: I have a terrible migraine headache, and it just will not stop! I've tried every medicine the doctor prescribed, more Excedrin than I care to remember, hot compresses, cold compresses, resting in a dark, quiet room and just giving up and going to sleep. But it's still there when I wake up! This has been going on for 3 days now, and I don't know what to do. My last trip to the emergency room for a bad migraine was a disaster–after waiting for 4 hours under the neon lights and with all the noise and chaos, I just gave up and went back home without being seen. I am sick of feeling so sick, but what can I do?

[Pause] *I know. I'll call my doctor*

You call and leave a message. Hours pass. Evening comes. The phone rings…

Doctor: "I have a message here that you called. What can I do for you?"
You: "I have a headache."
Doctor: [silence]
You [breaking silence]: "It's really a bad one. I've been too sick to go to work for the past 3 days."
Doctor: "Have you taken your medications for acute headache and nausea?"
You: "Yes. They're not helping."
Doctor: "Well, I'm sorry, but there's not much I can do over the phone. Maybe it's time to go to the ER?"
You: "Okay" [thinking: Thanks for nothing.]

Call ends.

Not a very satisfying or productive interaction. And I know, believe me, because I participated on the doctor end in an awful lot of these interactions over the years. So many, in fact, that I eventually decided to do something about it.

With the help of my clinic nurse, we established what we decided to name "the headache rescue room." Put simply, we restructured one of the exam rooms in clinic to make it as comfortable as possible for a patient with acute severe migraine headache and associated symptoms. We obtained an arsenal of intramuscularly and intravenously administered medications for acute headache, medications for nausea, a few medications to treat elevated blood pressure and numerous bags of normal saline for intravenous hydration.

We developed a management strategy that ran the gamut from the initial evaluation to an evidence-based, stepwise treatment algorithm to an exit evaluation that would include confirmation patients had appropriate transportation for the trip back home. To evaluate prospectively the effectiveness of our new "rescue room" we

Nurtec® ODT
(rimegepant)
orally disintegrating tablets 75 mg

THE FIRST & ONLY MEDICATION PROVEN TO TREAT & PREVENT MIGRAINES

Ellie W
Actual Nurtec ODT patient

With one medication you can:

STOP MIGRAINE PAIN
Take Nurtec ODT as soon as a migraine strikes to help stop pain and other symptoms.*

PREVENT MIGRAINES
Take Nurtec ODT every other day to get ahead of migraines and known triggers.

Ask your doctor about Nurtec ODT

& learn how you can get savings and support at **nurtec.com/savings**

*Light sensitivity, sound sensitivity, or nausea.

IMPORTANT SAFETY INFORMATION

Do not take Nurtec ODT if you are allergic to Nurtec ODT (rimegepant) or any of its ingredients.

Before you take Nurtec ODT, tell your healthcare provider (HCP) about all your medical conditions, including if you:
• have liver problems, • have kidney problems, • are pregnant or plan to become pregnant, • breastfeeding or plan to breastfeed.

Tell your HCP about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.
Nurtec ODT may cause serious side effects including allergic reactions, including trouble breathing and rash. This can happen days after you take Nurtec ODT. Call your HCP or get emergency help right away if you have swelling of the face, mouth, tongue, or throat or trouble breathing. This occurred in less than 1% of patients treated with Nurtec ODT.

The most common side effects of Nurtec ODT were nausea (2.7%) and stomach pain/indigestion (2.4%). These are not the only possible side effects of Nurtec ODT. Tell your HCP if you have any side effects.

WHAT IS NURTEC ODT?
Nurtec ODT orally disintegrating tablets is a prescription medicine that is used to treat migraine in adults. It is for the acute treatment of migraine attacks with or without aura and the preventive treatment of episodic migraine. It is not known if Nurtec ODT is safe and effective in children.

You are encouraged to report side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088 or report side effects to Biohaven at 1-833-4Nurtec.

Please see a Brief Summary of the Prescribing Information on the following page.

BRIEF SUMMARY OF PRESCRIBING INFORMATION

(For complete product information, see Full Prescribing Information.)

NURTEC® ODT (rimegepant) orally disintegrating tablets 75 mg, for sublingual or oral use

1 INDICATIONS AND USAGE

1.1 Acute Treatment of Migraine

NURTEC ODT is indicated for the acute treatment of migraine with or without aura in adults.

1.2 Preventive Treatment of Migraine

NURTEC ODT is indicated for the preventive treatment of episodic migraine in adults.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosing for Acute Treatment of Migraine

The recommended dose of NURTEC ODT is 75 mg taken orally, as needed.

The maximum dose in a 24-hour period is 75 mg. The safety of using more than 18 doses in a 30-day period has not been established.

2.2 Recommended Dosing for Preventive Treatment of Episodic Migraine

The recommended dosage of NURTEC ODT is 75 mg taken orally every other day.

4 CONTRAINDICATIONS

NURTEC ODT is contraindicated in patients with a history of hypersensitivity reaction to rimegepant, NURTEC ODT, or any of its components. Delayed serious hypersensitivity has occurred *[see Warnings and Precautions (5.1)]*.

5 WARNING AND PRECAUTIONS

5.1 Hypersensitivity Reactions

Hypersensitivity reactions, including dyspnea and rash, have occurred with NURTEC ODT in clinical studies. Hypersensitivity reactions can occur days after administration, and delayed serious hypersensitivity has occurred. If a hypersensitivity reaction occurs, discontinue NURTEC ODT and initiate appropriate therapy *[see Contraindications (4)]*.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are discussed in greater detail in other sections of the labeling:

• Hypersensitivity Reactions *[see Warnings and Precautions (5.1)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

Acute Treatment of Migraine

The safety of NURTEC ODT for the acute treatment of migraine in adults has been evaluated in a randomized, double-blind, placebo-controlled trial (Study 1) in 682 patients with migraine who received one 75 mg dose of NURTEC ODT *[see Clinical Studies (14)]*. Approximately 85% were female, 74% were White, 21% were Black, and 17% were Hispanic or Latino. The mean age at study entry was 40 years (range 18-75 years of age).

Long-term safety was assessed in an open-label extension study using a different oral dosage form of rimegepant. That study evaluated 1,798 patients, dosing intermittently for up to 1-year, including 1,131 patients who were exposed to rimegepant 75 mg for at least 6 months, and 863 who were exposed for at least one year, all of whom treated an average of at least two migraine attacks per month.

The most common adverse reaction in Study 1 was nausea (2% in patients who received NURTEC ODT compared to 0.4% of patients who received placebo).

Hypersensitivity, including dyspnea and severe rash, occurred in less than 1% of patients treated with NURTEC ODT *[see Contraindications (4) and Warnings and Precautions (5.1)]*.

Preventive Treatment of Episodic Migraine

The safety of NURTEC ODT for the preventive treatment of episodic migraine in adults has been established in a randomized, double-blind, placebo-controlled trial with an open-label extension (Study 2) using a different oral dosage form of rimegepant *[see Clinical Studies (14)]*. In the 12-week, double-blind treatment period, 370 patients with migraine received one 75 mg dose of rimegepant every other day. Approximately 81% were female, 80% were White, 17% were Black, and 28% were Hispanic or Latino. The mean age at study entry was 41 years (range 18-74 years of age). Long-term safety was assessed in an open-label extension study that included 603 patients who were treated for up to one year. Overall, 527 patients were exposed to rimegepant 75 mg for at least 6 months, and 311 were exposed for at least one year.

The most common adverse reactions (occurring in at least 2% of rimegepant-treated patients and at a frequency of at least 1% higher than placebo) in Study 2 were nausea (2.7% in patients who received rimegepant compared with 0.8% of patients who received placebo) and abdominal pain/dyspepsia (2.4% in patients who received rimegepant compared with 0.8% of patients who received placebo).

7 DRUG INTERACTIONS

7.1 CYP3A4 Inhibitors

Concomitant administration of NURTEC ODT with strong inhibitors of CYP3A4 results in a significant increase in rimegepant exposure. Avoid concomitant administration of NURTEC ODT with strong inhibitors of CYP3A4 *[see Clinical Pharmacology (12.3)]*.

Concomitant administration of NURTEC ODT with moderate inhibitors of CYP3A4 may result in increased exposure of rimegepant. Avoid another dose of NURTEC ODT within 48 hours when it is concomitantly administered with moderate inhibitors of CYP3A4 *[see Clinical Pharmacology (12.3)]*.

7.2 CYP3A Inducers

Concomitant administration of NURTEC ODT with strong or moderate inducers of CYP3A can result in a significant reduction in rimegepant exposure, which may lead to loss of efficacy of NURTEC ODT. Avoid concomitant administration of NURTEC ODT with strong or moderate inducers of CYP3A *[see Clinical Pharmacology (12.3)]*.

7.3 Transporters

Rimegepant is a substrate of P-gp and BCRP effux transporters. Concomitant administration of NURTEC ODT with inhibitors of P-gp or BCRP may result in a significant increase in rimegepant exposure *[see Clinical Pharmacology (12.3)]*. Avoid NURTEC ODT with inhibitors of P-gp or BCRP.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate data on the developmental risk associated with the use of NURTEC ODT in pregnant women. In animal studies, oral administration of rimegepant during organogenesis resulted in adverse effects on development in rats (decreased fetal body weight and increased incidence of fetal variations) at exposures greater than those used clinically and which were associated with maternal toxicity. The evaluation of developmental effects following oral administration of rimegepant throughout pregnancy and lactation was inadequate (see Data).

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. The estimated rate of major birth defects (2.2 to 2.9%) and miscarriage (17%) among deliveries to women with migraine are similar to rates reported in women without migraine.

Clinical Considerations

Disease-Associated Maternal and/or Embryo/Fetal Risk

Published data have suggested that women with migraine may be at increased risk of preeclampsia and gestational hypertension during pregnancy.

8.2 Lactation

There are no data on the presence of rimegepant or its metabolites in human milk, the effects of rimegepant on the breastfed infant, or the effects of rimegepant on milk production. There are no animal data on the excretion of rimegepant in milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for NURTEC ODT and any potential adverse effects on the breastfed infant from NURTEC ODT or from the underlying maternal condition.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use

In pharmacokinetic studies, no clinically significant pharmacokinetic differences were observed between elderly and younger subjects. Clinical studies of NURTEC ODT did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently from younger patients.

8.6 Hepatic Impairment

No dosage adjustment of NURTEC ODT is required in patients with mild (Child-Pugh A) or moderate (Child-Pugh B) hepatic impairment. Plasma concentrations of rimegepant were significantly higher in subjects with severe (Child-Pugh C) hepatic impairment. Avoid use of NURTEC ODT in patients with severe hepatic impairment *[see Clinical Pharmacology (12.3)]*.

8.7 Renal Impairment

No dosage adjustment of NURTEC ODT is required in patients with mild, moderate, or severe renal impairment. NURTEC ODT has not been studied in patients with end-stage renal disease and in patients on dialysis. Avoid use of NURTEC ODT in patients with end-stage renal disease (CLcr < 15 mL/min) *[see Clinical Pharmacology (12.3)]*.

10 OVERDOSAGE

There is limited clinical experience with NURTEC ODT overdosage. Treatment of an overdose of NURTEC ODT should consist of general supportive measures including monitoring of vital signs and observation of the clinical status of the patient. No specific antidote for the treatment of rimegepant overdose is available. Rimegepant is unlikely to be significantly removed by dialysis because of high serum protein binding *[see Clinical Pharmacology (12.3)]*.

Manufactured for:

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developed a research protocol that included assessments of clinical effectiveness, safety, cost and patient satisfaction. In accordance with the protocol, all patients were contacted 24 hours after treatment for a follow-up assessment.

When we were all set, we advised our clinic's established migraine patients that if they experienced an episode of severe migraine that resisted self-administered therapy, they could call a dedicated phone number and request to be evaluated and treated in the "rescue room". The rescue room was available to them all day on weekdays.

Each of the initial 100 consecutive patients treated in the rescue room provided informed consent to participate in our study. To summarize, virtually all of the 100 patients reported significant headache relief or freedom from headache at the time of exit from the clinic. On a five-point scale, 95% reported their degree of satisfaction with the rescue room to be "good" (32%) or "excellent" (63%). The average total cost for a rescue room visit was just over $160. Many of the patient's involved in our study previously had sought care for acute migraine headache at an emergency room, and the average cost for an ER visit was approximately $1700…10 times that of the cost associated with use of the rescue room.

At my present institution we have a small suite devoted exclusively to rescue room patients, 3 nurse practitioners who alternate in managing the rescue room, 2 faculty physicians who supervise the nurse practitioners and a registered nurse who assists with hands-on patient care. When the COVID pandemic shut down our rescue room for months, it provided both us, the providers, and our migraine population an all too clear view of how nicely this service had met the needs of patients who now were left once again to choose between the potential discomfort and inconvenience of an ER versus suffering in silence at home.

Thankfully, the doors have reopened, and our patients once again have the security of knowing that another and more attractive option exists for those times "when the headache just won't quit".