FDA Approves the First Oral Medication for the Management of Heavy Menstrual Bleeding Due to Uterine Fibroids in Pre-menopausal Women

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- Uterine fibroids are the most common type of benign tumor in women of reproductive age[1]
- ORIAHNN™ (elagolix, estradiol, and norethindrone acetate capsules; elagolix capsules) is expected to be available in the U.S. by the end of June 2020

NORTH CHICAGO, Ill., May 29, 2020 /PRNewswire/ -- AbbVie (NYSE: ABBV), in cooperation with Neurocrine Biosciences, Inc. (Nasdaq: NBIX), announced that the U.S. Food and Drug Administration (FDA) approved ORIAHNN™ (elagolix, estradiol, and norethindrone acetate capsules; elagolix capsules), with a treatment duration of up to 24 months.[2] ORIAHNN is the first FDA-approved non-surgical, oral medication option for the management of heavy menstrual bleeding associated with uterine fibroids in pre-menopausal women.[2] ORIAHNN is expected to be available in the U.S. by the end of June 2020.

"Women who experience heavy menstrual bleeding as a symptom not only deal with the physical toll of uterine fibroids, but also the burdens surrounding its management while trying to get through with their day-to-day routines," said Ayman Al-Hendy, M.D., Ph.D., investigator for the ELARIS UF-2 clinical trials, and professor of gynecology and director of translational research at the University of Illinois at Chicago. "This approval provides women with a non-surgical option to help address unresolved heavy menstrual bleeding in an impactful way."

Uterine fibroids, also called leiomyomas, are estrogen and progesterone-dependent non-cancerous tumors of the uterus and are the most common type of benign tumor in women of reproductive age, affecting up to 70 percent of Caucasian women and up to 80 percent of African American women by age 50.[1,3,4,5,6,7] Traditionally, uterine fibroids have been primarily managed by surgery and are the leading reason for the hysterectomies performed in the U.S.[1,3,5,8]

"It is always deeply rewarding when the years of development our researchers and scientists dedicate to creating a new way to treat patients is successful," said Michael Severino, M.D., vice chairman and president, AbbVie. "ORIAHNN signifies an important advance in how we can care for women with uterine fibroids."

In the two, randomized Phase 3 uterine fibroid clinical trials, ELARIS UF-I and ELARIS UF-II, ORIAHNN achieved the primary endpoint of clinically meaningful reduction in bleeding (defined as the proportion of women who achieved both at least a 50 percent reduction in menstrual blood loss at final month of treatment and a total menstrual blood loss amount of less than 80 ml), compared with placebo in final month of study for patients, with seven out of 10 women no longer experiencing heavy menstrual bleeding versus one out of 10 women on placebo ($P<0.001$ for both trials).[9] ORIAHNN also reduced heavy menstrual bleeding due to uterine fibroids by 50 percent within the first month of use.[9] The results from these studies were recently published in *The New England Journal of Medicine*.

ORIAHNN may increase your chances of heart attack, stroke, or blood clots, especially if you are a smoker over 35 years of age with high blood pressure.[2] Please see the important safety information below for more information. ORIAHNN is taken twice daily (morning and evening) at approximately the same time each day, with or without food. Use of ORIAHNN should be limited to 24 months due to the risk of continued bone loss, which may not be reversible.[2]

"We have heard from women with fibroids across the country who have been hopeful for a treatment with the potential to address their bleeding effectively," said Jenny Rosenberg, executive director of CARE About Fibroids. "The FDA's approval of an oral treatment for women suffering from heavy menstrual bleeding due to uterine fibroids marks a step forward in women's health."[10]

About Uterine Fibroids
Uterine fibroids (also called leiomyomas or myomas) are non-cancerous, hormonally-responsive muscle tissue tumors of the uterus.[1,3] Fibroids are the most common type of abnormal growth in a woman's pelvis and can affect up to 70 percent of Caucasian women and up to 80 of African American women by age 50.[1,3,4,5,6,7] Fibroids can range in size, shape, number and location.[5] Fibroids can be asymptomatic but, in some women, they can cause symptoms such as heavy menstrual bleeding.[3,4,5] Treatment options for uterine fibroids include surgery (hysterectomy, myomectomy), endometrial ablation, uterine artery embolization, magnetic resonance imaging (MRI)-guided focused ultrasound and medical management with treatments such as oral contraceptives, progestins, selective progesterone receptor modulators, and gonadotropin-releasing hormone (GnRH) agonists and antagonists.[1,9]

About ORIAHNN™ (elagolix, estradiol, and norethindrone acetate capsules; elagolix capsules)
ORIAHNN is approved by the U.S. Food and Drug Administration (FDA) as an oral medication for the management of heavy menstrual bleeding due to uterine fibroids in pre-menopausal women.[2] ORIAHNN is an oral combination of elagolix and E2/NETA (estradiol/norethindrone acetate) to help achieve a balance between the reduction of heavy bleeding and associated hypoestrogenic side effects.[2]

The full U.S. prescribing information, including the medication guide, for ORIAHNN can be found on rxabbvie.com.

USE

ORIAHNN™ (elagolix, estradiol, and norethindrone acetate capsules; elagolix capsules) is a prescription medicine used to control heavy menstrual bleeding related to uterine fibroids in women before menopause. It should not be taken for more than 24 months. It is not known if ORIAHNN is safe and effective in children under 18 years of age.

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about ORIAHNN?
ORIAHNN may cause serious side effects, including:

- **Cardiovascular Conditions**
  - **ORIAHNN may increase your chances of heart attack, stroke, or blood clots, especially if you are over 35 years of age and smoke, have uncontrolled high blood pressure,** high cholesterol, diabetes, or are obese. **Stop taking ORIAHNN and call your healthcare provider right away or go to the nearest hospital emergency room right away if you have:**
    - Leg pain or swelling that will not go away
    - Sudden shortness of breath
    - Double vision, bulging of the eyes, or sudden blindness (partial or complete)
    - Pain or pressure in your chest, arm, or jaw
    - Sudden, severe headache unlike your usual headaches
    - Weakness or numbness in an arm or leg, or trouble speaking
- **Bone Loss (Decreased Bone Mineral Density [BMD])**
  - While taking ORIAHNN, your estrogen levels may be low. Low estrogen levels can lead to BMD loss.
  - If you have bone loss on ORIAHNN, your BMD may improve after you stop taking ORIAHNN, but complete recovery may not occur. It is unknown if these BMD changes could increase your risk for broken bones as you age. For this reason, **you should not take ORIAHNN for more than 24 months.**
  - Your healthcare provider may order an X-ray test called a DXA scan to check your bone mineral density when you start taking ORIAHNN and periodically after you start.
  - Your doctor may advise you to take vitamin D and calcium supplements as part of a healthy lifestyle.
- **Effects on Pregnancy**
  - **Do not take** ORIAHNN if you are pregnant or trying to become pregnant, as it may increase the risk of early pregnancy loss.
  - **If you think you may be pregnant,** stop taking ORIAHNN right away and call your HCP.
  - ORIAHNN can decrease your menstrual bleeding or result in no menstrual bleeding at all, making it hard to know if you are pregnant. Watch for other pregnancy signs like breast tenderness, weight gain, and nausea.
  - ORIAHNN does not prevent pregnancy. You will need to use effective methods of birth control while taking ORIAHNN and for 1 week after you stop taking ORIAHNN. Examples of effective methods can include condoms or spermicide, which do not contain hormones.
  - Talk to your HCP about which birth control to use during treatment with ORIAHNN. Your HCP may change the birth control you are on before you start taking ORIAHNN.

Do not take ORIAHNN if you:

- Have or have had:
  - A stroke or heart attack
  - A problem that makes your blood clot more than normal
  - Blood circulation disorder
  - Certain heart valve problems or heart rhythm abnormalities that can cause blood clots to form in the heart
  - Blood clots in your legs (deep vein thrombosis), lungs (pulmonary embolism), or eyes (retinal thrombosis)
  - High blood pressure not well controlled by medicine
  - Diabetes with kidney, eye, nerve, or blood vessel damage
  - Certain kinds of headaches with numbness, weakness, or changes in vision, or have migraine headaches with aura if you are over age 35
  - Breast cancer or any cancer that is sensitive to female hormones
  - Osteoporosis
  - Unexplained vaginal bleeding that has not been diagnosed
  - Liver problems including liver disease
- Smoke and are over 35 years old

- Are taking medicines known as strong OATP1B1 inhibitors that are known or expected to significantly increase the blood levels of elagolix. Ask your HCP if you are not sure if you are taking this type of medicine.
- Have had a serious allergic reaction to elagolix, estradiol, norethindrone acetate, or any of the ingredients in ORIAHNN. Ask your HCP if you are not sure.
- FD&C Yellow No. 5 (tartrazine) is an ingredient in ORIAHNN, which may cause an allergic type reaction such as bronchial asthma in some patients who are also allergic to aspirin.

What should I discuss with my HCP before taking ORIAHNN?
Tell your HCP about all your medical conditions, including if you:

- Have or have had:
  - Broken bones or other conditions that may cause bone problems
  - Depression, mood swings, or suicidal thoughts or behavior
  - Yellowing of the skin or eyes (jaundice) or jaundice caused by pregnancy (cholestasis of pregnancy)
- Are scheduled for surgery. ORIAHNN may increase your risk of blood clots after surgery. Your doctor may advise you to stop taking ORIAHNN before you have surgery. If this happens, talk to your HCP about when to restart ORIAHNN after surgery.
- Are pregnant or think you may be pregnant.
- Are breastfeeding. It is not known if ORIAHNN can pass into your breastmilk. Talk to your HCP about the best way to feed your baby if you take ORIAHNN.

Tell your HCP about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Women on thyroid or cortisol replacement therapy may need increased doses of the hormone.

Keep a list of your medicines with you to show to your HCP and pharmacist when you get a new medicine.

What should I avoid while taking ORIAHNN?

- Avoid grapefruit and grapefruit juice during treatment with ORIAHNN since they may affect the level of ORIAHNN in your blood, which may increase side effects.

What are the possible side effects of ORIAHNN?
ORIAHNN can cause additional serious side effects, including:

- **Suicidal thoughts, suicidal behavior, and worsening of mood.** ORIAHNN may cause suicidal thoughts or actions. **Call your HCP or get emergency medical help right away if you have any of these symptoms, especially if they are new, worse, or bother you:** thoughts about suicide or dying, attempts to commit suicide, new or worse depression or anxiety, or other unusual changes in behavior or mood. Pay attention to any changes, especially sudden changes, in your mood, behaviors, thoughts, or feelings.
- **Abnormal liver tests. Call your HCP right away if you have any of these signs and symptoms of liver problems:** jaundice, dark amber-colored urine, feeling tired, nausea and vomiting, generalized swelling, right upper stomach area pain, or bruising easily.
- **High blood pressure.** You should see your HCP to check your blood pressure regularly.
- **Gallbladder problems** (cholestasis), especially if you had cholestasis of pregnancy.
- **Increases in blood sugar, cholesterol, and fat (triglyceride) levels.**
- **Hair loss (alopecia).** Hair loss and hair thinning can happen while taking ORIAHNN, and it can continue even after you stop taking ORIAHNN. It is not known if this hair loss or hair thinning is reversible. Talk to your HCP if this is a concern for you.
- **Changes in laboratory tests,** including thyroid and other hormone, cholesterol, and blood clotting tests.

The most common side effects of ORIAHNN include: hot flashes, headache, fatigue, and irregular periods.

These are not all of the possible side effects of ORIAHNN. Tell your HCP if you have any side effect that bothers you or that does not go away. Call your HCP for medical advice about side effects.

Take ORIAHNN exactly as your HCP tells you. The recommended oral dosage of ORIAHNN is one yellow/white capsule in the morning and one blue/white capsule in the evening, with or without food.

This is the most important information to know about ORIAHNN. For more information, talk to your doctor or HCP.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit http://www.fda.gov/medwatch or call 1-800-FDA-1088.

If you are having difficulty paying for your medicine, AbbVie may be able to help. Visit AbbVie.com/myAbbVieAssist to learn more.

About AbbVie

AbbVie's mission is to discover and deliver innovative medicines that solve serious health issues today and address the medical challenges of tomorrow. We strive to have a remarkable impact on people's lives across several key therapeutic areas: immunology, oncology, neuroscience, eye care, virology, women's health and gastroenterology, in addition to products and services across its Allergan Aesthetics portfolio. For more information about AbbVie, please visit us at www.abbvie.com. Follow @abbvie on Twitter, Facebook, Instagram, YouTube and LinkedIn.

Forward-Looking Statements

Some statements in this news release are, or may be considered, forward-looking statements for purposes of the Private Securities Litigation Reform Act of 1995. The words "believe," "expect," "anticipate," "project" and similar expressions, among others, generally identify forward-looking statements. AbbVie cautions that these forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those indicated in the forward-looking statements. Such risks and uncertainties include, but are not limited to, competition from other products, challenges to intellectual property, difficulties inherent in the research and development process, adverse litigation or government action, and changes to laws and regulations applicable to our industry. Additional information about the economic, competitive, governmental, technological and other factors that may affect AbbVie's operations is set forth in Item 1A, "Risk Factors," of AbbVie's 2019 Annual Report on Form 10-K, which has been filed with the Securities and Exchange Commission. AbbVie undertakes no obligation to release publicly any revisions to forward-looking statements as a result of subsequent events or developments, except as required by law.

[1] De La Cruz MS, Buchanan EM. Uterine Fibroids: Diagnosis and Treatment. Am Fam Physician. 2017 Jan 15;95(2):100-107.

[2] ORIAHNN™ (elagolix, estradiol and norethindrone acetate capsules co-formulated) [Package Insert]. North Chicago, Ill.: AbbVie Inc.

[3] Office on Women's Health, WomensHealth.gov. Uterine Fibroids. https://www.womenshealth.gov/a-z-topics/uterine-fibroids.

[4] Khan A et al. Uterine fibroids: current perspectives. Int J Women's Health. 2014;6:95-114.

[5] The American College of Obstetricians and Gynecologists: FAQ Uterine Fibroids. https://www.acog.org/patient-resources/faqs/gynecologic-problems/uterine-fibroids.

[6] Wallach EE et al. Uterine myomas: an overview of development, clinical features, and management. Obstet Gynecol. 2004;104:393–406.

[7] Baird DD, Dunson DB, Hill MC, Cousins D, Schectman JM. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. *Am J Obstet Gynecol*. 2013;188:100-107.

[8] Alternatives to hysterectomy in the management of leiomyomas. ACOG Practice Bulletin No. 96. American College of Obstetricians and Gynecologist. Obstet Gynecol 2008; 112:387-400.

[9] Data on file.

[10] Reference to CARE About Fibroids reflects their recognition of the need for medical management options for this patient population, but is not meant to be an endorsement or recommendation of use by this organization of ORIAHNN or AbbVie.

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U.S. Media: Bret Coons, +1 (847) 938-6310, bret.coons@abbvie.com, or Investors: Liz Shea, +1 (847) 935-2211, liz.shea@abbvie.com