Important New Update to the Prescribing Information for ORILISSA® (elagolix) tablets, for oral use

In February 2021, the ORILISSA Prescribing Information (PI) was updated. The following describes several of the changes in the ORILISSA PI. Please refer to the full PI to review additional changes.

The following items have been added to the Prescribing Information (PI):

- **Section 1 Indications and Usage**
  - **Limitations of Use:** Limit the duration of use based on the dose and coexisting condition (see Table 1).
- **Section 4 Contraindications**
  - With known hypersensitivity reaction to ORILISSA or any of its inactive components. Reactions have included anaphylaxis and angioedema [see Adverse Reactions (6.2)].
- **Section 6 Adverse Reactions**
  - **6.2 Postmarketing Experience**

    The following adverse reactions have been identified during post-approval use of ORILISSA. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

    Immune system disorders: hypersensitivity reactions (including anaphylaxis, angioedema, and urticaria).

The following items have been updated in the PI to read:

- **Section 4 Contraindications**
  - Taking inhibitors of organic anion transporting polypeptide (OATP) 1B1 (a hepatic uptake transporter) that are known or expected to significantly increase elagolix plasma concentrations [see Drug Interactions (7.2)].
- **Section 5 Warnings and Precautions**
  - **5.5 Interactions with Hormonal Contraceptives**

    Advise women to use effective non-hormonal contraceptives during treatment with ORILISSA and for 28 days after discontinuing ORILISSA [see Use in Specific Populations (8.1, 8.3), Drug Interactions (7.1), Clinical Pharmacology (12.3)].

    <u>Increase in Estrogen Exposure and Potential Associated Increased Risks When ORILISSA 200 mg Twice Daily is Taken With Combined Hormonal Contraceptives</u>

    Co-administration of a combined oral contraceptive (COC) (containing 20 mcg ethinyl estradiol/0.1 mg levonorgestrel) following administration of ORILISSA 200 mg twice daily for 14 days increases the plasma ethinyl estradiol concentration by 2.2-fold compared to this COC alone. ORILISSA 200 mg twice daily co-administered with a COC containing ethinyl estradiol may lead to increased risk of ethinyl estradiol-related adverse events including thromboembolic disorders and vascular events and is not recommended [see Drug Interactions (7.1), Clinical Pharmacology (12.3)].

Please see Indication and additional Important Safety Information on pages 2-3.
Please click here for full Prescribing Information.

Potential for Reduced Efficacy of Progestin-Containing Hormonal Contraceptives

Co-administration of ORILISSA 200 mg twice daily and a COC containing 0.1 mg levonorgestrel decreases the plasma concentrations of levonorgestrel by 27%, potentially affecting contraceptive efficacy. Co-administration of ORILISSA with COCs containing norethindrone acetate did not show reduction in plasma concentrations of norethindrone [see Drug Interactions (7.1), Clinical Pharmacology (12.3)].

Co-administration of ORILISSA with progestin-containing intrauterine contraceptive systems has not been studied.

Reduced Efficacy of ORILISSA

Based on the mechanism of action of ORILISSA, estrogen-containing contraceptives are expected to reduce the efficacy of ORILISSA. The effect of progestin-only contraceptives on the efficacy of ORILISSA is unknown.

The following items have been removed in the PI:

- **Section 6 Adverse Reactions**

Endometrial Effects

Endometrial biopsies were performed in subjects in Study EM-1 and its extension at Month 6 and Month 12. These biopsies showed a dose-dependent decrease in proliferative and secretory biopsy patterns and an increase in quiescent/minimally stimulated biopsy patterns. There were no abnormal biopsy findings on treatment, such as endometrial hyperplasia or cancer.

Based on transvaginal ultrasound, during the course of a 3-menstrual cycle study in healthy women, ORILISSA 150 mg once daily and 200 mg twice daily resulted in a dose-dependent decrease from baseline in mean endometrial thickness.

This is not a complete list of all the changes made to the Prescribing Information for ORILISSA. Please refer to the full Prescribing Information for more details.

INDICATION[1]

ORILISSA® (elagolix) is indicated for the management of moderate to severe pain associated with endometriosis. Limit the duration of use based on the dose and coexisting condition.

IMPORTANT SAFETY INFORMATION[1]

CONTRAINDICATIONS

- ORILISSA is contraindicated in women who are pregnant (exposure to ORILISSA early in pregnancy may increase the risk of early pregnancy loss), in women with known osteoporosis or severe hepatic impairment, in women taking organic anion transporting polypeptide (OATP) 1B1 inhibitors that are known or expected to significantly increase elagolix plasma concentrations, and in women with known hypersensitivity reaction to ORILISSA or any of its inactive components. Reactions have included anaphylaxis and angioedema.

WARNINGS AND PRECAUTIONS

Bone Loss

- ORILISSA causes a dose-dependent decrease in bone mineral density (BMD), which is greater with increasing duration of use and may not be completely reversible after stopping treatment.
- The impact of ORILISSA-associated decreases in BMD on long-term bone health and future fracture risk is unknown. ORILISSA is contraindicated in women with known osteoporosis. Consider assessment of BMD in patients with a history of low-trauma fracture or other risk factors for osteoporosis or bone loss.
- Limit the duration of use to reduce the extent of bone loss.

Please click here for full Prescribing Information.

Change in Menstrual Bleeding Pattern and Reduced Ability to Recognize Pregnancy

- Women who take ORILISSA may experience a reduction in the amount, intensity, or duration of menstrual bleeding, which may reduce the ability to recognize the occurrence of pregnancy in a timely manner. Perform pregnancy testing if pregnancy is suspected, and discontinue ORILISSA if pregnancy is confirmed.

Suicidal Ideation, Suicidal Behavior, and Exacerbation of Mood Disorders

- Suicidal ideation and behavior, including one completed suicide, occurred in subjects treated with ORILISSA in the endometriosis clinical trials.
- ORILISSA users had a higher incidence of depression and mood changes compared to placebo and ORILISSA users with a history of suicidality or depression had an increased incidence of depression. Promptly evaluate patients with depressive symptoms to determine whether the risks of continued therapy outweigh the benefits. Patients with new or worsening depression, anxiety, or other mood changes should be referred to a mental health professional, as appropriate.
- Advise patients to seek immediate medical attention for suicidal ideation and behavior. Reevaluate the benefits and risks of continuing ORILISSA if such events occur.

Hepatic Transaminase Elevations

- In clinical trials, dose-dependent elevations of serum alanine aminotransferase (ALT) at least 3 times the upper limit of the reference range occurred with ORILISSA.
- Use the lowest effective dose and instruct patients to promptly seek medical attention in case of symptoms or signs that may reflect liver injury, such as jaundice.
- Promptly evaluate patients with elevations in liver tests to determine whether the benefits of continued therapy outweigh the risks.

Interactions with Hormonal Contraceptives

- Advise women to use effective non-hormonal contraceptives during treatment and for 28 days after discontinuing ORILISSA.
- Coadministration of ORILISSA 200 mg twice daily with an estrogen-containing contraceptive is not recommended because of the potential for increased estrogen-associated risks including thromboembolic disorders and vascular events. Coadministration of ORILISSA with an estrogen-containing contraceptive is expected to reduce the efficacy of ORILISSA.
- Coadministration with progestin-containing oral contraceptives may reduce the efficacy of the contraceptive. The effect of progestin-only contraceptives on the efficacy of ORILISSA is unknown. Coadministration of ORILISSA with progestin-containing intrauterine contraceptive systems has not been studied.

ADVERSE REACTIONS

- The most common adverse reactions (>5%) in clinical trials included hot flushes and night sweats, headache, nausea, insomnia, amenorrhea, anxiety, arthralgia, depression-related adverse reactions, and mood changes.

These are not all the possible side effects of ORILISSA.

Safety and effectiveness of ORILISSA in pediatric patients have not been established.

Please click here for full Prescribing Information.

Reference: 1. ORILISSA [package insert]. North Chicago, IL: AbbVie Inc.