Oriahnn™

elagolix, estradiol and norethindrone acetate capsules and elagolix capsules 300 mg/1 mg/0.5 mg and 300 mg

ORIAHNN CLINICAL OVERVIEW

INDICATION[1]

ORIAHNN™ (elagolix, estradiol, and norethindrone acetate capsules; elagolix capsules) is indicated for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women. Use of ORIAHNN should be limited to 24 months due to the risk of continued bone loss, which may not be reversible.

SAFETY CONSIDERATIONS[1]

Estrogen and progestin combinations, including ORIAHNN, increase the risk of thrombotic or thromboembolic disorders, including pulmonary embolism, deep vein thrombosis, stroke, and myocardial infarction, especially in women at increased risk for these events.

ORIAHNN is contraindicated in women with current or a history of thrombotic or thromboembolic disorders and in women at increased risk for these events, including women over 35 years of age who smoke and women with uncontrolled hypertension.

- ORIAHNN is contraindicated in women who are at a high risk of arterial, venous thrombotic, or thromboembolic disorders; who are pregnant; with known osteoporosis; current or history of breast cancer or other hormonally sensitive malignancies; known hepatic impairment or disease; undiagnosed abnormal uterine bleeding; known anaphylactic reaction, angioedema, or hypersensitivity to ingredients of ORIAHNN; or with concomitant use of organic anion transporting polypeptide (OATP) 1B1 inhibitors that are known or expected to significantly increase elagolix plasma concentrations.
- Discontinue ORIAHNN if an arterial or venous thrombotic, cardiovascular, or cerebrovascular event occurs. If feasible, discontinue ORIAHNN at least 4 to 6 weeks before surgery of the type associated with an increased risk of thromboembolism, or during periods of prolonged immobilization. Stop ORIAHNN if there is sudden, unexplained partial or complete loss of vision, proptosis, diplopia, papilledema, or retinal vascular lesions and evaluate for retinal vein thrombosis immediately.
- ORIAHNN may cause a decrease in bone mineral density (BMD), which is greater with increasing duration of use and may not be completely reversible after stopping treatment. Assessment of BMD by dual-energy X-ray absorptiometry (DXA) is recommended at baseline and periodically thereafter. Limit the duration of use to 24 months to reduce the extent of bone loss.
- ORIAHNN should not be used in women with current or a history of breast cancer and in women at increased risk for hormonally sensitive malignancies, such as those with mutations in BRCA genes. Discontinue ORIAHNN if a hormonally sensitive malignancy is diagnosed.
- Depression, depressed mood, and/or tearfulness have occurred in women taking ORIAHNN. Advise patients to seek medical attention for suicidal ideation, suicidal behavior, new onset or worsening depression, anxiety, or other mood changes.
- ORIAHNN may delay the ability to recognize the occurrence of a pregnancy, as it may reduce the intensity, duration, and amount of menstrual bleeding. Discontinue ORIAHNN if pregnancy is confirmed.
- Alopecia, hair loss, and hair thinning have occurred with ORIAHNN. No specific pattern was described. Whether the hair loss is reversible is unknown. Consider discontinuing ORIAHNN if hair loss becomes a concern.
- The following events/conditions were either reported in clinical trials of ORIAHNN and/or may be potentially caused or exacerbated by the estrogen and progestin components in ORIAHNN: transaminase elevations, an increase in blood pressure, an increased risk of developing gallbladder disease, diabetes mellitus, hereditary angioedema, adverse lipid changes, and change in the results of some laboratory tests such as coagulation factors, lipids, glucose tolerance, and binding proteins.
- ORIAHNN contains FD&C Yellow No. 5 (tartrazine), which may cause allergic-type reactions (including bronchial asthma) in certain susceptible persons.

Please see additional Important Safety Information, including **BOXED WARNING on THROMBOEMBOLIC AND VASCULAR EVENTS**, on pages 18-19 and please see accompanying Full Prescribing Information.

TABLE OF CONTENTS

INDICATION[1]

ORIAHNN™ (elagolix, estradiol, and norethindrone acetate capsules; elagolix capsules) is indicated for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women. Use of ORIAHNN should be limited to 24 months due to the risk of continued bone loss, which may not be reversible.

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EXECUTIVE SUMMARY

ORIAHNN is an oral medication specifically approved for the management of heavy menstrual bleeding (HMB) associated with uterine leiomyomas (fibroids) in premenopausal women. Use of ORIAHNN should be limited to 24 months due to the risk of continued bone loss, which may not be reversible. ORIAHNN is administered twice daily. The morning capsule contains elagolix 300 mg in combination with estradiol (E2) 1 mg and norethindrone acetate (NETA) 0.5 mg (an exogenous combination of estrogen and progestin), and the evening capsule contains elagolix 300 mg alone.[1]

The safety and efficacy of ORIAHNN were evaluated in 2 replicate, double-blind, placebo-controlled phase 3 studies, ELARIS UF-1 and ELARIS UF-2. The studies randomized 790 premenopausal women aged 18 to 51 years who had uterine fibroids (UF) and HMB to placebo, ORIAHNN, and a reference arm.* Women who completed the 6-month treatment period and met eligibility criteria entered an uncontrolled, blinded, 6-month extension study, UF-EXTEND (UF-3), for a total treatment duration of up to 12 months receiving either ORIAHNN or the reference arm.[1,2,*]

The primary endpoint was menstrual blood loss (MBL) <80 mL during the final month of treatment and ≥50% reduction in MBL from baseline to the final month. Of the women treated with ORIAHNN, 68.5% in ELARIS UF-1 and 76.5% in ELARIS UF-2 achieved treatment response compared with 8.7% and 10.5% of those receiving placebo, respectively.[1]

In both ELARIS UF-1 and ELARIS UF-2, treatment with ORIAHNN was statistically significant for all ranked secondary endpoints, including change in MBL from baseline to final month; change in MBL from baseline to months 1, 3, and 6; percentage of women with suppression of bleeding (spotting allowed) at final month; and percentage of women with a baseline hemoglobin level ≤10.5 g/dL who had an increase of >2 g/dL at 6 months. Other prespecified endpoints included the percentage of women with amenorrhea and the change from baseline in Uterine Fibroid Symptom and Quality of Life (UFS-QoL) score.[2]

*Elagolix 300 mg BID alone was included as a reference arm and is not intended to be commercialized.

SAFETY CONSIDERATIONS[1] (cont'd)

ORIAHNN is contraindicated in women who are at a high risk of arterial, venous thrombotic, or thromboembolic disorders; who are pregnant; with known osteoporosis; current or history of breast cancer or other hormonally sensitive malignancies; known hepatic impairment or disease; undiagnosed abnormal uterine bleeding; known anaphylactic reaction, angioedema, or hypersensitivity to ingredients of ORIAHNN; or with concomitant use of organic anion transporting polypeptide (OATP) 1B1 inhibitors that are known or expected to significantly increase elagolix plasma concentrations.

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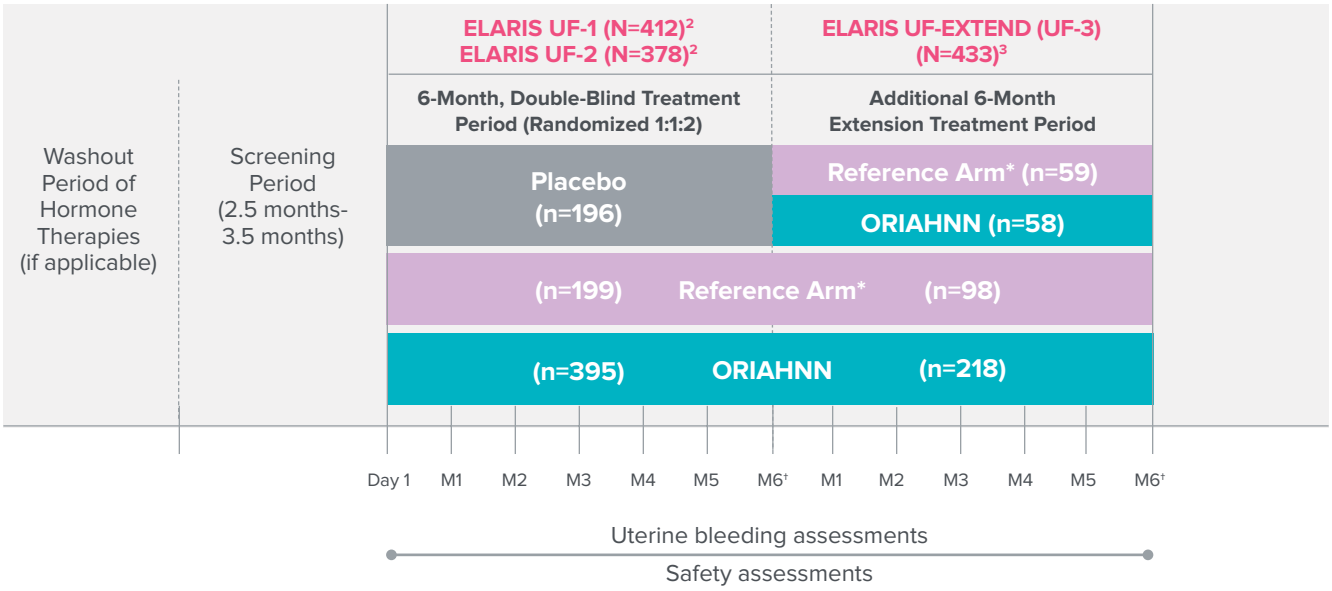
ELARIS UF-1 AND ELARIS UF-2

ORIAHNN was studied in 2 replicate, double-blind, randomized, placebo-controlled, 6-month, phase 3 studies[2]

The studies evaluated the efficacy and safety of ORIAHNN compared with placebo for the management of HMB associated with UF.[2]

- Patients were randomized in a 2:1:1 ratio to receive ORIAHNN, reference arm,* or placebo
- The 6-month treatment period across all treatment arms in ELARIS UF-1 and ELARIS UF-2 was completed by 79.6% and 76.5% of women, respectively

Women who completed the 6-month treatment period and met eligibility criteria entered an uncontrolled, blinded, 6-month extension study, UF-EXTEND (UF-3), receiving either ORIAHNN or reference arm for a total treatment duration of up to 12 months.[1]



Primary endpoint[1]

The primary endpoint in ELARIS UF-1 and ELARIS UF-2 was the proportion of women who achieved treatment response, defined as attaining both MBL volume <80 mL at the final month and ≥50 % reduction in MBL volume from baseline to the final month. Final month was defined as the last 28 days before and including the last treatment visit date or the last dose date.

*Elagolix 300 mg BID alone was included as a reference arm and is not intended to be commercialized.
†A 12-month posttreatment follow-up period was used for women who prematurely discontinued treatment during the 6-month treatment period, who completed the 6-month treatment, but declined to participate in the extension study, or who did not meet eligibility criteria for the extension study.

SAFETY CONSIDERATIONS[1] (cont'd)

ORIAHNN may cause a decrease in bone mineral density (BMD), which is greater with increasing duration of use and may not be completely reversible after stopping treatment. Assessment of BMD by dual-energy X-ray absorptiometry (DXA) is recommended at baseline and periodically thereafter. Limit the duration of use to 24 months to reduce the extent of bone loss.

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ELARIS UF-1 AND ELARIS UF-2 (cont'd)

Select ranked secondary endpoints[2]

- Percentage of women with suppression of bleeding at final month
- Change in MBL from baseline to months 1, 3, and 6
- Percentage of women with baseline hemoglobin level ≤10.5 g/dL with increase >2 g/dL at 6 months

Other prespecified endpoints included the percentage of women with amenorrhea and the change from baseline in UFS-QoL score.

Select enrollment criteria[2]

- Premenopausal women aged 18 to 51 years
- Ultrasonography-confirmed diagnosis of UF
  - ≥1 fibroid ≥2 cm in diameter if intramural, submucosal, nonpedunculated or ≥4 cm if solitary subserosal
    OR
  - Multiple small fibroids with total uterine volume (UV) of ≥200 cm^3 to ≤2500 cm^3
- MBL of >80 mL per cycle for at least 2 separate cycles

Select patient characteristics[2]

		ELARIS UF-1		ELARIS UF-2	
Characteristic Mean (SD)		Placebo (n=102)	ORIAHNN (n=206)	Placebo (n=94)	ORIAHNN (n=189)
Age, years		41.6±5.7	42.6±5.3	42.5±5.4	42.5±5.3
Race, n (%)*	Black	70 (68.6)	141 (68.4)	63 (67.0)	124 (66.0)†
	White	30 (29.4)	59 (28.6)	30 (32.0)	59 (31.4)†
	Other	2 (2.0)	6 (3.0)	1 (1.0)	5 (2.7)†
BMI,‡ kg/m^2		33.8±7.7	33.3±6.8§	33.8±7.2	33.2±6.9
MBL/menstrual cycle, mL		255.3±174.0	238.0±150.1	254.3±178.5	228.5±148.8
Hemoglobin, g/dL		11.0±1.4	11.1±1.5	11.0±1.6	11.1±1.5
Total UV, cm^3					
By TAU/TVU		478.1±356.9	474.9±388.2	549.6± 452.1	496.1±381.6
By MRI‖		561.9±437.2	508.6±342.2	798.6±730.9	676.8±559.1
UFS-QoL Scores¶					
Symptom Severity#		61.7±19.2	57.3±22.2	60.5±23.4	60.9±21.6
Total HRQoL**		40.7±20.3	44.1±23.5	43.0±22.8	43.3±24.2
Z-score for BMD					
Lumbar Spine		0.9±1.0	1.0±1.0§	1.1±1.1	1.1±1.2
Total Hip		0.7±0.9	0.8±0.9§	0.7±1.0	0.8±0.9
Femoral Neck		0.5±0.8	0.6±0.9§	0.6±0.9	0.6±0.9

*Race was reported by the women.
†n=188.
‡BMI is the weight in kilograms divided by the square of the height in meters.
§n=205.
‖ELARIS UF-1: placebo n=48, elagolix alone n=51, ORIAHNN n=96; ELARIS UF-2: placebo n=51, elagolix alone n=52, ORIAHNN n=89.
¶On the UFS-QoL Questionnaire, scores for symptom severity range from 0 to 100, with higher scores indicating increased severity. Total scores for health-related quality of life range from 0 to 100, with higher scores indicating a better quality of life.
#ELARIS UF-1: placebo n=102, elagolix alone n=103, ORIAHNN n=206; ELARIS UF-2: placebo n=92, elagolix alone n=94, ORIAHNN n=186.
**ELARIS UF-1: placebo n=102, elagolix alone n=103, ORIAHNN n=206; ELARIS UF-2: placebo n=90, elagolix alone n=94, ORIAHNN n=185.
BMI=body mass index; MRI=magnetic resonance imaging; SD=standard deviation; TAU=transabdominal ultrasound; TVU=transvaginal ultrasound.

SAFETY CONSIDERATIONS[1] (cont'd)

Discontinue ORIAHNN if an arterial or venous thrombotic, cardiovascular, or cerebrovascular event occurs. If feasible, discontinue ORIAHNN at least 4 to 6 weeks before surgery of the type associated with an increased risk of thromboembolism, or during periods of prolonged immobilization. Stop ORIAHNN if there is sudden, unexplained partial or complete loss of vision, proptosis, diplopia, papilledema, or retinal vascular lesions and evaluate for retinal vein thrombosis immediately.

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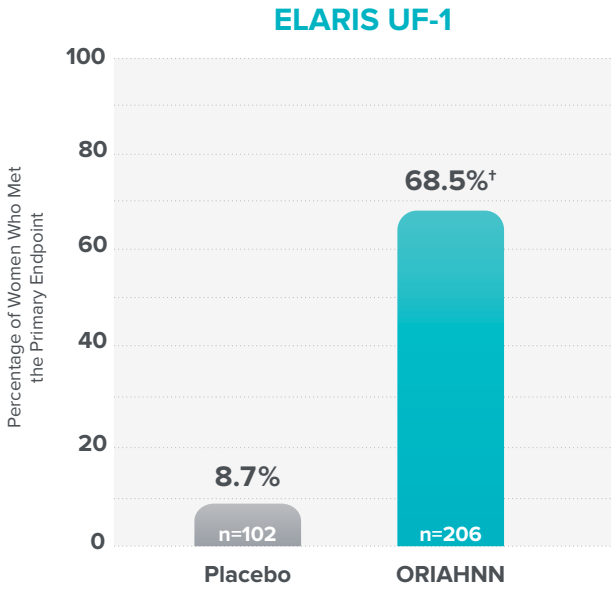
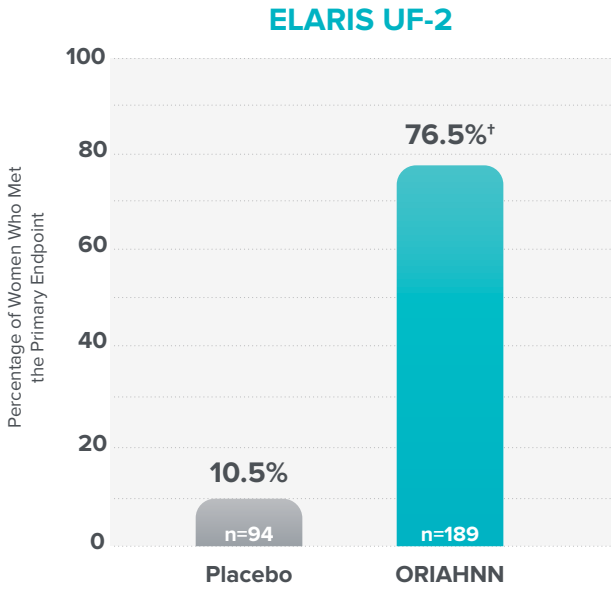
PRIMARY EFFICACY RESULTS

In order to meet the primary endpoint and be a responder, patients had to have[1,*]

MBL volume **<80 mL** at the final month + **≥50% reduction** in MBL from baseline to the final month = **TREATMENT RESPONSE**





In ELARIS UF-2, 77% of patients taking ORIAHNN achieved treatment response at final month vs 11% receiving placebo[1]

*Women who met these criteria but who had prematurely discontinued treatment due to ARs or lack of efficacy or had surgery or invasive intervention for UF during the trial were not considered to have met the endpoint.[2]

†*P*<0.001; statistical significance vs placebo from a logistic regression model that included treatment as the main effect and baseline MBL volume as a covariate.[1,2]

SAFETY CONSIDERATIONS[1] (cont'd)

ORIAHNN should not be used in women with current or a history of breast cancer and in women at increased risk for hormonally sensitive malignancies, such as those with mutations in BRCA genes.
Discontinue ORIAHNN if a hormonally sensitive malignancy is diagnosed.

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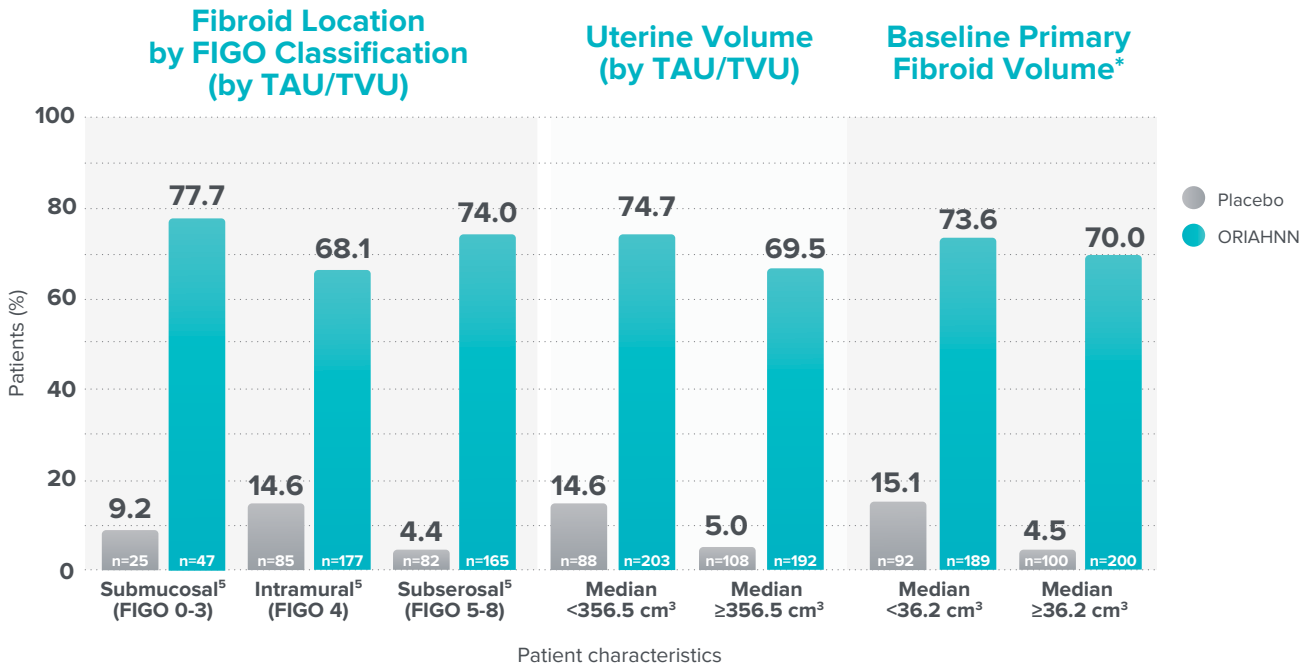
PRIMARY ENDPOINT RESULTS BY SUBGROUP

Percentage of women who met primary endpoint in ELARIS UF-1 and ELARIS UF-2 (n=590)[4]



Subgroup analyses of the primary endpoint were explored to assess potential differences in treatment effect based on uterine and fibroid volume and fibroid location and were not controlled for multiplicity.[2,4]

FIGO=International Federation of Gynecology and Obstetrics.
*Defined as size of largest fibroid as measured by transabdominal/transvaginal ultrasound (TAU/TVU) at baseline.[2]

SAFETY CONSIDERATIONS[1] (cont'd)

ORIAHNN is contraindicated in women who are at a high risk of arterial, venous thrombotic, or thromboembolic disorders; who are pregnant; with known osteoporosis; current or history of breast cancer or other hormonally sensitive malignancies; known hepatic impairment or disease; undiagnosed abnormal uterine bleeding; known anaphylactic reaction, angioedema, or hypersensitivity to ingredients of ORIAHNN; or with concomitant use of organic anion transporting polypeptide (OATP) 1B1 inhibitors that are known or expected to significantly increase elagolix plasma concentrations.

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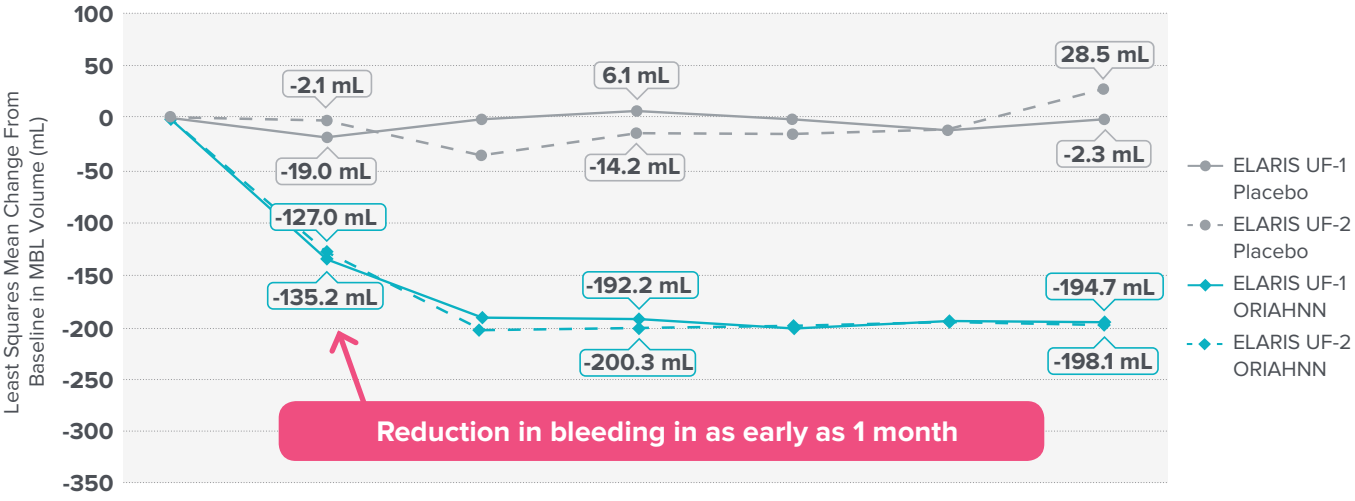
SECONDARY EFFICACY RESULTS

ORIAHNN met all ranked secondary endpoints evaluated in ELARIS UF-1 and ELARIS UF-2.[2]

ORIAHNN quickly reduced mean MBL volume from baseline at month 1

Average MBL volume was reduced by >50% with ORIAHNN at month 1.[6]

Change in MBL Volume Time Points Through Month 6[1,2,*]



	Baseline	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6
ELARIS UF-1 Placebo (n)	99	95	90	85	85	81	71
ELARIS UF-2 Placebo (n)	91	88	83	78	75	73	64
ELARIS UF-1 ORIAHNN (n)	199	187	175	172	164	158	132
ELARIS UF-2 ORIAHNN (n)	182	175	161	157	149	149	124

Most women were able to manage their HMB associated with UF without the need for surgery while on ORIAHNN[7]

In the two 6-month pivotal trials, 3 out of 395 women discontinued for UF surgery.

*Months 2, 4, and 5 were not prespecified ranked endpoints.

SAFETY CONSIDERATIONS[1] (cont'd)

ORIAHNN may delay the ability to recognize the occurrence of a pregnancy, as it may reduce the intensity, duration, and amount of menstrual bleeding. Discontinue ORIAHNN if pregnancy is confirmed.

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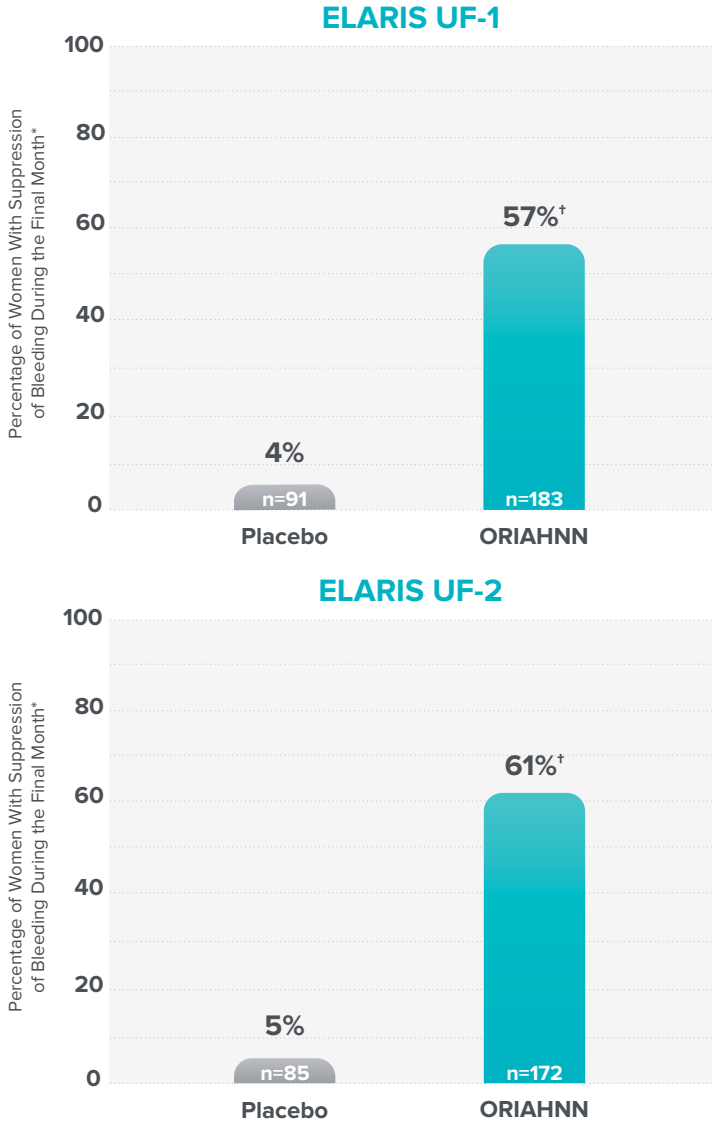
SECONDARY EFFICACY RESULTS (cont'd)

Proportion of women with suppression of bleeding[1,2]

Most women achieved suppression of bleeding (spotting allowed) in the final month with ORIAHNN.



*Final month was defined as the last 28 days before and including the last treatment period visit date. If data on MBL (measured with the use of the alkaline hematin method) that could be evaluated were available between the last treatment period visit date and the last dose date, then the last dose date was used. The missing data on MBL in the final month were imputed with the use of multiple imputation.[2]

†*P*<0.001; statistical significance vs placebo based on the chi-square test.[2]

SAFETY CONSIDERATIONS[1] (cont'd)

ORIAHNN may delay the ability to recognize the occurrence of a pregnancy, as it may reduce the intensity, duration, and amount of menstrual bleeding. Discontinue ORIAHNN if pregnancy is confirmed.

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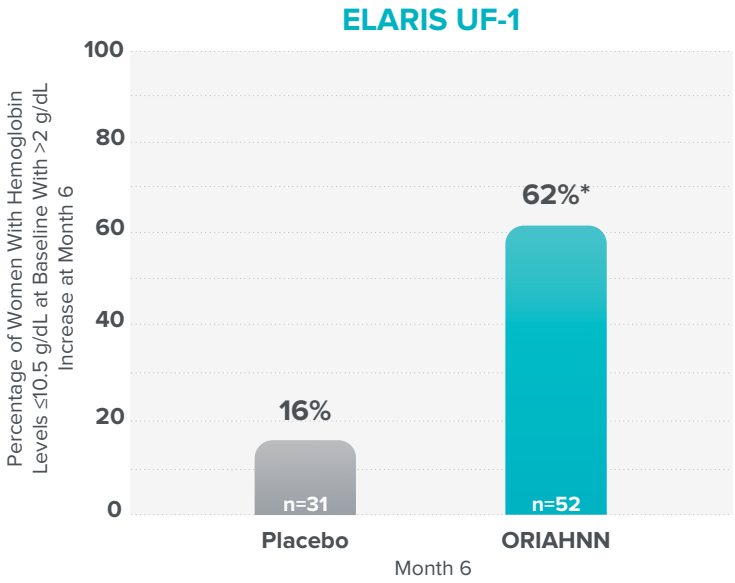
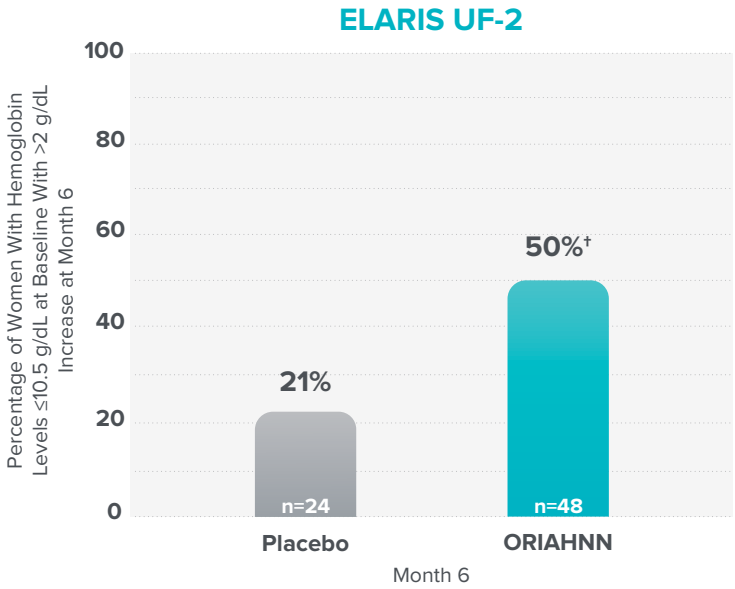
SECONDARY EFFICACY RESULTS (cont'd)

Proportion of women with increase in hemoglobin[1,2]

Hemoglobin levels increased >2 g/dL in patients treated with ORIAHNN who had ≤10.5 g/dL at baseline compared with placebo at month 6.





*P<0.001; statistical significance vs placebo based on the chi-square test.
†P=0.02; statistical significance vs placebo based on the chi-square test.

SAFETY CONSIDERATIONS[1] (cont'd)

Depression, depressed mood, and/or tearfulness have occurred in women taking ORIAHNN. Advise patients to seek medical attention for suicidal ideation, suicidal behavior, new onset or worsening depression, anxiety, or other mood changes.

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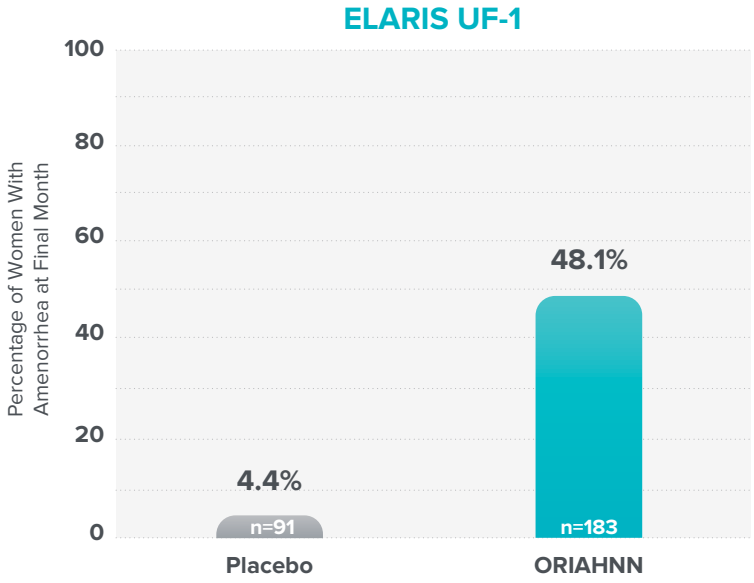
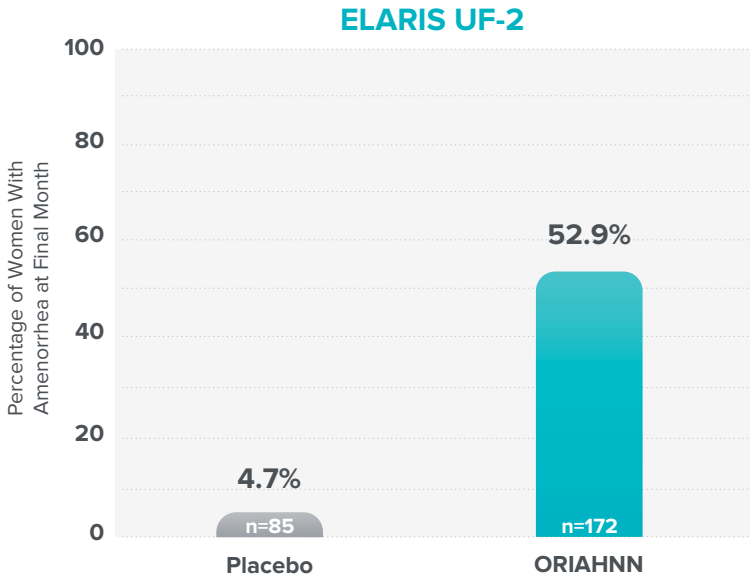
OTHER ENDPOINTS

Proportion of women with amenorrhea[2]

Amenorrhea was defined as having 0 days of bleeding or spotting during the final month. Amenorrhea data were a nonranked endpoint that was not controlled for multiplicity.[2]





SAFETY CONSIDERATIONS[1] (cont'd)

ORIAHNN may delay the ability to recognize the occurrence of a pregnancy, as it may reduce the intensity, duration, and amount of menstrual bleeding. Discontinue ORIAHNN if pregnancy is confirmed.

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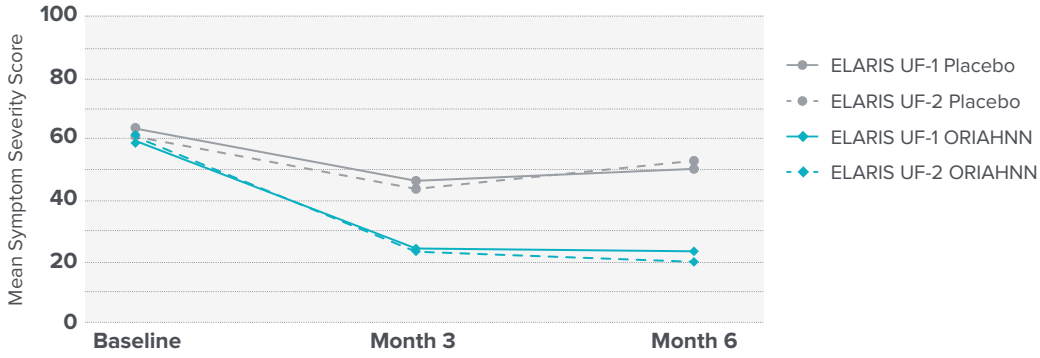
OTHER ENDPOINTS (cont'd)

Symptom severity and total HRQoL score

UFS-QoL is a validated questionnaire that measures QoL across 2 scales—symptom severity and HRQoL.[8,9]

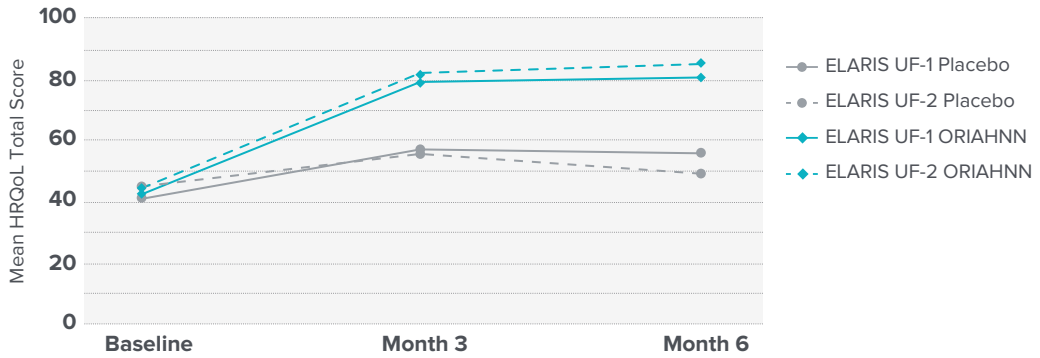
- The symptom severity scale consists of 8 items that assess the level of distress caused by UF-related symptoms[9]
- The HRQoL scale consists of 29 items that measure the impact of UF-related symptoms over 6 subscales: concern, control, activities, self-consciousness, energy/mood, and sexual function[9]
- In a study validating the UFS-QoL Questionnaire, 29 normal control patients had an average symptom severity score of 22.5 and an average HRQoL total of 86.4[9]
- UFS-QoL data from ELARIS UF-1 and ELARIS UF-2 were a nonranked endpoint that was not controlled for multiplicity[2]

Symptom Severity[2,10,*]



	Baseline	Month 3	Month 6
ELARIS UF-1 Placebo (n)	102	88	81
ELARIS UF-2 Placebo (n)	92	78	71
ELARIS UF-1 ORIAHNN (n)	206	179	158
ELARIS UF-2 ORIAHNN (n)	186	160	144

HRQoL[2,10,†]



	Baseline	Month 3	Month 6
ELARIS UF-1 Placebo (n)	102	88	81
ELARIS UF-2 Placebo (n)	90	77	70
ELARIS UF-1 ORIAHNN (n)	206	179	158
ELARIS UF-2 ORIAHNN (n)	185	159	143

HRQoL=health-related quality of life.
*Scores for symptom severity range from 0 to 100, with higher scores indicating increased severity.
†Total scores for HRQoL range from 0 to 100, with higher scores indicating a better HRQoL.

SAFETY CONSIDERATIONS[1] (cont'd)

Depression, depressed mood, and/or tearfulness have occurred in women taking ORIAHNN. Advise patients to seek medical attention for suicidal ideation, suicidal behavior, new onset or worsening depression, anxiety, or other mood changes.

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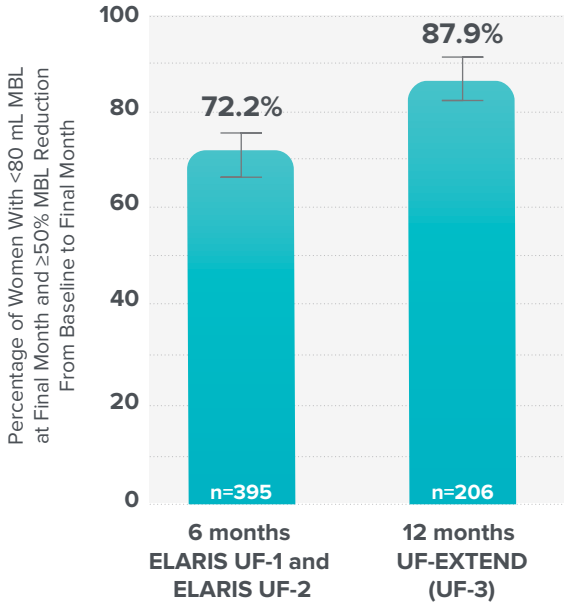
UF-EXTEND (UF-3) RESULTS

UF-EXTEND (UF-3) assessed the percentage of women who achieved the primary endpoint for an additional 6 months for a treatment duration of up to 12 months.[3]

MBL volume **<80 mL** at the final month + **≥50% reduction** in MBL from baseline to the final month = **PRIMARY ENDPOINT**

Primary endpoint responder rate during final month for women treated with ORIAHNN[3,11]



- The most commonly reported ARs were similar to those in the placebo-controlled trials[1,3]

Reductions in MBL for women taking ORIAHNN were observed out to 12 months[3]

SAFETY CONSIDERATIONS[1] (cont'd)

ORIAHNN may cause a decrease in bone mineral density (BMD), which is greater with increasing duration of use and may not be completely reversible after stopping treatment. Assessment of BMD by dual-energy X-ray absorptiometry (DXA) is recommended at baseline and periodically thereafter. Limit the duration of use to 24 months to reduce the extent of bone loss.

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CLINICAL TRIAL SAFETY INFORMATION

Adverse reactions[1]

The most common side effects reported for women treated with ORIAHNN in ELARIS UF-1 and ELARIS UF-2 trials (incidence ≥5%) were hot flush, headache, fatigue, and metrorrhagia. In ELARIS UF-1 and ELARIS UF-2, discontinuation from therapy due to any adverse reactions (ARs) occurred in 10% of women treated with ORIAHNN and 7% of those who received placebo. The most common discontinuations due to ARs were for nausea (1%), headache (1%), alopecia (1%), metrorrhagia (1%), menorrhagia (1%), and hot flush (1%).

ARs Occurring in ≥5% of Women Receiving ORIAHNN and at a Greater Incidence Than Placebo[1]

	Placebo (n=196)	ORIAHNN (n=395)
Hot flush	9%	22%
Headache	7%	9%
Fatigue	4%	6%
Metrorrhagia	1%	5%

For more information on ARs seen in the ELARIS clinical studies, see section 6 of the Prescribing Information.

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LIMITATION OF USE

Use of ORIAHNN should be limited to 24 months due to the risk of continued bone loss, which may not be reversible.[1]

- ORIAHNN is contraindicated in women with known osteoporosis
- Consider the benefits and risks of ORIAHNN treatment in patients with a history of a low trauma fracture or other risk factors for osteoporosis or bone loss, including taking medications that may decrease BMD
- Assessment of BMD by DXA is recommended at baseline and periodically thereafter
  - Consider discontinuing ORIAHNN if the risk associated with bone loss exceeds the potential benefit of treatment

In clinical trials, there was a greater decrease in BMD in women treated with ORIAHNN for 6 months compared with placebo.[1]

- Following 12 months of ORIAHNN treatment in ELARIS UF-EXTEND (UF-3), a decline in lumbar spine BMD of >3% was seen in 27% of women (48/175) and a decline of ≥8% was seen in 1.7% of women (3/175)

Mean Percent Change From Baseline in Lumbar Spine BMD[1,*]

	ELARIS UF-1 and ELARIS UF-2: Treatment Month 6		ELARIS UF-EXTEND (UF-3): Treatment Month 12
	ORIAHNN (n=305)	Placebo (n=150)	ORIAHNN (n=175)
Percent change from baseline	-0.7%	-0.1%	-1.5%
Treatment difference, % (95% CI)	-0.6% (-1.0, -0.1)		

The change in BMD over time was measured for women receiving ORIAHNN for up to 12 months and an additional 12 months after cessation of therapy.[1]

Percentage of Women With Continued Bone Loss or Recovery 12 Months After Cessation of ORIAHNN[1]

	Lumbar Spine	Total Hip	Femoral Neck
Continued bone loss	24%	32%	40%
Partial recovery	46%	33%	38%
Full recovery	30%	35%	22%

Partial recovery was defined as an increase in BMD after cessation of treatment that did not return to baseline. Full recovery was characterized by BMD levels returning to baseline by 12 months after cessation of treatment.

*The effect of ORIAHNN on BMD was assessed by dual-energy X-ray absorptiometry (DXA).

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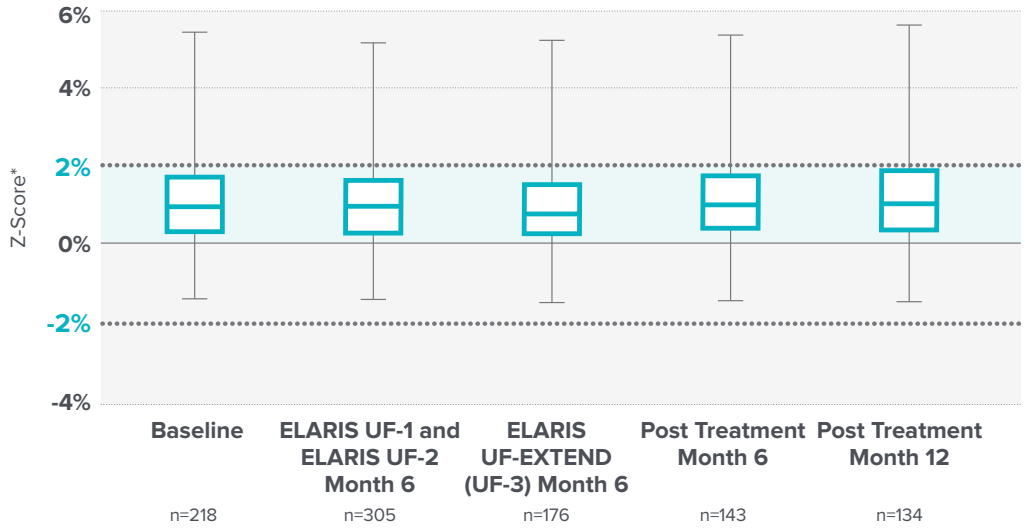
LIMITATION OF USE (cont'd)

BMD assessment using Z-score for premenopausal women.

In clinical trials, Z-scores were measured for up to 12 months of treatment and 12 months after cessation of ORIAHNN.[3]

Z-Score in Lumbar Spine in ELARIS UF-1, ELARIS UF-2, and ELARIS UF-EXTEND (UF-3)[3]



- ORIAHNN baseline Z-scores ranged from 0.7 to 1.1[3]
- In the Phase 3 studies, 7 of 453 women experienced fractures during treatment or in the posttreatment follow-up period, one of them experiencing a fragility fracture[1]
- Z-scores for all women treated with ORIAHNN were above -2.0 at 6 months and 12 months after cessation of treatment[3]

*Z-scores are presented as median, quartile 1, quartile 3, and range.[3]

SAFETY CONSIDERATIONS[1] (cont'd)

ORIAHNN may cause a decrease in bone mineral density (BMD), which is greater with increasing duration of use and may not be completely reversible after stopping treatment. Assessment of BMD by dual-energy X-ray absorptiometry (DXA) is recommended at baseline and periodically thereafter. Limit the duration of use to 24 months to reduce the extent of bone loss.

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SERIOUS ADVERSE REACTIONS[1]

Thromboembolic Disorders and Vascular Events

- Discontinue ORIAHNN if an arterial or venous thrombotic, cardiovascular, or cerebrovascular event occurs. If feasible, discontinue ORIAHNN at least 4 to 6 weeks before surgery of the type associated with an increased risk of thromboembolism, or during periods of prolonged immobilization. Stop ORIAHNN if there is sudden unexplained partial or complete loss of vision, proptosis, diplopia, papilledema, or retinal vascular lesions and evaluate for retinal vein thrombosis immediately

Bone Loss

- ORIAHNN is contraindicated in women with known osteoporosis. ORIAHNN may cause a decrease in BMD in some patients, which is greater with increasing duration of use and may not be completely reversible after stopping treatment. Assessment of BMD by dual-energy X-ray absorptiometry is recommended at baseline and periodically thereafter. Consider discontinuing ORIAHNN if the risk associated with bone loss exceeds the potential benefit of treatment. Limit the duration of use to 24 months to reduce the extent of bone loss

Suicidal Ideation, Suicidal Behavior, and Exacerbation of Mood Disorders

- Depression, depressed mood, and/or tearfulness have occurred in women taking ORIAHNN. Advise patients to seek medical attention for suicidal ideation, suicidal behavior, new onset or worsening depression, anxiety, or other mood changes

Hepatic Transaminase Elevations

- ORIAHNN is contraindicated in women with known hepatic impairment or disease. Transaminase elevations, in alanine aminotransferase and aspartate aminotransferase, occurred with ORIAHNN in Phase 3 clinical trials. No pattern in time to onset of these liver transaminase elevations was identified. Transaminase levels returned to baseline within 4 months after peak values in these patients. Instruct patients to promptly seek medical attention in case of symptoms or signs that may reflect liver injury, such as jaundice

Elevated Blood Pressure

- ORIAHNN is contraindicated in women with uncontrolled hypertension. Maximum mean increases in systolic blood pressure occurred at Month 5, and a mean maximum increase in diastolic blood pressure occurred at Month 4 in ORIAHNN-treated women, as compared with placebo-treated women. For women with well-controlled hypertension, continue to monitor blood pressure and stop ORIAHNN if blood pressure rises significantly. Monitor blood pressure in normotensive women treated with ORIAHNN

Effects on Carbohydrate and Lipid Metabolism

- ORIAHNN may decrease glucose tolerance and result in increased glucose levels. More frequent monitoring in ORIAHNN-treated women with prediabetes and diabetes may be needed. In women with pre-existing hypertriglyceridemia, estrogen therapy may be associated with elevations of plasma triglycerides leading to pancreatitis. Use of elagolix is associated with increases in total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and serum triglycerides. Monitor lipid levels and consider discontinuing ORIAHNN if hypercholesterolemia or hypertriglyceridemia worsens

Alopecia

- In Phase 3 clinical trials more women experienced alopecia, hair loss and hair thinning with ORIAHNN (3.5%) compared to placebo (1.0%). In almost one-third of affected ORIAHNN-treated women, alopecia was the reason for discontinuing treatment. No specific pattern was described. In the majority of these women, hair loss was continuing when ORIAHNN was stopped. Whether the hair loss is reversible is unknown. Consider discontinuing ORIAHNN if the patient is concerned about hair loss

For more information on warnings and precautions, see section 5 of the Prescribing Information.

Please see additional Important Safety Information, including **BOXED WARNING on THROMBOEMBOLIC AND VASCULAR EVENTS**, on pages 18-19 and please see accompanying Full Prescribing Information.

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IMPORTANT SAFETY INFORMATION[1]

INDICATION[1]

ORIAHNN™ (elagolix, estradiol, and norethindrone acetate capsules; elagolix capsules) is indicated for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women. Use of ORIAHNN should be limited to 24 months due to the risk of continued bone loss, which may not be reversible.

IMPORTANT SAFETY INFORMATION[1]

THROMBOEMBOLIC AND VASCULAR EVENTS

Estrogen and progestin combinations, including ORIAHNN, increase the risk of thrombotic or thromboembolic disorders, including pulmonary embolism, deep vein thrombosis, stroke, and myocardial infarction, especially in women at increased risk for these events.

ORIAHNN is contraindicated in women with current or a history of thrombotic or thromboembolic disorders and in women at increased risk for these events, including women over 35 years of age who smoke and women with uncontrolled hypertension.

CONTRAINDICATIONS

- ORIAHNN is contraindicated in women at a high risk of arterial, venous thrombotic, or thromboembolic disorders; who are pregnant; with known osteoporosis; current or history of breast cancer or other hormonally sensitive malignancies; known hepatic impairment or disease; undiagnosed abnormal uterine bleeding; known anaphylactic reaction, angioedema, or hypersensitivity to ingredients of ORIAHNN; or with concomitant use of organic anion transporting polypeptide (OATP) 1B1 inhibitors that are known or expected to significantly increase elagolix plasma concentrations.

WARNINGS AND PRECAUTIONS

Thromboembolic Disorders and Vascular Events

- ORIAHNN is contraindicated in women with current or a history of thrombotic or thromboembolic disorders and in women at increased risk for these events. Components of ORIAHNN increase the risk of thrombotic or thromboembolic disorders, including pulmonary embolism, deep vein thrombosis, stroke, and myocardial infarction, especially in women at high risk for these events. In general, the risk is greatest among women over 35 years of age who smoke, and women with uncontrolled hypertension, dyslipidemia, vascular disease, or obesity.
- Discontinue ORIAHNN if an arterial or venous thrombotic, cardiovascular, or cerebrovascular event occurs. If feasible, discontinue ORIAHNN at least 4 to 6 weeks before surgery of the type associated with an increased risk of thromboembolism, or during periods of prolonged immobilization. Stop ORIAHNN if there is sudden, unexplained partial or complete loss of vision, proptosis, diplopia, papilledema, or retinal vascular lesions and evaluate for retinal vein thrombosis immediately.

Bone Loss

- ORIAHNN is contraindicated in women with known osteoporosis. ORIAHNN may cause a decrease in bone mineral density (BMD) in some patients, which is greater with increasing duration of use and may not be completely reversible after stopping treatment.
- The impact of ORIAHNN-associated decreases in BMD on long-term bone health and future fracture risk is unknown. Consider the benefits and risks of ORIAHNN in patients with a history of low-trauma fracture or other risk factors for osteoporosis or bone loss, including those taking medications that may decrease BMD (e.g., systemic or chronic inhaled corticosteroids, anticonvulsants, or proton pump inhibitors).
- Assessment of BMD by dual-energy X-ray absorptiometry (DXA) is recommended at baseline and periodically thereafter. Consider discontinuing ORIAHNN if the risk associated with bone loss exceeds the potential benefit of treatment. Limit the duration of use to 24 months to reduce the extent of bone loss.

Hormonally Sensitive Malignancies

- ORIAHNN is contraindicated in women with current or a history of breast cancer and in women at increased risk for hormonally sensitive malignancies, such as those with mutations in BRCA genes.
- The use of estrogen alone and estrogen plus progestin has been reported to result in an increase in abnormal mammograms requiring further evaluation. Surveillance measures, such as breast examinations and regular mammography, are recommended. Discontinue ORIAHNN if a hormonally sensitive malignancy is diagnosed.

Suicidal Ideation, Suicidal Behavior, and Exacerbation of Mood Disorders

- Depression, depressed mood, and/or tearfulness were reported at a higher incidence in women taking ORIAHNN (3%) compared with placebo (1%) in the Phase 3 clinical trials. Suicidal ideation and behavior, including a completed suicide, occurred in women treated with lower doses of elagolix in clinical trials conducted for a different indication.
- 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 ORIAHNN if such events occur.

Please see accompanying Full Prescribing Information.

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IMPORTANT SAFETY INFORMATION[1] (cont'd)

Hepatic Impairment and Transaminase Elevations

- ORIAHNN is contraindicated in women with known hepatic impairment or disease.
- Transaminase elevations in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) occurred with ORIAHNN in Phase 3 clinical trials. No pattern in time to onset of these liver transaminase elevations was identified. Transaminase levels returned to baseline within 4 months after peak values in these patients.
- Instruct patients to promptly seek medical attention in case of symptoms or signs that may reflect liver injury, such as jaundice.

Elevated Blood Pressure

- ORIAHNN is contraindicated in women with uncontrolled hypertension. Maximum mean increases in systolic blood pressure occurred at Month 5, and a mean maximum increase in diastolic blood pressure occurred at Month 4 in ORIAHNN-treated women, as compared to placebo-treated women.
- For women with well-controlled hypertension, continue to monitor blood pressure and stop ORIAHNN if blood pressure rises significantly. Monitor blood pressure in normotensive women treated with ORIAHNN.

Gallbladder Disease or History of Cholestatic Jaundice

- Studies among estrogen users suggest a small increased relative risk of developing gallbladder disease. For women with a history of cholestatic jaundice associated with past estrogen use or with pregnancy, assess the risk-benefit of continuing therapy. Discontinue ORIAHNN if jaundice occurs.

Change in Menstrual Bleeding Pattern and Reduced Ability to Recognize Pregnancy

- ORIAHNN may delay the ability to recognize the occurrence of a pregnancy because it may reduce the intensity, duration, and amount of menstrual bleeding. Perform pregnancy testing if pregnancy is suspected and discontinue ORIAHNN if pregnancy is confirmed.
- The effect of hormonal contraceptives on the efficacy of ORIAHNN is unknown. Advise women to use non-hormonal contraception during treatment and for 1 week after discontinuing ORIAHNN.

Effects on Carbohydrate and Lipid Metabolism

- ORIAHNN may decrease glucose tolerance and result in increased glucose levels. More frequent monitoring in ORIAHNN-treated women with prediabetes and diabetes may be needed.
- In women with preexisting hypertriglyceridemia, estrogen therapy may be associated with elevations of plasma triglycerides leading to pancreatitis. Use of elagolix is associated with increases in total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and serum triglycerides. Monitor lipid levels and consider discontinuing ORIAHNN if hypercholesterolemia or hypertriglyceridemia worsens.

Alopecia

- In Phase 3 clinical trials, more women experienced alopecia, hair loss, and hair thinning with ORIAHNN (3.5%) compared to placebo (1.0%). In almost one-third of affected ORIAHNN-treated women, alopecia was the reason for discontinuing treatment. No specific pattern was described. In the majority of these women, hair loss was continuing when ORIAHNN was stopped. Whether the hair loss is reversible is unknown. Consider discontinuing ORIAHNN if hair loss becomes a concern.

Effect on Other Laboratory Results

- The use of estrogen and progestin combinations may raise serum concentrations of binding proteins (e.g., thyroid-binding globulin, corticosteroid-binding globulin), which may reduce the free thyroid or corticosteroid hormone levels. Patients with hypothyroidism and hypoadrenalism may require higher doses of thyroid hormone or cortisol replacement therapy, respectively.
- The use of estrogen and progestin may also affect the levels of sex hormone-binding globulin, coagulation factors, lipids, and glucose.

RISK OF ALLERGIC REACTIONS DUE TO THE INACTIVE INGREDIENT (FD&C YELLOW NO. 5)

- ORIAHNN contains FD&C Yellow No. 5 (tartrazine), which may cause allergic-type reactions (including bronchial asthma) in certain susceptible persons. Although the overall incidence of FD&C Yellow No. 5 (tartrazine) sensitivity in the general population is low, it is frequently seen in patients who also have aspirin hypersensitivity.

ADVERSE REACTIONS

- Most common adverse reactions occurring in ≥5% of women receiving ORIAHNN in clinical trials were hot flush, headache, fatigue, and metrorrhagia.

These are not all of the possible side effects of ORIAHNN.

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

For more information, see accompanying Full Prescribing Information.

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REFERENCES

1. ORIAHNN [package insert]. North Chicago, IL: AbbVie Inc; 2020. **2.** Schlaff WD, Ackerman RT, Al-Hendy A, et al. Elagolix for heavy menstrual bleeding in women with uterine fibroids. *N Engl J Med*. 2020;382(4):328-340. **3.** Simon JA, Al-Hendy A, Archer DF, Barnhart KT, Bradley LD, Carr BR, et al. elagolix Treatment for up to 12 months in women with heavy menstrual bleeding and uterine leiomyomas [published online ahead of print April 26, 2020]. *Obstet Gynecol*. doi:10.1097/AOG.0000000000003869. **4.** Al-Hendy A, Simon J, Hurtado S, et al. Effect of fibroid location and size on efficacy of elagolix: results from phase 3 clinical trials. Presented at: American Society for Reproductive Medicine 2019 Scientific Congress and Expo; October 12-16, 2019; Philadelphia, PA. **5.** Munro MG, Critchley HOD, Fraser IS, et al. The two FIGO systems for normal and abnormal uterine bleeding symptoms and classification of causes of abnormal uterine bleeding in the reproductive years: 2018 revisions. *Int J Gynaecol Obstet*. 2018;143(3):393-408. **6.** Data on File. ABVRRTI70254. AbbVie Inc. March 24, 2020. **7.** Data on File. ABVRRTI70090. AbbVie Inc. February 2, 2019. **8.** Coyne KS, Margolis MK, Bradley LD, Guido R, Maxwell GL, Spies JB. Further validation of the uterine fibroid symptom and quality-of-life questionnaire. *Value Health*. 2012;15(1):135-142. **9.** Spies JB, Coyne K, Guaou Guaou N, Boyle D, Skymarz-Murphy K, Gonzalves SM. The UFS-QOL, a new disease-specific symptom and health-related quality of life questionnaire for leiomymata. *Obstet Gynecol*. 2002;99(2):290-300. **10.** Al-Hendy A, Soliman AM, Wang H, Coyne K, Carr BR. Elagolix improves quality of life among uterine fibroids patients with heavy menstrual bleeding in phase 3 trials. Presented at: 2019 American College of Obstetricians and Gynecologists Annual Clinical and Scientific Meeting; May 3-6, 2019; Nashville, TN. **11.** Gillispie V. Up to 12 months of efficacy and safety of elagolix treatment in women with heavy menstrual bleeding associated with uterine fibroids. Presented at: AAGL 48th Global Congress on MIGS; November 9-13; Vancouver, BC.

Please see Important Safety Information, including **BOXED WARNING on THROMBOEMBOLIC AND VASCULAR EVENTS**, on pages 18-19 and please see accompanying Full Prescribing Information.

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FREQUENTLY ASKED QUESTIONS ABOUT ORIAHNN

FOR FORMULARY DECISION-MAKERS

The following materials are approved for use with payers, or members of a formulary committee or other similar entity, or an authorized agent(s) of that committee. An authorized agent is someone whom the committee has specifically asked to evaluate information related to the formulary decision-making or drug selection.

INDICATION[1]

ORIAHNN™ (elagolix, estradiol, and norethindrone acetate capsules; elagolix capsules) is indicated for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women. Use of ORIAHNN should be limited to 24 months due to the risk of continued bone loss, which may not be reversible.

SAFETY CONSIDERATIONS[1]

Estrogen and progestin combinations, including ORIAHNN, increase the risk of thrombotic or thromboembolic disorders, including pulmonary embolism, deep vein thrombosis, stroke, and myocardial infarction, especially in women at increased risk for these events.

ORIAHNN is contraindicated in women with current or a history of thrombotic or thromboembolic disorders and in women at increased risk for these events, including women over 35 years of age who smoke and women with uncontrolled hypertension.

- ORIAHNN is contraindicated in women who are at a high risk of arterial, venous thrombotic, or thromboembolic disorders; who are pregnant; with known osteoporosis; current or history of breast cancer or other hormonally sensitive malignancies; known hepatic impairment or disease; undiagnosed abnormal uterine bleeding; known anaphylactic reaction, angioedema, or hypersensitivity to ingredients of ORIAHNN; or with concomitant use of organic anion transporting polypeptide (OATP) 1B1 inhibitors that are known or expected to significantly increase elagolix plasma concentrations.
- Discontinue ORIAHNN if an arterial or venous thrombotic, cardiovascular, or cerebrovascular event occurs. If feasible, discontinue ORIAHNN at least 4 to 6 weeks before surgery of the type associated with an increased risk of thromboembolism, or during periods of prolonged immobilization. Stop ORIAHNN if there is sudden, unexplained partial or complete loss of vision, proptosis, diplopia, papilledema, or retinal vascular lesions and evaluate for retinal vein thrombosis immediately.
- ORIAHNN may cause a decrease in bone mineral density (BMD), which is greater with increasing duration of use and may not be completely reversible after stopping treatment. Assessment of BMD by dual-energy X-ray absorptiometry (DXA) is recommended at baseline and periodically thereafter. Limit the duration of use to 24 months to reduce the extent of bone loss.
- ORIAHNN should not be used in women with current or a history of breast cancer and in women at increased risk for hormonally sensitive malignancies, such as those with mutations in BRCA genes. Discontinue ORIAHNN if a hormonally sensitive malignancy is diagnosed.
- Depression, depressed mood, and/or tearfulness have occurred in women taking ORIAHNN. Advise patients to seek medical attention for suicidal ideation, suicidal behavior, new onset or worsening depression, anxiety, or other mood changes.
- ORIAHNN may delay the ability to recognize the occurrence of a pregnancy, as it may reduce the intensity, duration, and amount of menstrual bleeding. Discontinue ORIAHNN if pregnancy is confirmed.
- Alopecia, hair loss, and hair thinning have occurred with ORIAHNN. No specific pattern was described. Whether the hair loss is reversible is unknown. Consider discontinuing ORIAHNN if hair loss becomes a concern.
- The following events/conditions were either reported in clinical trials of ORIAHNN and/or may be potentially caused or exacerbated by the estrogen and progestin components in ORIAHNN: transaminase elevations, an increase in blood pressure, an increased risk of developing gallbladder disease, diabetes mellitus, hereditary angioedema, adverse lipid changes, and change in the results of some laboratory tests such as coagulation factors, lipids, glucose tolerance, and binding proteins.
- ORIAHNN contains FD&C Yellow No. 5 (tartrazine), which may cause allergic-type reactions (including bronchial asthma) in certain susceptible persons.

Please see additional Important Safety Information, including **BOXED WARNING on THROMBOEMBOLIC AND VASCULAR EVENTS**, on pages 11-12 and please see accompanying Full Prescribing Information.

TABLE OF CONTENTS

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UTERINE FIBROIDS AND HEAVY MENSTRUAL BLEEDING

Q WHAT IS UTERINE FIBROIDS?

A Uterine fibroids (UF) is a hormone-driven gynecological disease characterized by benign tumors that grow from smooth muscle cells in the uterus.[2]

Q WHAT IS THE MOST COMMON SYMPTOM OF UF?

A The most common symptom of UF is heavy menstrual bleeding (HMB).[3,4]

Based on a 2012 survey analysis, more than 70% of women with UF reported HMB as a primary symptom.[3]

Q HOW MANY WOMEN IN THE UNITED STATES ARE AFFECTED BY UF?

A Symptomatic UF affects approximately 6 million women aged 18 to 54 years in the United States, 4 million of whom have HMB related to UF.[3,5]

Q HOW DOES THE SIZE OF THE FIBROID(S) AFFECT THE SEVERITY OF HMB?

A HMB severity in UF is not related to fibroid size or location. Fibroid effects may span the entire endometrium and may not be localized to the areas near the fibroids. Submucosal fibroids have been shown to affect the endometrium throughout the uterine cavity.[6,7]

Q HOW ARE PATIENTS WITH UF CURRENTLY MANAGED?

A Currently, there are a number of surgical interventions and short-term medical treatments used to manage UF. Treatment goals will vary based on a woman's need for symptom relief and desires, such as future family plans and preference to not have surgery at this time.[8,9]

US guidelines do not provide guidance on selecting first- or second-line treatment options.[8,10]

ABOUT ORIAHNN

Q WHAT IS ORIAHNN INDICATED FOR?

A ORIAHNN™ (elagolix, estradiol, and norethindrone acetate capsules; elagolix capsules) is indicated for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women. Use of ORIAHNN should be limited to 24 months due to the risk of continued bone loss, which may not be reversible.[1]

Q WHEN WAS ORIAHNN APPROVED?

A The US Food and Drug Administration approved ORIAHNN on May 29, 2020.[11] ORIAHNN is the first oral gonadotropin-releasing hormone (GnRH) receptor antagonist specifically developed for women with UF-related HMB.[1]

ORIAHNN MECHANISM OF ACTION

Q HOW DOES ORIAHNN WORK?

A UF is a hormone-driven disease.[2] By competitively binding to GnRH receptors, elagolix inhibits GnRH signaling in the pituitary gland. This, in turn, suppresses luteinizing hormone and follicle-stimulating hormone, which leads to decreased production of both estradiol and progesterone by the ovaries. With these decreased levels of estrogen and progesterone, menstrual bleeding may be reduced. The combination of elagolix with estradiol/norethindrone acetate (E2/NETA) allows ORIAHNN to suppress hormones while helping to mitigate the hypoestrogenic effects associated with decreased hormone levels.[1]

ORIAHNN DOSING

Q HOW IS ORIAHNN DOSED?

A ORIAHNN dosing consists of an orally administered AM capsule containing a combination of 300 mg elagolix, 1 mg estradiol, and 0.5 mg norethindrone acetate and a PM capsule containing 300 mg elagolix. Exclude pregnancy before starting ORIAHNN or start ORIAHNN within 7 days from the onset of menses. Each capsule should be taken at approximately the same time each day and can be taken with or without food for up to 24 months.[1]

Assessment of bone mineral density (BMD) by dual-energy X-ray absorptiometry (DXA) is recommended at baseline and periodically thereafter.[1]

SAFETY CONSIDERATIONS[1] (cont'd)

ORIAHNN is contraindicated in women who are at a high risk of arterial, venous thrombotic, or thromboembolic disorders; who are pregnant; with known osteoporosis; current or history of breast cancer or other hormonally sensitive malignancies; known hepatic impairment or disease; undiagnosed abnormal uterine bleeding; known anaphylactic reaction, angioedema, or hypersensitivity to ingredients of ORIAHNN; or with concomitant use of organic anion transporting polypeptide (OATP) 1B1 inhibitors that are known or expected to significantly increase elagolix plasma concentrations.

Please see additional Important Safety Information, including **BOXED WARNING on THROMBOEMBOLIC AND VASCULAR EVENTS**, on pages 11-12 and please see accompanying Full Prescribing Information.

Oriahnn™
elagolix, estradiol and norethindrone acetate capsules and elagolix capsules 300 mg/1 mg/0.5 mg and 300 mg

ORIAHNN CLINICAL TRIALS

Q HOW WAS ORIAHNN STUDIED?

A ORIAHNN was studied in two 6-month, randomized, double-blind, placebo-controlled, phase 3 studies, ELARIS UF-1 and ELARIS UF-2. These studies include 790 premenopausal women who had ≤2 menstrual cycles with >80 mL menstrual blood loss (MBL). Women who completed the 6-month treatment period and met eligibility criteria entered an uncontrolled, blinded, 6-month extension study, UF-EXTEND (UF-3), for a total treatment duration of up to 12 months.[1,12]

ORIAHNN EFFICACY

Q HOW EFFECTIVE WAS ORIAHNN IN CLINICAL TRIALS?

A The primary endpoint in ELARIS UF-1 and ELARIS UF-2 was the proportion of women who achieved treatment response, defined as attaining both MBL volume <80 mL at the final month and ≥50% reduction in MBL volume from baseline to the final month.* A higher proportion of women treated with ORIAHNN were responders compared with placebo.[1]

- In ELARIS UF-1, 68.5% of women receiving ORIAHNN (n=206) met the primary endpoint vs 8.7% of women receiving placebo (n=102); *P*<0.001
- In ELARIS UF-2, 76.5% of women receiving ORIAHNN (n=189) met the primary endpoint vs 10.5% of women receiving placebo (n=94); *P*<0.001

*Final month was defined as the last 28 days before and including the last treatment visit date or the last dose date.

Q HOW QUICKLY DOES ORIAHNN REDUCE BLEEDING?

A In clinical trials, women treated with ORIAHNN experienced a greater reduction in MBL compared with placebo at 1 month.[1,12]

- Least squares mean change from baseline in ELARIS UF-1 was -135.2 mL with ORIAHNN (n=187; baseline 238.0 mL) vs -19.0 mL with placebo (n=95; baseline 255.3 mL) (*P*<0.001)[12]
- Least squares mean change from baseline in ELARIS UF-2 was -127.0 mL with ORIAHNN (n=175; baseline 228.5 mL) vs -2.1 mL with placebo (n=88; baseline 254.3 mL) (*P*<0.001)[12]

For more information on the clinical trials, including design and results, please see the ORIAHNN Clinical Overview.

SAFETY CONSIDERATIONS[1] (cont'd)

Discontinue ORIAHNN if an arterial or venous thrombotic, cardiovascular, or cerebrovascular event occurs. If feasible, discontinue ORIAHNN at least 4 to 6 weeks before surgery of the type associated with an increased risk of thromboembolism, or during periods of prolonged immobilization. Stop ORIAHNN if there is sudden, unexplained partial or complete loss of vision, proptosis, diplopia, papilledema, or retinal vascular lesions and evaluate for retinal vein thrombosis immediately.

Please see additional Important Safety Information, including **BOXED WARNING on THROMBOEMBOLIC AND VASCULAR EVENTS**, on pages 11-12 and please see accompanying Full Prescribing Information.

Oriahnn™
elagolix, estradiol and norethindrone acetate capsules and elagolix capsules 300 mg/1 mg/0.5 mg and 300 mg

ORIAHNN SAFETY

Q WHAT ARE THE MOST COMMON ADVERSE REACTIONS ASSOCIATED WITH ORIAHNN?

A The most common adverse reactions (ARs) reported for women treated with ORIAHNN in ELARIS UF-1 and ELARIS UF-2 trials (incidence ≥5%) were hot flush, headache, fatigue, and metrorrhagia.[1]

ARs Occurring in ≥5% of Women Receiving ORIAHNN and at a Greater Incidence than Placebo

	Placebo (n=196)	ORIAHNN (n=395)
Hot flush	9%	22%
Headache	7%	9%
Fatigue	4%	6%
Metrorrhagia	1%	5%

Q WHAT WERE THE MOST COMMON REASONS FOR DISCONTINUATION OF ORIAHNN IN THE CLINICAL TRIALS?

A In ELARIS UF-1 and ELARIS UF-2, discontinuation from therapy due to any ARs occurred in 10% of women treated with ORIAHNN and 7% of those who received placebo. The most common ARs leading to drug discontinuations in the ORIAHNN group were nausea (1%), headache (1%), alopecia (1%), metrorrhagia (1%), menorrhagia (1%), and hot flush (1%).[1]

Q WHAT IS INCLUDED IN THE BLACK BOXED WARNING FOR ORIAHNN?

A Estrogen and progestin combinations, including ORIAHNN, increase the risk of thrombotic or thromboembolic disorders, including pulmonary embolism, deep vein thrombosis, stroke, and myocardial infarction, especially in women at increased risk for these events.[1]

ORIAHNN is contraindicated in women with current or a history of thrombotic or thromboembolic disorders and in women at increased risk for these events, including women over 35 years of age who smoke and women with uncontrolled hypertension.[1]

For more information on warnings and precautions, see section 5 of the Prescribing Information.

Please see additional Important Safety Information, including **BOXED WARNING on THROMBOEMBOLIC AND VASCULAR EVENTS**, on pages 11-12 and please see accompanying Full Prescribing Information.

Oriahnn™
elagolix, estradiol and norethindrone acetate capsules and elagolix capsules 300 mg/1 mg/0.5 mg and 300 mg

ORIAHNN SAFETY (cont'd)

Q ARE THERE ANY CONTRAINDICATIONS FOR ORIAHNN?

A Yes, ORIAHNN is contraindicated in women with[1]

- High risk of arterial, venous thrombotic, or thromboembolic disorder
- Pregnancy
- Known osteoporosis
- Current or history of breast cancer or other hormonally sensitive malignancies
- Known liver impairment or disease
- Undiagnosed abnormal uterine bleeding
- Known hypersensitivity to the ingredients of ORIAHNN
- Organic anion transporting polypeptide (OATP) 1B1 inhibitors that are known or expected to significantly increase elagolix plasma concentrations

Q IS THERE ANY MONITORING RECOMMENDED FOR BONE LOSS WHILE TAKING ORIAHNN?

A Yes, it is recommended that BMD be assessed by DXA at baseline and periodically thereafter.[1]

ORIAHNN may cause a decrease in BMD. BMD loss is greater with increasing duration of use and may not be completely reversible after stopping treatment. Limit the duration of use to 24 months to reduce the extent of bone loss.[1]

The effects of ORIAHNN-associated decreases in BMD on long-term bone health and future fracture are unknown; therefore, the benefits and risks of treatment with ORIAHNN should be considered in women who have a history of low-trauma bone fracture or other risk factors for osteoporosis or bone loss and the use of ORIAHNN should be avoided in women with known osteoporosis.[1]

Q IS ORIAHNN CONSIDERED A CONTRACEPTIVE?

A ORIAHNN was not evaluated as a contraceptive and should not be used as such. Women are advised to use nonhormonal contraception during treatment and for 1 week after discontinuing ORIAHNN. ORIAHNN may delay the ability to recognize the occurrence of a pregnancy because it may reduce the intensity, duration, and amount of menstrual bleeding. Perform pregnancy testing if pregnancy is suspected, and discontinue ORIAHNN if pregnancy is confirmed.[1]

Please see additional Important Safety Information, including **BOXED WARNING on THROMBOEMBOLIC AND VASCULAR EVENTS**, on pages 11-12 and please see accompanying Full Prescribing Information.

Oriahnn™
elagolix, estradiol and norethindrone acetate capsules and elagolix capsules 300 mg/1 mg/0.5 mg and 300 mg

ORIAHNN SAFETY (cont'd)

Q ARE THERE ANY OTHER WARNINGS AND PRECAUTIONS FOR ORIAHNN?

A Yes, the warnings and precautions for ORIAHNN include[1]

- Discontinue ORIAHNN if an arterial or venous thrombotic, cardiovascular, or cerebrovascular event occurs. If feasible, discontinue ORIAHNN at least 4 to 6 weeks before surgery of the type associated with an increased risk of thromboembolism, or during periods of prolonged immobilization. Stop ORIAHNN if there is sudden, unexplained partial or complete loss of vision, proptosis, diplopia, papilledema, or retinal vascular lesions and evaluate for retinal vein thrombosis immediately.
- ORIAHNN may cause a decrease in BMD, which is greater with increasing duration of use and may not be completely reversible after stopping treatment. Assessment of BMD by dual-energy X-ray absorptiometry (DXA) is recommended at baseline and periodically thereafter. Limit the duration of use to 24 months to reduce the extent of bone loss.
- ORIAHNN should not be used in women with current or a history of breast cancer and in women at increased risk for hormonally sensitive malignancies, such as those with mutations in BRCA genes. Discontinue ORIAHNN if a hormonally sensitive malignancy is diagnosed.
- Depression, depressed mood, and/or tearfulness have occurred in women taking ORIAHNN. Advise patients to seek medical attention for suicidal ideation, suicidal behavior, new onset or worsening depression, anxiety, or other mood changes.
- ORIAHNN may delay the ability to recognize the occurrence of a pregnancy, as it may reduce the intensity, duration, and amount of menstrual bleeding. Discontinue ORIAHNN if pregnancy is confirmed.
- Alopecia, hair loss, and hair thinning have occurred with ORIAHNN. No specific pattern was described. Whether the hair loss is reversible is unknown. Consider discontinuing ORIAHNN if hair loss becomes a concern.
- The following events/conditions were either reported in clinical trials of ORIAHNN and/or may be potentially caused or exacerbated by the estrogen and progestin components in ORIAHNN: transaminase elevations, an increase in blood pressure, an increased risk of developing gallbladder disease, diabetes mellitus, hereditary angioedema, adverse lipid changes, and change in the results of some laboratory tests such as coagulation factors, lipids, glucose tolerance, and binding proteins.
- ORIAHNN contains FD&C Yellow No. 5 (tartrazine), which may cause allergic-type reactions (including bronchial asthma) in certain susceptible persons.

For more information on warnings and precautions, see section 5 of the Prescribing Information.

Please see additional Important Safety Information, including **BOXED WARNING on THROMBOEMBOLIC AND VASCULAR EVENTS**, on pages 11-12 and please see accompanying Full Prescribing Information.

Oriahnn™
elagolix, estradiol and norethindrone acetate capsules and elagolix capsules 300 mg/1 mg/0.5 mg and 300 mg

DISTRIBUTION AND PACKAGING

Q HOW IS ORIAHNN DISTRIBUTED?

A ORIAHNN is available through an open distribution model and retail pharmacy.

Q HOW IS ORIAHNN PACKAGED AND SUPPLIED?

A ORIAHNN is packaged in weekly blister packs that contain 7 morning (AM) capsules and 7 evening (PM) capsules. Each carton contains 4 blister packs for a total of 56 capsules. The National Drug Code is 0074-1017-56.[1]

WOMEN'S HEALTH PORTFOLIO

Q HOW IS ORIAHNN DIFFERENT FROM ORILISSA® (elagolix)?

A ORIAHNN is a combination therapy with different indication and dosing than ORILISSA.

ORILISSA is available in 2 doses, elagolix 150 mg once daily and elagolix 200 mg twice daily, for the management of moderate to severe pain associated with endometriosis.[13]

ORIAHNN is taken twice daily for the management of HMB associated with UF. The morning capsule contains elagolix 300 mg plus estradiol 1 mg/norethindrone acetate 0.5 mg and the evening capsule contains elagolix 300 mg.[1]

The therapies included here are not interchangeable. No comparisons regarding safety or efficacy can be made.

Q HOW DOES THE PREVALENCE OF THE TARGET PATIENT POPULATION FOR ORIAHNN COMPARE WITH THAT OF ORILISSA?

A The prevalence of HMB associated with UF is comparable with that of endometriosis. It is estimated that 4.1 million women aged 18 to 49 years in the United States have been diagnosed with endometriosis.[14] Approximately 4 million women aged 18 to 54 years are affected by HMB associated with UF in the United States.[3,5]

The therapies included here are not interchangeable. No comparisons regarding safety or efficacy can be made.

ORILISSA INDICATION[13]

ORILISSA® (elagolix) is indicated for the management of moderate to severe pain associated with endometriosis.

ORILISSA SAFETY CONSIDERATIONS[13]

ORILISSA is contraindicated in women who are pregnant, women with known osteoporosis, women with severe hepatic impairment, or in women taking strong organic anion transporting polypeptide (OATP) 1B1 inhibitors such as cyclosporine and gemfibrozil.

Please see additional Important Safety Information for ORILISSA on page 13 and see accompanying ORILISSA Full Prescribing Information.

Please see additional Important Safety Information, including **BOXED WARNING on THROMBOEMBOLIC AND VASCULAR EVENTS**, on pages 11-12 and please see accompanying Full Prescribing Information.

Oriahnn™
elagolix, estradiol and norethindrone acetate capsules and elagolix capsules 300 mg/1 mg/0.5 mg and 300 mg

WOMEN'S HEALTH PORTFOLIO (cont'd)

Q WHY DID ABBVIE PRICE ORIAHNN AT $907.39 WAC?

A AbbVie has taken a thoughtful pricing approach to help facilitate broad access for women with HMB associated with UF.

At $907.39,* ORIAHNN has the same wholesale acquisition cost (WAC) as ORILISSA per 28-day pack, providing flat pricing across all elagolix products with the potential to limit per-member per-month budget impact (pharmacy $0.05; medical -$0.04; total $0.02).[15]

The therapies included here are not interchangeable. No comparisons regarding safety or efficacy can be made.

*Current WAC as of June 2020. Subject to change. Acquisition costs do not necessarily reflect the actual price paid by consumers, pharmacies, or third-party payers.

ORILISSA SAFETY CONSIDERATIONS[13]

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. Consider assessment of BMD in patients with a history of fracture or other risk factors for bone loss, and do not use in women with known osteoporosis. Limit the duration of use to reduce the extent of bone loss.

Please see additional Important Safety Information for ORILISSA on page 13 and see accompanying ORILISSA Full Prescribing Information.

Please see additional Important Safety Information, including **BOXED WARNING on THROMBOEMBOLIC AND VASCULAR EVENTS**, on pages 11-12 and please see accompanying Full Prescribing Information.

Oriahnn™
elagolix, estradiol and norethindrone acetate capsules and elagolix capsules 300 mg/1 mg/0.5 mg and 300 mg

IMPORTANT SAFETY INFORMATION FOR ORIAHNN

INDICATION[1]

ORIAHNN™ (elagolix, estradiol, and norethindrone acetate capsules; elagolix capsules) is indicated for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women. Use of ORIAHNN should be limited to 24 months due to the risk of continued bone loss, which may not be reversible.

IMPORTANT SAFETY INFORMATION[1]

THROMBOEMBOLIC AND VASCULAR EVENTS

Estrogen and progestin combinations, including ORIAHNN, increase the risk of thrombotic or thromboembolic disorders, including pulmonary embolism, deep vein thrombosis, stroke, and myocardial infarction, especially in women at increased risk for these events.

ORIAHNN is contraindicated in women with current or a history of thrombotic or thromboembolic disorders and in women at increased risk for these events, including women over 35 years of age who smoke and women with uncontrolled hypertension.

CONTRAINDICATIONS

- ORIAHNN is contraindicated in women at a high risk of arterial, venous thrombotic, or thromboembolic disorders; who are pregnant; with known osteoporosis; current or history of breast cancer or other hormonally sensitive malignancies; known hepatic impairment or disease; undiagnosed abnormal uterine bleeding; known anaphylactic reaction, angioedema, or hypersensitivity to ingredients of ORIAHNN; or with concomitant use of organic anion transporting polypeptide (OATP) 1B1 inhibitors that are known or expected to significantly increase elagolix plasma concentrations.

WARNINGS AND PRECAUTIONS

Thromboembolic Disorders and Vascular Events

- ORIAHNN is contraindicated in women with current or a history of thrombotic or thromboembolic disorders and in women at increased risk for these events. Components of ORIAHNN increase the risk of thrombotic or thromboembolic disorders, including pulmonary embolism, deep vein thrombosis, stroke, and myocardial infarction, especially in women at high risk for these events. In general, the risk is greatest among women over 35 years of age who smoke, and women with uncontrolled hypertension, dyslipidemia, vascular disease, or obesity.
- Discontinue ORIAHNN if an arterial or venous thrombotic, cardiovascular, or cerebrovascular event occurs. If feasible, discontinue ORIAHNN at least 4 to 6 weeks before surgery of the type associated with an increased risk of thromboembolism, or during periods of prolonged immobilization. Stop ORIAHNN if there is sudden, unexplained partial or complete loss of vision, proptosis, diplopia, papilledema, or retinal vascular lesions and evaluate for retinal vein thrombosis immediately.

Bone Loss

- ORIAHNN is contraindicated in women with known osteoporosis. ORIAHNN may cause a decrease in bone mineral density (BMD) in some patients, which is greater with increasing duration of use and may not be completely reversible after stopping treatment.
- The impact of ORIAHNN-associated decreases in BMD on long-term bone health and future fracture risk is unknown. Consider the benefits and risks of ORIAHNN in patients with a history of low-trauma fracture or other risk factors for osteoporosis or bone loss, including those taking medications that may decrease BMD (e.g., systemic or chronic inhaled corticosteroids, anticonvulsants, or proton pump inhibitors).
- Assessment of BMD by dual-energy X-ray absorptiometry (DXA) is recommended at baseline and periodically thereafter. Consider discontinuing ORIAHNN if the risk associated with bone loss exceeds the potential benefit of treatment. Limit the duration of use to 24 months to reduce the extent of bone loss.

Hormonally Sensitive Malignancies

- ORIAHNN is contraindicated in women with current or a history of breast cancer and in women at increased risk for hormonally sensitive malignancies, such as those with mutations in BRCA genes.
- The use of estrogen alone and estrogen plus progestin has been reported to result in an increase in abnormal mammograms requiring further evaluation. Surveillance measures, such as breast examinations and regular mammography, are recommended. Discontinue ORIAHNN if a hormonally sensitive malignancy is diagnosed.

Suicidal Ideation, Suicidal Behavior, and Exacerbation of Mood Disorders

- Depression, depressed mood, and/or tearfulness were reported at a higher incidence in women taking ORIAHNN (3%) compared with placebo (1%) in the Phase 3 clinical trials. Suicidal ideation and behavior, including a completed suicide, occurred in women treated with lower doses of elagolix in clinical trials conducted for a different indication.
- 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 ORIAHNN if such events occur.

Please see accompanying Full Prescribing Information.

Oriahnn™
elagolix, estradiol and norethindrone acetate capsules and elagolix capsules 300 mg/1 mg/0.5 mg and 300 mg

IMPORTANT SAFETY INFORMATION FOR ORIAHNN[1] (cont'd)

Hepatic Impairment and Transaminase Elevations

- ORIAHNN is contraindicated in women with known hepatic impairment or disease.
- Transaminase elevations in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) occurred with ORIAHNN in Phase 3 clinical trials. No pattern in time to onset of these liver transaminase elevations was identified. Transaminase levels returned to baseline within 4 months after peak values in these patients.
- Instruct patients to promptly seek medical attention in case of symptoms or signs that may reflect liver injury, such as jaundice.

Elevated Blood Pressure

- ORIAHNN is contraindicated in women with uncontrolled hypertension. Maximum mean increases in systolic blood pressure occurred at Month 5, and a mean maximum increase in diastolic blood pressure occurred at Month 4 in ORIAHNN-treated women, as compared to placebo-treated women.
- For women with well-controlled hypertension, continue to monitor blood pressure and stop ORIAHNN if blood pressure rises significantly. Monitor blood pressure in normotensive women treated with ORIAHNN.

Gallbladder Disease or History of Cholestatic Jaundice

- Studies among estrogen users suggest a small increased relative risk of developing gallbladder disease. For women with a history of cholestatic jaundice associated with past estrogen use or with pregnancy, assess the risk-benefit of continuing therapy. Discontinue ORIAHNN if jaundice occurs.

Change in Menstrual Bleeding Pattern and Reduced Ability to Recognize Pregnancy

- ORIAHNN may delay the ability to recognize the occurrence of a pregnancy because it may reduce the intensity, duration, and amount of menstrual bleeding. Perform pregnancy testing if pregnancy is suspected and discontinue ORIAHNN if pregnancy is confirmed.
- The effect of hormonal contraceptives on the efficacy of ORIAHNN is unknown. Advise women to use non-hormonal contraception during treatment and for 1 week after discontinuing ORIAHNN.

Effects on Carbohydrate and Lipid Metabolism

- ORIAHNN may decrease glucose tolerance and result in increased glucose levels. More frequent monitoring in ORIAHNN-treated women with prediabetes and diabetes may be needed.
- In women with preexisting hypertriglyceridemia, estrogen therapy may be associated with elevations of plasma triglycerides leading to pancreatitis. Use of elagolix is associated with increases in total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and serum triglycerides. Monitor lipid levels and consider discontinuing ORIAHNN if hypercholesterolemia or hypertriglyceridemia worsens.

Alopecia

- In Phase 3 clinical trials, more women experienced alopecia, hair loss, and hair thinning with ORIAHNN (3.5%) compared to placebo (1.0%). In almost one-third of affected ORIAHNN-treated women, alopecia was the reason for discontinuing treatment. No specific pattern was described. In the majority of these women, hair loss was continuing when ORIAHNN was stopped. Whether the hair loss is reversible is unknown. Consider discontinuing ORIAHNN if hair loss becomes a concern.

Effect on Other Laboratory Results

- The use of estrogen and progestin combinations may raise serum concentrations of binding proteins (e.g., thyroid-binding globulin, corticosteroid-binding globulin), which may reduce the free thyroid or corticosteroid hormone levels. Patients with hypothyroidism and hypoadrenalism may require higher doses of thyroid hormone or cortisol replacement therapy, respectively.
- The use of estrogen and progestin may also affect the levels of sex hormone-binding globulin, coagulation factors, lipids, and glucose.

RISK OF ALLERGIC REACTIONS DUE TO THE INACTIVE INGREDIENT (FD&C YELLOW NO. 5)

- ORIAHNN contains FD&C Yellow No. 5 (tartrazine), which may cause allergic-type reactions (including bronchial asthma) in certain susceptible persons. Although the overall incidence of FD&C Yellow No. 5 (tartrazine) sensitivity in the general population is low, it is frequently seen in patients who also have aspirin hypersensitivity.

ADVERSE REACTIONS

- Most common adverse reactions occurring in ≥5% of women receiving ORIAHNN in clinical trials were hot flush, headache, fatigue, and metrorrhagia.

These are not all of the possible side effects of ORIAHNN.

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

For more information, see accompanying Full Prescribing Information.

Oriahnn™
elagolix, estradiol and norethindrone acetate capsules and elagolix capsules 300 mg/1 mg/0.5 mg and 300 mg

IMPORTANT SAFETY INFORMATION FOR ORILISSA® (elagolix)[13]

INDICATION[13]

ORILISSA® (elagolix) is indicated for the management of moderate to severe pain associated with endometriosis.

IMPORTANT SAFETY INFORMATION[13]

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, or with concomitant use of strong organic anion transporting polypeptide (OATP) 1B1 inhibitors (e.g., cyclosporine and gemfibrozil).

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. Consider assessment of BMD in patients with a history of low-trauma fracture or other risk factors for osteoporosis or bone loss, and do not use in women with known osteoporosis.
- Limit the duration of use to reduce the extent of bone loss.

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.

Reduced Efficacy with Estrogen-Containing Contraceptives

- 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.
- Advise women to use non-hormonal contraceptives during treatment and for one week after discontinuing ORILISSA.

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 patients less than 18 years of age have not been established.

For more information, see accompanying Full Prescribing Information.

Orilissa®
elagolix tablets 150 mg 200 mg

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Please see additional Important Safety Information, including **BOXED WARNING on THROMBOEMBOLIC AND VASCULAR EVENTS**, on pages 11-12 and please see accompanying Full Prescribing Information.

abbvie

Oriahnn™
elagolix, estradiol and norethindrone acetate capsules and elagolix capsules 300 mg/1 mg/0.5 mg and 300 mg

 US-GYNUF-200077 June 2020

COMPANY: AbbVie Inc.

PRODUCT TRADE NAME: ORIAHNN

INDICATION[1]: ORIAHNN™ (elagolix, estradiol, and norethindrone acetate capsules; elagolix capsules) is indicated for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women. Use of ORIAHNN should be limited to 24 months due to the risk of continued bone loss, which may not be reversible.

Images of pills and packaging are not actual size.

HOW SUPPLIED[1]	**ORIAHNN Capsules** (twice daily) • Yellow and white morning (AM) capsules contain elagolix 300 mg, estradiol 1 mg, and norethindrone acetate 0.5 mg • Light blue and white evening (PM) capsules contain elagolix 300 mg
PACKAGING[1]	• Each weekly blister pack contains 7 AM capsules and 7 PM capsules • Each monthly carton contains 4 weekly blister packs for a total of 56 capsules
STORAGE[1]	Store at 20°C to 25°C (68°F to 77°F).
SHIPPING CASE DIMENSIONS	There are 24 monthly cartons per case. • Monthly carton: 2.5" x 4.1875" x 6.125" • Case: 10.66" x 8.86" x 18.86"
WAC*	$907.39
NDC NUMBER[1]	Monthly carton: 0074-1017-56

NDC=National Drug Code; WAC=wholesale acquisition cost.

*WAC is the price for this drug submitted to certain pricing compendia in June 2020 for publication and does not include prompt-pay discounts or other discounts, rebates, or reductions in price. The actual price paid by wholesalers and other customers and the retail price paid by consumers at a pharmacy may vary.

SAFETY CONSIDERATIONS[1]

Estrogen and progestin combinations, including ORIAHNN, increase the risk of thrombotic or thromboembolic disorders, including pulmonary embolism, deep vein thrombosis, stroke, and myocardial infarction, especially in women at increased risk for these events.

ORIAHNN is contraindicated in women with current or a history of thrombotic or thromboembolic disorders and in women at increased risk for these events, including women over 35 years of age who smoke and women with uncontrolled hypertension.

Please see additional Important Safety Information, including **BOXED WARNING on THROMBOEMBOLIC AND VASCULAR EVENTS**, on pages 2-3 and please see accompanying Full Prescribing Information.

Oriahnn™
elagolix, estradiol and norethindrone acetate capsules and elagolix capsules 300 mg/1 mg/0.5 mg and 300 mg

INDICATION[1]

ORIAHNN™ (elagolix, estradiol, and norethindrone acetate capsules; elagolix capsules) is indicated for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women. Use of ORIAHNN should be limited to 24 months due to the risk of continued bone loss, which may not be reversible.

IMPORTANT SAFETY INFORMATION[1]

THROMBOEMBOLIC AND VASCULAR EVENTS

Estrogen and progestin combinations, including ORIAHNN, increase the risk of thrombotic or thromboembolic disorders, including pulmonary embolism, deep vein thrombosis, stroke, and myocardial infarction, especially in women at increased risk for these events.

ORIAHNN is contraindicated in women with current or a history of thrombotic or thromboembolic disorders and in women at increased risk for these events, including women over 35 years of age who smoke and women with uncontrolled hypertension.

CONTRAINDICATIONS

- ORIAHNN is contraindicated in women at a high risk of arterial, venous thrombotic, or thromboembolic disorders; who are pregnant; with known osteoporosis; current or history of breast cancer or other hormonally sensitive malignancies; known hepatic impairment or disease; undiagnosed abnormal uterine bleeding; known anaphylactic reaction, angioedema, or hypersensitivity to ingredients of ORIAHNN; or with concomitant use of organic anion transporting polypeptide (OATP) 1B1 inhibitors that are known or expected to significantly increase elagolix plasma concentrations.

WARNINGS AND PRECAUTIONS

Thromboembolic Disorders and Vascular Events

- ORIAHNN is contraindicated in women with current or a history of thrombotic or thromboembolic disorders and in women at increased risk for these events. Components of ORIAHNN increase the risk of thrombotic or thromboembolic disorders, including pulmonary embolism, deep vein thrombosis, stroke, and myocardial infarction, especially in women at high risk for these events. In general, the risk is greatest among women over 35 years of age who smoke, and women with uncontrolled hypertension, dyslipidemia, vascular disease, or obesity.
- Discontinue ORIAHNN if an arterial or venous thrombotic, cardiovascular, or cerebrovascular event occurs. If feasible, discontinue ORIAHNN at least 4 to 6 weeks before surgery of the type associated with an increased risk of thromboembolism, or during periods of prolonged immobilization. Stop ORIAHNN if there is sudden, unexplained partial or complete loss of vision, proptosis, diplopia, papilledema, or retinal vascular lesions and evaluate for retinal vein thrombosis immediately.

Bone Loss

- ORIAHNN is contraindicated in women with known osteoporosis. ORIAHNN may cause a decrease in bone mineral density (BMD) in some patients, which is greater with increasing duration of use and may not be completely reversible after stopping treatment.
- The impact of ORIAHNN-associated decreases in BMD on long-term bone health and future fracture risk is unknown. Consider the benefits and risks of ORIAHNN in patients with a history of low-trauma fracture or other risk factors for osteoporosis or bone loss, including those taking medications that may decrease BMD (e.g., systemic or chronic inhaled corticosteroids, anticonvulsants, or proton pump inhibitors).
- Assessment of BMD by dual-energy X-ray absorptiometry (DXA) is recommended at baseline and periodically thereafter. Consider discontinuing ORIAHNN if the risk associated with bone loss exceeds the potential benefit of treatment. Limit the duration of use to 24 months to reduce the extent of bone loss.

Hormonally Sensitive Malignancies

- ORIAHNN is contraindicated in women with current or a history of breast cancer and in women at increased risk for hormonally sensitive malignancies, such as those with mutations in BRCA genes.
- The use of estrogen alone and estrogen plus progestin has been reported to result in an increase in abnormal mammograms requiring further evaluation. Surveillance measures, such as breast examinations and regular mammography, are recommended. Discontinue ORIAHNN if a hormonally sensitive malignancy is diagnosed.

Suicidal Ideation, Suicidal Behavior, and Exacerbation of Mood Disorders

- Depression, depressed mood, and/or tearfulness were reported at a higher incidence in women taking ORIAHNN (3%) compared with placebo (1%) in the Phase 3 clinical trials. Suicidal ideation and behavior, including a completed suicide, occurred in women treated with lower doses of elagolix in clinical trials conducted for a different indication.
- 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 ORIAHNN if such events occur.

Please see accompanying Full Prescribing Information.

Oriahnn™
elagolix, estradiol and norethindrone acetate capsules and elagolix capsules 300 mg/1 mg/0.5 mg and 300 mg

IMPORTANT SAFETY INFORMATION[1] (cont'd)

Hepatic Impairment and Transaminase Elevations

- ORIAHNN is contraindicated in women with known hepatic impairment or disease.
- Transaminase elevations in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) occurred with ORIAHNN in Phase 3 clinical trials. No pattern in time to onset of these liver transaminase elevations was identified. Transaminase levels returned to baseline within 4 months after peak values in these patients.
- Instruct patients to promptly seek medical attention in case of symptoms or signs that may reflect liver injury, such as jaundice.

Elevated Blood Pressure

- ORIAHNN is contraindicated in women with uncontrolled hypertension. Maximum mean increases in systolic blood pressure occurred at Month 5, and a mean maximum increase in diastolic blood pressure occurred at Month 4 in ORIAHNN-treated women, as compared to placebo-treated women.
- For women with well-controlled hypertension, continue to monitor blood pressure and stop ORIAHNN if blood pressure rises significantly. Monitor blood pressure in normotensive women treated with ORIAHNN.

Gallbladder Disease or History of Cholestatic Jaundice

- Studies among estrogen users suggest a small increased relative risk of developing gallbladder disease. For women with a history of cholestatic jaundice associated with past estrogen use or with pregnancy, assess the risk-benefit of continuing therapy. Discontinue ORIAHNN if jaundice occurs.

Change in Menstrual Bleeding Pattern and Reduced Ability to Recognize Pregnancy

- ORIAHNN may delay the ability to recognize the occurrence of a pregnancy because it may reduce the intensity, duration, and amount of menstrual bleeding. Perform pregnancy testing if pregnancy is suspected and discontinue ORIAHNN if pregnancy is confirmed.
- The effect of hormonal contraceptives on the efficacy of ORIAHNN is unknown. Advise women to use non-hormonal contraception during treatment and for 1 week after discontinuing ORIAHNN.

Effects on Carbohydrate and Lipid Metabolism

- ORIAHNN may decrease glucose tolerance and result in increased glucose levels. More frequent monitoring in ORIAHNN-treated women with prediabetes and diabetes may be needed.
- In women with preexisting hypertriglyceridemia, estrogen therapy may be associated with elevations of plasma triglycerides leading to pancreatitis. Use of elagolix is associated with increases in total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and serum triglycerides. Monitor lipid levels and consider discontinuing ORIAHNN if hypercholesterolemia or hypertriglyceridemia worsens.

Alopecia

- In Phase 3 clinical trials, more women experienced alopecia, hair loss, and hair thinning with ORIAHNN (3.5%) compared to placebo (1.0%). In almost one-third of affected ORIAHNN-treated women, alopecia was the reason for discontinuing treatment. No specific pattern was described. In the majority of these women, hair loss was continuing when ORIAHNN was stopped. Whether the hair loss is reversible is unknown. Consider discontinuing ORIAHNN if hair loss becomes a concern.

Effect on Other Laboratory Results

- The use of estrogen and progestin combinations may raise serum concentrations of binding proteins (e.g., thyroid-binding globulin, corticosteroid-binding globulin), which may reduce the free thyroid or corticosteroid hormone levels. Patients with hypothyroidism and hypoadrenalism may require higher doses of thyroid hormone or cortisol replacement therapy, respectively.
- The use of estrogen and progestin may also affect the levels of sex hormone-binding globulin, coagulation factors, lipids, and glucose.

RISK OF ALLERGIC REACTIONS DUE TO THE INACTIVE INGREDIENT (FD&C YELLOW NO. 5)

- ORIAHNN contains FD&C Yellow No. 5 (tartrazine), which may cause allergic-type reactions (including bronchial asthma) in certain susceptible persons. Although the overall incidence of FD&C Yellow No. 5 (tartrazine) sensitivity in the general population is low, it is frequently seen in patients who also have aspirin hypersensitivity.

ADVERSE REACTIONS

- Most common adverse reactions occurring in ≥5% of women receiving ORIAHNN in clinical trials were hot flush, headache, fatigue, and metrorrhagia.

These are not all of the possible side effects of ORIAHNN.

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

Please see accompanying Full Prescribing Information.

Oriahnn™
elagolix, estradiol and norethindrone acetate capsules and elagolix capsules 300 mg/1 mg/0.5 mg and 300 mg

REFERENCE

1. ORIAHNN [package insert]. North Chicago, IL: AbbVie Inc; 2020.

Please see Important Safety Information, including **BOXED WARNING on THROMBOEMBOLIC AND VASCULAR EVENTS**, on pages 2-3 and please see accompanying Full Prescribing Information.

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 US-GYNUF-200075 June 2020

Oriahnn™
elagolix, estradiol and norethindrone acetate capsules and elagolix capsules 300 mg/1 mg/0.5 mg and 300 mg

SUMMARY OF RELEVANT CODES

Physician attestation of uterine fibroids is sufficient; however, if your plan decides a code is necessary, please refer to the list below.

Oriahnn™
elagolix, estradiol and norethindrone acetate capsules and elagolix capsules 300 mg/1 mg/0.5 mg and 300 mg

Uterine Fibroid Codes[1,2]

CONDITION	ICD-9-CM CODE	ICD-10-CM CODE
Submucous leiomyoma of uterus	218.0	D25.0
Intramural leiomyoma of uterus	218.1	D25.1
Subserosal leiomyoma of uterus	218.2	D25.2
Leiomyoma of uterus, unspecified	218.9	D25.9

Please refer to the list below for additional codes related to heavy menstrual bleeding symptoms.

Heavy Menstrual Bleeding Codes[1,2]

ICD-9-CM CONDITION AND CODE		ICD-10-CM CONDITION AND CODE	
Excessive or frequent menstruation	626.2	Excessive and frequent menstruation with regular cycle	N92.0
Metrorrhagia	626.6	Excessive and frequent menstruation with irregular cycle	N92.1
Ovulation bleeding	626.5	Ovulation bleeding	N92.3
Premenopausal menorrhagia	627.0	Excessive bleeding in the premenopausal period	N92.4
Other disorders of menstruation and other abnormal bleeding from female genital tract	626.8	Other specified irregular menstruation	N92.5
		Other specified abnormal uterine and vaginal bleeding	N93.8
Unspecified disorders of menstruation and other abnormal bleeding from female genital tract	626.9	Irregular menstruation, unspecified	N92.6
		Abnormal uterine and vaginal bleeding, unspecified	N93.9

ICD-9-CM=*International Classification of Diseases, Ninth Edition, Clinical Manifestation*; ICD-10-CM=*International Classification of Diseases, Tenth Edition, Clinical Manifestation*.

The National Drug Code for the ORIAHNN monthly carton is 0074-1017-56.[3]

INDICATION[3]

ORIAHNN™ (elagolix, estradiol, and norethindrone acetate capsules; elagolix capsules) is indicated for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women. Use of ORIAHNN should be limited to 24 months due to the risk of continued bone loss, which may not be reversible.

SAFETY CONSIDERATIONS[3]

Estrogen and progestin combinations, including ORIAHNN, increase the risk of thrombotic or thromboembolic disorders, including pulmonary embolism, deep vein thrombosis, stroke, and myocardial infarction, especially in women at increased risk for these events.

ORIAHNN is contraindicated in women with current or a history of thrombotic or thromboembolic disorders and in women at increased risk for these events, including women over 35 years of age who smoke and women with uncontrolled hypertension.

Please see Important Safety Information, including **BOXED WARNING on THROMBOEMBOLIC AND VASCULAR EVENTS**, on pages 2-3 and please see accompanying Full Prescribing Information.

INDICATION[3]

ORIAHNN™ (elagolix, estradiol, and norethindrone acetate capsules; elagolix capsules) is indicated for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women. Use of ORIAHNN should be limited to 24 months due to the risk of continued bone loss, which may not be reversible.

IMPORTANT SAFETY INFORMATION[3]

THROMBOEMBOLIC AND VASCULAR EVENTS

Estrogen and progestin combinations, including ORIAHNN, increase the risk of thrombotic or thromboembolic disorders, including pulmonary embolism, deep vein thrombosis, stroke, and myocardial infarction, especially in women at increased risk for these events.

ORIAHNN is contraindicated in women with current or a history of thrombotic or thromboembolic disorders and in women at increased risk for these events, including women over 35 years of age who smoke and women with uncontrolled hypertension.

CONTRAINDICATIONS

- ORIAHNN is contraindicated in women at a high risk of arterial, venous thrombotic, or thromboembolic disorders; who are pregnant; with known osteoporosis; current or history of breast cancer or other hormonally sensitive malignancies; known hepatic impairment or disease; undiagnosed abnormal uterine bleeding; known anaphylactic reaction, angioedema, or hypersensitivity to ingredients of ORIAHNN; or with concomitant use of organic anion transporting polypeptide (OATP) 1B1 inhibitors that are known or expected to significantly increase elagolix plasma concentrations.

WARNINGS AND PRECAUTIONS

Thromboembolic Disorders and Vascular Events

- ORIAHNN is contraindicated in women with current or a history of thrombotic or thromboembolic disorders and in women at increased risk for these events. Components of ORIAHNN increase the risk of thrombotic or thromboembolic disorders, including pulmonary embolism, deep vein thrombosis, stroke, and myocardial infarction, especially in women at high risk for these events. In general, the risk is greatest among women over 35 years of age who smoke, and women with uncontrolled hypertension, dyslipidemia, vascular disease, or obesity.
- Discontinue ORIAHNN if an arterial or venous thrombotic, cardiovascular, or cerebrovascular event occurs. If feasible, discontinue ORIAHNN at least 4 to 6 weeks before surgery of the type associated with an increased risk of thromboembolism, or during periods of prolonged immobilization. Stop ORIAHNN if there is sudden, unexplained partial or complete loss of vision, proptosis, diplopia, papilledema, or retinal vascular lesions and evaluate for retinal vein thrombosis immediately.

Bone Loss

- ORIAHNN is contraindicated in women with known osteoporosis. ORIAHNN may cause a decrease in bone mineral density (BMD) in some patients, which is greater with increasing duration of use and may not be completely reversible after stopping treatment.
- The impact of ORIAHNN-associated decreases in BMD on long-term bone health and future fracture risk is unknown. Consider the benefits and risks of ORIAHNN in patients with a history of low-trauma fracture or other risk factors for osteoporosis or bone loss, including those taking medications that may decrease BMD (e.g., systemic or chronic inhaled corticosteroids, anticonvulsants, or proton pump inhibitors).
- Assessment of BMD by dual-energy X-ray absorptiometry (DXA) is recommended at baseline and periodically thereafter. Consider discontinuing ORIAHNN if the risk associated with bone loss exceeds the potential benefit of treatment. Limit the duration of use to 24 months to reduce the extent of bone loss.

Hormonally Sensitive Malignancies

- ORIAHNN is contraindicated in women with current or a history of breast cancer and in women at increased risk for hormonally sensitive malignancies, such as those with mutations in BRCA genes.
- The use of estrogen alone and estrogen plus progestin has been reported to result in an increase in abnormal mammograms requiring further evaluation. Surveillance measures, such as breast examinations and regular mammography, are recommended. Discontinue ORIAHNN if a hormonally sensitive malignancy is diagnosed.

Suicidal Ideation, Suicidal Behavior, and Exacerbation of Mood Disorders

- Depression, depressed mood, and/or tearfulness were reported at a higher incidence in women taking ORIAHNN (3%) compared with placebo (1%) in the Phase 3 clinical trials. Suicidal ideation and behavior, including a completed suicide, occurred in women treated with lower doses of elagolix in clinical trials conducted for a different indication.
- 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 ORIAHNN if such events occur.

Please see accompanying Full Prescribing Information.

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elagolix, estradiol and norethindrone acetate capsules and elagolix capsules 300 mg/1 mg/0.5 mg and 300 mg

IMPORTANT SAFETY INFORMATION[3] (cont'd)

Hepatic Impairment and Transaminase Elevations

- ORIAHNN is contraindicated in women with known hepatic impairment or disease.
- Transaminase elevations in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) occurred with ORIAHNN in Phase 3 clinical trials. No pattern in time to onset of these liver transaminase elevations was identified. Transaminase levels returned to baseline within 4 months after peak values in these patients.
- Instruct patients to promptly seek medical attention in case of symptoms or signs that may reflect liver injury, such as jaundice.

Elevated Blood Pressure

- ORIAHNN is contraindicated in women with uncontrolled hypertension. Maximum mean increases in systolic blood pressure occurred at Month 5, and a mean maximum increase in diastolic blood pressure occurred at Month 4 in ORIAHNN-treated women, as compared to placebo-treated women.
- For women with well-controlled hypertension, continue to monitor blood pressure and stop ORIAHNN if blood pressure rises significantly. Monitor blood pressure in normotensive women treated with ORIAHNN.

Gallbladder Disease or History of Cholestatic Jaundice

- Studies among estrogen users suggest a small increased relative risk of developing gallbladder disease. For women with a history of cholestatic jaundice associated with past estrogen use or with pregnancy, assess the risk-benefit of continuing therapy. Discontinue ORIAHNN if jaundice occurs.

Change in Menstrual Bleeding Pattern and Reduced Ability to Recognize Pregnancy

- ORIAHNN may delay the ability to recognize the occurrence of a pregnancy because it may reduce the intensity, duration, and amount of menstrual bleeding. Perform pregnancy testing if pregnancy is suspected and discontinue ORIAHNN if pregnancy is confirmed.
- The effect of hormonal contraceptives on the efficacy of ORIAHNN is unknown. Advise women to use non-hormonal contraception during treatment and for 1 week after discontinuing ORIAHNN.

Effects on Carbohydrate and Lipid Metabolism

- ORIAHNN may decrease glucose tolerance and result in increased glucose levels. More frequent monitoring in ORIAHNN-treated women with prediabetes and diabetes may be needed.
- In women with preexisting hypertriglyceridemia, estrogen therapy may be associated with elevations of plasma triglycerides leading to pancreatitis. Use of elagolix is associated with increases in total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and serum triglycerides. Monitor lipid levels and consider discontinuing ORIAHNN if hypercholesterolemia or hypertriglyceridemia worsens.

Alopecia

- In Phase 3 clinical trials, more women experienced alopecia, hair loss, and hair thinning with ORIAHNN (3.5%) compared to placebo (1.0%). In almost one-third of affected ORIAHNN-treated women, alopecia was the reason for discontinuing treatment. No specific pattern was described. In the majority of these women, hair loss was continuing when ORIAHNN was stopped. Whether the hair loss is reversible is unknown. Consider discontinuing ORIAHNN if hair loss becomes a concern.

Effect on Other Laboratory Results

- The use of estrogen and progestin combinations may raise serum concentrations of binding proteins (e.g., thyroid-binding globulin, corticosteroid-binding globulin), which may reduce the free thyroid or corticosteroid hormone levels. Patients with hypothyroidism and hypoadrenalism may require higher doses of thyroid hormone or cortisol replacement therapy, respectively.
- The use of estrogen and progestin may also affect the levels of sex hormone-binding globulin, coagulation factors, lipids, and glucose.

RISK OF ALLERGIC REACTIONS DUE TO THE INACTIVE INGREDIENT (FD&C YELLOW NO. 5)

- ORIAHNN contains FD&C Yellow No. 5 (tartrazine), which may cause allergic-type reactions (including bronchial asthma) in certain susceptible persons. Although the overall incidence of FD&C Yellow No. 5 (tartrazine) sensitivity in the general population is low, it is frequently seen in patients who also have aspirin hypersensitivity.

ADVERSE REACTIONS

- Most common adverse reactions occurring in ≥5% of women receiving ORIAHNN in clinical trials were hot flush, headache, fatigue, and metrorrhagia.

These are not all of the possible side effects of ORIAHNN.

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

Please see accompanying Full Prescribing Information.

Oriahnn™
elagolix, estradiol and norethindrone acetate capsules and elagolix capsules 300 mg/1 mg/0.5 mg and 300 mg

REFERENCES

1. ICD-9-CM diagnosis and procedure codes: abbreviated and full code titles. Centers for Disease Control and Prevention website. https://www.cms.gov/Medicare/Coding/ICD9ProviderDiagnosticCodes/codes. Accessed April 2, 2020. **2.** ICD-10-CM tabular list of diseases and injuries. Centers for Disease Control and Prevention website. https://www.cdc.gov/nchs/icd/icd10cm.htm. Accessed February 27, 2020. **3.** ORIAHNN [package insert]. North Chicago, IL: AbbVie Inc; 2020.

Please see Important Safety Information, including **BOXED WARNING on THROMBOEMBOLIC AND VASCULAR EVENTS**, on pages 2-3 and please see accompanying Full Prescribing Information.

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Oriahnn™
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ORIAHNN PRIOR AUTHORIZATION CONSIDERATIONS

INDICATION[1]

ORIAHNN™ (elagolix, estradiol, and norethindrone acetate capsules; elagolix capsules) is indicated for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women. Use of ORIAHNN should be limited to 24 months due to the risk of continued bone loss, which may not be reversible.

SAFETY CONSIDERATIONS[1]

Estrogen and progestin combinations, including ORIAHNN, increase the risk of thrombotic or thromboembolic disorders, including pulmonary embolism, deep vein thrombosis, stroke, and myocardial infarction, especially in women at increased risk for these events.

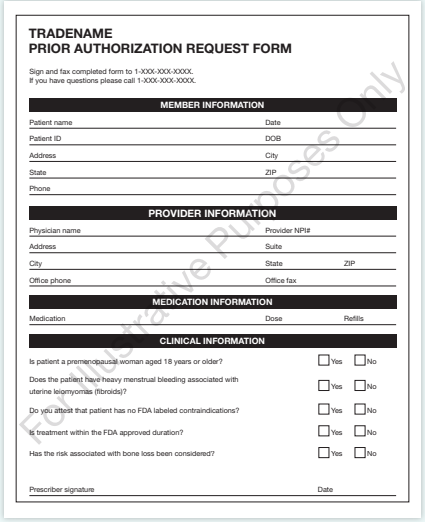
ORIAHNN is contraindicated in women with current or a history of thrombotic or thromboembolic disorders and in women at increased risk for these events, including women over 35 years of age who smoke and women with uncontrolled hypertension.

- ORIAHNN is contraindicated in women who are at a high risk of arterial, venous thrombotic, or thromboembolic disorders; who are pregnant; with known osteoporosis; current or history of breast cancer or other hormonally sensitive malignancies; known hepatic impairment or disease; undiagnosed abnormal uterine bleeding; known anaphylactic reaction, angioedema, or hypersensitivity to ingredients of ORIAHNN; or with concomitant use of organic anion transporting polypeptide (OATP) 1B1 inhibitors that are known or expected to significantly increase elagolix plasma concentrations.
- Discontinue ORIAHNN if an arterial or venous thrombotic, cardiovascular, or cerebrovascular event occurs. If feasible, discontinue ORIAHNN at least 4 to 6 weeks before surgery of the type associated with an increased risk of thromboembolism, or during periods of prolonged immobilization. Stop ORIAHNN if there is sudden, unexplained partial or complete loss of vision, proptosis, diplopia, papilledema, or retinal vascular lesions and evaluate for retinal vein thrombosis immediately.
- ORIAHNN may cause a decrease in bone mineral density (BMD), which is greater with increasing duration of use and may not be completely reversible after stopping treatment. Assessment of BMD by dual-energy X-ray absorptiometry (DXA) is recommended at baseline and periodically thereafter. Limit the duration of use to 24 months to reduce the extent of bone loss.
- ORIAHNN should not be used in women with current or a history of breast cancer and in women at increased risk for hormonally sensitive malignancies, such as those with mutations in BRCA genes. Discontinue ORIAHNN if a hormonally sensitive malignancy is diagnosed.
- Depression, depressed mood, and/or tearfulness have occurred in women taking ORIAHNN. Advise patients to seek medical attention for suicidal ideation, suicidal behavior, new onset or worsening depression, anxiety, or other mood changes.
- ORIAHNN may delay the ability to recognize the occurrence of a pregnancy, as it may reduce the intensity, duration, and amount of menstrual bleeding. Discontinue ORIAHNN if pregnancy is confirmed.
- Alopecia, hair loss, and hair thinning have occurred with ORIAHNN. No specific pattern was described. Whether the hair loss is reversible is unknown. Consider discontinuing ORIAHNN if hair loss becomes a concern.
- The following events/conditions were either reported in clinical trials of ORIAHNN and/or may be potentially caused or exacerbated by the estrogen and progestin components in ORIAHNN: transaminase elevations, an increase in blood pressure, an increased risk of developing gallbladder disease, diabetes mellitus, hereditary angioedema, adverse lipid changes, and change in the results of some laboratory tests such as coagulation factors, lipids, glucose tolerance, and binding proteins.
- ORIAHNN contains FD&C Yellow No. 5 (tartrazine), which may cause allergic-type reactions (including bronchial asthma) in certain susceptible persons.

Please see additional Important Safety Information, including **BOXED WARNING on THROMBOEMBOLIC AND VASCULAR EVENTS**, on pages 4-5 and please see accompanying Full Prescribing Information.

SAMPLE PRIOR AUTHORIZATION

If your plan assesses that a prior authorization (PA) is necessary for ORIAHNN, this sample form reflects possible criteria aligned to the label.



TRADENAME
PRIOR AUTHORIZATION REQUEST FORM

Sign and fax completed form to 1-XXX-XXX-XXXX.
If you have questions please call 1-XXX-XXX-XXXX.

MEMBER INFORMATION

Patient name | Date
Patient ID | DOB
Address | City
State | ZIP
Phone

PROVIDER INFORMATION

Physician name | Provider NPI#
Address | Suite
City | State | ZIP
Office phone | Office fax

MEDICATION INFORMATION

Medication | Dose | Refills

CLINICAL INFORMATION

Is patient a premenopausal woman aged 18 years or older? ☐Yes ☐No
Does the patient have heavy menstrual bleeding associated with uterine leiomyomas (fibroids)? ☐Yes ☐No
Do you attest that patient has no FDA labeled contraindications? ☐Yes ☐No
Is treatment within the FDA approved duration? ☐Yes ☐No
Has the risk associated with bone loss been considered? ☐Yes ☐No

Prescriber signature | Date

The content below and on the following pages provide additional information on the sample clinical criteria and label considerations.

PA CONSIDERATIONS

ORIAHNN is an oral medication specifically approved for heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women. Use of ORIAHNN should be limited to 24 months due to the risk of continued bone loss, which may not be reversible.[1] The patient population should be consistent with the label. PA language may include **physician attestation** of the following:

Patient age

The safety and efficacy of ORIAHNN was studied in two 6-month, randomized, double-blind, placebo-controlled trials with **790 premenopausal women aged ≥18 years**. The safety and effectiveness of ORIAHNN in patients aged <18 years have not been established.[1,2]

Uterine fibroids diagnosis

Uterine fibroids are often **detected by the presentation of symptoms**, such as heavy menstrual bleeding, during routine pelvic exams or incidentally during imaging. Imaging techniques, such as ultrasonography, can also be used for the detection and evaluation of uterine fibroids.[3,4]

SAFETY CONSIDERATIONS[1]

Estrogen and progestin combinations, including ORIAHNN, increase the risk of thrombotic or thromboembolic disorders, including pulmonary embolism, deep vein thrombosis, stroke, and myocardial infarction, especially in women at increased risk for these events.

ORIAHNN is contraindicated in women with current or a history of thrombotic or thromboembolic disorders and in women at increased risk for these events, including women over 35 years of age who smoke and women with uncontrolled hypertension.

Please see additional Important Safety Information, including **BOXED WARNING on THROMBOEMBOLIC AND VASCULAR EVENTS**, on pages 4-5 and please see accompanying Full Prescribing Information.

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PA CONSIDERATIONS (cont'd)

ORIAHNN is an oral medication specifically approved for heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women. Use of ORIAHNN should be limited to 24 months due to the risk of continued bone loss, which may not be reversible.[1] The patient population should be consistent with the label. PA language may include **physician attestation** of the following:

Heavy menstrual bleeding

Heavy menstrual bleeding is a common symptom of uterine fibroids and may often be a driver for treatment.[5,6] In clinical trials, menstrual blood loss was assessed by the alkaline hematin method. This method is **not typical of or practical for real-world practice**.[1,7] The physician should determine whether or not their patient is experiencing heavy menstrual bleeding.

FDA-labeled contraindications for ORIAHNN do not preclude the patient

Physicians should be aware of the contraindications and known risks of prescribing ORIAHNN in those patient populations.

ORIAHNN is contraindicated in women at a high risk of arterial, venous thrombotic, or thromboembolic disorders; who are pregnant; with known osteoporosis; current or history of breast cancer or other hormonally sensitive malignancies; known hepatic impairment or disease; undiagnosed abnormal uterine bleeding; known anaphylactic reaction, angioedema, or hypersensitivity to ingredients of ORIAHNN; or with concomitant use of organic anion transporting polypeptide 1B1 inhibitors that are known or expected to significantly increase elagolix plasma concentrations.[1]

Label-consistent authorization period

The prescription should not exceed the label treatment duration of **24 months** due to the risk of continued bone loss, which may not be reversible.[1]

Bone loss considerations

Consider the benefits and risks of ORIAHNN treatment in patients with a history of a low-trauma fracture or other risk factors for osteoporosis or bone loss. Assessment of BMD by dual-energy X-ray absorptiometry is recommended at baseline and periodically thereafter.[1] There are currently no guidelines available for BMD assessment in women taking ORIAHNN. There are very limited guidelines available that speak to BMD assessment in premenopausal women.[8] **Healthcare providers should use their clinical judgment to determine when to perform the recommended DXA scans for their patients taking ORIAHNN**.

DXA=dual-energy X-ray absorptiometry; FDA=US Food and Drug Administration.

SAFETY CONSIDERATIONS[1]

ORIAHNN may cause a decrease in bone mineral density (BMD), which is greater with increasing duration of use and may not be completely reversible after stopping treatment. Assessment of BMD by dual-energy X-ray absorptiometry (DXA) is recommended at baseline and periodically thereafter. Limit the duration of use to 24 months to reduce the extent of bone loss.

Please see additional Important Safety Information, including **BOXED WARNING on THROMBOEMBOLIC AND VASCULAR EVENTS**, on pages 4-5 and please see accompanying Full Prescribing Information.

Oriahnn™
elagolix, estradiol and norethindrone acetate capsules and elagolix capsules 300 mg/1 mg/0.5 mg and 300 mg

IMPORTANT SAFETY INFORMATION FOR ORIAHNN

INDICATION[1]

ORIAHNN™ (elagolix, estradiol, and norethindrone acetate capsules; elagolix capsules) is indicated for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women. Use of ORIAHNN should be limited to 24 months due to the risk of continued bone loss, which may not be reversible.

IMPORTANT SAFETY INFORMATION[1]

THROMBOEMBOLIC AND VASCULAR EVENTS

Estrogen and progestin combinations, including ORIAHNN, increase the risk of thrombotic or thromboembolic disorders, including pulmonary embolism, deep vein thrombosis, stroke, and myocardial infarction, especially in women at increased risk for these events.

ORIAHNN is contraindicated in women with current or a history of thrombotic or thromboembolic disorders and in women at increased risk for these events, including women over 35 years of age who smoke and women with uncontrolled hypertension.

CONTRAINDICATIONS

- ORIAHNN is contraindicated in women at a high risk of arterial, venous thrombotic, or thromboembolic disorders; who are pregnant; with known osteoporosis; current or history of breast cancer or other hormonally sensitive malignancies; known hepatic impairment or disease; undiagnosed abnormal uterine bleeding; known anaphylactic reaction, angioedema, or hypersensitivity to ingredients of ORIAHNN; or with concomitant use of organic anion transporting polypeptide (OATP) 1B1 inhibitors that are known or expected to significantly increase elagolix plasma concentrations.

WARNINGS AND PRECAUTIONS

Thromboembolic Disorders and Vascular Events

- ORIAHNN is contraindicated in women with current or a history of thrombotic or thromboembolic disorders and in women at increased risk for these events. Components of ORIAHNN increase the risk of thrombotic or thromboembolic disorders, including pulmonary embolism, deep vein thrombosis, stroke, and myocardial infarction, especially in women at high risk for these events. In general, the risk is greatest among women over 35 years of age who smoke, and women with uncontrolled hypertension, dyslipidemia, vascular disease, or obesity.
- Discontinue ORIAHNN if an arterial or venous thrombotic, cardiovascular, or cerebrovascular event occurs. If feasible, discontinue ORIAHNN at least 4 to 6 weeks before surgery of the type associated with an increased risk of thromboembolism, or during periods of prolonged immobilization. Stop ORIAHNN if there is sudden, unexplained partial or complete loss of vision, proptosis, diplopia, papilledema, or retinal vascular lesions and evaluate for retinal vein thrombosis immediately.

Bone Loss

- ORIAHNN is contraindicated in women with known osteoporosis. ORIAHNN may cause a decrease in bone mineral density (BMD) in some patients, which is greater with increasing duration of use and may not be completely reversible after stopping treatment.
- The impact of ORIAHNN-associated decreases in BMD on long-term bone health and future fracture risk is unknown. Consider the benefits and risks of ORIAHNN in patients with a history of low-trauma fracture or other risk factors for osteoporosis or bone loss, including those taking medications that may decrease BMD (e.g., systemic or chronic inhaled corticosteroids, anticonvulsants, or proton pump inhibitors).
- Assessment of BMD by dual-energy X-ray absorptiometry (DXA) is recommended at baseline and periodically thereafter. Consider discontinuing ORIAHNN if the risk associated with bone loss exceeds the potential benefit of treatment. Limit the duration of use to 24 months to reduce the extent of bone loss.

Hormonally Sensitive Malignancies

- ORIAHNN is contraindicated in women with current or a history of breast cancer and in women at increased risk for hormonally sensitive malignancies, such as those with mutations in BRCA genes.
- The use of estrogen alone and estrogen plus progestin has been reported to result in an increase in abnormal mammograms requiring further evaluation. Surveillance measures, such as breast examinations and regular mammography, are recommended. Discontinue ORIAHNN if a hormonally sensitive malignancy is diagnosed.

Suicidal Ideation, Suicidal Behavior, and Exacerbation of Mood Disorders

- Depression, depressed mood, and/or tearfulness were reported at a higher incidence in women taking ORIAHNN (3%) compared with placebo (1%) in the Phase 3 clinical trials. Suicidal ideation and behavior, including a completed suicide, occurred in women treated with lower doses of elagolix in clinical trials conducted for a different indication.
- 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 ORIAHNN if such events occur.

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IMPORTANT SAFETY INFORMATION FOR ORIAHNN[1] (cont'd)

Hepatic Impairment and Transaminase Elevations

- ORIAHNN is contraindicated in women with known hepatic impairment or disease.
- Transaminase elevations in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) occurred with ORIAHNN in Phase 3 clinical trials. No pattern in time to onset of these liver transaminase elevations was identified. Transaminase levels returned to baseline within 4 months after peak values in these patients.
- Instruct patients to promptly seek medical attention in case of symptoms or signs that may reflect liver injury, such as jaundice.

Elevated Blood Pressure

- ORIAHNN is contraindicated in women with uncontrolled hypertension. Maximum mean increases in systolic blood pressure occurred at Month 5, and a mean maximum increase in diastolic blood pressure occurred at Month 4 in ORIAHNN-treated women, as compared to placebo-treated women.
- For women with well-controlled hypertension, continue to monitor blood pressure and stop ORIAHNN if blood pressure rises significantly. Monitor blood pressure in normotensive women treated with ORIAHNN.

Gallbladder Disease or History of Cholestatic Jaundice

- Studies among estrogen users suggest a small increased relative risk of developing gallbladder disease. For women with a history of cholestatic jaundice associated with past estrogen use or with pregnancy, assess the risk-benefit of continuing therapy. Discontinue ORIAHNN if jaundice occurs.

Change in Menstrual Bleeding Pattern and Reduced Ability to Recognize Pregnancy

- ORIAHNN may delay the ability to recognize the occurrence of a pregnancy because it may reduce the intensity, duration, and amount of menstrual bleeding. Perform pregnancy testing if pregnancy is suspected and discontinue ORIAHNN if pregnancy is confirmed.
- The effect of hormonal contraceptives on the efficacy of ORIAHNN is unknown. Advise women to use non-hormonal contraception during treatment and for 1 week after discontinuing ORIAHNN.

Effects on Carbohydrate and Lipid Metabolism

- ORIAHNN may decrease glucose tolerance and result in increased glucose levels. More frequent monitoring in ORIAHNN-treated women with prediabetes and diabetes may be needed.
- In women with preexisting hypertriglyceridemia, estrogen therapy may be associated with elevations of plasma triglycerides leading to pancreatitis. Use of elagolix is associated with increases in total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and serum triglycerides. Monitor lipid levels and consider discontinuing ORIAHNN if hypercholesterolemia or hypertriglyceridemia worsens.

Alopecia

- In Phase 3 clinical trials, more women experienced alopecia, hair loss, and hair thinning with ORIAHNN (3.5%) compared to placebo (1.0%). In almost one-third of affected ORIAHNN-treated women, alopecia was the reason for discontinuing treatment. No specific pattern was described. In the majority of these women, hair loss was continuing when ORIAHNN was stopped. Whether the hair loss is reversible is unknown. Consider discontinuing ORIAHNN if hair loss becomes a concern.

Effect on Other Laboratory Results

- The use of estrogen and progestin combinations may raise serum concentrations of binding proteins (e.g., thyroid-binding globulin, corticosteroid-binding globulin), which may reduce the free thyroid or corticosteroid hormone levels. Patients with hypothyroidism and hypoadrenalism may require higher doses of thyroid hormone or cortisol replacement therapy, respectively.
- The use of estrogen and progestin may also affect the levels of sex hormone-binding globulin, coagulation factors, lipids, and glucose.

RISK OF ALLERGIC REACTIONS DUE TO THE INACTIVE INGREDIENT (FD&C YELLOW NO. 5)

- ORIAHNN contains FD&C Yellow No. 5 (tartrazine), which may cause allergic-type reactions (including bronchial asthma) in certain susceptible persons. Although the overall incidence of FD&C Yellow No. 5 (tartrazine) sensitivity in the general population is low, it is frequently seen in patients who also have aspirin hypersensitivity.

ADVERSE REACTIONS

- Most common adverse reactions occurring in ≥5% of women receiving ORIAHNN in clinical trials were hot flush, headache, fatigue, and metrorrhagia.

These are not all of the possible side effects of ORIAHNN.

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

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REFERENCES

1. ORIAHNN [package insert]. North Chicago, IL: AbbVie Inc; 2020. **2.** Schlaff WD, Ackerman RT, Al-Hendy A, et al. Elagolix for heavy menstrual bleeding in women with uterine fibroids. *N Engl J Med*. 2020;382(4):328-340. **3.** De La Cruz MS, Buchanan EM. Uterine fibroids: diagnosis and treatment. *Am Fam Physician*. 2017;95(2):100-107. **4.** Uterine fibroids. American College of Obstetricians and Gynecologists website. https://www.acog.org/patient-resources/faqs/gynecologic-problems/uterine-fibroids. Accessed March 27, 2020. **5.** Stewart EA, Laughlin-Tommasco SK, Catherino WH, Lalikumar S, Gupta D, Vollenhoven B. Uterine fibroids. *Nat Rev Dis Primers*. 2016;2:16043. **6.** Marsh EE, Al-Hendy A, Kappus D, Galitsky A, Stewart EA, Kerolous M. Burden, prevalence, and treatment of uterine fibroids: a survey of US women. *J Womens Health (Larchmt)*. 2018;27(11):1359-1367. **7.** Herman MC, Mol BW, Bongers MY. Diagnosis of heavy menstrual bleeding. *Womens Health (Lond)*. 2016;12(1):15-20. **8.** The International Society for Clinical Densitometry. *2019 ISCD Official Positions: Adult*. https://www.iscd.org/official-positions/2019-iscd-official-positions-adult/. Accessed June 5, 2020.

ORIAHNN is an oral medication specifically approved for the management of heavy menstrual bleeding associated with uterine leiomyomas (fibroids) in premenopausal women. Use of ORIAHNN should be limited to 24 months due to the risk of continued bone loss, which may not be reversible.[1]

In order to ensure timely access to treatment, PA criteria should align with FDA-approved labeling.

SAFETY CONSIDERATIONS[1]

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