

BENEFITS AND RISKS OF HORMONE THERAPY

This tool, designed for primary care physicians, pharmacists and nurses, was developed to promote discussions on the topic of hormone therapy for the management of clinical manifestations associated with perimenopause and postmenopause. It is provided solely for information purposes and does not seek to replace the judgement of healthcare professionals. This document is based on the INESSS' systematic review of the scientific literature, available on the Web site inesss.qc.ca.

KEY POINTS TO DISCUSS WITH WOMEN

The management of clinical manifestations associated with perimenopause or postmenopause do not systemically require treatment. However, the women who report experiencing clinical manifestations with a significant impact on their quality of life could benefit from a therapeutic approach, and more specifically, hormone therapy.

SHARED DECISION-MAKING

The decision as to whether or not hormone therapy should be initiated depends on existing scientific knowledge, as well as the values and preferences of the woman in question regarding the various available options for the management of clinical manifestations.

If hormone therapy is being considered, the benefits and risks of treatment will need to be discussed with the woman in question, to identify the best option in this regard.

SYSTEMIC HORMONE THERAPY OPTIONS

Hormones labelled as bioidentical	Classical hormones	Other hormonal agents
The molecule's structure is identical to that of the hormones produced by the human body (17β-estradiol, micronized progesterone).	The molecule's structure is different than that of the hormones produced by the human body (conjugated estrogens, medroxyprogesterone acetate and other progestins).	Agents with a different mechanism of action (tibolone, bazedoxifene combined with conjugated estrogens).
All of the systemic hormone therapy options are manufactured in a laboratory setting.		

SCIENTIFIC DATA

The data analyzed mainly concerns postmenopausal women. Very few studies have included women in the perimenopausal stage.

Very few analyses were carried out on individual molecules and administration routes (oral 17β-estradiol, transdermal 17β-estradiol) and the ensuing level of evidence is generally low or very low.

Quantitative results concerning benefits and risks are included in the statements when available. Absolute risks are calculated when baseline risks are known. The baseline risk corresponds to the likelihood of instances of a given event occurring in the comparison group population.

This document provides a recap of the main scientific data available on systemic hormone therapy gathered as at March 2024. The benefits and risks of topical hormone therapy to address clinical manifestations of genitourinary syndrome of menopause (GSM) have not been analyzed.

View the [report](#) to learn more.

LEVEL OF EVIDENCE

The findings with regard to the benefits and risks of hormone therapy discussed in this tool are graded according to the GRADE approach (Grades of Recommendations, Assessment, Development and Evaluation):


- **High (⊕⊕⊕⊕):** The evidence-based data analysed constitutes a very good indication of the estimated effect. There is a very low likelihood that the actual effect would be markedly different from the estimated effect.
- **Moderate (⊕⊕⊕⊖):** The evidence-based data analysed constitutes a good indication of the estimated effect. There is a moderate likelihood that the actual effect would be markedly different from the estimated effect.
- **Low (⊕⊕⊖⊖):** The evidence-based data analysed constitutes an indication of the estimated effect. There is a high likelihood that the actual effect would be markedly different from the estimated effect.
- **Very low (⊕⊖⊖⊖):** The evidence-based data does not constitute a reliable indication of the estimated effect. There is a very high likelihood that the actual effect would be markedly different from the estimated effect.

SUMMARY



- Key points to discuss with women 1
- Scientific data 1
- List of topics by type of hormone therapy. 2
- Combined hormone therapy 3
- Estrogen-only hormone therapy 11
- Tibolone 17
- Bazedoxifene/conjugated estrogens 21
- Micronized progesterone only 22

LIST OF TOPICS BY TYPE OF HORMONE THERAPY

Click on a topic to go to the corresponding page. 

COMBINED HORMONE THERAPY	ESTROGEN-ONLY HORMONE THERAPY	TIBOLONE	BAZEDOXIFENE/CONJUGATED ESTROGENS	MICRONIZED PROGESTERONE ONLY
<ul style="list-style-type: none"> Alzheimer's disease Breast cancer Colorectal cancer Dementia Emotional instability Endometrial cancer Fractures Gallbladder diseases Hot flashes Joint pain Libido, desire and sexual function Mortality (all cause combined) Mortality (cardiovascular cause) Mortality linked to breast cancer Myocardial infarction Night sweats Ovarian cancer Skin aging Sleep disorders Stroke Symptoms of anxiety Symptoms of depression Thinning hair and hair loss Type 2 diabetes Venous thrombo-embolism Weight gain 	<ul style="list-style-type: none"> Alzheimer's disease Breast cancer Colorectal cancer Dementia Emotional instability Fractures Gallbladder diseases Hot flashes Joint pain Libido, desire and sexual function Mortality (all cause combined) Mortality (cardiovascular cause) Mortality linked to breast cancer Myocardial infarction Night sweats Ovarian cancer Skin aging Sleep disorders Stroke Symptoms of anxiety Symptoms of depression Thinning hair and hair loss Type 2 diabetes Venous thrombo-embolism Weight gain 	<ul style="list-style-type: none"> Alzheimer's disease Breast cancer Colorectal cancer Dementia Emotional instability Endometrial cancer Fractures Gallbladder diseases Hot flashes Joint pain Libido, desire and sexual function Mortality (all cause combined) Mortality (cardiovascular cause) Mortality linked to breast cancer Myocardial infarction Night sweats Ovarian cancer Skin aging Sleep disorders Stroke Symptoms of anxiety Symptoms of depression Thinning hair and hair loss Type 2 diabetes Venous thrombo-embolism Weight gain 	<ul style="list-style-type: none"> Alzheimer's disease Breast cancer Colorectal cancer Dementia Emotional instability Endometrial cancer Fractures Gallbladder diseases Hot flashes Joint pain Libido, desire and sexual function Mortality (all cause combined) Mortality (cardiovascular cause) Mortality linked to breast cancer Myocardial infarction Night sweats Ovarian cancer Skin aging Sleep disorders Stroke Symptoms of anxiety Symptoms of depression Thinning hair and hair loss Type 2 diabetes Venous thrombo-embolism Weight gain 	<ul style="list-style-type: none"> Alzheimer's disease Breast cancer Colorectal cancer Dementia Emotional instability Endometrial cancer Fractures Gallbladder diseases Hot flashes Joint pain Libido, desire and sexual function Mortality (all cause combined) Mortality (cardiovascular cause) Mortality linked to breast cancer Myocardial infarction Night sweats Ovarian cancer Skin aging Sleep disorders Stroke Symptoms of anxiety Symptoms of depression Thinning hair and hair loss Type 2 diabetes Venous thrombo-embolism Weight gain

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- Combined hormone therapy
- Estrogen-only hormone therapy
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- Micronized progesterone only

Unless otherwise indicated, the effects are observed in **postmenopausal women**.

	COMBINED HORMONE THERAPY (LABELLED AS BIOIDENTICAL) 17β-estradiol combined with a micronized progesterone <i>Unless otherwise indicated</i>	COMBINED HORMONE THERAPY (CLASSICAL) Conjugated estrogens combined with MPA <i>Unless otherwise indicated</i>
Hot flashes	Transdermal route for the past 3 months:	Used for the past 12 months:
	<ul style="list-style-type: none"> Relative decrease of around 68% in the severity of moderate to severe hot flashes, compared to 36% for the placebo. ⊕⊕○○ No difference with the effect of conjugated estrogens combined with micronized progesterone on the severity of moderate to severe hot flashes. ⊕⊕○○ 	<ul style="list-style-type: none"> Relative decrease of around 94% in the number of moderate to severe hot flashes, compared to 66% for the placebo. ⊕⊕○○ Significant decrease in the severity of moderate to severe hot flashes, compared to the placebo. ⊕⊕○○ to ⊕⊕⊕○
	Combined with a progestin other than MPA:	
	<ul style="list-style-type: none"> Decrease in the average number of moderate to severe hot flashes per day, i.e., around 10, compared to 6 per day for the placebo. ⊕⊕○○ 	
	Oral route for the past 3 months:	
	<ul style="list-style-type: none"> Relative decrease of around 68% to 73% in the average number of moderate to severe hot flashes, depending on the dose, compared to 52% for the placebo. ⊕⊕⊕○ Decrease in the severity of moderate to severe hot flashes, compared to the placebo. ⊕⊕⊕○ 	
Night sweats	Transdermal route for the past 3 months:	Used for the past 12 months:
	<ul style="list-style-type: none"> Relative decrease of around 68% in the intensity of night sweats, compared to 44% for the placebo. ⊕⊕○○ No difference with the effect of conjugated estrogens, when both are combined with micronized progesterone. ⊕○○○ Frequency of night sweats. ⊖ 	<ul style="list-style-type: none"> Significant decrease in the frequency and intensity of night sweats, compared to the placebo. ⊕⊕⊕○
	Oral route:	
	⊖	
Joint pain	⊖	Used for the past 12 months:
		<ul style="list-style-type: none"> Increase in relief from and decrease of the prevalence of moderate to severe joint pain, compared to the placebo. ⊕⊕⊕○
Libido, desire and sexual function	Transdermal route for the past 18 months:	Used for the past 4 months:
	<ul style="list-style-type: none"> Improvement in sexual function, compared to the placebo. ⊕⊕⊕○ 	<ul style="list-style-type: none"> Improvement in the level of interest in sexual relations, compared to the placebo. ⊕⊕⊕○
	Oral route:	Used for the past 6 months:
	⊖	<ul style="list-style-type: none"> No difference with the effect of a placebo on sexual function. ⊕○○○

Summary

Combined hormone therapy

Estrogen-only hormone therapy

Tibolone

Bazedoxifene/ conjugated estrogens

Micronized progesterone only

LEGEND

MPA = medroxyprogesterone acetate Hormone therapy effect: ● Benefit ● No observed effect ● Increased risk ⊖ No data available in the literature reviewed

Level of evidence: High ⊕⊕⊕⊕ Moderate ⊕⊕⊕○ Low ⊕⊕○○ Very low ⊕○○○

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Sleep disorders	Transdermal route for the past 4 years: ● Improvement in sleep quality, compared to the placebo. ⊕⊕⊕○ ● No difference with the effect of conjugated estrogens combined with MPA on sleep quality. ⊕⊕⊕○	Used for the past 12 months: ● Improvement in sleep quality, compared to the placebo. ⊕⊕⊕○
	Voie orale ⊖	
Emotional instability	⊖ Irritability and general symptoms of emotional instability.	Used for the past 4 to 12 months: ● No difference with the effect of a placebo on general symptoms of emotional instability. ⊕⊕○○ to ⊕⊕⊕○
		Used for the past 12 to 60 months: ● No difference with the effect of a placebo on symptoms of irritability. ⊕⊕○○
Symptoms of anxiety	♀♂ Transdermal route for the past 4 years: ● No difference with the effect of a placebo. ⊕⊕⊕○	Used for the past 5 years: ● No difference with the effect of a placebo or in the absence of hormone therapy. ⊕○○○
	Oral route for the past 3 to 12 months, combined with a progestin other than MPA: ● Improvement in symptoms of anxiety, compared to a placebo. ⊕○○○	
Symptoms of depression	♀♂ Transdermal route for the past 2 years: ● No difference with the effect in the absence of hormone therapy. ⊕⊕⊕○	Used for the past 12 months: ● No difference with the effect of a placebo. ⊕⊕⊕○
	Oral or transdermal route, combined with a progestogen: ● No difference with the effect of a placebo among women aged 65 years or more. ⊕○○○	
	Oral route, combined with norethindrone: ● <i>For the past 3 months, among women with no history of depression:</i> No difference with the effect of a placebo. ⊕⊕○○ ● <i>For the past 12 months:</i> Decrease in symptoms of depression, compared to the effect of the placebo, among women in the postmenopausal stage for 2 years or less. ⊕○○○	
Skin aging	⊖	⊖
Thinning hair and hair loss	⊖	⊖

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♀♂: Effect observed in perimenopausal and postmenopausal women

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Weight gain	Transdermal route: ⊖	Used for the past 2 years ● No difference with the effect of a placebo. ⊕⊕⊕⊕
	Oral route for the past 12 months, combined with micronized progesterone: ● <i>Dose of 0.5/100 mg/day:</i> Increase in body weight, compared to the placebo. ⊕⊕⊕⊕ ● <i>Dose of 1.0/100 mg/day:</i> No difference with the effect of a placebo. ⊕⊕⊕⊕	
Type 2 diabetes	Voie transdermique, usage actuel: ● - 20 cases out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 4 years. <i>Baseline risk: 42 cases out of 1,000</i> ⊕⊕⊕⊕	Current use: ● - 9 to 18 cases out of 1,000 women treated, compared to the effect of a placebo or the absence of hormone therapy, follow-up over an average period of 5 years or undefined. <i>Baseline risk: 48 to 49 cases out of 1,000, depending on the duration of the follow-up.</i> ⊕⊕⊕⊕
	Oral route: ⊖	
Fractures (all sites)	⊖	Ever use: ● - 29 cases out of 1,000 women treated, compared to the effect of a placebo, follow-up over an average period of 8 years. <i>Baseline risk: 154 cases out of 1,000</i> ⊕⊕⊕⊕
		Current use: ● - 20 cases out of 1,000 women treated, compared to the effect of a placebo or the absence of hormone therapy, follow-up over an average period of 1 to 5 years. <i>Baseline risk: 79 cases out of 1,000.</i> ⊕⊕⊕⊕
		● No difference with the effect in the absence of hormone therapy, follow-up over an average period of 10 years. ⊕⊕⊕⊕
Stroke	♀♂ Transdermal route, current use: ● No difference with the effect in the absence of hormone therapy, follow-up over an average period of 7 years. ⊕○○○	Current use: ● + 3 cases out of 1,000 women treated, compared to the effect of a placebo, follow-up over an average period of 3 to 5 years. <i>Baseline risk: 9 cases out of 1,000</i> ⊕⊕⊕⊕
	Oral route: ⊖	
		Age at the initiation of treatment, current use: <i>Between 50 – 59 years OR between 70 – 79 years</i> ● No difference with the effect in the absence of hormone therapy, follow-up over an average period of 5 years. ⊕○○○ <i>Between 60 – 69 years</i> ● 78% increase in the risk of a stroke, compared to the increase with a placebo, follow-up over an average period of 5 years. ⊕⊕⊕⊕

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Level of evidence: High ⊕⊕⊕⊕ Moderate ⊕⊕⊕⊕ Low ⊕⊕○○ Very low ⊕○○○ ♀♂ Effect observed in perimenopausal and postmenopausal women

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Myocardial infarction	Transdermal route, current use: ● No difference with the effect in the absence of hormone therapy, follow-up over an average period of 7 years. ⊕○○○	Current use: ● No difference with the effect of the placebo or in the absence of hormone therapy, follow-up over an average period of 5 to 7 years. ⊕○○○
	Oral route: ⊖	
Mortality (cardiovascular cause)	Transdermal or oral route, for 5 years or less OR more than 5 years: ● No difference with the effect in the absence of hormone therapy, follow-up over an average period of 7 years. ⊕○○○	● No difference with the effect in the absence of hormone therapy, follow-up over an average period of 5 years. ⊕⊕⊕○
Gallbladder diseases	Transdermal route, current use: ● No difference with the effect in the absence of hormone therapy on instances of cholecystectomy, follow-up over an average period of 12 years. ⊕⊕○○	Current use: ● + 10 cases of cholecystectomy, out of 1,000 women treated, compared to the effect of a placebo, follow-up over an average period of 6 years. <i>Baseline risk: 16 cases out of 1,000</i> ⊕⊕⊕○
	Oral route, current use, combined with a progestin other than MPA: ● + 14 cases of cholecystectomy, out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 14 years. <i>Baseline risk: 27 cases out of 1,000</i> ⊕⊕○○	● + 9 cases of cholecystitis, out of 1,000 women treated, compared to the effect of a placebo, follow-up over an average period of 6 years. <i>Baseline risk: 17 cases out of 1,000</i> ⊕⊕⊕○ ● + 11 cases of cholelithiasis, out of 1,000 women treated, compared to the effect of a placebo, follow-up over an average period of 6 years. <i>Baseline risk: 17 cases out of 1,000</i> ⊕⊕⊕○
Venous thrombo-embolism	Transdermal route, current use: ● No difference with the effect in the absence of hormone therapy, follow-up over an average period of 10 years. ⊕○○○	♀♂ Combined with a progestogen, current use: ● Significant increase in cases of venous thromboembolism, compared to the number of cases in the absence of hormone therapy. ⊕⊕○○
	Oral route, current use: ● 70% increase in risk, compared to the increase in the absence of hormone therapy, follow-up over an average period of 10 years. ⊕⊕○○	
	Micronized progesterone combined with an estrogen, current use: ● No difference with the effect in the absence of hormone therapy, follow-up over an average period of 11 years. ⊕⊕○○	MPA combined with an estrogen: ● + 3 cases out of 1,000 persons, compared to the absence of hormone therapy, follow-up over an average period of 3 years. <i>Baseline risk: 2 cases out of 1,000</i> ⊕⊕○○

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Colorectal cancer	Transdermal route: ● No difference with the effect in the absence of hormone therapy, follow-up over an average period of 11 years. ⊕⊕⊕⊕	● No difference with the effect of a placebo, follow-up over an average period of 13 years. ⊕⊕⊕⊕
	♀♀ Transdermal or oral route: ● No difference with the effect in the absence of hormone therapy, follow-up over an average period of 5 years. ⊕⊕⊕⊕	
	Micronized progesterone combined with an estrogen ● No difference with the effect in the absence of hormone therapy, follow-up over an average period of 11 years. ⊕⊕⊕⊕	
Endometrial cancer	Transdermal or oral route, combined with micronized progesterone: <i>For less than 5 years</i> ● No difference with the effect in the absence of hormone therapy, follow-up over an average period of 11 years. ⊕⊕⊕⊕	● - 4 cases out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 13 years. <i>Baseline risk: 12 cases out of 1,000</i> ⊕⊕⊕⊕
	<i>For more than 5 years</i> ● + 8 cases out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 11 years. <i>Baseline risk: 5 cases out of 1,000</i> ⊕⊕⊕⊕	
	♀♀ Transdermal or oral route, combined with a progestin: ● No difference with the effect in the absence of hormone therapy. ⊕⊕⊕⊕	MPA combined with an estrogen: ● - 3 cases out of 1,000 women treated, compared to the effect of a placebo or the absence of hormone therapy, follow-up over an average period of 13 years or undefined. <i>Baseline risk: 9 cases out of 1,000</i> ⊕⊕⊕⊕ to ⊕⊕⊕⊕
		Combined with micronized progesterone: ● 33% increase in the risk of endometrial cancer, compared to the absence of hormone therapy, follow-up over an average period of 19 years. Increased risk if treatment duration is 5 years or more. ⊕⊕⊕⊕

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Ovarian cancer	<p>Transdermal route:</p> <p>● No difference with the effect in the absence of hormone therapy, follow-up over an average period of 7 years. ⊕○○○</p>	<p>● No difference with the effect of a placebo or in the absence of hormone therapy, follow-up over an average period of 13 years. ⊕⊕○○</p>
	<p>Oral route:</p> <p>● + 1 case out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 7 years. ⊕⊕⊕○ <i>Baseline risk: 4 cases out of 1,000</i></p>	
	<p>Age at the initiation of treatment, transdermal or oral route:</p> <p><i>Less than 60 years</i></p> <p>● - 1 case out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 7 years. ⊕⊕⊕○ <i>Baseline risk: 4 cases out of 1,000</i></p> <p><i>Between 60 – 69 years</i></p> <p>● + 3 cases out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 7 years. ⊕⊕⊕○ <i>Baseline risk: 4 cases out of 1,000</i></p> <p><i>70 years or older</i></p> <p>● No difference with the effect in the absence of hormone therapy, follow-up over an average period of 7 years. ⊕⊕⊕○</p>	
	<p>Micronized progesterone combined with an estrogen:</p> <p>● + 2 cases out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 15 years. ⊕⊕○○ <i>Baseline risk: 5 cases out of 1,000</i></p>	

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Breast cancer	Transdermal route: No difference with the effect in the absence of hormone therapy, follow-up over an average period of 8 years or unknown.	+ 9 cases out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 15 to 20 years. <i>Baseline risk: 39 cases out of 1,000</i>
	Oral route: + 6 cases out of 1,000 women treated, compared to the absence of hormone therapy. <i>Baseline risk: 22 cases out of 1,000 (average follow-up period unknown)</i>	
	Transdermal or oral route, all ages at the initiation of treatment combined: Increased cases of breast cancer, compared to the number of cases in the absence of hormone therapy. Effect increases with the duration of treatment.	Increased cases of breast cancer, compared to the number of cases in the absence of hormone therapy, follow-up over an unknown period. This effect increases with the duration of hormone therapy.
	Age at the initiation of treatment, transdermal or oral route: <i>Less than 60 years</i> - 7 cases out of 1,000 women treated, compared to the absence of hormone therapy. <i>Between 60 – 69 years</i> + 8 cases out of 1,000 women treated, compared to the absence of hormone therapy. <i>70 years or older</i> + 19 cases out of 1,000 women treated, compared to the absence of hormone therapy. <i>Baseline risk: 22 cases out of 1,000 (average follow-up period unknown)</i>	MPA combined with an estrogen: + 10 cases out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 15 to 20 years. <i>Baseline risk: 39 cases out of 1,000</i>
	Micronized progesterone combined with an estrogen: No difference with the effect in the absence of hormone therapy, follow-up over an average period of 8 years.	Progestin other than MPA combined with an estrogen: Increased cases of breast cancer, compared to the number of cases in the absence of hormone therapy. When considering treatment duration, the effect among women treated for 5 years or more is double that among women treated for less than 5 years.
	Mortality linked to breast cancer 	No difference with the effect of a placebo on deaths, follow-up over an average period of 20 years.

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 Level of evidence: High Moderate Low Very low Effect observed in perimenopausal and postmenopausal women

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	COMBINED HORMONE THERAPY (LABELLED AS BIOIDENTICAL) 17β-estradiol combined with a progestogen <i>Unless otherwise indicated</i>	COMBINED HORMONE THERAPY (CLASSICAL) Conjugated estrogens combined with MPA <i>Unless otherwise indicated</i>
Dementia (including Alzheimer's disease)	<p>Transdermal or oral route, combined with norethindrone:</p> <p>● No difference with the effect in the absence of hormone therapy. ⊕⊕○○</p>	<p>Current use: ⊕⊕⊕○</p> <p>● +9 cases out of 1,000 women treated, aged 65 to 79 years, compared to the absence of hormone therapy, follow-up over an average period of 4 years. <i>Baseline risk: 9 cases out of 1,000</i></p>
	<p>Micronized progesterone combined with an estrogen:</p> <p>● -24 cases out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 5 years. <i>Baseline risk: 29 cases out of 1,000</i></p>	
Alzheimer's disease	<p>Age at the initiation of treatment, transdermal or oral route:</p> <p><i>Less than 60 years, used for less than 10 years</i></p> <p>● No difference with the effect in the absence of hormone therapy. ⊕⊕○○</p>	<p>● -21 cases out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 5 years. <i>Baseline risk: 29 cases out of 1,000</i></p> <p>MPA combined with an estrogen:</p> <p>● No difference with the effect in the absence of hormone therapy. ⊕○○○ to ⊕⊕⊕○</p>
	<p><i>Less than 60 years, used for 10 years or more</i></p> <p>● Increased cases of Alzheimer's disease, compared to the number of cases in the absence of hormone therapy ⊕⊕○○ Note: Number of cases not estimated due to missing data.</p>	
	<p><i>60 years or older, all usage durations</i></p> <p>● Increased cases of Alzheimer's disease, compared to the number of cases in the absence of hormone therapy. ⊕⊕○○ Note: Number of cases not estimated due to missing data.</p>	
	<p>Micronized progesterone combined with an estrogen:</p> <p>● -25 cases out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 5 years. <i>Baseline risk: 29 cases out of 1,000</i></p>	
Mortality (all causes combined)	<p>Transdermal or oral route:</p> <p>● -26 cases out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 9 years. <i>Baseline risk: 120 cases out of 1,000</i></p>	<p>Age at the initiation of treatment, between 50 – 79 years:</p> <p>● No difference with the effect in the absence of hormone therapy, follow-up over an average period of 19 years. ⊕○○○ to ⊕⊕⊕○</p>

Summary

Combined hormone therapy

Estrogen-only hormone therapy

Tibolone

Bazedoxifene/
conjugated estrogens

Micronized progesterone only

LEGEND

MPA = medroxyprogesterone acetate

Hormone therapy effect: ● Benefit ● No observed effect ● Increased risk ○ No data available in the literature reviewed

Level of evidence: High ⊕⊕⊕⊕ Moderate ⊕⊕⊕○ Low ⊕⊕○○ Very low ⊕○○○

●●●● Effect observed in perimenopausal and postmenopausal women

Unless otherwise indicated, the effects are observed in **postmenopausal women**.

	ESTROGEN-ONLY HORMONE THERAPY (LABELLED AS BIOIDENTICAL) 17β-estradiol	ESTROGEN-ONLY THERAPY (CLASSICAL) Conjugated estrogens
Hot flashes	Transdermal route for the past 3 months: ● Relative decrease of 73% in the average number of hot flashes, compared to 53% for the placebo. ⊕⊕○○	Used for the past 12 months: ● Relative decrease in the number of moderate to severe hot flashes, compared to the placebo. ⊕⊕○○ ● Decrease of 49% in the instances of moderate to severe hot flashes, compared to the placebo. ⊕⊕⊕⊕ ♀♀ ● Significant decrease in the severity of moderate to severe hot flashes, compared to the placebo. ⊕⊕○○ to ⊕⊕⊕⊕
	Oral route: ⊖	
	⊖ Intensity of hot flashes.	
Night sweats	⊖ Frequency and intensity of night sweats.	⊖ Frequency of night sweats. Used for the past 12 months: ● Decrease of 37% in the intensity of night sweats, compared to the placebo. ⊕⊕⊕⊕
Joint pain	⊖	Used for the past 12 months: ● No difference with the effect of a placebo on moderate to severe joint pain. ⊕⊕⊕⊕
Libido, desire and sexual function	Transdermal route for the past 12 months: <i>Age at the initiation of treatment, between 50 – 59 years</i> ● Improvement in the frequency of sexual desire of about 1 day per week, compared to the absence of treatment. ⊕○○○	⊖
	Oral route: ⊖	
Sleep disorders	Transdermal route for the past 3 months: ● Improvement in sleep quality, compared to the placebo. ⊕⊕○○	Used for the past 12 months: ● Improvement in sleep quality, compared to a placebo. ⊕⊕⊕⊕
	Oral route: ⊖	

Summary
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LEGEND

Hormone therapy effect: ● Benefit ● No observed effect ● Increased risk ⊖ No data available in the literature reviewed

Level of evidence: High ⊕⊕⊕⊕ Moderate ⊕⊕⊕○ Low ⊕⊕○○ Very low ⊕○○○

♀♀: Effect observed in perimenopausal and postmenopausal women

Unless otherwise indicated, the effects are observed in **postmenopausal women**.

	ESTROGEN-ONLY HORMONE THERAPY (LABELLED AS BIOIDENTICAL) 17β-estradiol	ESTROGEN-ONLY THERAPY (CLASSICAL) Conjugated estrogens
Emotional instability	⊖ Irritability and general symptoms of emotional instability.	Used for the past 12 months: ● No difference with the effect of a placebo on general symptoms of emotional instability. ⊕⊕⊕⊕ ⊖ Irritability.
Symptoms of anxiety	Transdermal route for the past 6 months: ● Improvement in symptoms, compared to the placebo. ⊕⊕○○	Used for the past 6 months: ● No difference with the effect of a placebo. ⊕⊕○○
	Oral route for the past 5 months: <i>Among women aged 70 and older</i> ● No difference with the effect of a placebo. ⊕⊕○○	
Symptoms of depression	Transdermal route: <i>Used for the past 7 months, among women with no history of depression</i> ● No difference with the effect of a placebo. ⊕⊕○○ <i>Among women aged 65 and older</i> ● No difference with the effect in the absence of hormone therapy. ⊕⊕○○	Used for the past 12 months: ● No difference with the effect of a placebo. ⊕⊕⊕⊕
	Oral route: <i>Used for the past 6 months, among women with no history of depression</i> ● Decrease in symptoms of depression, compared to a placebo. ⊕○○○ <i>Among women aged 65 and older</i> ● No difference with the effect of a placebo on symptoms of depression or instances of depression. ⊕○○○	
Skin aging	⊖	⊖
Thinning hair and hair loss	⊖	⊖
Weight gain	⊖	Used for the past 6 months: ● No difference with the effect of a placebo. ⊕⊕○○

Summary

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Hormone therapy effect: ● Benefit ● No observed effect ● Increased risk ⊖ No data available in the literature reviewed

Level of evidence: High ⊕⊕⊕⊕ Moderate ⊕⊕⊕○ Low ⊕⊕○○ Very low ⊕○○○

Unless otherwise indicated, the effects are observed in **postmenopausal women**.

	ESTROGEN-ONLY HORMONE THERAPY (LABELLED AS BIOIDENTICAL) 17β-estradiol	ESTROGEN-ONLY THERAPY (CLASSICAL) Conjugated estrogens
Type 2 Diabetes	⊖	Current use: ● - 14 cases out of 1,000 women treated, compared to the effect of a placebo, follow-up over an average period of 7 years. <i>Baseline risk: 105 cases out of 1,000</i> ⊕⊕○○ ● - 31 cases out of 1,000 women treated, compared to the effect of a placebo, follow-up over an unknown average period. <i>Baseline risk: 83 cases out of 1,000</i> ⊕⊕○○
Fractures (all sites)	Transdermal route: ● - 14 cases out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 3 years. <i>Baseline risk: 43 cases out of 1,000</i> ⊕⊕○○	● - 22 cases out of 1,000 women treated, compared to the effect of a placebo or the absence of hormone therapy, follow-up over an average period of 3 to 10 years. <i>Baseline risk: 75 cases out of 1,000</i> ⊕⊕○○
	Oral route: ● - 20 cases out of 1,000 women treated with a dose of ≤ 1 mg per day, compared to the absence of hormone therapy, follow-up over an average period of 3 years. ⊕⊕○○ ● - 23 cases out of 1,000 women treated with a dose of > 1 mg per day, compared to the absence of hormone therapy, follow-up over an average period of 3 years. ⊕⊕○○ <i>Baseline risk: 43 cases out of 1,000</i>	
Stroke	👤👤 Transdermal route: ● - 2 cases out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 7 to 8 years. <i>Baseline risk: 13 cases out of 1,000</i> ⊕○○○	● + 8 cases out of 1,000 women treated, compared to the effect of a placebo, follow-up over an average period of 7 years. <i>Baseline risk: 24 cases out of 1,000</i> ⊕○○○
	Oral route: ⊖	<i>Age at the initiation of treatment, between 50 – 79 years</i> ● No difference with the effect of a placebo, follow-up over an average period of 7 years. ⊕○○○ to ⊕⊕○○
Myocardial infarction	Transdermal route, current use: ● - 9 cases out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 7 years. <i>Baseline risk: 24 cases out of 1,000</i> ⊕○○○	Current use: ● No difference with the effect of a placebo or in the absence of hormone therapy, follow-up over an average period of 5 to 7 years. ⊕○○○
	Oral route: ⊖	

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Hormone therapy effect: ● Benefit ● No observed effect ● Increased risk ⊖ No data available in the literature reviewed

Level of evidence: High ⊕⊕⊕⊕ Moderate ⊕⊕⊕○ Low ⊕⊕○○ Very low ⊕○○○

👤👤: Effect observed in perimenopausal and postmenopausal women

Unless otherwise indicated, the effects are observed in **postmenopausal women**.

	ESTROGEN-ONLY HORMONE THERAPY (LABELLED AS BIOIDENTICAL) 17β-estradiol	ESTROGEN-ONLY THERAPY (CLASSICAL) Conjugated estrogens
Mortality (cardiovascular cause)	Transdermal or oral route: ● - 18 cases out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 9 years. <i>Baseline risk: 50 cases out of 1,000</i> ⊕○○○	● No difference with the effect in the absence of hormone therapy, follow-up over an average period of 18 years. ⊕⊕⊕○
Gallbladder diseases	Transdermal route: <i>Ever use</i> ● No difference with the effect in the absence of hormone therapy on instances of cholecystectomy, follow-up over an average period of 12 years. ⊕⊕○○	Current use ● + 13 cases of gallbladder diseases, out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 7 years. <i>Baseline risk: 16 cases out of 1,000</i> ⊕⊕○○ ● + 22 cases of cholecystectomy, out of 1,000 women treated, compared to the effect of a placebo, follow-up over an average period of 7 years. <i>Baseline risk: 25 cases out of 1,000</i> ⊕⊕⊕○
	Oral route: <i>Current use</i> ● + 10 cases of gallbladder diseases, out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 7 years. <i>Baseline risk: 16 cases out of 1,000</i> ⊕⊕○○	● + 22 cases of cholelithiasis, out of 1,000 women treated, compared to the effect of a placebo, follow-up over an average period of 7 years. <i>Baseline risk: 26 cases out of 1,000</i> ⊕⊕⊕○
	<i>Ever use</i> ● + 35 cases of cholecystectomy, out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 12 years. <i>Baseline risk: 44 cases out of 1,000</i> ⊕⊕○○	● + 20 cases of cholecystitis, out of 1,000 women treated, compared to the effect of a placebo, follow-up over an average period of 7 years. <i>Baseline risk: 25 cases out of 1,000</i> ⊕⊕⊕○
		Ever use ● + 38 cases of cholecystectomy, out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 12 years. <i>Baseline risk: 44 cases out of 1,000</i> ⊕⊕○○
Venous thrombo-embolism	Transdermal route: ● The effect was no different than that in the absence of hormone therapy. ⊕⊕○○ ● Decrease of 56% in the risk of instances of venous thromboembolism, compared to oral estrogens only , follow-up over an average period of 2 years. ⊕○○○	● + 1 case out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 3 years. <i>Baseline risk: 2 cases out of 1,000</i> ⊕⊕○○
	Oral route: ● - 1 case out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 3 years. <i>Baseline risk: 2 cases out of 1,000</i> ⊕⊕○○	
Colorectal cancer	Transdermal or oral route: ● - 3 cases out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 11 years. <i>Baseline risk: 9 cases out of 1,000</i> ⊕⊕⊕○	● No difference with the effect in the absence of hormone therapy, follow-up over an average period of 13 years. ⊕⊕○○

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Bazedoxifene/
conjugated estrogens

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Hormone therapy effect: ● Benefit ● No observed effect ● Increased risk ● No data available in the literature reviewed

Level of evidence: High ⊕⊕⊕⊕ Moderate ⊕⊕⊕○ Low ⊕⊕○○ Very low ⊕○○○

● Effect observed in perimenopausal and postmenopausal women

Unless otherwise indicated, the effects are observed in **postmenopausal women**.

	ESTROGEN-ONLY HORMONE THERAPY (LABELLED AS BIOIDENTICAL) 17β-estradiol	ESTROGEN-ONLY THERAPY (CLASSICAL) Conjugated estrogens	
Ovarian cancer	Transdermal route: ● No difference with the effect in the absence of hormone therapy, follow-up over an average period of 8 years. ⊕○○○	● No difference with the effect in the absence of hormone therapy. ⊕○○○	Summary
	Transdermal or oral route, for less than 5 years or for 5 years or more: ● No difference with the effect in the absence of hormone therapy. ⊕○○○		
Breast cancer	Transdermal route: ● No difference with the effect of a placebo or in the absence of hormone therapy, follow-up over an average period of 8 to 17 years. ⊕○○○	● - 9 cases out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 15 to 20 years. <i>Baseline risk: 52 cases out of 1,000</i> <i>For less than 5 years</i> ● No difference with the effect in the absence of hormone therapy. ⊕○○○ <i>For 5 years or more</i> ● Increased cases of breast cancer, compared to the number of cases in the absence of hormone therapy. ⊕○○○	Combined hormone therapy
	Transdermal route: ● No difference with the effect of a placebo or in the absence of hormone therapy, follow-up over an average period of 8 to 16 years. ⊕○○○		
	♀♀ Transdermal or oral route: ● - 2 cases out of 1,000 women treated, compared to a placebo or in the absence of hormone therapy. ⊕○○○ ● There does not appear to be a trend as regards effect and the duration of hormone therapy. <i>Baseline risk: 22 cases out of 1,000 (average follow-up period unknown)</i> ⊕○○○ to ⊕○○○	♀♀ ● No difference with the effect in the absence of hormone therapy on instances of breast cancer. ⊕○○○ <i>For less than 4 years</i> ● Decrease in cases of breast cancer, compared to the number of cases in the absence of hormone therapy. ⊕○○○ <i>For 4 years or more</i> ● No difference with the effect in the absence of hormone therapy. ⊕○○○	Estrogen-only hormone therapy
	Mortality linked to breast cancer ⊖	● - 3 cases out of 1,000 women treated, compared to the effect of a placebo, follow-up over an average period of 20 years. <i>Baseline risk: 8 cases out of 1,000</i> ⊕○○○	
Dementia (including Alzheimer's disease)	♀♀ Transdermal or oral route: ● No difference with the effect in the absence of hormone therapy. ⊕○○○	● Among women aged 65 to 79 years and undergoing treatment, no difference with the effect of a placebo, follow-up over an average period of 5 years. ⊕○○○	Tibolone
	♀♀ Oral route: ● - 16 cases out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 5 years. <i>Baseline risk: 29 cases out of 1,000</i> ⊕○○○		
			Bazedoxifene/ conjugated estrogens
			Micronized progesterone only

LEGEND

Hormone therapy effect: ● Benefit ● No observed effect ● Increased risk ⊖ No data available in the literature reviewed

Level of evidence: High ⊕⊕⊕⊕ Moderate ⊕⊕⊕○ Low ⊕⊕○○ Very low ⊕○○○

♀♀: Effect observed in perimenopausal and postmenopausal women

Unless otherwise indicated, the effects are observed in **postmenopausal women**.

	ESTROGEN-ONLY HORMONE THERAPY (LABELLED AS BIOIDENTICAL) 17β-estradiol	ESTROGEN-ONLY THERAPY (CLASSICAL) Conjugated estrogens
Alzheimer's disease	Transdermal route: <ul style="list-style-type: none"> - 22 cases out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 5 years. <i>Baseline risk: 29 cases out of 1,000</i> 	<ul style="list-style-type: none"> - 16 cases out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 5 years. <i>Baseline risk: 29 cases out of 1,000</i>
	Oral route: <ul style="list-style-type: none"> - 15 cases out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 5 years. <i>Baseline risk: 29 cases out of 1,000</i> 	
	Transdermal or oral route: <i>For the past 1 to 5 years</i> <ul style="list-style-type: none"> Decrease in cases of Alzheimer's disease, compared to the absence of hormone therapy, regardless of age at the initiation of treatment. <i>For less than 1 year or for 5 years or more</i> <ul style="list-style-type: none"> No difference with the effect of a placebo, regardless of age at the initiation of treatment. 	
Mortality (all causes combined)	Transdermal or oral route: <ul style="list-style-type: none"> - 42 cases out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 9 years. <i>Baseline risk: 120 cases out of 1,000</i> 	Age at the initiation of treatment, between 50 – 79 years: <ul style="list-style-type: none"> No difference with the effect of a placebo or in the absence of hormone therapy, follow-up over an average period of 19 years.
	Oral route: <ul style="list-style-type: none"> No difference with the effect in the absence of hormone therapy, follow-up over an average period of 16 years. 	

- Summary
- Combined hormone therapy
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- Micronized progesterone only

LEGEND

Hormone therapy effect: ● Benefit ● No observed effect ● Increased risk ● No data available in the literature reviewed

Level of evidence: High ⊕⊕⊕⊕ Moderate ⊕⊕⊕ Low ⊕⊕○○ Very low ⊕○○○

OTHER HORMONAL AGENTS

Unless otherwise indicated, the effects are observed in **postmenopausal women**.

	TIBOLONE	
Hot flashes	<p>For the past 1 to 4 months:</p> <ul style="list-style-type: none"> ● Decrease in the number of hot flashes compared to the placebo. <p>This decrease is around 37% among women who have been taking tibolone for the past 4 months, compared to 12% among women taking a placebo.</p>	<p>⊕○○○ to ⊕⊕○○ ⊕○○○</p>
	<p>For the past 3 to 6 months:</p> <ul style="list-style-type: none"> ● Decrease in the intensity of hot flashes, compared to the placebo. 	<p>⊕○○○ to ⊕⊕○○</p>
	<p>For the past 11 months:</p> <ul style="list-style-type: none"> ● Decrease in the intensity of hot flashes of about 49%, compared to 60% among women taking oral 17β-estradiol combined with norethindrone. 	<p>⊕⊕⊕○</p>
Night sweats	<ul style="list-style-type: none"> ⊖ Frequency of night sweats. 	
	<p>For the past 3 months:</p> <ul style="list-style-type: none"> ● No difference with the effect of a placebo on the intensity of night sweats. 	<p>⊕⊕○○</p>
Joint pain	<p>For the past 4 months:</p> <ul style="list-style-type: none"> ● No difference with the effect of a placebo on complaints of joint pain. 	<p>⊕○○○</p>
Libido, desire and sexual function	<p>For the past 6 months:</p> <ul style="list-style-type: none"> ● Improvement in sexual function, compared to the placebo. ● No difference with the effect of oral 17β-estradiol combined with norethindrone on sexual function. 	<p>⊕○○○ ⊕⊕○○</p>
	<p>For the past 3, 6 or 12 months:</p> <ul style="list-style-type: none"> ● Improvement in sexual function, sexual desire or interest in sexual relations, compared to conjugated estrogens combined with MPA. 	<p>⊕○○○</p>
	<p>For the past 12 months:</p> <ul style="list-style-type: none"> ● Improvement in sexual function, compared to oral 17β-estradiol combined with norethindrone. 	<p>⊕○○○</p>
	<p>For the past 1.5 to 3 months:</p> <ul style="list-style-type: none"> ● No difference with the effect of a placebo on sexual desire or decrease in libido. 	<p>⊕○○○ to ⊕⊕○○</p>

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MPA = medroxyprogesterone acetate

Hormone therapy effect: ● Benefit ● No observed effect ● Increased risk ⊖ No data available in the literature reviewed

Level of evidence: High ⊕⊕⊕⊕ Moderate ⊕⊕⊕○ Low ⊕⊕○○ Very low ⊕○○○

Unless otherwise indicated, the effects are observed in **postmenopausal women**.

	TIBOLONE	
Sleep disorders	<p>For the past 3 months:</p> <p>● No difference with the effect of a placebo on the quality of sleep the previous evening.</p>	⊕⊕○○
Emotional instability	<p>For the past 1.5 to 6 months:</p> <p>● No difference with the effect of a placebo on general symptoms of emotional instability.</p>	⊕○○○
	<p>For the past 12 months:</p> <p>● Decrease in symptoms of irritability, compared to the placebo.</p>	⊕○○○
Symptoms of anxiety	<p>For the past 3 to 6 months:</p> <p>● Improvement in symptoms of anxiety, compared to the placebo.</p>	⊕○○○ to ⊕⊕○○
Symptoms of depression	<p>For the past 3 to 12 months:</p> <p>● No difference with the effect of a placebo.</p>	⊕○○○
	<p>For the past 6 months, among women having undergone a hysterectomy and with no history of depression:</p> <p>● Decrease in symptoms of depression, compared to the placebo.</p>	⊕○○○
Skin aging	⊖	
Thinning hair and hair loss	⊖	
Weight gain	<p>For the past 6 to 12 months:</p> <p>● No difference with the effect of a placebo or in the absence of hormone therapy.</p>	⊕○○○ to ⊕⊕○○
	<p>For the past 13 months:</p> <p>● Increase in body weight, compared to conjugated estrogens combined with MPA.</p>	⊕⊕○○
Type 2 diabetes	<p>● + 32 cases out of 1,000 women treated, compared to the absence of hormone therapy. <i>Baseline risk: 152 cases out of 1,000</i></p>	⊕○○○

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LEGEND

MPA = medroxyprogesterone acetate Hormone therapy effect: ● Benefit ● No observed effect ● Increased risk ⊖ No data available in the literature reviewed
 Level of evidence: High ⊕⊕⊕⊕ Moderate ⊕⊕⊕○ Low ⊕⊕○○ Very low ⊕○○○

Unless otherwise indicated, the effects are observed in **postmenopausal women**.

	TIBOLONE	
Fractures (all sites)	● - 14 cases out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 3 years. <i>Baseline risk: 43 cases out of 1,000</i>	⊕⊕○○
Stroke	👩👩 ● + 4 cases out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 5 to 8 years. <i>Baseline risk: 13 cases out of 1,000</i>	⊕⊕○○
Myocardial infarction	● No difference with the effect in the absence of hormone therapy, follow-up over an average period of 7 years.	⊕○○○
Mortality (cardiovascular cause)	👩👩 ● - 25 cases out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 9 years. <i>Baseline risk: 50 cases out of 1,000</i>	⊕○○○
Gallbladder diseases	Current use: ● + 13 cases of gallbladder diseases, out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 7 years. <i>Baseline risk: 16 cases out of 1,000</i>	⊕⊕○○
	● + 9 cases of cholelithiasis, out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 12 years. <i>Baseline risk: 27 cases out of 1,000</i>	⊕⊕○○
	Ever use: ● Increased risk of cholecystitis, compared to the absence of hormone therapy, follow-up over an average period of 12 years.	⊕⊕○○
Venous thromboembolism	👩👩 ● No difference with the effect in the absence of hormone therapy.	⊕⊕○○
Colorectal cancer	👩👩 ● No difference with the effect in the absence of hormone therapy, follow-up over an average period of 6 years.	⊕○○○
Endometrial cancer	Insufficient data to come to any conclusion.	
Ovarian cancer	👩👩 ● No difference with the effect in the absence of hormone therapy, follow-up over an average period of 7 years.	⊕⊕○○

Summary

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LEGEND

Hormone therapy effect: ● Benefit ● No observed effect ● Increased risk ● No data available in the literature reviewed

Level of evidence: High ⊕⊕⊕⊕ Moderate ⊕⊕⊕○ Low ⊕⊕○○ Very low ⊕○○○

👩👩: Effect observed in perimenopausal and postmenopausal women

Unless otherwise indicated, the effects are observed in **postmenopausal women**.

	TIBOLONE	
Breast Cancer	All durations combined: No difference with the effect in the absence of hormone therapy.	⊕○○○
	For less than 6 months: + 3 cases out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 4 years. <i>Baseline risk: 9 cases out of 1,000</i>	⊕○○○
	For the past 6 to 12 months: No difference with the effect in the absence of hormone therapy, follow-up over an average period of 4 years.	⊕○○○
	For over 12 months: + 1 case out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 4 years. <i>Baseline risk: 9 cases out of 1,000</i>	⊕○○○
Mortality (breast cancer)	- 5 cases out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 17 years. <i>Baseline risk: 9 cases out of 1,000</i>	⊕⊕○○
Dementia (including Alzheimer's disease)	+ 20 cases out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 12 years. <i>Baseline risk: 96 cases out of 1,000</i>	⊕○○○
	No difference with the effect in the absence of hormone therapy.	⊕○○○ to ⊕⊕○○
Alzheimer's disease	+ 3 cases Out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 12 years. <i>Baseline risk: 63 cases out of 1,000</i>	⊕○○○
	No difference with the effect in the absence of hormone therapy.	⊕○○○ to ⊕⊕○○
Mortality (all causes combined)	Current use: - 48 cases out of 1,000 women treated, compared to the absence of hormone therapy, follow-up over an average period of 9 years. <i>Baseline risk: 120 cases out of 1,000</i>	⊕○○○

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Hormone therapy effect: Benefit No observed effect Increased risk No data available in the literature reviewed

Level of evidence: High ⊕⊕⊕⊕ Moderate ⊕⊕⊕○ Low ⊕⊕○○ Very low ⊕○○○

Effect observed in perimenopausal and postmenopausal women

Unless otherwise indicated, the effects are observed in **postmenopausal women**.

BAZEDOXIFENE/CONJUGATED ESTROGENS						
Hot flashes	<p>For the past 3 months:</p> <ul style="list-style-type: none"> ● Significant decrease in the number and intensity of hot flashes, compared to the placebo. 	⊕⊕○○	Thinning hair or hair loss	⊖	Colorectal cancer	⊖
Night sweats	<ul style="list-style-type: none"> ⊖ Frequency and intensity of night sweats. 		Weight gain	⊖	Endometrial cancer	⊖
Joint pain	<ul style="list-style-type: none"> ⊖ 		Type 2 diabetes	⊖	Ovarian cancer	⊖
Libido, desire and sexual function	<p><i>Among women with at least one moderate to severe symptom of vulvovaginal atrophy:</i></p> <p>For the past 3 months:</p> <ul style="list-style-type: none"> ● No difference with the effect of a placebo on sexual function. 	⊕○○○	Fractures (all sites)	⊖	Breast cancer	⊖
Sleep disorders	<p>For the past 3 months:</p> <ul style="list-style-type: none"> ● Improvement in sleep quality, compared to the placebo. <p><i>Among women who begin hormone therapy less than 5 years after the onset of menopause</i></p> <ul style="list-style-type: none"> ● Increase in sleep duration, compared to the placebo. <p><i>Among women who begin hormone therapy more than 5 years after the onset of menopause</i></p> <ul style="list-style-type: none"> ● No difference with the effect of a placebo. 	<p>⊕○○○ to ⊕⊕○○</p> <p>⊕○○○</p> <p>⊕○○○</p>	Stroke	⊖	Mortality (breast cancer)	⊖
Emotional instability	<ul style="list-style-type: none"> ⊖ 		Myocardial infarction	⊖	Dementia (including Alzheimer's disease)	⊖
Symptoms of anxiety	<ul style="list-style-type: none"> ⊖ 		Mortality (cardiovascular cause)	⊖	Alzheimer's disease	⊖
Symptoms of depression	<ul style="list-style-type: none"> ⊖ 		Gallbladder diseases	⊖	Mortality (all causes combined)	⊖
Skin aging	<ul style="list-style-type: none"> ⊖ 		Venous thrombo-embolism	⊖		

LEGEND

Hormone therapy effect: ● Benefit ● No observed effect ● Increased risk ⊖ No data available in the literature reviewed

Level of evidence: High ⊕⊕⊕⊕ Moderate ⊕⊕⊕○ Low ⊕⊕○○ Very low ⊕○○○

Unless otherwise indicated, the effects are observed in **postmenopausal women**.

MICRONIZED PROGESTERONE ONLY					
Hot flashes	<p>For the past 2 months:</p> <p>● No difference with the effect of a placebo on the number of hot flashes.</p> <p>⊕⊕○○</p>	Thinning hair or hair loss	⊖	Colorectal cancer	⊖
Night sweats	⊖	Weight gain	<p>For the past 3 months:</p> <p>● No difference with the effect of a placebo on body weight.</p> <p>⊕⊕○○</p>	Endometrial cancer	<p>● No difference with the effect in the absence of hormone therapy, follow-up over an average period of 12 years.</p> <p>⊕○○○</p>
Joint pain	⊖	Type 2 diabetes	⊖	Ovarian cancer	⊖
Libido, desire and sexual function	⊖	Fractures (all sites)	⊖	Breast cancer	⊖
Sleep disorders	<p>For the past 2 months:</p> <p>● No difference with the effect of a placebo on sleep duration.</p> <p>⊕⊕○○</p>	Stroke	⊖	Mortality (breast cancer)	⊖
Emotional instability	⊖	Myocardial infarction	⊖	Dementia (including Alzheimer's disease)	⊖
Symptoms of anxiety	⊖	Mortality (cardiovascular cause)	⊖	Alzheimer's disease	⊖
Symptoms of depression	⊖	Gallbladder diseases	⊖	Mortality (all causes combined)	⊖
Skin aging	⊖	Venous thrombo-embolism	⊖		

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Hormone therapy effect: ● Benefit ● No observed effect ● Increased risk ⊖ No data available in the literature reviewed

Level of evidence: High ⊕⊕⊕⊕ Moderate ⊕⊕⊕○ Low ⊕⊕○○ Very low ⊕○○○