PREMARIN® (conjugated estrogens) 0.625 mg/g
VAGINAL CREAM

PREMARIN®
(conjugated estrogens tablets, USP)

PREMPRO®
(conjugated estrogens/medroxyprogesterone acetate tablets)
0.3 mg / 1.5 mg

Pfizer U.S. Pharmaceuticals

Parent Slide 1
Slide External Name: Premarin Landing Page
Message Category: Non Specific Messaging

PREMARIN® (conjugated estrogens) 0.625 mg/g
VAGINAL CREAM

Relief—inside and out.

She may only say this much about her vaginal symptoms.

Next →

Study description

Dosing

SELECTED SAFETY INFORMATION

WARNING: ENDOMETRIAL CANCER, CARDIOVASCULAR DISORDERS AND PROBABLE DEMENTIA FOR ESTROGEN-ALONE THERAPY
ENDOMETRIAL CANCER

There is an increased risk of endometrial cancer in a woman with a uterus who uses unopposed estrogens. Adding a progestin to estrogen therapy has been shown to reduce the risk of endometrial hyperplasia, which may be a precursor to endometrial cancer. Adequate diagnostic measures, including directed or random endometrial sampling when indicated, should be undertaken to rule out malignancy in postmenopausal women with undiagnosed persistent or recurring

CLICK HERE FOR PRODUCT INDICATION AND IMPORTANT SAFETY INFORMATION

REF

PI PPI

Parent Slide 2
Slide External Name: Premarin Cream Intro
Message Category: Non Specific Messaging

PREMARIN® (conjugated estrogens) 0.625 mg/g
VAGINAL CREAM

Relief—inside and out.

63%

of postmenopausal women surveyed reported vaginal discomfort, yet **less than half** discussed it with their healthcare professionals[1]

Study description

Dosing

SELECTED SAFETY INFORMATION

WARNING: ENDOMETRIAL CANCER, CARDIOVASCULAR DISORDERS AND PROBABLE DEMENTIA FOR ESTROGEN-ALONE THERAPY
ENDOMETRIAL CANCER

There is an increased risk of endometrial cancer in a woman with a uterus who uses unopposed estrogens. Adding a progestin to estrogen therapy has been shown to reduce the risk of endometrial hyperplasia, which may be a precursor to endometrial cancer. Adequate diagnostic measures, including directed or random endometrial sampling when indicated, should be undertaken to rule out malignancy in postmenopausal women with undiagnosed persistent or recurring

CLICK HERE FOR PRODUCT INDICATION AND IMPORTANT SAFETY INFORMATION

REF

PI PPI

This is a progression of the previous slide
Product Message: 63% report vaginal discomfort

PREMARIN® (conjugated estrogens) 0.625 mg/g
VAGINAL CREAM
Relief—inside and out.

PREMARIN® (conjugated estrogens tablets, USP) is indicated in the treatment of moderate to severe vasomotor symptoms due to menopause, the treatment of moderate to severe symptoms of vulvar and vaginal atrophy due to menopause, and the prevention of postmenopausal osteoporosis.
PREMARIN Vaginal Cream is indicated in the treatment of atrophic vaginitis and kraurosis vulvae and the treatment of moderate to severe dyspareunia, a symptom of vulvar and vaginal atrophy, due to menopause.

IMPORTANT SAFETY INFORMATION

WARNING: ENDOMETRIAL CANCER, CARDIOVASCULAR DISORDERS AND PROBABLE DEMENTIA FOR ESTROGEN-ALONE THERAPY

ENDOMETRIAL CANCER

There is an increased risk of endometrial cancer in a woman with a uterus who uses unopposed estrogens. Adding a progestin to estrogen therapy has been shown to reduce the risk of endometrial hyperplasia, which may be a precursor to endometrial cancer.
Adequate diagnostic measures, including directed or random endometrial sampling when indicated, should be undertaken to rule out malignancy in postmenopausal women with undiagnosed persistent or recurring abnormal genital bleeding [see Warnings and Precautions (5.3)].

CARDIOVASCULAR DISORDERS AND PROBABLE DEMENTIA

Estrogen-alone therapy should not be used for the prevention of cardiovascular disease or dementia [see Warnings and Precautions (5.2, 5.4), and Clinical Studies (14.2, 14.3)].

The Women's Health Initiative (WHI) estrogen-alone substudy reported increased risks of stroke and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age) during 7.1 years of treatment with daily oral conjugated estrogens (CE) [0.625 mg], relative to placebo [see Warnings and Precautions (5.2), and Clinical Studies (14.2)].

The Women's Health Initiative Memory Study (WHIMS) estrogen-alone ancillary study of WHI reported an increased risk of developing probable dementia in postmenopausal women 65 years of age or older during 5.2 years of treatment with daily CE (0.625 mg) alone, relative to placebo. It is unknown whether this finding

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PPI

younger postmenopausal women [see Warnings and Precautions (5.4), Use in Specifi c Populations (8.5), and Clinical Studies (14.3)].
In the absence of comparable data, these risks should be assumed to be similar for other doses of CE and other dosage forms of estrogens.
Estrogens with or without progestins should be prescribed at the lowest effective doses and for the shortest duration consistent with treatment goals and risks for the individual woman.

WARNING: CARDIOVASCULAR DISORDERS, BREAST CANCER AND PROBABLE DEMENTIA FOR ESTROGEN PLUS PROGESTIN THERAPY

Estrogen plus progestin therapy should not be used for the prevention of cardiovascular disease or dementia [see Warnings and Precautions (5.2, 5.4), and Clinical Studies (14.2, 14.3)].

The WHI estrogen plus progestin substudy reported increased risks of DVT, pulmonary embolism, stroke and myocardial infarction in postmenopausal women (50 to 79 years of age) during 5.6 years of treatment with daily oral CE (0.625 mg) combined with medroxyprogesterone acetate (MPA) [2.5 mg], relative to placebo [see Warnings and Precautions (5.2), and Clinical Studies (14.2)].

The WHI estrogen plus progestin substudy also demonstrated an increased risk of invasive breast cancer [see Warnings and Precautions (5.3), and Clinical Studies (14.2)].
The WHIMS estrogen plus progestin ancillary study of the WHI, reported an increased risk of developing probable dementia in postmenopausal women 65 years of age or older during 4 years of treatment with daily CE (0.625 mg) combined with MPA (2.5 mg), relative to placebo. It is unknown whether this finding applies to younger post-menopausal women [see Warnings and Precautions (5.4), Use in Specific Populations (8.5), and Clinical Studies (14.3)].

In the absence of comparable data, these risks should be assumed to be similar for other doses of CE and MPA, and other combinations and dosage forms of estrogens and progestins.

Estrogens with or without progestins should be prescribed at the lowest effective doses and for the shortest duration consistent with treatment goals and risks for the individual woman.

PREMARIN® (conjugated estrogens) 0.625 mg/g
VAGINAL CREAM
Relief—inside and out.

• When prescribing solely for the treatment of symptoms of vulvar and vaginal atrophy, topical vaginal products should be considered. When prescribing solely for the prevention of postmenopausal osteoporosis, therapy should only be considered for women at significant risk of osteoporosis and for whom non-estrogen medications are not considered to be appropriate.

• PREMARIN and PREMARIN Vaginal Cream should not be used under any of the following conditions or circumstances: undiagnosed abnormal genital bleeding; known, suspected, or a history of breast cancer; known or suspected estrogen-dependent neoplasia; active venous thromboembolism or a history of this condition; active or recent arterial thromboembolism; known liver dysfunction or disease; known or suspected pregnancy.

• In a clinical trial, the most commonly reported (≥5%) adverse events for PREMARIN that were statistically different than placebo included vaginal moniliasis, vaginitis, vaginal bleeding, dysmenorrhea, and leg cramps. In a prospective, randomized, placebo-controlled, double-blind study, the most common adverse reactions (≥5%) for PREMARIN Vaginal Cream are headache, infection, abdominal pain, back pain, accidental injury, and vaginitis.

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PREMARIN® (conjugated estrogens) 0.625 mg/g
VAGINAL CREAM
Relief—inside and out.

Study description

A Web-based sexual health survey that included 214 postmenopausal women.

SELECTED SAFETY INFORMATION

WARNING: ENDOMETRIAL CANCER, CARDIOVASCULAR DISORDERS AND PROBABLE DEMENTIA FOR ESTROGEN-ALONE THERAPY
ENDOMETRIAL CANCER

There is an increased risk of endometrial cancer in a woman with a uterus who uses unopposed estrogens. Adding a progestin to estrogen therapy has been shown to reduce the risk of endometrial hyperplasia, which may be a precursor to endometrial cancer. Adequate diagnostic measures, including directed or random endometrial sampling when indicated, should be undertaken to rule out malignancy in postmenopausal women with undiagnosed persistent or recurring

CLICK HERE FOR PRODUCT INDICATION AND IMPORTANT SAFETY INFORMATION

REF

PI PPI

PREMARIN® (conjugated estrogens) 0.625 mg/g
VAGINAL CREAM
Relief—inside and out.

Reference

1. Cumming GP, Herald J, Moncur R, et al. Women's attitudes to hormone replacement therapy, alternative therapy and sexual health: a web-based survey. *Menopause Int*. 2007;13:79-83.

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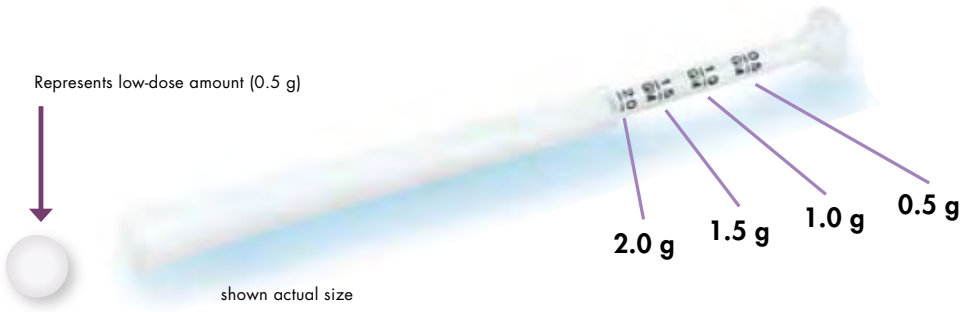
PREMARIN® (conjugated estrogens) 0.625 mg/g
VAGINAL CREAM
Relief—inside and out.

Dosing

PREMARIN Vaginal Cream delivers low cream volume with an easy-to-use applicator[1]

- Flexible dosing (0.5 g, 1.0 g, 1.5 g, or 2.0 g) daily for individualized therapy[1]
- The lowest dose that controls symptoms should be chosen[1]



SELECTED SAFETY INFORMATION

WARNING: ENDOMETRIAL CANCER, CARDIOVASCULAR DISORDERS AND PROBABLE DEMENTIA FOR ESTROGEN-ALONE THERAPY
ENDOMETRIAL CANCER

There is an increased risk of endometrial cancer in a woman with a uterus who uses unopposed estrogens. Adding a progestin to estrogen therapy has been shown to reduce the risk of endometrial hyperplasia, which may be a precursor to endometrial cancer. Adequate diagnostic measures, including directed or random endometrial sampling when indicated, should be undertaken to rule out malignancy in postmenopausal women with undiagnosed persistent or recurring

CLICK HERE FOR PRODUCT INDICATION AND IMPORTANT SAFETY INFORMATION

REF

PI PPI

Pop Up 1.0.1
Message Category: Dosing
Product Message: easy to use applicator

PREMARIN® (conjugated estrogens) 0.625 mg/g
VAGINAL CREAM
Relief—inside and out.

Reference

1. PREMARIN® (conjugated estrogens) Vaginal Cream Prescribing Information, Wyeth Pharmaceuticals Inc.

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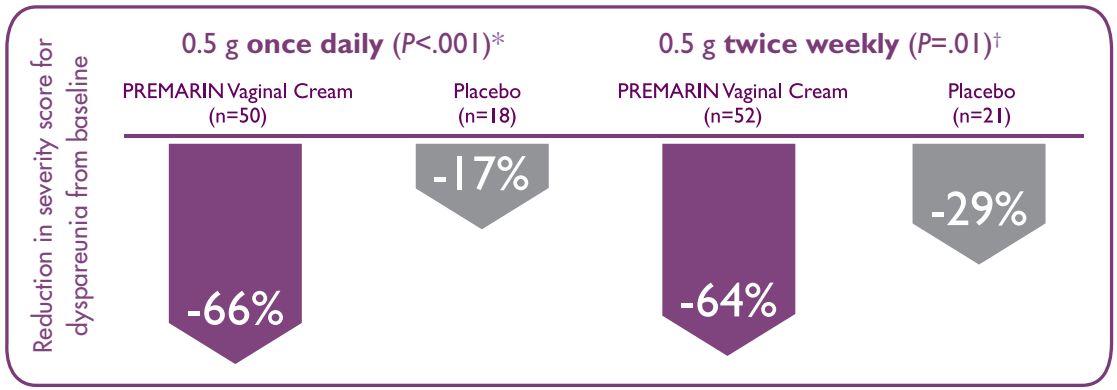
PREMARIN Vaginal Cream—effective relief with a **low** dose and **low** volume[1]

PREMARIN® (conjugated estrogens) 0.625 mg/g
VAGINAL CREAM
Relief—inside and out.

Low-dose efficacy (0.5 g)

- Effectively relieved moderate to severe dyspareunia, a symptom of vulvar and vaginal atrophy, due to menopause[1]

Significant reduction in severity score for dyspareunia compared with placebo at 12 weeks[1]



- Restores natural lubrication and reverses atrophic changes in the vagina for sustained relief with continued use[1-4]

In this study of PREMARIN Vaginal Cream 0.5 g, there were no cases of endometrial hyperplasia or carcinoma at 52 weeks[1*†]

*21 days of PREMARIN Vaginal Cream followed by 7 days of no therapy.
†As measured by endometrial biopsy in all women who had evaluable endometrial sampling.

Study description

Dosing

SELECTED SAFETY INFORMATION

WARNING: ENDOMETRIAL CANCER, CARDIOVASCULAR DISORDERS AND PROBABLE DEMENTIA FOR ESTROGEN-ALONE THERAPY
ENDOMETRIAL CANCER

There is an increased risk of endometrial cancer in a woman with a uterus who uses unopposed estrogens. Adding a progestin to estrogen therapy has been shown to reduce the risk of endometrial hyperplasia, which may be a precursor to endometrial cancer. Adequate diagnostic measures, including directed or random endometrial sampling when indicated, should be undertaken to rule out malignancy in postmenopausal women with undiagnosed persistent or recurring

CLICK HERE FOR PRODUCT INDICATION AND IMPORTANT SAFETY INFORMATION

REF

PI PPI

Parent Slide 3
Slide External Name: Low dose efficacy
Message Category: Efficacy
Product Message: Effective relief with low dose and volume

PREMARIN Vaginal Cream—effective relief with a **low** dose and **low** volume[1]

PREMARIN® (conjugated estrogens) 0.625 mg/g
VAGINAL CREAM
Relief—inside and out.

Study description

Results from a 12-week, randomized, double-blind, placebo-controlled trial that included generally healthy postmenopausal women (N=423) aged 44 to 77 years. Study consisted of an initial 12-week trial followed by an open-label extension to assess endometrial safety through week 52 (n=155).

SELECTED SAFETY INFORMATION

WARNING: ENDOMETRIAL CANCER, CARDIOVASCULAR DISORDERS AND PROBABLE DEMENTIA FOR ESTROGEN-ALONE THERAPY
ENDOMETRIAL CANCER

There is an increased risk of endometrial cancer in a woman with a uterus who uses unopposed estrogens. Adding a progestin to estrogen therapy has been shown to reduce the risk of endometrial hyperplasia, which may be a precursor to endometrial cancer. Adequate diagnostic measures, including directed or random endometrial sampling when indicated, should be undertaken to rule out malignancy in postmenopausal women with undiagnosed persistent or recurring

CLICK HERE FOR PRODUCT INDICATION AND IMPORTANT SAFETY INFORMATION

REF

PI PPI

PREMARIN® (conjugated estrogens) 0.625 mg/g
VAGINAL CREAM
Relief—inside and out.

References

1. PREMARIN® (conjugated estrogens) Vaginal Cream Prescribing Information, Wyeth Pharmaceuticals Inc.

2. Data on file, Wyeth Pharmaceuticals Inc.

3. Manonai J, Theppisai U, Suthutvoravut S, et al. The effect of estradiol vaginal tablet and conjugated estrogen cream on urogenital symptoms in postmenopausal women: a comparative study. *J Obstet Gynaecol Res.* 2001;27:255-260.

4. Semmens JP, Tsai CC, Semmens EC, et al. Effects of estrogen therapy on vaginal physiology during menopause. *Obstet Gynecol.* 1985;66:15-18.

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PPI

PREMARIN Vaginal Cream—the soothing comfort of a cream with a **low** dose[1,2]

PREMARIN® (conjugated estrogens) 0.625 mg/g
VAGINAL CREAM
Relief—inside and out.

PREMARIN Vaginal Cream delivers low cream volume with an easy-to-use applicator[1]

- Flexible dosing (0.5 g, 1.0 g, 1.5 g, or 2.0 g) daily for individualized therapy[1]
- The lowest dose that controls symptoms should be chosen[1]

Low systemic absorption

- In a pharmacokinetic study, after 7 days of dosing with PREMARIN Vaginal Cream 0.5 g daily, levels of estradiol (9.1 pg/mL) did not exceed levels seen in postmenopausal women (0-50 pg/mL) not receiving therapy. Clinical relevance of these data is unknown[1]

Study description

Dosing

SELECTED SAFETY INFORMATION

WARNING:

CARDIOVASCULAR DISORDERS, BREAST CANCER AND PROBABLE DEMENTIA FOR ESTROGEN PLUS PROGESTIN THERAPY

Estrogen plus progestin therapy should not be used for the prevention of cardiovascular disease or dementia [see Warnings and Precautions (5.2, 5.4), and Clinical Studies (14.2, 14.3)].

The WHI estrogen plus progestin substudy reported increased risks of DVT, pulmonary embolism, stroke and myocardial infarction in postmenopausal women (50 to 79 years of age) during 5.6 years of treatment with daily oral CE (0.625

CLICK HERE FOR PRODUCT INDICATION AND IMPORTANT SAFETY INFORMATION

REF

PI PPI

Parent Slide 4
Slide External Name: Dosing/Absorption
Message Category: Dosing
Product Message: low cream volume, low systemic absorption

PREMARIN Vaginal Cream—the soothing comfort of a cream with a **low** dose[1,2]

PREMARIN® (conjugated estrogens) 0.625 mg/g
VAGINAL CREAM
Relief—inside and out.

Study description

Data from an open-label, randomized, multiple-dose, 2-treatment, 2-period, relative bioavailability crossover study (n=24). PREMARIN Vaginal Cream 0.5 g daily and PREMARIN® (conjugated estrogens tablets, USP) oral tablets 0.3 mg daily were used.

SELECTED SAFETY INFORMATION

WARNING:

CARDIOVASCULAR DISORDERS, BREAST CANCER AND PROBABLE DEMENTIA FOR ESTROGEN PLUS PROGESTIN THERAPY

Estrogen plus progestin therapy should not be used for the prevention of cardiovascular disease or dementia [see Warnings and Precautions (5.2, 5.4), and Clinical Studies (14.2, 14.3)].

The WHI estrogen plus progestin substudy reported increased risks of DVT, pulmonary embolism, stroke and myocardial infarction in postmenopausal women (50 to 79 years of age) during 5.6 years of treatment with daily oral CE (0.625

CLICK HERE FOR PRODUCT INDICATION AND IMPORTANT SAFETY INFORMATION

REF

PI PPI

PREMARIN® (conjugated estrogens) 0.625 mg/g
VAGINAL CREAM
Relief—inside and out.

References

1. PREMARIN® (conjugated estrogens) Vaginal Cream Prescribing Information, Wyeth Pharmaceuticals Inc.

2. Data on file, Wyeth Pharmaceuticals Inc.

PI
PPI

PREMARIN Vaginal Cream—effective relief with a **low** dose and **low** volume[1]

PREMARIN® (conjugated estrogens) 0.625 mg/g
VAGINAL CREAM
Relief—inside and out.

Low-dose efficacy (0.5 g)

- Effectively relieved moderate to severe dyspareunia, a symptom of vulvar and vaginal atrophy, due to menopause[1]
- Restores natural lubrication and reverses atrophic changes for sustained relief with continued use[1-4]
- In this study of PREMARIN Vaginal Cream 0.5 g, there were no cases of endometrial hyperplasia or carcinoma at 52 weeks[1]*

(0.5-g dose shown actual size)

Low cream volume (0.5 g)

- Can minimize the potential mess of larger doses
- Can be applied directly to vulvar and vaginal tissues for relief inside and out

Low systemic absorption

- In a pharmacokinetic study, after 7 days of dosing with PREMARIN Vaginal Cream 0.5 g daily, levels of estradiol (9.1 pg/mL) did not exceed levels seen in postmenopausal women (0-50 pg/mL) not receiving therapy. Clinical relevance of these data is unknown[1†]

Prescribe PREMARIN Vaginal Cream—a little bit of cream can help make a difference in her symptoms.

Study description

Dosing

SELECTED SAFETY INFORMATION

WARNING:

CARDIOVASCULAR DISORDERS, BREAST CANCER AND PROBABLE DEMENTIA FOR ESTROGEN PLUS PROGESTIN THERAPY

Estrogen plus progestin therapy should not be used for the prevention of cardiovascular disease or dementia [see Warnings and Precautions (5.2, 5.4), and Clinical Studies (14.2, 14.3)].

The WHI estrogen plus progestin substudy reported increased risks of DVT, pulmonary embolism, stroke and myocardial infarction in postmenopausal women (50 to 79 years of age) during 5.6 years of treatment with daily oral CE (0.625

CLICK HERE FOR PRODUCT INDICATION AND IMPORTANT SAFETY INFORMATION

REF

PI PPI

Parent Slide 5
Slide External Name: Premarin Cream Summary
Message Category: Summary
Product Message: A little bit of cream can help make a difference

PREMARIN Vaginal Cream—effective relief with a **low** dose and **low** volume[†]

PREMARIN® (conjugated estrogens) 0.625 mg/g
VAGINAL CREAM
Relief—inside and out.

Study description

*Results from a 12-week, randomized, double-blind, placebo-controlled trial that included generally healthy postmenopausal women (N=423) aged 44 to 77 years. Study consisted of an initial 12-week trial followed by an open-label extension to assess endometrial safety through week 52 (n=155), as measured by endometrial biopsy in all women who had evaluable endometrial sampling.

†Data from an open-label, randomized, multiple-dose, 2-treatment, 2-period, relative bioavailability crossover study (n=24). PREMARIN Vaginal Cream 0.5 g daily and PREMARIN® (conjugated estrogens tablets, USP) oral tablets 0.3 mg daily were used.

SELECTED SAFETY INFORMATION

WARNING:

CARDIOVASCULAR DISORDERS, BREAST CANCER AND PROBABLE DEMENTIA FOR ESTROGEN PLUS PROGESTIN THERAPY

Estrogen plus progestin therapy should not be used for the prevention of cardiovascular disease or dementia [see Warnings and Precautions (5.2, 5.4), and Clinical Studies (14.2, 14.3)].

The WHI estrogen plus progestin substudy reported increased risks of DVT, pulmonary embolism, stroke and myocardial infarction in postmenopausal women (50 to 79 years of age) during 5.6 years of treatment with daily oral CE (0.625

CLICK HERE FOR PRODUCT INDICATION AND IMPORTANT SAFETY INFORMATION

REF

PI PPI

PREMARIN® (conjugated estrogens) 0.625 mg/g
VAGINAL CREAM
Relief—inside and out.

References

1. PREMARIN® (conjugated estrogens) Vaginal Cream Prescribing Information, Wyeth Pharmaceuticals Inc.

2. Data on file, Wyeth Pharmaceuticals Inc.

3. Manonai J, Theppisai U, Suthutvoravut S, et al. The effect of estradiol vaginal tablet and conjugated estrogen cream on urogenital symptoms in postmenopausal women: a comparative study. *J Obstet Gynaecol Res.* 2001;27:255-260.

4. Semmens JP, Tsai CC, Semmens EC, et al. Effects of estrogen therapy on vaginal physiology during menopause. *Obstet Gynecol.* 1985;66:15-18.

PI
PPI

PREMARIN® (conjugated estrogens) 0.625 mg/g
VAGINAL CREAM
Relief—inside and out.

Prescribing Information

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Premarin, conjugated estrogens, Vaginal Cream safely and effectively. See full prescribing information for Premarin Vaginal Cream.

Premarin, conjugated estrogens, Vaginal Cream in a nonliquefying base Initial U.S. Approval: 1946

WARNING: ENDOMETRIAL CANCER, CARDIOVASCULAR DISORDERS AND PROBABLE DEMENTIA FOR ESTROGEN-ALONE THERAPY

See full prescribing information for complete boxed warning.

- There is an increased risk of endometrial cancer in a woman with a uterus who uses unopposed estrogens. (5.3)
- Estrogen-alone therapy should not be used for the prevention of cardiovascular disease or dementia. (5.2, 5.4)
- The Women's Health Initiative (WHI) estrogen-alone substudy reported increased risks of stroke and deep vein thrombosis. (5.2)
- The Women's Health Initiative Memory Study (WHIMS) estrogen-alone ancillary study of WHI reported an increased risk of probable dementia in postmenopausal women 65 years of age and older. (5.4)

WARNING: CARDIOVASCULAR DISORDERS, BREAST CANCER AND PROBABLE DEMENTIA FOR ESTROGEN PLUS PROGESTIN THERAPY

See full prescribing information for complete boxed warning.

- Estrogen plus progestin therapy should not be used for the prevention of cardiovascular disease or dementia. (5.2, 5.4)
- The WHI estrogen plus progestin substudy reported increased risks of stroke, deep vein thrombosis, pulmonary embolism, and myocardial infarction. (5.2)
- The WHI estrogen plus progestin substudy reported increased risks of invasive breast cancer. (5.3)
- The WHIMS estrogen plus progestin ancillary study of WHI reported an increased risk of probable dementia in postmenopausal women 65 years of age and older. (5.4)

————————RECENT MAJOR CHANGES————————

Indications and Usage (1) 11/2008

PREMARIN® (conjugated estrogens) 0.625 mg/g
VAGINAL CREAM
Relief—inside and out.

Prescribing Information

What are the ingredients in PREMARIN Vaginal Cream?
PREMARIN Vaginal Cream contains a mixture of conjugated estrogens, which are a mixture of sodium estrone sulfate and sodium equilin sulfate and other components, including sodium sulfate conjugates: 17 -dihydroequilin, 17 -estradiol, and 17 -dihydroequilin. PREMARIN Vaginal Cream also contains cetyl esters wax, cetyl alcohol, white wax, glyceryl monostearate, propylene glycol monostearate, methyl stearate, benzyl alcohol, sodium lauryl sulfate, glycerin, and mineral oil.
PREMARIN (conjugated estrogens) Vaginal Cream—Each gram contains 0.625 mg conjugated estrogens, USP.
Combination package: Each contains a net wt. 1.5 oz (42.5 g) tube with one plastic applicator calibrated in 0.5 g increments to a maximum of 2 g (NDC 0046-0872-93).
Store at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].
Wyeth®
Wyeth Pharmaceuticals Inc.
Philadelphia, PA 19101

PATIENT INFORMATION
PREMARIN® (conjugated estrogens) Vaginal Cream
Read this PATIENT INFORMATION before you start using PREMARIN Vaginal Cream and read what you get each time you refill your PREMARIN Vaginal Cream prescription. There may be new information. This information does not take the place of talking to your healthcare provider about your menopausal symptoms and their treatment.
What is the most important information I should know about PREMARIN Vaginal Cream (an estrogen mixture)?
- Estrogens may increase the chances of getting cancer of the uterus.
- Report any unusual vaginal bleeding right away while you are using PREMARIN Vaginal Cream. Vaginal bleeding after menopause may be a warning sign of cancer of the uterus (womb). Your healthcare provider should check any unusual vaginal bleeding to find the cause.
- Do not use estrogens with or without progestins to prevent heart disease, heart attacks, strokes or dementia.
Using estrogens, with or without progestins, may increase your chance of getting heart attacks, strokes, breast cancer, and blood clots. Using estrogens, with or without progestins, may increase your chance of getting dementia, based on a study of women age 65 years or older. You and your healthcare provider should talk regularly about whether you still need treatment

PREMARIN® (conjugated estrogens) 0.625 mg/g
VAGINAL CREAM
Relief—inside and out.

Prescribing Information

This product's label may have been updated. For current package insert and further product information, please visit www.wyeth.com or call our medical communications department toll-free at 1-800-934-5556.

Wyeth®
Wyeth Pharmaceuticals Inc.
Philadelphia, PA 19101
W10413C016
ET01
Rev 03/09

Evidence supports starting appropriate symptomatic menopausal women on estrogen therapy[1]

PREMARIN®
(conjugated estrogens tablets, USP)

Dosing

SELECTED SAFETY INFORMATION

WARNINGS

ENDOMETRIAL CANCER
Adequate diagnostic measures, including endometrial sampling when indicated, should be undertaken to rule out malignancy in all cases of undiagnosed persistent or recurring abnormal vaginal bleeding. (See WARNINGS, Malignant neoplasms, Endometrial cancer in the Prescribing Information.)

CARDIOVASCULAR AND OTHER RISKS
Estrogens with or without progestins should not be used for the prevention of cardiovascular disease or dementia. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders and Dementia in the Prescribing Information.)
The estrogen alone substudy of the Women's Health Initiative (WHI) reported increased risks of stroke and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age)

CLICK HERE FOR PRODUCT INDICATION AND IMPORTANT SAFETY INFORMATION

REF

PI
PPI

Parent Slide 6
Slide External Name: Premarin Oral Title
Message Category: Non Specific Messaging
Product Message: Evidence supports

PREMARIN®
(conjugated estrogens tablets, USP)

PREMARIN is indicated in the treatment of moderate to severe vasomotor symptoms due to menopause, the treatment of moderate to severe symptoms of vulvar and vaginal atrophy due to menopause, and the prevention of postmenopausal osteoporosis.

IMPORTANT SAFETY INFORMATION

WARNINGS

ENDOMETRIAL CANCER

Adequate diagnostic measures, including endometrial sampling when indicated, should be undertaken to rule out malignancy in all cases of undiagnosed persistent or recurring abnormal vaginal bleeding. (See WARNINGS, Malignant neoplasms, Endometrial cancer in the Prescribing Information.)

CARDIOVASCULAR AND OTHER RISKS

Estrogens with or without progestins should not be used for the prevention of cardiovascular disease or dementia. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders and Dementia in the Prescribing Information.)

The estrogen alone substudy of the Women's Health Initiative (WHI) reported increased risks of stroke and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age) during 6.8 years and 7.1 years, respectively, of treatment with daily oral conjugated estrogens (CE 0.625 mg), relative to placebo. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders in the Prescribing Information.)

The estrogen plus progestin substudy of WHI reported increased risks of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli, and DVT in postmenopausal women (50 to 79 years of age) during 5.6 years of treatment with daily CE 0.625 mg combined with medroxyprogesterone acetate (MPA 2.5 mg), relative to placebo. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders and Malignant neoplasms, Breast cancer in the Prescribing Information.)

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PPI

PREMARIN®
(conjugated estrogens tablets, USP)

The Women's Health Initiative Memory Study (WHIMS), a substudy of WHI, reported an increased risk of developing probable dementia in postmenopausal women 65 years of age or older during 5.2 years of treatment with daily CE 0.625 mg alone and during 4 years of treatment with daily CE 0.625 mg combined with MPA 2.5 mg, relative to placebo. It is unknown whether this finding applies to younger postmenopausal women. (See CLINICAL STUDIES and WARNINGS, Dementia and PRECAUTIONS, Geriatric Use in the Prescribing Information.)

In the absence of comparable data, these risks should be assumed to be similar for other doses of CE and MPA and other combinations and dosage forms of estrogens and progestins. Because of these risks, estrogens with or without progestins should be prescribed at the lowest effective doses and for the shortest duration consistent with treatment goals and risks for the individual woman.

- When prescribing solely for the treatment of symptoms of vulvar and vaginal atrophy, topical vaginal products should be considered. When prescribing solely for the prevention of postmenopausal osteoporosis, therapy should only be considered for women at significant risk of osteoporosis and for whom non-estrogen medications are not considered to be appropriate.

- PREMARIN should not be used under any of the following conditions or circumstances: undiagnosed abnormal genital bleeding; known, suspected, or a history of breast cancer; known or suspected estrogen-dependent neoplasia; active venous thromboembolism or a history of this condition; active or recent arterial thromboembolism; liver dysfunction or disease; in patients with a known hypersensitivity to its ingredients; known or suspected pregnancy.

- In a clinical trial, the most commonly reported (5%) adverse events for PREMARIN that were statistically different than placebo included vaginal moniliasis, vaginitis, vaginal bleeding, dysmenorrhea, and leg cramps.

PI
PPI

PREMARIN®
(conjugated estrogens tablets, USP)

Reference

1. PREMARIN® (conjugated estrogens tablets, USP) Prescribing Information, Wyeth Pharmaceuticals Inc.

PI
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PREMARIN: evidence to support your recommendations[1-15]

PREMARIN®
(conjugated estrogens tablets, USP)

Breast cancer safety profile

Cardiovascular safety profile

Dosing

SELECTED SAFETY INFORMATION

WARNINGS

ENDOMETRIAL CANCER
Adequate diagnostic measures, including endometrial sampling when indicated, should be undertaken to rule out malignancy in all cases of undiagnosed persistent or recurring abnormal vaginal bleeding. (See WARNINGS, Malignant neoplasms, Endometrial cancer in the Prescribing Information.)

CARDIOVASCULAR AND OTHER RISKS
Estrogens with or without progestins should not be used for the prevention of cardiovascular disease or dementia. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders and Dementia in the Prescribing Information.)
The estrogen alone substudy of the Women's Health Initiative (WHI) reported increased risks of stroke and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age)

CLICK HERE FOR PRODUCT INDICATION AND IMPORTANT SAFETY INFORMATION

REF

PI
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Parent Slide 7
Slide External Name: Breast/CV Safety
Message Category: Safety

PREMARIN®
(conjugated estrogens tablets, USP)

References

1. The Women's Health Initiative Steering Committee. Effects of conjugated equine estrogen in postmenopausal women with hysterectomy: the Women's Health Initiative randomized controlled trial. *JAMA*. 2004;291:1701-1712.

2. Utian WH, Shoupe D, Bachmann G, et al. Relief of vasomotor symptoms and vaginal atrophy with lower doses of conjugated equine estrogens and medroxyprogesterone acetate. *Fertil Steril*. 2001;75:1065-1079.

3. Lindsay R, Gallagher JC, Kleerekoper M, et al. Effect of lower doses of conjugated equine estrogens with and without medroxyprogesterone acetate on bone in early postmenopausal women. *JAMA*. 2002;287:2668-2676.

4. Pickar JH, Yeh I-T, Wheeler JE, et al. Endometrial effects of lower doses of conjugated equine estrogens and medroxyprogesterone acetate. *Fertil Steril*. 2001;76:25-31.

5. Archer DF, Dorin M, Lewis V, et al. Effects of lower doses of conjugated equine estrogens and medroxyprogesterone acetate on endometrial bleeding. *Fertil Steril*. 2001;75:1080-1087.

6. Greendale GA, Reboussin BA, Hogan P, et al, for the Postmenopausal Estrogen/Progestin Interventions Trial Investigators. Symptom relief and side effects of postmenopausal hormones: results from the Postmenopausal Estrogen/Progestin Interventions Trial. *Obstet Gynecol.* 1998;92:982-988.

7. The Writing Group for the PEPI Trial. Effects of hormone replacement therapy on endometrial histology in postmenopausal women: the Postmenopausal Estrogen/Progestin Interventions (PEPI) Trial. *JAMA*.1996;275:370-375.

8. The Writing Group for the PEPI Trial. Effects of hormone therapy on bone mineral density: results from the Postmenopausal Estrogen/Progestin Interventions (PEPI) trial. *JAMA*.1996;276:1389-1396.

PI
PPI

PREMARIN®
(conjugated estrogens tablets, USP)

References

9. Shumaker SA, Legault C, Kuller L, et al, for the Women's Health Initiative Memory Study Investigators. Conjugated equine estrogens and incidence of probable dementia and mild cognitive impairment in postmenopausal women: Women's Health Initiative Memory Study. *JAMA*. 2004;291:2947-2958.

10. Archer DF, Pickar JH, Bottiglioni F, for The Menopause Study Group. Bleeding patterns in postmenopausal women taking continuous combined or sequential regimens of conjugated estrogens with medroxyprogesterone acetate. *Obstet Gynecol*. 1994;83:686-692.

11. Woodruff JD, Pickar JH, for The Menopause Study Group. Incidence of endometrial hyperplasia in postmenopausal women taking conjugated estrogens (Premarin) with medroxyprogesterone acetate or conjugated estrogens alone. *Am J Obstet Gynecol.* 1994;170:1213-1223.

12. Hsia J, Langer RD, Manson JE, et al, for the Women's Health Initiative Investigators. Conjugated equine estrogens and coronary heart disease: the Women's Health Initiative. *Arch Intern Med.* 2006;166:357-365.

13. Curb JD, Prentice RL, Bray PF, et al. Venous thrombosis and conjugated equine estrogen in women without a uterus. *Arch Intern Med.* 2006;166:772-780.

14. Stefanick ML, Anderson GL, Margolis KL, et al, for the WHI Investigators. Effects of conjugated equine estrogens on breast cancer and mammography screening in postmenopausal women with hysterectomy. *JAMA*.2006;295:1647-1657.

15. Hendrix SL, Wassertheil-Smoller S, Johnson KC, et al, for the WHI Investigators. Effects of conjugated equine estrogen on stroke in the Women's Health Initiative. *Circulation*. 2006;113:2425-2434.

PI
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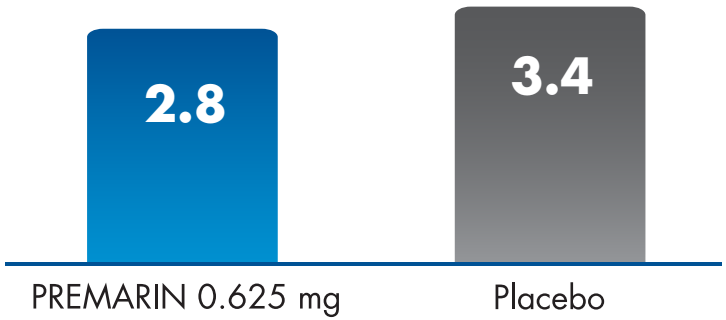
PREMARIN: evidence to support your recommendations[1-15]

PREMARIN®
(conjugated estrogens tablets, USP)

In the Women's Health Initiative (WHI), the most important randomized clinical trial providing information about breast cancer in postmenopausal women using hormone therapy

No increased risk of invasive breast cancer with PREMARIN was found after an average follow-up of 7.1 years[14]

Number of cases of invasive breast cancer by age group*†
(per 1000 women per year)



**P*=nonsignificant.

†Adjudicated data from the WHI Estrogen-Alone Substudy, a prospective, randomized, double-blind trial comparing estrogen alone with placebo in 10,739 women aged 50-79 years who had undergone a hysterectomy.

The use of estrogens alone and estrogens plus progestin has been reported to result in an increase in abnormal mammograms requiring further evaluation.[16]

SELECTED SAFETY INFORMATION

PREMARIN should not be used under any of the following conditions or circumstances: undiagnosed abnormal genital bleeding; known, suspected, or a history of breast cancer; known or suspected estrogen-dependent neoplasia; active venous thromboembolism or a history of this condition; active or recent arterial thromboembolism; liver dysfunction or disease; in patients with a known hypersensitivity to its ingredients; known or suspected pregnancy.

CARDIOVASCULAR AND OTHER RISKS

Estrogens with or without progestins should not be used for the prevention of cardiovascular disease or dementia. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders and Dementia in the Prescribing Information.)

WARNINGS

CLICK HERE FOR PRODUCT INDICATION AND IMPORTANT SAFETY INFORMATION

REF

PI
PPI

Pop Up 7.0.1
Message Category: Safety
Product Message: No increased risk of breast cancer

PREMARIN®
(conjugated estrogens tablets, USP)

References

1. The Women's Health Initiative Steering Committee. Effects of conjugated equine estrogen in postmenopausal women with hysterectomy: the Women's Health Initiative randomized controlled trial. *JAMA*. 2004;291:1701-1712.

2. Utian WH, Shoupe D, Bachmann G, et al. Relief of vasomotor symptoms and vaginal atrophy with lower doses of conjugated equine estrogens and medroxyprogesterone acetate. *Fertil Steril.* 2001;75:1065-1079.

3. Lindsay R, Gallagher JC, Kleerekoper M, et al. Effect of lower doses of conjugated equine estrogens with and without medroxyprogesterone acetate on bone in early postmenopausal women. *JAMA*. 2002;287:2668-2676.

4. Pickar JH, Yeh I-T, Wheeler JE, et al. Endometrial effects of lower doses of conjugated equine estrogens and medroxyprogesterone acetate. *Fertil Steril.* 2001;76:25-31.

5. Archer DF, Dorin M, Lewis V, et al. Effects of lower doses of conjugated equine estrogens and medroxyprogesterone acetate on endometrial bleeding. *Fertil Steril*. 2001;75:1080-1087.

6. Greendale GA, Reboussin BA, Hogan P, et al, for the Postmenopausal Estrogen/Progestin Interventions Trial Investigators. Symptom relief and side effects of postmenopausal hormones: results from the Postmenopausal Estrogen/Progestin Interventions Trial. *Obstet Gynecol.* 1998;92:982-988.

7. The Writing Group for the PEPI Trial. Effects of hormone replacement therapy on endometrial histology in postmenopausal women: the Postmenopausal Estrogen/Progestin Interventions (PEPI) Trial. *JAMA*. 1996;275:370-375.

8. The Writing Group for the PEPI Trial. Effects of hormone therapy on bone mineral density: results from the Postmenopausal Estrogen/Progestin Interventions (PEPI) trial. *JAMA*. 1996;276:1389-1396.

PI
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PREMARIN®
(conjugated estrogens tablets, USP)

References

9. Shumaker SA, Legault C, Kuller L, et al, for the Women's Health Initiative Memory Study Investigators. Conjugated equine estrogens and incidence of probable dementia and mild cognitive impairment in postmenopausal women: Women's Health Initiative Memory Study. *JAMA*. 2004;291:2947-2958.

10. Archer DF, Pickar JH, Bottiglioni F, for The Menopause Study Group. Bleeding patterns in postmenopausal women taking continuous combined or sequential regimens of conjugated estrogens with medroxyprogesterone acetate. *Obstet Gynecol.* 1994;83:686-692.

11. Woodruff JD, Pickar JH, for The Menopause Study Group. Incidence of endometrial hyperplasia in postmenopausal women taking conjugated estrogens (Premarin) with medroxyprogesterone acetate or conjugated estrogens alone. *Am J Obstet Gynecol.* 1994;170:1213-1223.

12. Hsia J, Langer RD, Manson JE, et al, for the Women's Health Initiative Investigators. Conjugated equine estrogens and coronary heart disease: the Women's Health Initiative. *Arch Intern Med*. 2006;166:357-365.

13. Curb JD, Prentice RL, Bray PF, et al. Venous thrombosis and conjugated equine estrogen in women without a uterus. *Arch Intern Med.* 2006;166:772-780.

14. Stefanick ML, Anderson GL, Margolis KL, et al, for the WHI Investigators. Effects of conjugated equine estrogens on breast cancer and mammography screening in postmenopausal women with hysterectomy. *JAMA*. 2006;295:1647-1657.

15. Hendrix SL, Wassertheil-Smoller S, Johnson KC, et al, for the WHI Investigators. Effects of conjugated equine estrogen on stroke in the Women's Health Initiative. *Circulation*. 2006;113:2425-2434.

16. PREMARIN® (conjugated estrogens tablets, USP) Prescribing Information, Wyeth Pharmaceuticals Inc.

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PREMARIN: evidence to support your recommendations[1-15]

PREMARIN®
(conjugated estrogens tablets, USP)

No increased risk of coronary heart disease with PREMARIN after an average follow-up of 7.1 years[16]

A significant increased risk of stroke and deep vein thrombosis associated with PREMARIN after an average follow-up of 7.1 years[13,16]

PREMARIN should not be used in patients with active venous thromboembolism, a history of venous thromboembolism, or active/recent arterial thromboembolism.

SELECTED SAFETY INFORMATION

WARNINGS

ENDOMETRIAL CANCER
Adequate diagnostic measures, including endometrial sampling when indicated, should be undertaken to rule out malignancy in all cases of undiagnosed persistent or recurring abnormal vaginal bleeding. (See WARNINGS, Malignant neoplasms, Endometrial cancer in the Prescribing Information.)

CARDIOVASCULAR AND OTHER RISKS
Estrogens with or without progestins should not be used for the prevention of cardiovascular disease or dementia. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders and Dementia in the Prescribing Information.)
The estrogen alone substudy of the Women's Health Initiative (WHI) reported increased risks of stroke and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age)

CLICK HERE FOR PRODUCT INDICATION AND IMPORTANT SAFETY INFORMATION

REF

PI PPI

Pop Up 7.0.2
Message Category: Safety
Product Message: No increased risk of coronary heart disease

PREMARIN®
(conjugated estrogens tablets, USP)

References

1. The Women's Health Initiative Steering Committee. Effects of conjugated equine estrogen in postmenopausal women with hysterectomy: the Women's Health Initiative randomized controlled trial. *JAMA*. 2004;291:1701-1712.

2. Utian WH, Shoupe D, Bachmann G, et al. Relief of vasomotor symptoms and vaginal atrophy with lower doses of conjugated equine estrogens and medroxyprogesterone acetate. *Fertil Steril.* 2001;75:1065-1079.

3. Lindsay R, Gallagher JC, Kleerekoper M, et al. Effect of lower doses of conjugated equine estrogens with and without medroxyprogesterone acetate on bone in early postmenopausal women. *JAMA*. 2002;287:2668-2676.

4. Pickar JH, Yeh I-T, Wheeler JE, et al. Endometrial effects of lower doses of conjugated equine estrogens and medroxyprogesterone acetate. *Fertil Steril.* 2001;76:25-31.

5. Archer DF, Dorin M, Lewis V, et al. Effects of lower doses of conjugated equine estrogens and medroxyprogesterone acetate on endometrial bleeding. *Fertil Steril*. 2001;75:1080-1087.

6. Greendale GA, Reboussin BA, Hogan P, et al, for the Postmenopausal Estrogen/Progestin Interventions Trial Investigators. Symptom relief and side effects of postmenopausal hormones: results from the Postmenopausal Estrogen/Progestin Interventions Trial. *Obstet Gynecol.* 1998;92:982-988.

7. The Writing Group for the PEPI Trial. Effects of hormone replacement therapy on endometrial histology in postmenopausal women: the Postmenopausal Estrogen/Progestin Interventions (PEPI) Trial. *JAMA*. 1996;275:370-375.

8. The Writing Group for the PEPI Trial. Effects of hormone therapy on bone mineral density: results from the Postmenopausal Estrogen/Progestin Interventions (PEPI) trial. *JAMA*. 1996;276:1389-1396.

PI
PPI

PREMARIN®
(conjugated estrogens tablets, USP)

References

9. Shumaker SA, Legault C, Kuller L, et al, for the Women's Health Initiative Memory Study Investigators. Conjugated equine estrogens and incidence of probable dementia and mild cognitive impairment in postmenopausal women: Women's Health Initiative Memory Study. *JAMA*. 2004;291:2947-2958.

10. Archer DF, Pickar JH, Bottiglioni F, for The Menopause Study Group. Bleeding patterns in postmenopausal women taking continuous combined or sequential regimens of conjugated estrogens with medroxyprogesterone acetate. *Obstet Gynecol.* 1994;83:686-692.

11. Woodruff JD, Pickar JH, for The Menopause Study Group. Incidence of endometrial hyperplasia in postmenopausal women taking conjugated estrogens (Premarin) with medroxyprogesterone acetate or conjugated estrogens alone. *Am J Obstet Gynecol.* 1994;170:1213-1223.

12. Hsia J, Langer RD, Manson JE, et al, for the Women's Health Initiative Investigators. Conjugated equine estrogens and coronary heart disease: the Women's Health Initiative. *Arch Intern Med*. 2006;166:357-365.

13. Curb JD, Prentice RL, Bray PF, et al. Venous thrombosis and conjugated equine estrogen in women without a uterus. *Arch Intern Med.* 2006;166:772-780.

14. Stefanick ML, Anderson GL, Margolis KL, et al, for the WHI Investigators. Effects of conjugated equine estrogens on breast cancer and mammography screening in postmenopausal women with hysterectomy. *JAMA*. 2006;295:1647-1657.

15. Hendrix SL, Wassertheil-Smoller S, Johnson KC, et al, for the WHI Investigators. Effects of conjugated equine estrogen on stroke in the Women's Health Initiative. *Circulation*. 2006;113:2425-2434.

16. Rossouw JE, Prentice RL, Manson JE, et al. Postmenopausal hormone therapy and risk of cardiovascular disease by age and years since menopause. *JAMA*. 2007;297:1465-1477.

PI
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PREMARIN: proven efficacy to help meet her needs[1-3]

PREMARIN®
(conjugated estrogens tablets, USP)

Significant impact on multiple symptoms of menopause

Dosing

Vasomotor symptom efficacy

Bone mineral density efficacy

SELECTED SAFETY INFORMATION

IMPORTANT SAFETY INFORMATION

ENDOMETRIAL CANCER
Adequate diagnostic measures, including endometrial sampling when indicated, should be undertaken to rule out malignancy in all cases of undiagnosed persistent or recurring abnormal vaginal bleeding. (See WARNINGS, Malignant neoplasms, Endometrial cancer in the Prescribing Information.)

CARDIOVASCULAR AND OTHER RISKS
Estrogens with or without progestins should not be used for the prevention of cardiovascular disease or dementia. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders and Dementia in the Prescribing Information.)

The estrogen alone substudy of the Women's Health Initiative (WHI) reported increased risks of stroke and

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REF

PI
PPI

Parent Slide 8
Slide External Name: Vasomotor/BMD Safety
Message Category: Non Specific Messaging

PREMARIN®
(conjugated estrogens tablets, USP)

References

1. Utian WH, Shoupe D, Bachmann G, et al. Relief of vasomotor symptoms and vaginal atrophy with lower doses of conjugated equine estrogens and medroxyprogesterone acetate. *Fertil Steril.* 2001;75:1065-1079.

2. Lindsay R, Gallagher JC, Kleerekoper M, et al. Effect of lower doses of conjugated equine estrogens with and without medroxyprogesterone acetate on bone in early postmenopausal women. *JAMA.* 2002;287:2668-2676.

3. PREMARIN® (conjugated estrogens tablets, USP) Prescribing Information, Wyeth Pharmaceuticals Inc.

PI
PPI

PREMARIN: proven efficacy to help meet her needs[1-3]

PREMARIN®
(conjugated estrogens tablets, USP)

Significant relief of moderate to severe vasomotor symptoms as early as 3 weeks[1]

84%
reduction in the number of hot flashes by week 4 with PREMARIN 0.625 mg (n=27)[1,3]

94%
reduction in the number of hot flashes by week 12 with PREMARIN 0.625 mg (n=27)[1,3]

In the Women's Health, Osteoporosis, Progestin, Estrogen (HOPE) Study, a randomized, double-blind trial comparing estrogens alone (or in combination with MPA) with placebo in 2673 healthy, postmenopausal women with an intact uterus (including an efficacy-evaluable population [n=241 at baseline] in the vasomotor substudy).

SELECTED SAFETY INFORMATION

IMPORTANT SAFETY INFORMATION

ENDOMETRIAL CANCER
Adequate diagnostic measures, including endometrial sampling when indicated, should be undertaken to rule out malignancy in all cases of undiagnosed persistent or recurring abnormal vaginal bleeding. (See WARNINGS, Malignant neoplasms, Endometrial cancer in the Prescribing Information.)

CARDIOVASCULAR AND OTHER RISKS
Estrogens with or without progestins should not be used for the prevention of cardiovascular disease or dementia. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders and Dementia in the Prescribing Information.)

The estrogen alone substudy of the Women's Health Initiative (WHI) reported increased risks of stroke and

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REF PI PPI

Pop Up 8.0.1
Message Category: Efficacy
Product Message: Significant relief of vasomotor symptoms

PREMARIN®
(conjugated estrogens tablets, USP)

References

1. Utian WH, Shoupe D, Bachmann G, et al. Relief of vasomotor symptoms and vaginal atrophy with lower doses of conjugated equine estrogens and medroxyprogesterone acetate. *Fertil Steril.* 2001;75:1065-1079.

2. Lindsay R, Gallagher JC, Kleerekoper M, et al. Effect of lower doses of conjugated equine estrogens with and without medroxyprogesterone acetate on bone in early postmenopausal women. *JAMA.* 2002;287:2668-2676.

3. PREMARIN® (conjugated estrogens tablets, USP) Prescribing Information, Wyeth Pharmaceuticals Inc.

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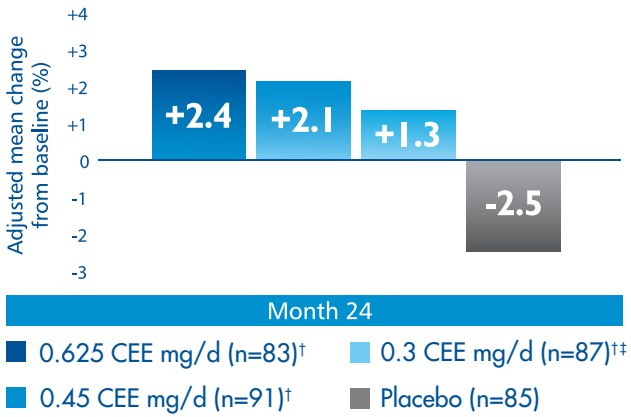
PREMARIN: proven efficacy to help meet her needs[1-3]

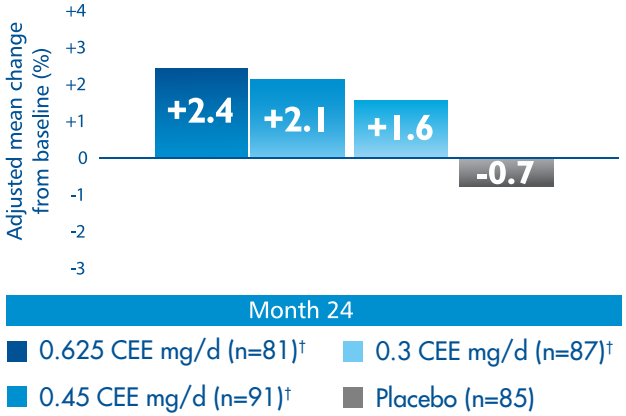
PREMARIN®
(conjugated estrogens tablets, USP)

Significant increase in spine and hip bone mineral density (BMD)[2,4]

Change in spine BMD[4]*



Change in hip BMD[4]*



Data from the Women's HOPE Study: a 2-year study of 2673 healthy postmenopausal women (average age of 53.3 years). The BMD substudy included 822 women.

*Modified intent-to-treat population.
†Differences from baseline and placebo were significant ($P<.05$).
‡$P=.02$ for 0.3 mg vs 0.625 mg. Percentages rounded to nearest tenth. All patients received one 600-mg tablet of Caltrate® daily.

SELECTED SAFETY INFORMATION

IMPORTANT SAFETY INFORMATION

ENDOMETRIAL CANCER
Adequate diagnostic measures, including endometrial sampling when indicated, should be undertaken to rule out malignancy in all cases of undiagnosed persistent or recurring abnormal vaginal bleeding. (See WARNINGS, Malignant neoplasms, Endometrial cancer in the Prescribing Information.)

CARDIOVASCULAR AND OTHER RISKS
Estrogens with or without progestins should not be used for the prevention of cardiovascular disease or dementia. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders and Dementia in the Prescribing Information.)

The estrogen alone substudy of the Women's Health Initiative (WHI) reported increased risks of stroke and

CLICK HERE FOR PRODUCT INDICATION AND IMPORTANT SAFETY INFORMATION

REF

PI PPI

Pop Up 8.0.2
Message Category: Efficacy
Product Message: Significant increase in spine and hip BMD

PREMARIN®
(conjugated estrogens tablets, USP)

References

1. Utian WH, Shoupe D, Bachmann G, et al. Relief of vasomotor symptoms and vaginal atrophy with lower doses of conjugated equine estrogens and medroxyprogesterone acetate. *Fertil Steril.* 2001;75:1065-1079.

2. Lindsay R, Gallagher JC, Kleerekoper M, et al. Effect of lower doses of conjugated equine estrogens with and without medroxyprogesterone acetate on bone in early postmenopausal women. *JAMA.* 2002;287:2668-2676.

3. PREMARIN® (conjugated estrogens tablets, USP) Prescribing Information, Wyeth Pharmaceuticals Inc.

4. Data on file, Wyeth Pharmaceuticals Inc.

PI
PPI

PREMARIN: proven efficacy to help meet her needs[1-3]

PREMARIN®
(conjugated estrogens tablets, USP)

PREMARIN can provide symptom relief and bone protection at every dose[1-3]

0.3 mg | 0.45 mg | 0.625 mg | 0.9 mg | 1.25 mg

SELECTED SAFETY INFORMATION

IMPORTANT SAFETY INFORMATION

ENDOMETRIAL CANCER
Adequate diagnostic measures, including endometrial sampling when indicated, should be undertaken to rule out malignancy in all cases of undiagnosed persistent or recurring abnormal vaginal bleeding. (See WARNINGS, Malignant neoplasms, Endometrial cancer in the Prescribing Information.)

CARDIOVASCULAR AND OTHER RISKS
Estrogens with or without progestins should not be used for the prevention of cardiovascular disease or dementia. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders and Dementia in the Prescribing Information.)

The estrogen alone substudy of the Women's Health Initiative (WHI) reported increased risks of stroke and

CLICK HERE FOR PRODUCT INDICATION AND IMPORTANT SAFETY INFORMATION

REF | PI PPI

Pop Up
Message Category: Dosing
Product Message: symptom relief and bone protection at every dose

PREMARIN®
(conjugated estrogens tablets, USP)

References

1. Utian WH, Shoupe D, Bachmann G, et al. Relief of vasomotor symptoms and vaginal atrophy with lower doses of conjugated equine estrogens and medroxyprogesterone acetate. *Fertil Steril.* 2001;75:1065-1079.

2. Lindsay R, Gallagher JC, Kleerekoper M, et al. Effect of lower doses of conjugated equine estrogens with and without medroxyprogesterone acetate on bone in early postmenopausal women. *JAMA.* 2002;287:2668-2676.

3. PREMARIN® (conjugated estrogens tablets, USP) Prescribing Information, Wyeth Pharmaceuticals Inc.

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PREMARIN®
(conjugated estrogens tablets, USP)

Prescribing Information

PREMARIN®
(conjugated estrogens tablets, USP)
Rx only
WARNINGS
ENDOMETRIAL CANCER
Adequate diagnostic measures, including endometrial sampling when indicated, should be undertaken to rule out malignancy in all cases of undiagnosed persistent or recurring abnormal vaginal bleeding. (See WARNINGS, Malignant neoplasms, Endometrial cancer.)

CARDIOVASCULAR AND OTHER RISKS
Estrogens with or without progestins should not be used for the prevention of cardiovascular disease or dementia. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders and Dementia.)
The estrogen alone substudy of the Women's Health Initiative (WHI) reported increased risks of stroke and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age) during 6.8 years and 7.1 years, respectively, of treatment with daily oral conjugated estrogens (CE 0.625 mg), relative to placebo. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders.)
The estrogen plus progestin substudy of WHI reported increased risks of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli, and DVT in postmenopausal women (50 to 79 years of age) during 5.6 years of treatment with daily CE 0.625 mg combined with medroxyprogesterone acetate (MPA 2.5 mg), relative to placebo. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders and Malignant neoplasms, Breast cancer.)
The Women's Health Initiative Memory Study (WHIMS), a substudy of WHI, reported an increased risk of developing probable dementia in postmenopausal women 65 years of age or older during 5.2 years of treatment with daily CE 0.625 mg alone and during 4 years of treatment with daily CE 0.625 mg combined with MPA 2.5 mg, relative to placebo. It is unknown whether this finding applies to younger postmenopausal women. (See CLINICAL STUDIES and WARNINGS, Dementia and PRECAUTIONS, Geriatric Use.)
In the absence of comparable data, these risks should be assumed to be similar for other doses of CE and MPA and other combinations and dosage forms of estrogens and progestins. Because of these risks, estrogens with or without progestins should be prescribed at the lowest effective doses and for the shortest duration consistent with treatment goals and risks for the individual woman.
DESCRIPTION

PREMARIN®
(conjugated estrogens tablets, USP)

Prescribing Information

PREMARIN® (conjugated estrogens tablets, USP) for oral administration contains a mixture of conjugated estrogens obtained exclusively from natural sources, occurring as the sodium salts of water-soluble estrogen sulfates blended to represent the average composition of material derived

PATIENT INFORMATION
PREMARIN®
(conjugated estrogens tablets, USP)
Read this PATIENT INFORMATION before you start taking PREMARIN and read what you get each time you refill your PREMARIN prescription. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.
What is the most important information I should know about PREMARIN (an estrogen mixture)?
- Estrogens increase the chance of getting cancer of the uterus.
Report any unusual vaginal bleeding right away while you are taking PREMARIN.
Vaginal bleeding after menopause may be a warning sign of cancer of the uterus (womb).
Your healthcare provider should check any unusual vaginal bleeding to find out the cause.
- Do not use estrogens with or without progestins to prevent heart disease, heart attacks, strokes, or dementia.
Using estrogens, with or without progestins, may increase your chance of getting heart attacks, strokes, breast cancer, and blood clots. Using estrogens, with or without progestins, may increase your chance of getting dementia, based on a study of women age 65 years or older. You and your healthcare provider should talk regularly about whether you still need treatment with PREMARIN.
What is PREMARIN?
PREMARIN is a medicine that contains a mixture of estrogen hormones.
PREMARIN is used after menopause to:
- Reduce moderate to severe hot flashes. Estrogens are hormones made by a woman's ovaries. The ovaries normally stop making estrogens when a woman is between 45 and 55 years old. This drop in body estrogen levels causes the “change of life” or menopause (the end of monthly menstrual periods). Sometimes both ovaries are removed during an operation before natural menopause takes place. The sudden drop in estrogen levels causes “surgical menopause.”
When the estrogen levels begin dropping, some women get very uncomfortable symptoms, such as feelings of warmth in the face, neck, and chest, or sudden strong feelings of heat and sweating (“hot flashes” or “hot flushes”). In some women the symptoms are mild, and they will not need to take estrogens. In other

Prescribing Information

women, symptoms can be more severe. You and your healthcare provider should talk regularly about whether you still need treatment with PREMARIN.

The tablets come in different strengths and each strength tablet is a different color. The color ingredients are:
— 0.3 mg tablet (green color): D&C Yellow No. 10 and FD&C Blue No. 2.
— 0.45 mg tablet (blue color): FD&C Blue No. 2.
— 0.625 mg tablet (maroon color): FD&C Blue No. 2 and FD&C Red No. 40.
— 0.9 mg tablet (white color): D&C Red No. 30 and D&C Red No. 7.
— 1.25 mg tablet (yellow color): black iron oxide, D&C Yellow No. 10, and
FD&C Yellow No. 6.
The appearance of these tablets is a trademark of Wyeth Pharmaceuticals.
Store at Controlled Room Temperature 20° – 25°C (68° – 77°F).
This product's label may have been updated. For current package insert and further product information, please visit www.wyeth.com or call our medical communications department toll-free at 1-800-934-5556.
Wyeth®
Wyeth Pharmaceuticals Inc.
Philadelphia, PA 19101
W10405C023
ET01
Rev 05/08

Individualize her therapy with a range of dosing options

PREMPRO®
(conjugated estrogens/medroxyprogesterone acetate tablets)
0.3 mg / 1.5 mg

Dosing

Evidence supports starting appropriate symptomatic menopausal women on hormone therapy[1]

SELECTED SAFETY INFORMATION

WARNINGS

CARDIOVASCULAR AND OTHER RISKS
Estrogens plus progestins should not be used for the prevention of cardiovascular disease or dementia. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders and Dementia in the Prescribing Information.)

The estrogen plus progestin substudy of the Women's Health Initiative (WHI) reported increased risks of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli, and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age) during 5.6 years of treatment with daily oral conjugated estrogens (CE 0.625 mg) combined with medroxyprogesterone acetate (MPA 2.5 mg), relative to placebo. (See CLINICAL STUDIES and WARNINGS, Cardiovas-

CLICK HERE FOR PRODUCT INDICATION AND IMPORTANT SAFETY INFORMATION

REF

PI
PPI

Parent Slide 9
Slide External Name: Prempro Title
Message Category: Non Specific Messaging
Product Message: Individualize her therapy

PREMPRO®
(conjugated estrogens/medroxyprogesterone acetate tablets)
0.3 mg / 1.5 mg

PREMPRO is indicated in women who have a uterus for the treatment of moderate to severe vasomotor symptoms due to menopause, the treatment of moderate to severe symptoms of vulvar and vaginal atrophy due to menopause, and the prevention of postmenopausal osteoporosis.

IMPORTANT SAFETY INFORMATION

WARNINGS

CARDIOVASCULAR AND OTHER RISKS

Estrogens plus progestins should not be used for the prevention of cardiovascular disease or dementia. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders and Dementia in the Prescribing Information.)

The estrogen plus progestin substudy of the Women's Health Initiative (WHI) reported increased risks of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli, and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age) during 5.6 years of treatment with daily oral conjugated estrogens (CE 0.625 mg) combined with medroxyprogesterone acetate (MPA 2.5 mg), relative to placebo. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders and Malignant neoplasms, Breast cancer in the Prescribing Information.)

The estrogen alone substudy of the WHI reported increased risks of stroke and DVT in postmenopausal women (50 to 79 years of age) during 6.8 years and 7.1 years, respectively, of treatment with daily CE 0.625 mg, relative to placebo. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders in the Prescribing Information.)

The Women's Health Initiative Memory Study (WHIMS), a substudy of WHI, reported an increased risk of developing probable dementia in postmenopausal women 65 years of age or older during 4 years of treatment with daily CE 0.625 mg combined with MPA 2.5 mg and during 5.2 years of treatment with daily CE 0.625 mg alone, relative to placebo. It is unknown whether this fi nding applies to younger postmenopausal women. (See CLINICAL STUDIES and WARNINGS, Dementia and PRECAUTIONS, Geriatric Use in the Prescribing Information.)

PI
PPI

In the absence of comparable data, these risks should be assumed to be similar for other doses of CE and MPA and other combinations and dosage forms of estrogens and progestins. Because of these risks, estrogens with or without progestins should be prescribed at the lowest effective doses and for the shortest duration consistent with treatment goals and risks for the individual woman.

• When prescribing solely for the treatment of symptoms of vulvar and vaginal atrophy, topical vaginal products should be considered. When prescribing solely for the prevention of postmenopausal osteoporosis, therapy should only be considered for women at signifi cant risk of osteoporosis and for whom non-estrogen medications are not considered to be appropriate.

• PREMPRO should not be used under any of the following conditions or circumstances: undiagnosed abnormal genital bleeding; known, suspected, or a history of breast cancer; known or suspected estrogen-dependent neoplasia; active venous thromboembolism or a history of this condition; active or recent arterial thromboembolism; liver dysfunction or disease; in patients with a known hypersensitivity to its ingredients; known or suspected pregnancy.

• In a clinical trial, the most commonly reported (5%) adverse events for PREMPRO 0.45 mg/1.5 mg and PREMPRO 0.625 mg/2.5 mg that were statistically different than placebo were mastalgia, vaginal bleeding, vaginal moniliasis, leg cramps, dysmenorrhea, breast enlargement, and vaginitis. In a clinical trial, there was no difference in the commonly reported (5%) adverse events for women taking PREMPRO 0.3 mg/1.5 mg compared to those taking placebo.

PREMPRO®
(conjugated estrogens/medroxyprogesterone acetate tablets)
0.3 mg / 1.5 mg

Reference

1. PREMPRO®/PREMPHASE® (conjugated estrogens/medroxyprogesterone acetate tablets) Prescribing Information, Wyeth Pharmaceuticals Inc.

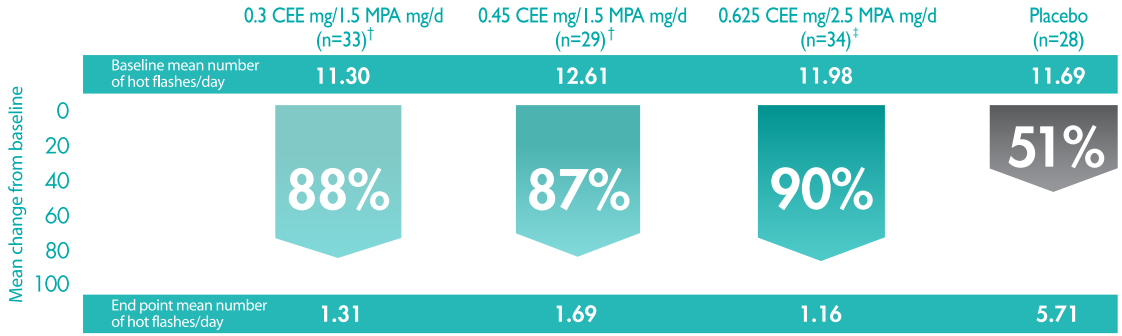
PI
PPI

PREMPRO: low doses can help manage her symptoms effectively[1,2]

PREMPRO®
(conjugated estrogens/medroxyprogesterone acetate tablets)
0.3 mg / 1.5 mg

Significant reduction in moderate to severe hot flashes—even at low doses[1,2]

Decrease in vasomotor symptoms at week 12*



*Efficacy-evaluable population (n=241).
†$P<.05$ from weeks 3 through 12 compared with placebo.
‡$P<.05$ from weeks 2 through 12 compared with placebo.

Study description

Dosing

SELECTED SAFETY INFORMATION

WARNINGS

CARDIOVASCULAR AND OTHER RISKS
Estrogens plus progestins should not be used for the prevention of cardiovascular disease or dementia. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders and Dementia in the Prescribing Information.)

The estrogen plus progestin substudy of the Women's Health Initiative (WHI) reported increased risks of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli, and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age) during 5.6 years of treatment with daily oral conjugated estrogens (CE 0.625 mg) combined with medroxyprogesterone acetate (MPA 2.5 mg), relative to placebo. (See CLINICAL STUDIES and WARNINGS, Cardiovas-

CLICK HERE FOR PRODUCT INDICATION AND IMPORTANT SAFETY INFORMATION

REF

PI PPI

Parent Slide 10
Slide External Name: Vasomotor efficacy
Message Category: Efficacy
Product Message: significant reduction in hot flashes

Chris - we can title this vasomotor to be consistent with Oral or Hot flashes. What do you think?

PREMPRO: low doses can help manage her symptoms effectively[1,2]

PREMPRO®
(conjugated estrogens/medroxyprogesterone acetate tablets)
0.3 mg / 1.5 mg

Study description

Data from the Women's Hope Study: a 2-year study of 2673 healthy, postmenopausal women (average age of 53.3 years).

SELECTED SAFETY INFORMATION

WARNINGS

CARDIOVASCULAR AND OTHER RISKS
Estrogens plus progestins should not be used for the prevention of cardiovascular disease or dementia. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders and Dementia in the Prescribing Information.)

The estrogen plus progestin substudy of the Women's Health Initiative (WHI) reported increased risks of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli, and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age) during 5.6 years of treatment with daily oral conjugated estrogens (CE 0.625 mg) combined with medroxyprogesterone acetate (MPA 2.5 mg), relative to placebo. (See CLINICAL STUDIES and WARNINGS, Cardiovas-

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REF

PI
PPI

PREMPRO®
(conjugated estrogens/medroxyprogesterone acetate tablets)
0.3 mg / 1.5 mg

References

1. Utian WH, Shoupe D, Bachmann G, et al. Relief of vasomotor symptoms and vaginal atrophy with lower doses of conjugated equine estrogens and medroxyprogesterone acetate. *Fertil Steril.* 2001;75:1065-1079.

2. PREMPRO®/PREMPHASE® (conjugated estrogens/medroxyprogesterone acetate tablets) Prescribing Information, Wyeth Pharmaceuticals Inc.

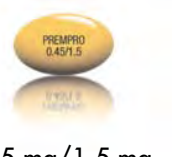
PI
PPI

PREMPRO: low doses can help manage her symptoms effectively[1,2]

PREMPRO®
(conjugated estrogens/medroxyprogesterone acetate tablets)
0.3 mg / 1.5 mg

More dosing options available than with any other single-tablet combination hormone therapy[2-7]

0.3 mg/1.5 mg



0.45 mg/1.5 mg

0.625 mg/2.5 mg

SELECTED SAFETY INFORMATION

WARNINGS

CARDIOVASCULAR AND OTHER RISKS
Estrogens plus progestins should not be used for the prevention of cardiovascular disease or dementia. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders and Dementia in the Prescribing Information.)

The estrogen plus progestin substudy of the Women's Health Initiative (WHI) reported increased risks of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli, and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age) during 5.6 years of treatment with daily oral conjugated estrogens (CE 0.625 mg) combined with medroxyprogesterone acetate (MPA 2.5 mg), relative to placebo. (See CLINICAL STUDIES and WARNINGS, Cardiovas-

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REF

PI
PPI

Pop Up
Message Category: Dosing
Product Message: more dosing option available than any other therapy

PREMPRO®
(conjugated estrogens/medroxyprogesterone acetate tablets)
0.3 mg / 1.5 mg

References

1. Utian WH, Shoupe D, Bachmann G, et al. Relief of vasomotor symptoms and vaginal atrophy with lower doses of conjugated equine estrogens and medroxyprogesterone acetate. *Fertil Steril*. 2001;75:1065-1079.

2. PREMPRO®/PREMPHASE® (conjugated estrogens/medroxyprogesterone acetate tablets) Prescribing Information, Wyeth Pharmaceuticals Inc.

3. Activella® (estradiol/norethindrone acetate) tablets Prescribing Information, Novo Nordisk, Inc., Princeton, NJ.

4. femhrt® (norethindrone acetate/ethinyl estradiol tablets) Prescribing Information, Warner Chilcott Inc., Rockaway, NJ.

5. PREFEST™ (estradiol/norgestimate) tablets Prescribing Information, Monarch Pharmaceuticals, Inc., Bristol, TN.

6. Climara Pro® (Estradiol/Levonorgestrel Transdermal System) Prescribing Information, Bayer HealthCare Pharmaceuticals Inc., Wayne, NJ.

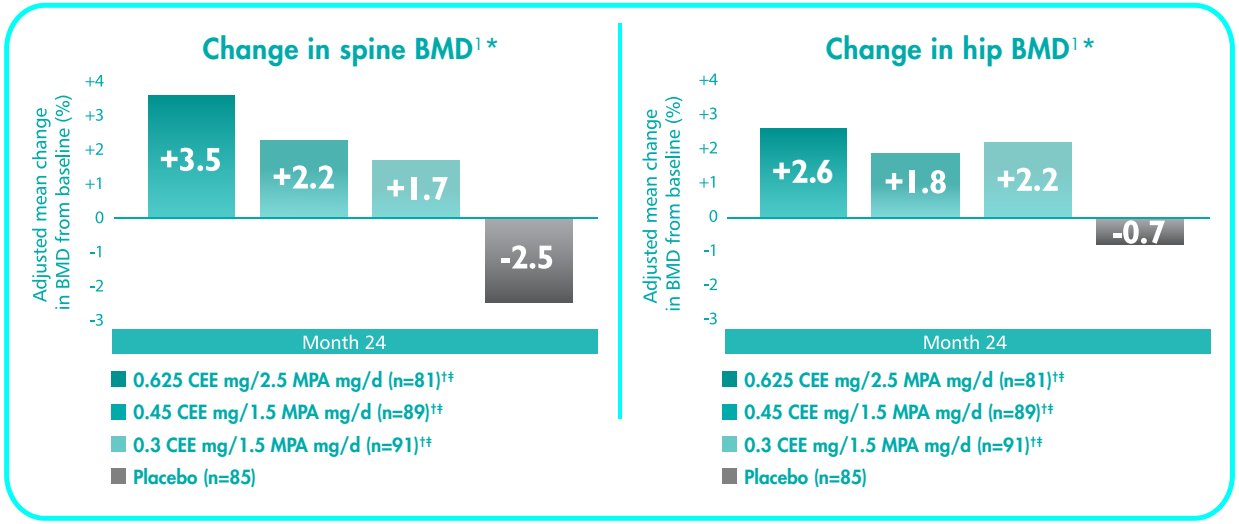
7. CombiPatch® (estradiol/norethindrone acetate transdermal system) Prescribing Information, Novartis Pharmaceuticals Corp., East Hanover, NJ.

PI
PPI

PREMPRO: bone protection even at low doses[1-3]

PREMPRO®
(conjugated estrogens/medroxyprogesterone acetate tablets)
0.3 mg / 1.5 mg

Significant increase in spine and hip bone mineral density (BMD)—even at low doses[1,2]



*Modified intent-to-treat population.
†Differences from baseline and placebo were significant ($P<.05$).
‡$P<.001$ vs placebo. Percentages rounded to nearest tenth. All patients received one 600-mg tablet of Caltrate® daily.

Study description

Dosing

SELECTED SAFETY INFORMATION

WARNINGS

CARDIOVASCULAR AND OTHER RISKS
Estrogens plus progestins should not be used for the prevention of cardiovascular disease or dementia. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders and Dementia in the Prescribing Information.)

The estrogen plus progestin substudy of the Women's Health Initiative (WHI) reported increased risks of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli, and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age) during 5.6 years of treatment with daily oral conjugated estrogens (CE 0.625 mg) combined with medroxyprogesterone acetate (MPA 2.5 mg), relative to placebo. (See CLINICAL STUDIES and WARNINGS,

CLICK HERE FOR PRODUCT INDICATION AND IMPORTANT SAFETY INFORMATION

REF

PI PPI

Parent Slide 11
Slide External Name: Bone protection
Message Category: Safety
Product Message: Bone protection even at low doses

PREMPRO: bone protection even at low doses[1-3]

PREMPRO®
(conjugated estrogens/medroxyprogesterone acetate tablets)
0.3 mg / 1.5 mg

Study description

Data from the Women's HOPE Study: a 2-year study of 2673 healthy, postmenopausal women (average age of 53.3 years). The BMD substudy included 822 women.

SELECTED SAFETY INFORMATION

WARNINGS

CARDIOVASCULAR AND OTHER RISKS
Estrogens plus progestins should not be used for the prevention of cardiovascular disease or dementia. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders and Dementia in the Prescribing Information.)

The estrogen plus progestin substudy of the Women's Health Initiative (WHI) reported increased risks of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli, and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age) during 5.6 years of treatment with daily oral conjugated estrogens (CE 0.625 mg) combined with medroxyprogesterone acetate (MPA 2.5 mg), relative to placebo. (See CLINICAL STUDIES and WARNINGS,

CLICK HERE FOR PRODUCT INDICATION AND IMPORTANT SAFETY INFORMATION

REF

PI PPI

PREMPRO®
(conjugated estrogens/medroxyprogesterone acetate tablets)
0.3 mg / 1.5 mg

References

1. Data on file, Wyeth Pharmaceuticals Inc.

2. Lindsay R, Gallagher JC, Kleerekoper M, et al. Effect of lower doses of conjugated equine estrogens with and without medroxyprogesterone acetate on bone in early postmenopausal women. *JAMA*. 2002;287:2668-2676.

3. PREMPRO®/PREMPHASE® (conjugated estrogens/medroxyprogesterone acetate tablets) Prescribing Information, Wyeth Pharmaceuticals Inc.

PI
PPI

PREMPRO: proven tolerablity at low doses[1-3]

PREMPRO®
(conjugated estrogens/medroxyprogesterone acetate tablets)
0.3 mg / 1.5 mg

Proven tolerability of PREMPRO 0.3 mg/1.5 mg[4,5]

No weight gain[5]
No clinically important change in average body weight compared with placebo

Less bleeding[4]
75% amenorrhea at 1 month compared with 51% with PREMPRO 0.625 mg/2.5 mg

Less breast pain[1]
Significantly less breast pain compared with PREMPRO 0.625 mg/2.5 mg

Low incidence of side effects[3]
No significant difference in the incidence of commonly reported (≥5%) side effects compared with placebo

Study description

Dosing

SELECTED SAFETY INFORMATION

WARNINGS
CARDIOVASCULAR AND OTHER RISKS
Estrogens plus progestins should not be used for the prevention of cardiovascular disease or dementia. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders and Dementia in the Prescribing Information.)

The estrogen plus progestin substudy of the Women's Health Initiative (WHI) reported increased risks of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli, and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age) during 5.6 years of treatment with daily oral conjugated estrogens (CE 0.625 mg) combined with medroxyprogesterone acetate (MPA 2.5 mg), relative to placebo. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders and Malignant neoplasms, Breast cancer in the Prescribing Information.)

CLICK HERE FOR PRODUCT INDICATION AND IMPORTANT SAFETY INFORMATION

REF

PI
PPI

Parent Slide 12
Slide External Name: Proven Tolerability
Message Category: Tolerability
Product Message: Proven tolerability at low doses

PREMPRO®
(conjugated estrogens/medroxyprogesterone acetate tablets)
0.3 mg / 1.5 mg

References

1. Data on file, Wyeth Pharmaceuticals Inc.

2. Lindsay R, Gallagher JC, Kleerekoper M, et al. Effect of lower doses of conjugated equine estrogens with and without medroxyprogesterone acetate on bone in early postmenopausal women. *JAMA*. 2002;287:2668-2676.

3. PREMPRO®/PREMPHASE® (conjugated estrogens/medroxyprogesterone acetate tablets) Prescribing Information, Wyeth Pharmaceuticals Inc.

4. Archer DF, Dorin M, Lewis V, et al. Effects of lower doses of conjugated equine estrogens and medroxyprogesterone acetate on endometrial bleeding. *Fertil Steril*. 2001;75:1080-1087.

5. Utian WH, Gass MLS, Pickar JH. Body mass index does not influence response to treatment, nor does body weight change with lower doses of conjugated estrogens and medroxyprogesterone acetate in early postmenopausal women. *Menopause*. 2004;11:306-314.

PI
PPI

PREMPRO: Contraindicated for the following patients[1]

PREMPRO®
(conjugated estrogens/medroxyprogesterone acetate tablets)
0.3 mg / 1.5 mg

PREMPRO is contraindicated for women with any of the following conditions:

- Undiagnosed abnormal genital bleeding.
- Known, suspected, or history of cancer of the breast.
- Known or suspected estrogen-dependent neoplasia.
- Active deep vein thrombosis, pulmonary embolism or a history of these conditions.
- Known or suspected pregnancy.
- Active or recent (within past year) arterial thromboembolic disease (for example, stroke, myocardial infarction).
- Liver dysfunction or disease.
- Known hypersensitivity to any of the ingredients in PREMPRO or PREMPHASE.

Dosing

SELECTED SAFETY INFORMATION

WARNINGS
CARDIOVASCULAR AND OTHER RISKS
Estrogens plus progestins should not be used for the prevention of cardiovascular disease or dementia. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders and Dementia in the Prescribing Information.)

The estrogen plus progestin substudy of the Women's Health Initiative (WHI) reported increased risks of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli, and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age) during 5.6 years of treatment with daily oral conjugated estrogens (CE 0.625 mg) combined with medroxyprogesterone acetate (MPA 2.5 mg), relative to placebo. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders and Malignant neoplasms, Breast cancer in the Prescribing Information.)

CLICK HERE FOR PRODUCT INDICATION AND IMPORTANT SAFETY INFORMATION

REF

PI
PPI

Parent Slide 13
Slide External Name: Contraindicated Patients
Message Category: Non Specific Messaging
Product Message: Contraindicated in the following patients

PREMPRO®
(conjugated estrogens/medroxyprogesterone acetate tablets)
0.3 mg / 1.5 mg

Reference

1. PREMPRO®/PREMPHASE® (conjugated estrogens/medroxyprogesterone acetate tablets) Prescribing Information, Wyeth Pharmaceuticals Inc.

PI
PPI

PREMPRO®
(conjugated estrogens/medroxyprogesterone acetate tablets)
0.3 mg / 1.5 mg

Prescribing Information

PREMPRO®
(conjugated estrogens/medroxyprogesterone acetate tablets)
PREMPHASE®
(conjugated estrogens/medroxyprogesterone acetate tablets)
Rx only

WARNINGS

CARDIOVASCULAR AND OTHER RISKS

Estrogens plus progestins should not be used for the prevention of cardiovascular disease or dementia. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders and Dementia.)

The estrogen plus progestin substudy of the Women's Health Initiative (WHI) reported increased risks of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli, and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age) during 5.6 years of treatment with daily oral conjugated estrogens (CE 0.625 mg) combined with medroxyprogesterone acetate (MPA 2.5 mg), relative to placebo. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders and Malignant neoplasms, Breast cancer.)

The estrogen alone substudy of the WHI reported increased risks of stroke and DVT in postmenopausal women (50 to 79 years of age) during 6.8 years and 7.1 years, respectively, of treatment with daily CE 0.625 mg, relative to placebo. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders.)

The Women's Health Initiative Memory Study (WHIMS), a substudy of WHI, reported an increased risk of developing probable dementia in postmenopausal women 65 years of age or older during 4 years of treatment with daily CE 0.625 mg combined with MPA 2.5 mg and during 5.2 years of treatment with daily CE 0.625 mg alone, relative to placebo. It is unknown whether this finding applies to younger postmenopausal women. (See CLINICAL STUDIES, and WARNINGS, Dementia and PRECAUTIONS, Geriatric Use.) In the absence of comparable data, these risks should be assumed to be similar for other doses of CE and MPA and other combinations and dosage forms of estrogens and progestins. Because of these risks, estrogens with or without progestins should be prescribed at the lowest effective doses and for the shortest duration consistent with treatment goals and risks for the individual woman.

DESCRIPTION

PREMPRO® 0.3 mg/1.5 mg therapy consists of a single tablet containing 0.3 mg of the conjugated estrogens (CE) found in Premarin® tablets and 1.5 mg of medroxyprogesterone acetate (MPA) for oral administration.

PREMPRO®
(conjugated estrogens/medroxyprogesterone acetate tablets)
0.3 mg / 1.5 mg

Prescribing Information

PATIENT INFORMATION
PREMPRO®
(conjugated estrogens/medroxyprogesterone acetate tablets)
PREMPHASE®
(conjugated estrogens/medroxyprogesterone acetate tablets)
Read this PATIENT INFORMATION before you start taking PREMPRO or PREMPHASE and read what you get each time you refill PREMPRO or PREMPHASE. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.
What is the most important information I should know about PREMPRO and
PREMPHASE (combinations of estrogens and a progestin)?
Do not use estrogens and progestins to prevent heart disease, heart attacks, strokes, or dementia. Using estrogens and progestins may increase your chances of getting heart attacks, strokes, breast cancer, or blood clots. Using estrogens, with or without progestins, may increase your chance of getting dementia, based on a study of women age 65 years or older. You and your healthcare provider should talk regularly about whether you still need treatment with PREMPRO or PREMPHASE.
What is PREMPRO or PREMPHASE?
PREMPRO or PREMPHASE are medicines that contain two kinds of hormones, estrogens and a progestin.
PREMPRO or PREMPHASE is used after menopause to:
- Reduce moderate to severe hot flashes. Estrogens are hormones made by a woman's ovaries. The ovaries normally stop making estrogens when a woman is between 45 and 55 years old. This drop in body estrogen levels causes the “change of life” or menopause (the end of monthly menstrual periods). Sometimes, both ovaries are removed during an operation before natural menopause takes place. The sudden drop in estrogen levels causes “surgical menopause.”
- When the estrogen levels begin dropping, some women get very uncomfortable symptoms, such as feelings of warmth in the face, neck, and chest, or sudden strong feelings of heat and sweating (“hot flashes” or “hot flushes”). In some women the symptoms are mild, and they will not need to take estrogens. In other women, symptoms can be more severe. You and your healthcare provider should talk regularly about whether you still need treatment with PREMPRO or PREMPHASE.
- Treat moderate to severe dryness, itching, and burning, in and around the vagina.

PREMPRO®
(conjugated estrogens/medroxyprogesterone acetate tablets)
0.3 mg / 1.5 mg

Prescribing Information

You and your healthcare provider should talk regularly about whether you still need treatment with PREMPRO or PREMPHASE to control these problems. If you use PREMPRO or PREMPHASE only to treat your dryness, itching, and burning in and

Each carton includes 1 blister card containing 28 tablets. One blister card contains 14 oval, maroon Premarin tablets containing 0.625 mg of conjugated estrogens and 14 oval, light-blue tablets that contain 0.625 mg of the conjugated estrogens found in Premarin tablets and 5 mg of medroxyprogesterone acetate for oral administration.
The appearance of PREMPRO tablets is a trademark of Wyeth Pharmaceuticals.
The appearance of PREMARIN tablets is a trademark of Wyeth Pharmaceuticals. The
appearance of the conjugated estrogens/medroxyprogesterone acetate combination tablets is a trademark.
Store at 20° - 25°C (68° - 77°F); excursions permitted to 15° - 30°C (59° - 86°F) [see USP Controlled Room Temperature].
United States Patent Number: 5,547,948 (PREMPRO).
This product's label may have been updated. For current package insert and further product information, please visit www.wyeth.com or call our medical communications department toll-free at 1-800-934-5556.
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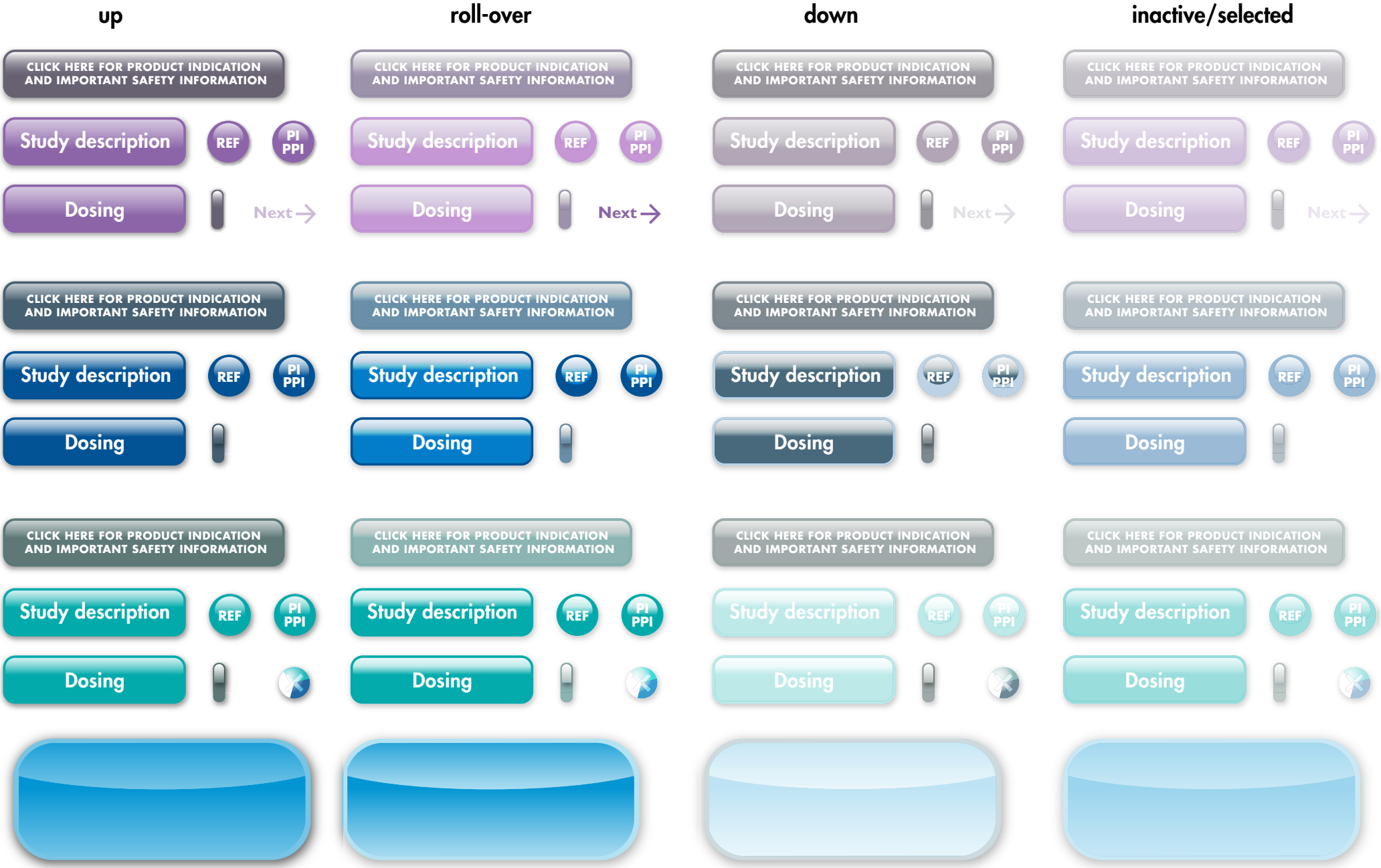
ET01
Rev 08/09


up
roll-over
down
inactive/selected
CLICK HERE FOR PRODUCT INDICATION AND IMPORTANT SAFETY INFORMATION
Study description
REF
PI PPI
Dosing
Next