Revision of PRECAUTIONS

Estradiol (oral dosage form)
Estradiol valerate
Estriol (oral dosage form)
Progesterone (oral dosage form)
Estradiol/Norethisterone acetate
Estradiol/Levonorgestrel
Testosterone enanthate/Estradiol valerate

October 22, 2025

Therapeutic category

Estrogen and progestogen preparations

Mixed hormone preparations

Non-proprietary name

Estradiol (oral dosage form)

Estradiol valerate

Estriol (oral dosage form)

Progesterone (oral dosage form)

Estradiol/Norethisterone acetate

Estradiol/Levonorgestrel

Testosterone enanthate/Estradiol valerate

Safety measure

PRECAUTIONS should be revised.

Revised language is underlined.

Current	Revision
15. OTHER PRECAUTIONS 15.1 Information Based on Clinical Use HRT and risk of breast cancer (N/A)	15. OTHER PRECAUTIONS 15.1 Information Based on Clinical Use HRT and risk of breast cancer The causal relationship between HRT and breast cancer development is not clear, but the following reports have been made. A meta-analysis of large-scale epidemiological studies in postmenopausal women showed that the risk of breast cancer was increased with the duration of menopausal hormone replacement therapy (MHT) in women treated with estrogen alone or in combination with estrogen and gestagen preparations as MHT (adjusted risk ratio [95% confidence interval], 1.60 [1.52 to 1.69] for the combination of estrogen and gestagen preparations for 1 to 4 years, 1.17 [1.10 to 1.26] for estrogen alone, 2.08 [2.02 to 2.15] for combination of estrogen and gestagen preparations for 5 to 14 years, and 1.33 [1.28 to 1.37] for estrogen alone), with the MHT non-users-adjusted risk ratio being higher in current MHT users than in prior MHT users. In addition, it has been reported that the risk of breast cancer may persist for 10 years or more in prior MHT users, depending on the duration of previous treatment, even after discontinuation.

N/A: Not Applicable. No corresponding language is included in the current PRECAUTIONS.

(References) Collaborative Group on Hormonal Factors in Breast Cancer: Lancet 2019;394:1159-1168