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

This document is an English-translated version of an attachment of a notification for Revision of PRECAUTIONS issued by the Ministry of Health, Labour and Welfare.

This English version is intended to be a reference material to provide convenience for users.

In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

Estriol (oral dosage form)

Progesterone (oral dosage form)

Estradiol/Norethisterone acetate

Estradiol/Levonorgestrel

Testosterone enanthate/Estradiol valerate

Safety measure

PRECAUTIONS should be revised.

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Revised language is underlined.

Current	Revision
15. OTHER PRECAUTIONS	15. OTHER PRECAUTIONS
15.1 Information Based on Clinical Use	15.1 Information Based on Clinical Use
HRT and risk of breast cancer	HRT and risk of breast cancer
(N/A)	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