HAUTE AUTORITÉ DE SANTÉ

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TRANSPARENCY COMMITTEE

Opinion
28 May 2014

ESTREVA, scored tablet
B/28 (CIP: 34009 339 632 3 1)

ESTREVA 0.1%, gel
B/1 tube of 50 g with metering pump (CIP: 34009 339 130 8 3)

FEMSEPT 50 micrograms/24 hours, transdermal patch
B/4 sachets of 1 patch (CIP: 34009 346 107 8 3)

FEMSEPT 75 micrograms/24 hours, transdermal patch
B/4 sachets of 1 patch (CIP: 34009 346 106 1 5)

FEMSEPT 100 micrograms/24 hours, transdermal patch
B/4 sachets of 1 patch (CIP: 34009 346 105 5 4)

Applicant: TEVA SANTE

INN	Estradiol
ATC code (2013)	G03CA03 (oestrogen)
Reason for the review	**Re-assessment of the Actual Benefit of all medicines indicated for menopausal hormone replacement therapy at the request of the Committee, pursuant to Article R-163-21 of the French Social Security Code** **Renewal of inclusion for ESTREVA scored tablet and ESTREVA 0.1% gel**
Lists concerned	**National Health Insurance (French Social Security Code L.162-17)** **Hospital use (French Public Health Code L.5123-2)**
Indications concerned	**ESTREVA scored tablet:** **'- Hormone replacement therapy (HRT) for symptoms of oestrogen deficiency in menopausal women.** **- Prevention of postmenopausal osteoporosis in women at increased risk of osteoporotic fracture and who are intolerant to or contraindicated for the other treatments indicated for the prevention of osteoporosis.** **Treatment experience in women over 65 years of age is limited. '** **ESTREVA 0.1% gel:** **'Hormone replacement therapy (HRT) for symptoms of oestrogen deficiency in menopausal women.** **Treatment experience in women over 65 years of age is limited. '** **FEMSEPT 50 micrograms/24 hours, 75 micrograms/24 hours, 100 micrograms/24 hours, transdermal patch:** **'Hormone replacement therapy (HRT) for symptoms of oestrogen deficiency in menopausal women whose last menstrual period was at least 6 months ago (for natural menopause).** **Treatment experience in women over 65 years of age is limited. '**

01 ADMINISTRATIVE AND REGULATORY INFORMATION

Marketing Authorisation	ESTREVA scored tablet: 09 October 1995 (national procedure) 0.1% gel: 10 July 1995 (mutual recognition procedure) FEMSEPT 50 µg/24 hours, 75 µg/24 hours, 100 µg/24 hours: 06 March 1998 (national procedure)
Prescribing and dispensing conditions	List II

02 TRANSPARENCY COMMITTEE CONCLUSIONS

Based on the assessment report attached to this opinion, the Committee considered that:

02.1 ACTUAL BENEFIT

2.1.1 Hormone replacement therapy (HRT) for symptoms of oestrogen deficiency in menopausal women.

◗ Vasomotor symptoms of menopause when they are frequent and intense may significantly impair quality of life.

◗ These proprietary medicinal products are intended as symptomatic therapy.

◗ The efficacy/adverse effects ratio is moderate in patients with climacteric disorders that are described as troublesome enough to impair their quality of life and in compliance with the Committee's recommendations.

◗ There are treatment alternatives to these proprietary medicinal products (other hormonal treatments for menopause).

◗ Menopausal hormonal therapies are first-line therapies for climacteric disorders when they are troublesome enough to impair quality of life.

◗ Public health benefit

At the time of menopause, in the general population, the proportion of women complaining of climacteric disorders is supposedly more than 50%.[1] The most common symptom is hot flashes; approximately one in three women present with night sweats. However, there may be other symptoms: vaginal dryness or urinary symptoms. The frequency and severity of these symptoms decrease with time but are still present 10 years after menopause in approximately one out of four women.

As a result, given the limitations of their use in menopausal women, HRTs have little impact on public health.

Consequently, the Committee considers that the actual benefit of the proprietary medicinal products ESTREVA scored tablet, 0.1% gel and FEMSEPT 50 µg/24 hours, 75 µg/24 hours, 100 µg/24 hours in hormone replacement therapy (HRT) for symptoms of oestrogen deficiency in menopausal women remains substantial in patients for whom climacteric disorders are described as troublesome enough to impair their quality of life when these proprietary medicinal products are used as per the Committee's recommendations.

[1] ANAES [National Health Accreditation and Assessment Agency]/ANSM [French National Agency for Medicines and Health Products Safety] Traitements hormonaux substitutifs de la ménopause. Rapport d'orientation, 11 May 2004

2.1.2 Prevention of postmenopausal osteoporosis in women at increased risk of osteoporotic fracture and who are intolerant to or contraindicated for the other treatments indicated for the prevention of osteoporosis.

◗ Postmenopausal osteoporosis is a serious disorder because of the risk of fractures. Femoral neck fractures in particular may be life-threatening.

◗ The proprietary medicinal product ESTREVA is intended as preventive therapy.

◗ Only for the duration of treatment, the efficacy/adverse effects ratio is high in the event of climacteric disorders and recent menopause, after a minor fracture or if there is a low T-score, in the case of intolerance to or failure of other treatments indicated in the prevention of osteoporosis.

◗ There are treatment alternatives (other hormonal treatments for menopause with the same indication).

◗ This proprietary medicinal product is intended as backup therapy.

◗ Public health benefit

Because of its high prevalence and the severity of its consequences, the public health burden of postmenopausal osteoporosis is substantial.

Given the role of hormonal menopause treatments in the management of osteoporosis, the number of patients for whom hormonal menopause treatments are indicated is very low.

Consequently, HRT does not have an impact on public health in this indication.

Consequently, the Committee considers that the actual benefit of the proprietary medicinal products ESTREVA remains substantial in the prevention of postmenopausal osteoporosis in women at increased risk of osteoporotic fracture and who are intolerant to or contraindicated for the other treatments indicated for the prevention of osteoporosis in the event of climacteric disorders and recent menopause, after a minor fracture or if there is a low T-score, when this proprietary medicinal product is used as per the Committee's recommendations.

03 TRANSPARENCY COMMITTEE RECOMMENDATIONS

The Committee recommends:

- Carefully weighing the benefit of hormone therapy against the symptoms and their impact on the patient's quality of life.
- Prescribing these treatments in accordance with their contraindications, in particular concerning the risk of thromboembolism and breast cancer.

These treatments should be prescribed when the climacteric disorders are described by the patient as troublesome enough to impair their quality of life, at the lowest effective dose, for the shortest duration possible as per the AFSSAPS's guidelines (see the appendix), in particular:

- before initiating or reinstituting HRT, a complete clinical and gynaecological examination (including an analysis of the family history) should be performed. A regular breast examination should be performed as per the current recommendations (palpation, mammography, ultrasound, etc.) and tailored to individual cases.
- at the start of treatment, patients must be given all relevant information enabling an appropriate and informed prescription. Thus, patients must be informed of the risks inherent to the treatment. In addition, the treatment should be re-assessed regularly, at least once a year, taking into account changes in the benefit/risk ratio. The treatment may be temporarily suspended during this reassessment in order to verify the persistence of the climacteric syndrome and its severity.

In the prevention of postmenopausal osteoporosis in women at increased risk of osteoporotic fracture and who are intolerant to, or contraindicated for, the other treatments indicated for the prevention of osteoporosis, these treatments should be prescribed in the event of climacteric disorders and recent menopause, after a minor fracture or if there is a low T-score.

The Committee recommends continued inclusion on the list of medicines refundable by National Health Insurance and on the list of medicines approved for hospital use in the indications in the Marketing Authorisation and as recommended by the Committee.

◗ **Proposed reimbursement rate: 65%**