HAUTE AUTORITÉ DE SANTÉ

The legally binding text is the original French version

TRANSPARENCY COMMITTEE

Opinion

28 May 2014

ACTIVELLE, film-coated tablet

B/1 calendar dial pack of 28 tablets (CIP: 3400934879944)

Applicant: NOVO NORDISK

INN	Estradiol / norethisterone acetate
ATC code (2013)	G03FA01 (progestogens and oestrogens, fixed combinations)
Reason for the review	**Reassessment of the Actual Benefit of all medicines indicated in hormone replacement therapy for menopause at the request of the Committee, pursuant to Article R-163-21 of the French Social Security Code**
Lists concerned	**National Health Insurance (French Social Security Code L.162-17)** **Hospital use (French Public Health Code L.5123 2)**
Indications concerned	**"Hormone Replacement Therapy (HRT) for oestrogen deficiency symptoms in postmenopausal women with more than 1 year since last menses.** **Prevention of osteoporosis in postmenopausal women at high risk of future fractures who are intolerant of or contraindicated for other medicinal products approved for the prevention of osteoporosis.** **The experience treating women older than 65 years is limited. "**

01 ADMINISTRATIVE AND REGULATORY INFORMATION

Marketing Authorisation	10 December 1998 (mutual recognition procedure)
Prescribing and dispensing conditions	List I

02 TRANSPARENCY COMMITTEE CONCLUSIONS

According to the evaluation report attached to this opinion, the Committee believes that:

02.1 ACTUAL BENEFIT

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

◗ When they are frequent and intense, vasomotor symptoms of menopause can significantly impair quality of life.

◗ This proprietary medicinal product is intended as symptomatic therapy.

◗ The efficacy / adverse effects ratio is modest in patients whose menopausal disorders are perceived as troublesome enough to impair their quality of life and in accordance with the committee's recommendations.

◗ There are treatment alternatives to this proprietary medicinal product (other hormone therapies for menopause).

◗ Hormone therapies for menopause are first-line treatments for menopausal disorders when they are sufficiently troublesome to cause impaired quality of life.

◗ Public health benefit

At the time of menopause, in the general population, the proportion of women complaining of menopausal disorders is more than 50%.[1] Hot flashes are the most common symptom: approximately 1 in 3 women has night sweats. However other symptoms may also be present: genital dryness or urinary symptoms. The frequency and severity of these symptoms decrease with time but they are still present more than 10 years after menopause in approximately a quarter of women.

Consequently, in regard to the limitations of its use in menopausal women, HRT has a low impact on public health.

Consequently, the Committee considers that the actual benefit of the proprietary medicinal product ACTIVELLE in hormone replacement therapy (HRT) for oestrogen deficiency symptoms in menopausal women remains substantial in patients for whom menopausal disorders are sufficiently troublesome to impair their quality of life when this proprietary medicinal product is used according to the Committee's recommendations.

[1] ANAES [National Health Accreditation and Assessment Agency]/AFSSAPS [French Healthcare Product Safety Agency]. Traitements hormonaux substitutifs de la ménopause [Hormone replacement therapies for menopause]. Orientation report, 11 May 2004

2.1.2 Prevention of osteoporosis in postmenopausal women at high risk of future fractures who are intolerant of or contraindicated for other medicinal products approved for the prevention of osteoporosis.

◗ Postmenopausal osteoporosis is a serious disorder because of the risk of fractures. Hip fractures in particular can be life-threatening.

◗ This proprietary medicinal product is intended as preventive therapy.

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

◗ There are treatment alternatives (other hormone therapies for menopause with the same indication).

◗ This proprietary medicinal product is intended as backup therapy.

◗ Public health benefit

Due to its high prevalence and the seriousness of its consequences, the public health burden of post-menopausal osteoporosis is substantial.

Given the role of hormone therapy for menopause in the management of osteoporosis, the number of patients for whom hormone therapy for menopause is indicated is very low.

Consequently, HRTs do not have any impact on public health in this indication.

Consequently, the Committee considers that the actual benefit of the proprietary medicinal product ACTIVELLE remains substantial in the prevention of postmenopausal osteoporosis in women with an increased risk of osteoporotic fracture and who are intolerant of or contraindicated for other treatments indicated in the prevention of menopausal and recent postmenopausal osteoporosis, after a minor fracture or if there is a low T-score, when this proprietary medicinal product is used according to the committee's recommendations.

03 TRANSPARENCY COMMITTEE RECOMMENDATIONS

The Committee recommends:

- Carefully considering the benefit of hormone therapy relative to the symptoms and their impact on patient quality of life.
- Complying with contraindications when prescribing these therapies, in particular concerning the risk of thromboembolism and breast cancer.

These therapies will be prescribed when the menopausal disorders experienced by the patient are sufficiently troublesome to impair her quality of life, at the minimum effective dose, for the shortest possible duration in compliance with AFSSAPS' recommendations (see appendix), in particular:

- before initiating or reinitiating HRT, a complete physical and gynaecological examination (including an analysis of family history) should be conducted. Regular breast examination should be done according to the current recommendations (palpation, mammography, ultrasound, etc.) and adapted in accordance with the individual case.
- when treatment is initiated, patients must be provided with all useful information for appropriate and informed prescription. Therefore, they must be informed of the risks inherent in the treatment. Furthermore, the treatment should be regularly reassessed, at least once a year, taking into consideration changes in the benefit/risk ratio. This reassessment may be accompanied by temporary treatment suspension in order to check whether menopausal syndrome is persisting and how severe it is.

In the prevention of osteoporosis in postmenopausal women at high risk of future fractures who are intolerant of or contraindicated for other medicinal products approved for the prevention of osteoporosis, these treatments will be prescribed in the event of menopausal and immediate menopausal disorders 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 indication in the Marketing Authorisation and according to the Committee's recommendations.

◗ Proposed reimbursement rate: 65%