HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
3 FEBRUARY 2021

abemaciclib
VERZENIOS 50 mg film-coated tablets
VERZENIOS 100 mg film-coated tablets
VERZENIOS 150 mg film-coated tablets

Reevaluation

Key points

Favourable opinion for reimbursement in combination with fulvestrant, in postmenopausal women with hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2) negative locally advanced or metastatic breast cancer, without short-term life-threatening symptomatic visceral involvement, as first-line treatment of metastatic disease in women in early relapse following adjuvant endocrine therapy, or as second-line treatment of metastatic disease following a first line of endocrine therapy.

What therapeutic improvement?

Therapeutic improvement compared to fulvestrant alone.

Role in the care pathway?

In the absence of short-term life-threatening symptomatic visceral involvement, the therapeutic strategy is based on endocrine therapy.

In postmenopausal women, treatment with non-steroidal aromatase inhibitors (letrozole or anastrozole) is recommended as a first-line treatment, unless they were previously administered as part of adjuvant therapy discontinued less than 12 months previously. The addition of a CDK4/6 inhibitor [IBRANCE (palbociclib), KISQALI (ribociclib) or VERZENIOS (abemaciclib)] to the aromatase inhibitor is recommended in current clinical practice guidelines. KISQALI (ribociclib) in combination with fulvestrant is also a treatment option in women diagnosed at the advanced stage or in relapse following adjuvant endocrine therapy. In the event of disease progression under endocrine therapy, the choice of treatment will depend primarily on the type of prior therapy, without the optimal endocrine therapy sequence having been clearly established. Following first-line therapy at an advanced stage combining an aromatase inhibitor and a CDK4/6 inhibitor, the treatments that may be proposed for second-line therapy are fulvestrant alone, tamoxifen or exemestane alone or in combination with everolimus. In the event of progression under endocrine therapy administered as monotherapy at an advanced stage, the co-administration of endocrine therapy, in particular with fulvestrant, with a CDK4/6 inhibitor is recommended. The use of cytotoxic chemotherapy is an available option that should only be considered in the event of aggressive disease presentation.

Role of the medicinal product in the care pathway

Considering demonstration of the superiority of the addition of VERZENIOS (abemaciclib) to fulvestrant compared to fulvestrant alone in terms of overall survival now, co-administration of VERZENIOS (abemaciclib) with fulvestrant, like co-administration of KISQALI (ribociclib) with fulvestrant, is a treatment option to be favoured compared to fulvestrant alone in postmenopausal women with HR-positive / HER2-negative locally advanced or metastatic breast cancer, without short-term life-threatening symptomatic visceral involvement, as first-line treatment of metastatic disease in women in early relapse following adjuvant endocrine therapy, or as second-line treatment of metastatic disease following a first line of endocrine therapy.

CDK4/6 inhibitors in combination with endocrine therapy have an indication as both first and second-line treatment at the advanced stage. However, no data is available enabling the optimal treatment sequence to be established. There is no evidence of a clinical benefit of further treatment with a CDK 4/6 inhibitor for patients having already received one in a previous line of treatment.

The choice of CDK4/6 inhibitor to be used in combination with fulvestrant between VERZENIOS (abemaciclib), KISQALI (ribociclib) and IBRANCE (palbociclib) should take into account, in particular, the level of evidence of the demonstration in terms of efficacy as well as the safety profile of each medicinal product. In particular, as regards VERZENIOS (abemaciclib), this choice should take into account demonstration of an improvement in overall survival compared to fulvestrant alone, as well as its specific safety profile, marked by venous thromboembolic events and frequent gastrointestinal disorders (diarrhoea), in addition to the risk of neutropenia already observed with the other two CDK4/6 inhibitors, requiring regular monitoring of complete blood count (see SPC).

As a reminder, in the absence of clinical data, VERZENIOS (abemaciclib) in combination with fulvestrant has no role (opinion of 12 December 2018) in the following cases:

- as first-line treatment of metastatic disease in women with cancer diagnosed at an advanced stage, and in women with late relapse following adjuvant endocrine therapy;
- in pre or perimenopausal women and/or those with short-term life-threatening symptomatic visceral involvement;
- following the failure of another CDK4/6 inhibitor (KISQALI or IBRANCE).

COMMITTEE'S CONCLUSIONS

Considering all of this information and further to debate and voting, the Committee considers:

Clinical benefit

◗ HR-positive/HER2-negative breast cancer, at the locally advanced or metastatic stage, is a serious, life-threatening disease.

◗ This is a specific curative cancer treatment.

◗ The efficacy/adverse effects ratio of VERZENIOS (abemaciclib) in combination with fulvestrant remains high in postmenopausal women with HR-positive / HER2-negative locally advanced or metastatic breast cancer, without short-term life-threatening symptomatic visceral involvement, as first-line treatment of metastatic disease in women in early relapse following adjuvant endocrine therapy, or as second-line treatment of metastatic disease following a first line of endocrine therapy.

◗ There are therapeutic alternatives.

◗ Considering demonstration of the superiority of the addition of VERZENIOS (abemaciclib) to fulvestrant compared to fulvestrant alone in terms of overall survival now, co-administration of VERZENIOS (abemaciclib) with fulvestrant, like co-administration of KISQALI (ribociclib) with fulvestrant, is a treatment option to be favoured compared to fulvestrant alone in postmenopausal women with HR-positive / HER2-negative locally advanced or metastatic breast cancer, without short-term life-threatening symptomatic visceral involvement, as first-line treatment of metastatic disease in women in early relapse following adjuvant endocrine therapy, or as second-line treatment of metastatic disease following a first line of endocrine therapy (see section 09).

Public health impact

Considering:

- the seriousness of HR-positive/HER2-negative locally advanced or metastatic breast cancer and its incidence at the advanced stage,
- the partially met medical need,
- the partial response to the identified need, with an additional impact on morbidity and mortality, and without any demonstrated impact to date on quality of life,
- the absence of data supporting an impact on the care and/or life pathway,

VERZENIOS (abemaciclib) in combination with fulvestrant is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of VERZENIOS (abemaciclib) remains substantial in combination with fulvestrant, in postmenopausal women with HR-positive / HER2-negative locally advanced or metastatic breast cancer, without short-term life-threatening symptomatic visceral involvement, as first-line treatment of metastatic disease in women in early relapse following adjuvant endocrine therapy, or as second-line treatment of metastatic disease following a first line of endocrine therapy.

The Committee issues a favourable opinion for maintenance of inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in combination with fulvestrant in the treatment of postmenopausal women with HR-positive / HER2-negative locally advanced or metastatic breast cancer, without short-term life-threatening symptomatic visceral involvement, as first-line treatment of metastatic disease in women in early relapse following adjuvant endocrine therapy, or as second-line treatment of metastatic disease following a first line of endocrine therapy, and at the MA dosages.

◗ **Recommended reimbursement rate: 100%**

Clinical Added Value

Considering:

- **demonstration of the superiority of the addition of VERZENIOS (abemaciclib) to fulvestrant compared to fulvestrant alone in terms of overall survival (absolute increase of 9.47 months with the addition of abemaciclib; HR=0.757, CI95% [0.606; 0.945]) following a median follow-up of 48 months, in patients receiving first-line treatment in the context of early relapse or second-line treatment of metastatic disease,**

and despite:

- **an increased toxicity with grade ≥ 3 adverse events observed in 68% of patients versus 28% with fulvestrant alone, haematological and gastrointestinal toxicity (diarrhoea reported in 87% of patients versus 28% with fulvestrant alone) having led to dosage adjustments or even treatment discontinuations, as well as the serious venous thromboembolic events observed,**
- **the absence of robust data on the patients' quality of life,**

the Committee considers that the addition of VERZENIOS (abemaciclib) to fulvestrant, like KISQALI (ribociclib) in combination with fulvestrant, provides a minor clinical added value (CAV IV) compared to fulvestrant alone in the treatment of postmenopausal women with HR-positive / HER2-negative locally advanced or metastatic breast cancer, without short-term life-threatening symptomatic visceral involvement, as first-line treatment of metastatic disease in women in early relapse following adjuvant endocrine therapy, or as second-line treatment of metastatic disease following a first line of endocrine therapy.