HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
20 JANUARY 2021

alpelisib
PIQRAY 50 mg film-coated tablets
PIQRAY 150 mg film-coated tablets
PIQRAY 200 mg film-coated tablets

First assessment

Key points

Unfavourable opinion for reimbursement in combination with fulvestrant for the treatment of postmenopausal women, and men, with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer with a PIK3CA mutation after disease progression following endocrine therapy as monotherapy.

Role in the care pathway?

In the absence of any available treatment to date in the specific management of patients with a PIK3CA mutation, these patients are treated independently of their mutation status.

In postmenopausal women, non-steroidal aromatase inhibitors (letrozole or anastrozole) used to be recommended as first-line treatment, unless they were previously administered as part of adjuvant therapy discontinued less than 12 months previously. Today, current clinical practice guidelines recommend the addition of a CDK4/6 inhibitor [IBRANCE (palbociclib), KISQALI (ribociclib) or VERZENIOS (abemaciclib)] to the aromatase inhibitor for the majority of patients. They position endocrine therapy + CDK4/6 inhibitors as the current standard-of-care therapy for RH-positive/HER2-negative cancer at the advanced stage. KISQALI (ribociclib) in combination with fulvestrant is also a treatment option in women diagnosed at the advanced stage or in late relapse following adjuvant endocrine therapy.

As second-line treatment of the advanced stage and in the event of progression following first-line endocrine therapy as monotherapy, combination of endocrine therapy with a CDK4/6 inhibitor is recommended. The superiority of CDK4/6 inhibitors in the context of their combination with second-line endocrine therapy, particularly with fulvestrant, in comparison with the latter as monotherapy, has been demonstrated in terms of progression-free survival, but with increased toxicity. An increase in overall survival has also been demonstrated for KISQALI (ribociclib) and VERZENIOS (abemaciclib).

Role of the medicinal product in the care pathway

According to its MA, PIQRAY (alpelisib) is indicated in combination with fulvestrant, following endocrine therapy administered as monotherapy, for the treatment of postmenopausal women, and men, with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer with a PIK3CA mutation. This restricted MA was granted in the absence of sufficient robust data to reach a conclusion with respect to the efficacy of PIQRAY (alpelisib) in combination with fulvestrant following endocrine therapy combined with a CDK 4/6 inhibitor. Only 20 patients, i.e. 6% of the patients in the phase 3 SOLAR-1 study, had previously been treated with a CDK4/6 inhibitor.

Considering:
- demonstration of a benefit of the alpelisib + fulvestrant combination compared to endocrine therapy as monotherapy (fulvestrant) in terms of progression-free survival, but without a demonstrated impact on overall survival, with no robust quality of life data and with significant toxicity, with, in particular, metabolic (hyperglycaemia), gastrointestinal (diarrhoea) and cutaneous events (skin rashes) and grade 3-4 adverse events reported in 76.1% of patients versus 35.5% of patients in the fulvestrant group alone, and
- the evolution of the strategy, which now makes the combination of endocrine therapy and CDK4/6 inhibitors the current standard of care for the majority of patients and makes the study comparator (fulvestrant as monotherapy) acceptable at the start of the study but not clinically relevant at the current time,

the Transparency Committee considers that, within the precise scope of its MA indication, the role of PIQRAY (alpelisib) in combination with fulvestrant in the current care pathway cannot be determined.

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 advanced stage (locally advanced or metastatic), is a serious, life-threatening disease.

◗ This is a specific curative cancer treatment.

◗ Considering:
- demonstration of a benefit of the alpelisib + fulvestrant combination in terms of progression-free survival without a demonstrated impact on overall survival compared to fluvestrant as monotherapy, with no robust quality of life data and with significant toxicity, with, in particular, metabolic (hyperglycaemia) gastrointestinal (diarrhoea) and cutaneous events (skin rashes) and grade 3-4 adverse events reported in 76.1% of patients versus 35.5% of patients in the fulvestrant group alone,
- the study comparator, acceptable at the start of the study but not clinically relevant on the day of the assessment in view of current guidelines, and which does not enable the position of alpelisib in the current care pathway to be determined,

the efficacy/adverse effects ratio of PIQRAY (alpelisib) in combination with fulvestrant has not been adequately established.

◗ There are alternatives not specific to the PIK3CA mutation.

◗ At the present time, in the absence of comparative data versus the currently recommended standard-of-care therapy in the indication assessed, i.e., the combination of a CDK 4/6 inhibitor with endocrine therapy, the role of PIQRAY (alpelisib) in combination with fulvestrant is not known (see section 08. Role in the care pathway).

Public health impact

Considering:
- the seriousness of locally advanced or metastatic HR-positive/HER2-negative breast cancer,
- its incidence at the advanced stage,
- the partially met medical need,
- the lack of response to the identified need considering the absence of a demonstrated additional impact on morbidity and mortality or quality of life, and the absence of data supporting an impact on the care and/or life pathway,

PIQRAY (alpelisib) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of PIQRAY (alpelisib) is insufficient to justify its public funding cover in view of the alternatives available in the MA indication.

The Committee issues an unfavourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the MA indication and dosages.