HAUTE AUTORITÉ DE SANTÉ

ONCOLOGY
New indication
September 2018

TRANSPARENCY COMMITTEE OPINION SUMMARY

DECAPEPTYL LP 3 mg (triptorelin), GnRH analogue

Insufficient clinical benefit to justify its reimbursement, in combination with tamoxifen or with an aromatase inhibitor, for the adjuvant treatment of hormone-sensitive breast cancer in non-menopausal women at high risk of relapse, after chemotherapy.

Main points

- DECAPEPTYL (triptorelin) LP 3 mg has been granted a marketing authorisation, in combination with tamoxifen or with an aromatase inhibitor, for the adjuvant treatment of hormone-sensitive breast cancer in non-menopausal women at high risk of relapse, after chemotherapy.
- Triptorelin is a natural GnRH (gonadotropin releasing hormone) analogue that suppresses oestrogen synthesis by the ovaries. Suppression of ovarian function, combined with tamoxifen, causes increased toxicity relative to tamoxifen alone.
- One study demonstrated the absence of benefit in terms of 5-year disease-free survival of ovarian function suppression (in particular by triptorelin) combined with tamoxifen compared to tamoxifen alone.
- DECAPEPTYL LP 3 mg has no role in the current management strategy for early stage hormone-sensitive breast cancer in non-menopausal women, a strategy which is based on tamoxifen used alone.

Pre-existing indications in oncology*

DECAPEPTYL has also been granted a marketing authorisation for the treatment of prostate cancer (for further details, see SPC).

Therapeutic strategy

The systemic adjuvant treatment of early-stage hormone-sensitive breast cancer consists of hormone therapy, with or without prior chemotherapy. The systemic adjuvant treatment should start within 3 to 6 weeks after surgery. If not contraindicated, adjuvant breast cancer chemotherapy is performed with anthracyclines and taxanes. Treatment targeting the HER2 receptor is only indicated in combination with chemotherapy and in the vent of significant HER2 over-expression. In non-menopausal women, the reference hormone therapy is tamoxifen for 5 years.

- **Role of the medicinal product in the therapeutic strategy**
  DECAPEPTYL LP 3 mg has no role in the current management strategy for early stage hormone-sensitive breast cancer in non-menopausal women.

Clinical data

- One open-label study compared tamoxifen combined with ovarian function suppression (OFS) to tamoxifen alone, in terms of disease-free survival, in 2,033 chemotherapy-naive non-menopausal women who received adjuvant or neo-adjuvant chemotherapy, with confirmed absence of menopause after chemotherapy. This study did not allow the therapeutic contribution of triptorelin to be evaluated, due to the fact that OFS was achieved, according to the patient's choice, by triptorelin administration for 5 years, bilateral ovariectomy, or ovarian irradiation. No specific data are available for the sub-group of women at high risk of recurrence, i.e. the

* This summary does not concern these indications.

population of the MA (not specified in the study protocol). Finally, the study included chemotherapy-naive women, a population not included in the MA.

- With a median follow-up of 5.6 years, no benefit of combining OFS with tamoxifen over tamoxifen alone in terms of disease-free survival (primary endpoint) was demonstrated: HR= 0.83; CI95% [0.66; 1.04]; p=0.10 (not significant), with a 5-year disease-free survival rate of 86.6% in the OFS plus tamoxifen group and of 84.7% in the tamoxifen alone group.
  No difference in overall survival was demonstrated between the two groups, with a median survival of 5.6 years (unranked secondary endpoint).
- Adverse events were more frequent when OFS was combined with tamoxifen than when tamoxifen was administered alone, with particular emphasis on grade 3-4 adverse events (31.3% vs 23.7%), in particular hot flushes (93.4% vs 79.8%). Adverse events of particular interest such as osteoporosis, hypertension and hyperglycaemia/diabetes, were more frequent when OFS was combined with tamoxifen.
- To date, the impact on quality of life has not been demonstrated, though combining OFS with tamoxifen is expected to deteriorate quality of life relative to tamoxifen alone, due to the safety profile, particularly in the short term, of the OFS-tamoxifen combination.

Benefit of the medicinal product

- The actual clinical benefit* of DECAPEPTYL LP 3 mg is insufficient to justify reimbursement for adjuvant treatment, in combination with tamoxifen or an aromatase inhibitor, of early-stage hormone-sensitive breast cancer in women at high risk of relapse, confirmed as non-menopausal upon completion of chemotherapy.
- Not approved for non-hospital pharmacy reimbursement or for hospital treatment.

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This document was drafted on the basis of the Transparency Committee opinion dated 19 September 2018 (CT-16663) available at **www.has-sante.fr**

* The actual clinical benefit (ACB) of a medicinal product consists of its benefit particularly on the basis of its clinical performances and the severity of the disease treated. The HAS Transparency Committee assesses the ACB, which may be high, moderate, low, or insufficient for the medicinal product to be covered by public funding.