OPINION ON MEDICINAL PRODUCTS

tezepelumab

TEZSPIRE 210 mg,

solution for injection in prefilled syringe

First assessment

Adopted by the Transparency Committee on 30 November 2022

SUMMARY

The legally binding text is the original French opinion version

Key points

Approval of reimbursement of TEZSPIRE (tezepelumab) for adults and adolescents aged 12 years and older as an add-on -maintenance treatment for uncontrolled severe asthma despite high-dose inhaled corticosteroid therapy associated with another maintenance treatment.

Therapeutic improvement?

Therapeutic improvement in the care of uncontrolled severe asthma despite high-dose inhaled corticosteroid therapy associated with another maintenance treatment.

Role in therapeutic strategy?

The objectives of pharmacological asthma treatment consist of long-term disease control, including: symptom reduction, exacerbation prevention, reduction of limitations in everyday life and limitation of adverse effects due to pharmacological treatments.

Therapeutic management is primarily based on two types of medicinal products aimed at acting upon bronchospasm, on one hand, and upon underlying inflammation, on the other. A distinction is traditionally made between:

- attack treatments: short-acting beta-2 agonist (SABA) bronchodilators;
- maintenance treatments: inhaled corticosteroids (ICS) as monotherapy or in association with a long-acting beta-2 agonist (LABA) bronchodilator.

This therapeutic dichotomy is currently receding, insofar as it has been demonstrated that attack treatment with an association of formoterol (LABA) and inhaled corticosteroid helps to reduce severe exacerbations.

Therapeutic management is adapted to disease severity and control. International consensus has separated 5 steps of severity with therapeutic escalation in cases where asthma is uncontrolled or partially controlled. The treatment adaptation strategy is defined by GINA. Severe asthma corresponds to steps 4 and 5:

- step 4: asthma requiring use of a maintenance treatment associating a medium-dose ICS and formoterol (preferential maintenance treatment);
- step 5: uncontrolled step 4 asthma requiring use of a maintenance treatment associating a high-dose ICS and formoterol, with, as needed, an add-on biological treatment according to asthma phenotype.

In any case, the preferred attack treatment consists of a formoterol/high-dose inhaled corticosteroid association.

Before establishing uncontrolled asthma involving potential therapeutic escalation, it is necessary to rule out a differential diagnosis, assess treatment compliance, verify and correct the inhalation technique where needed, detect and treat exacerbating factors (tobacco, household allergens, work environment, etc.), and associated conditions.

Therapeutic escalation of severe asthma consists of oral corticosteroid therapy and biotherapies as a last resort. Among the biotherapies, omalizumab (XOLAIR) in severe allergic asthma, benralizumab (FASENRA) and mepolizumab (NUCALA) in severe refractory eosinophilic asthma, and dupilumab (DUPIXENT) in severe asthma associated with type 2 inflammation have currently been granted a marketing authorisation in France.

Role of the medicinal product

TEZSPIRE (tezepelumab) is a therapeutic alternative used in the context of an add-on maintenance treatment of uncontrolled severe asthma despite high-dose inhaled corticosteroid therapy and another maintenance symptomatic treatment for adults and adolescents aged 12 years and older.

In corticosteroid-dependent asthma, the findings of a study demonstrated that TEZSPIRE (tezepelumab) does not enable corticosteroid sparing.

According to GINA 2022, TEZSPIRE (tezepelumab) may be used in the treatment of step 5 asthma patients, with or without type 2 inflammation.

As such, the patients suitable for treatment with TEZSPIRE (tezepelumab) are adult and adolescent patients aged 12 years and older with uncontrolled severe asthma despite high-dose inhaled corticosteroid therapy associated with another maintenance treatment.

In the absence of a direct comparison to other biological products (see 5.1 Clinical relevant comparators), the role of TEZSPIRE (tezepelumab) among the other biological products available in severe asthma has yet to be specified.

Committee's conclusions

Clinical Benefit

- Uncontrolled severe asthma has a major impact on quality of life and is associated with a risk of severe, potentially life-threatening exacerbations.
- The proprietary medicinal product TEZSPIRE (tezepelumab) is used as part of a maintenance symptomatic treatment.
- The efficacy/adverse effects ratio of TEZSPIRE (tezepelumab) is significant.
- Therapeutic alternatives are available (other biological products, see 5.1 Medicinal products).
- TEZSPIRE (tezepelumab) is a therapeutic option as an add-on treatment of uncontrolled severe asthma despite high-dose inhaled corticosteroid therapy associated with another maintenance treatment. (see 8. **Erreur ! Source du renvoi introuvable.**).

Public health benefit

Considering:

- the severity of severe asthma,
- its prevalence,
- the partially met medical need among patients with uncontrolled severe asthma;
- the partial additional response to the identified need on account of:
  - the expected additional impact on morbidity but in the absence of evidence of an additional impact on mortality and on quality of life;
  - the lack of evidence of any impact on delivery of care;

TEZSPIRE (tezepelumab) is not likely to have an additional public health benefit.

Considering all of these elements, the Committee deems that the clinical benefit of TEZSPIRE (tezepelumab) is significant as an add-on maintenance treatment for uncontrolled severe asthma despite high-dose inhaled corticosteroid therapy associated with another maintenance treatment.

The Committee approves inclusion in the list of proprietary medicinal products qualifying for reimbursement under social security and in the list of proprietary products approved for community use for the indication and at the dosages of the marketing authorisation.

Recommended reimbursement rate: 65%

Clinical Added Value

Considering:

- the evidence of superiority of TEZSPIRE (tezepelumab) versus placebo in two double-blind randomised studies, on the annualised rate of severe asthma exacerbations at 52 weeks, a clinically relative outcome measure with a modest effect size (RR=0.44 (99%CI [0.34;0.57], p<0.001 in the pivotal study and Rate Ratio = 0.29 (95%CI [0.16;0.51], p<0.001 in a phase IIb study);
- its acceptable safety profile;
- the partially met medical need in adult and adolescent patients aged 12 years and over with uncontrolled severe asthma;

but in view of:

- the lack of difference in respect of corticosteroid sparing versus placebo in a study in which it was the primary outcome measure;
- the lack of data available beyond two years regarding asthma progression in patients treated with tezepelumab;
- the lack of evidence of a clinically relevant difference on asthma control and quality of life;

the Transparency Committee deems that TEZSPIRE (tezepelumab) provides **minor clinical added value (CAV IV) in the treatment** of uncontrolled severe asthma despite high-dose inhaled corticosteroid therapy associated with another maintenance treatment, in the same way as DUPIXENT (dupilumab), FASENRA (benralizumab), NUCALA (mepolizumab), and XOLAIR (omalizumab).