SUMMARY

remimazolam

BYFAVO 20 mg and 50 mg

powder for solution for injection

BYFAVO 50 mg

powder for concentrate for solution for injection/infusion

First listing

Original French opinion adopted by the Transparency Committee on 24 April 2024

The legally binding text is the original French opinion version

Summary of opinion

Favourable opinion for reimbursement for:

- **BYFAVO (remimazolam) 20 mg powder for solution for injection in adults for procedural sedation,**
- **BYFAVO (remimazolam) 50 mg powder for concentrate for solution for injection/infusion in adults for intravenous induction and maintenance of general anaesthesia.**

Transparency Committee's conclusions

Clinical Benefit

Procedural sedation

- The pain caused by surgical and/or diagnostic procedures warrants sedation or even anaesthesia.
- This is a symptomatic medicinal product.
- The efficacy/adverse effects ratio of BYFAVO 20 mg (remimazolam) is high in the indication in adults for procedural sedation.
- It is a first-line treatment in adults for procedural sedation.

Public health benefit

Considering:

- the significant psychosocial impact of pain during surgical/diagnostic procedures and its prevalence,
- the identified medical need,

- the partial response to the identified need, given:
  - the lack of evidence of an additional impact on morbidity and the lack of evidence of an impact on quality of life,
  - the lack of evidence of an impact on the patient's care or life pathway,
  - the lack of evidence of an additional impact on the organisation of care,

BYFAVO (remimazolam) 20 mg powder for solution for injection is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of BYFAVO (remimazolam) 20 mg powder for solution for injection is substantial in the MA indication.

The Committee issues a favourable opinion for inclusion of BYFAVO (remimazolam) 20 mg powder for solution for injection in the list of covered drugs for inpatients approved for use in the MA indication and at the MA dosages.

General anaesthesia

- BYFAVO 50 mg (remimazolam) is intended for use in the context of any anaesthesia technique inducing partial or total loss of sensitivity of the body and, in particular, muscle relaxation, for the performance of a surgical, medical or obstetric procedure.
- This is a symptomatic medicinal product.
- The efficacy/adverse effects ratio of BYFAVO 50 mg (remimazolam) is high in the indication in adults for intravenous induction and maintenance of general anaesthesia.
- It is a first-line treatment in adults for intravenous induction and maintenance of general anaesthesia.

Public health benefit

Considering:

- the high incidence of patients requiring general anaesthesia,
- the met identified medical need,
- the partial response to the met identified need, given:
  - the lack of evidence of an additional impact on morbidity and the lack of evidence of an impact on quality of life,
  - the lack of evidence of an impact on the patient's care or life pathway,
  - the lack of evidence of an additional impact on the organisation of care,

BYFAVO 50 mg (remimazolam) powder for concentrate for solution for injection/infusion is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of BYFAVO 50 mg (remimazolam) powder for concentrate for solution for injection/infusion is substantial in the MA indication.

The Committee issues a favourable opinion for inclusion of BYFAVO 50 mg (remimazolam) powder for concentrate for solution for injection/infusion in the list of covered drugs for inpatients approved for use in the MA indication and at the MA dosages.

Clinical Added Value

Procedural sedation

Considering:

- demonstration of the superiority of remimazolam compared to placebo in two phase 3 studies (studies 006 and 008), in terms of procedure success rate (composite primary endpoint) in patients undergoing bronchoscopy or colonoscopy, in combination with fentanyl,
- demonstration of the non-inferiority of remimazolam compared to propofol in a phase 3 study, in terms of procedure success rate (composite primary endpoint) in patients undergoing colonoscopy;

but taking into account:

- the low robustness of the data available, due, in particular, to:
  - the open-label nature of pivotal studies 006 and 008 and confirmatory trial 015,
  - the single-blind design of study RF-6,
  - the exploratory nature of the secondary endpoints, such as the time to onset and the recovery time, in the absence of a method to control the α risk,
  - the debatable clinical relevance of the composite primary endpoint of these studies,
- the absence of robust comparative data demonstrating an advantage of remimazolam in terms of efficacy or safety compared to the available alternatives,
- the medical need already met by these alternatives,

the Committee deems that BYFAVO (remimazolam) 20 mg powder for solution for injection provides no clinical added value (CAV V) in the care pathway for procedural sedation in adults.

General anaesthesia

Considering:

- demonstration of the non-inferiority of remimazolam compared to propofol in two phase 3 studies (studies ONO 2745-05 and CNS7056-022), in patients undergoing elective surgery, in terms of:
  - functional capability as a general anaesthetic assessed using a composite primary endpoint evaluating the failure of the procedure via three variables: “intraoperative awakening or recall”, “requirement of rescue sedation with other sedatives” and “body movement”, in study ONO-2745-05,
  - maintenance of general anaesthesia, defined as a percentage of general anaesthesia maintenance time with Narcotrend index ≤ 60 (primary endpoint) during the general anaesthesia maintenance period, in study CNS7056-022,

but taking into account:

- the low robustness of the data available, due, in particular, to:
  - the single-blind design of the two studies, making it impossible to rule out an assessment bias,
  - the higher number of protocol deviations in the remimazolam group (13.6% vs 4.8%), calling into question the internal validity of the result obtained for the primary endpoint,

    - the impossibility of interpreting the results for the key secondary endpoints of study CNS7056-022, suggesting a better haemodynamic stability of remimazolam, given the post hoc changes made to the statistical analysis plan,
    - the debatable clinical relevance of the composite primary endpoint in study ONO-2745-05
- the absence of robust comparative data demonstrating an advantage of remimazolam in terms of efficacy or safety compared to the available alternatives, including propofol,
- the medical need already met by these alternatives,

the Committee deems that BYFAVO (remimazolam) 50 mg powder for concentrate for solution for injection/infusion provides no clinical added value (CAV V) in the care pathway for intravenous induction and maintenance of general anaesthesia in adults.