SUMMARY

pitolisant

WAKIX 4.5 mg and 18 mg,

film-coated tablet

Indication extension

Original French opinion adopted by the Transparency Committee on 19 July 2023

The legally binding text is the original French opinion version

Transparency Committee's conclusions

Clinical Benefit

- Narcolepsy is a chronic disease primarily manifested by excessive daytime sleepiness accompanied by cataplexy attacks depending on the form. These symptoms are incapacitating to various degrees depending on their severity, with severe forms very significantly impairing quality of life.
- This is a symptomatic medicinal product.
- Due to a modest efficacy demonstrated after 4 weeks at a fixed dose only versus placebo and uncertainties with respect to the long-term safety in paediatric treatment, the short-term efficacy/adverse effects ratio is moderate. The long-term efficacy/adverse effects ratio remains to be determined.
- This product is a first-line treatment in adolescents and children from the age of 6 years for the treatment of narcolepsy with or without cataplexy.

- **Public health benefit**

Considering:

- the seriousness of the disease, which, in particular, impairs patients' quality of life in severe forms,
- its prevalence,
- the partially met medical need,
- the lack of additional response to the identified need with:
  - the lack of a demonstrated additional impact on morbidity compared to the available alternatives,

- the lack of a demonstrated additional impact on quality of life,
- the lack of evidence of an additional impact on the organisation of care and the patient's life pathway,

WAKIX (pitolisant) 4.5 mg and 18 mg film-coated tablet is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of WAKIX (pitolisant) 4.5 mg and 18 mg film-coated tablet is moderate in the paediatric indication extension to adolescents and children from the age of 6 years for the treatment of narcolepsy with or without cataplexy.

The Committee issues a favourable opinion for inclusion of WAKIX (pitolisant) 4.5 mg and 18 mg film-coated tablet in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the paediatric indication extension to adolescents and children from the age of 6 years for the treatment of narcolepsy with or without cataplexy, and at the MA dosages.

➔ **Recommended reimbursement rate for inclusion in the retail list of reimbursed proprietary medicinal products approved for use: 30%**

Clinical Added Value

Considering:

- demonstration of the superiority of pitolisant compared to placebo assessed during a double-blind, randomised study over 8 weeks (including 4 weeks at a fixed dose) in adolescents and children from the age of 6 years for the treatment of narcolepsy with or without cataplexy on:
  - the primary efficacy endpoint of variation in UNS total score, with a modest effect size: mean difference of -3.7 points (CI95% [-6.38; -0.99]; p=0.0073),
  - and on the ranked secondary endpoint of PDSS total score: mean difference of -3.4 points, (CI95% [-5.52; -1.31]; p=0.0015),
- conflicting results in terms of efficacy on cataplexy during this same study reported in a non-stratified subgroup of patients with type 1 narcolepsy, with a superiority demonstrated versus placebo on the UNS-CTP subscore (mean difference of -1.8 points, CI95% [-3.29; -0.24]; p=0.0229) but not demonstrated on the variation in the number of cataplexy attacks per week,
- the short-term paediatric safety profile similar to that already known in adults,
- the medical need only partially met in paediatrics by the recommended therapeutic alternatives, some of which are used off-label,

and despite:

- questions concerning the relevance of the primary endpoint, corresponding to a scale that has not been validated in children,
- the lack of quality of life data,
- the absence of data versus an active comparator in a context in which the majority of patients (64% in the pitolisant group and 69% in the placebo group) had received no prior narcolepsy treatments,

the Committee deems that WAKIX (pitolisant) 4.5 mg and 18 mg provides a minor clinical added value (CAV IV) in the care pathway for the treatment of narcolepsy with or without cataplexy in adolescents and children from the age of 6 years.