HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
OPINION
24 JUNE 2020

solriamfetol
SUNOSI 75 mg film-coated tablets
SUNOSI 150 mg film-coated tablets

First assessment

Key points

Favourable opinion for reimbursement to improve wakefulness and reduce excessive daytime sleepiness (EDS):

- in adult patients with narcolepsy (with or without cataplexy), only in the event of non-response, intolerance or contraindication to the therapeutic alternatives currently available.
- in adult patients with obstructive sleep apnoea (OSA), only in treatment-compliant patients whose EDS has not been satisfactorily treated by primary OSA therapy, such as continuous positive airway pressure (CPAP).

Unfavourable opinion for reimbursement in the other MA situations.

What therapeutic improvement?

- No therapeutic improvement to improve wakefulness and reduce excessive daytime sleepiness (EDS) in patients with narcolepsy (with or without cataplexy) in the event of non-response, intolerance or contraindication to the therapeutic alternatives currently available.
- Therapeutic improvement to improve wakefulness and reduce excessive daytime sleepiness (EDS) in treatment-compliant patients with obstructive sleep apnoea (OSA) whose EDS has not been satisfactorily treated by primary OSA therapy (CPAP).

Role in the care pathway?

In the treatment of EDS in narcolepsy

Modafinil is the first-line treatment and must be accompanied by the implementation of lifestyle rules. Methylphenidate and, possibly, amphetamine derivatives (dexamfetamine available on a named-patient compassionate use programme basis) are recommended in the event of inefficacy of or intolerance to modafinil.

In the event of drug resistance, a combination of several medicinal products may be initiated, including, in particular, antidepressants (off-label), sodium oxybate (XYREM) and pitolisant (WAKIX).

Role of the medicinal product in the care pathway

SUNOSI (solriamfetol) is a therapeutic option to improve wakefulness and reduce excessive daytime sleepiness (EDS) in patients with narcolepsy (with or without cataplexy) in the event of non-response, intolerance or contraindication to the therapeutic alternatives currently available.

In the treatment of EDS in OSA

Lifestyle and dietary measures must be put in place in all OSA patients. The reference treatment is nasal ventilation by continuous positive airway pressure (CPAP). Mandibular advancement devices (MADs) may be proposed as second-line option following refusal of or intolerance to CPAP. As regards surgical procedures, there are no recommendations with a high level of evidence in favour of surgery (in particular surgery of the jaw or base of the tongue); it may be proposed in paediatric cases when the cause of the OSA is anatomical.

In the absence of a satisfactory response on sleepiness with primary therapy such as CPAP, there are currently no medicinal products available for either the overall treatment of OSA or the treatment of excessive daytime sleepiness, a symptom of OSA.

Role of the medicinal product in the care pathway

SUNOSI (solriamfetol) is the first-line medicinal treatment to improve wakefulness and reduce EDS, only in treatment-compliant patients whose EDS has not been satisfactorily treated by primary OSA therapy, such as CPAP.

According to article L. 165-1 of the French Social Security Code “Patient compliance is assessed over a period of 28 consecutive days. During this period, the patient must actually use his/her CPAP device for at least 112 hours”, i.e., an average of 4 hours per night.

Special recommendations

In the OSA indication, the Committee warns that it is important to adhere to the prescription restrictions indicated in the MA and to monitor good compliance with primary CPAP therapy, with objective measurements of compliance and the course of the OSA, along with blood pressure and cardiovascular monitoring, which are essential.

01 COMMITTEE'S CONCLUSIONS

01.1 Clinical benefit

1.1.1 EDS in narcolepsy

◗ Narcolepsy is a chronic disease with excessive daytime sleepiness as primary symptom, incapacitating to various degrees depending on its severity, which very significantly impairs quality of life in severe forms.
◗ This is a symptomatic treatment.
◗ Considering:

- the superiority of solriamfetol, with a clinically relevant effect size but only versus placebo and in the short term,
- the short and medium-term safety profile, marked, in particular, by the cardiovascular and psychiatric risk, mentioned in the RMP,
- the absence of a comparison versus modafinil or other treatment combinations recommended in the event of non-response to modafinil, whereas this comparison could have been performed,

the efficacy/adverse effects ratio of SUNOSI (solriamfetol) is:

- moderate to improve wakefulness and reduce excessive daytime sleepiness (EDS) in adult patients with narcolepsy (with or without cataplexy) in the event of non-response, intolerance or contraindication to the therapeutic alternatives currently available and at the MA dosages,
- inadequately established in the other clinical situations of the MA.

◗ There are alternatives in the treatment of narcolepsy with or without cataplexy (MODIODAL, RITALIN, XYREM, WAKIX).
◗ This is a therapeutic option in the event of non-response, intolerance or contraindication to the therapeutic alternatives currently available.

Public health impact

Considering:

- the seriousness of the disease, which can substantially impair patients' quality of life in severe forms,
- its prevalence of 1/2,800,
- the partial unmet medical need,
- the absence of conclusive data in terms of care or life pathway,
- the absence of any demonstrated impact on the organisation of care,
- the lack of additional response to the partial unmet medical need,

SUNOSI (solriamfetol) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of SUNOSI (solriamfetol) is:

- **moderate in the event of non-response, intolerance or contraindication to the therapeutic alternatives currently available, to improve wakefulness and reduce excessive daytime sleepiness (EDS) in adult patients with narcolepsy (with or without cataplexy);**
- **insufficient to justify public funding cover in the other MA situations in narcolepsy.**

The Committee issues a favourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use to improve wakefulness and reduce excessive daytime sleepiness (EDS) in adult patients with narcolepsy (with or without cataplexy) in the event of non-response, intolerance or contraindication to the therapeutic alternatives currently available and at the MA dosages.

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 patients with narcolepsy in the other MA situations in narcolepsy.

1.1.2 EDS in obstructive sleep apnoea syndrome (OSA)

◗ Excessive daytime sleepiness is one of the main clinical symptoms in OSA, incapacitating to various degrees depending on its severity, which significantly impairs quality of life in severe forms.
◗ This is a symptomatic treatment.
◗ Considering:

- the superiority of solriamfetol, with a clinically relevant effect size versus placebo and in the short term,
- the short and medium-term safety profile, marked, in particular, by the cardiovascular risk, whereas OSA is already a risk factor for cardiovascular morbidity and mortality,
- compliance with CPAP therapy by 70% of patients,

the efficacy/adverse effects ratio of SUNOSI (solriamfetol) is:

- high to improve wakefulness and reduce excessive daytime sleepiness (EDS) in treatment-compliant patients with obstructive sleep apnoea (OSA) whose EDS has not been satisfactorily treated by primary OSA therapy,
- inadequately established in the other clinical situations of the MA.

◗ There are no medicinal alternatives in adult patients with obstructive sleep apnoea (OSA) whose EDS has not been satisfactorily treated by primary OSA therapy, such as continuous positive airway pressure (CPAP).
◗ SUNOSI (solriamfetol) is the first-line medicinal treatment to improve wakefulness and reduce excessive daytime sleepiness (EDS) in treatment-compliant patients with obstructive sleep apnoea (OSA) whose EDS has not been satisfactorily treated by primary OSA therapy, such as continuous positive airway pressure (CPAP) (according to article L. 165-1 of the French Social Security Code "Patient compliance is assessed over a period of 28 consecutive days. During this period, the patient must actually use his/her CPAP device for at least 112 hours", i.e., an average of 4 hours per night).

Public health impact

Considering:

- the seriousness of the disease,
- its prevalence, with 4 to 10% of French people having OSA[Erreur ! Signet non défini.,Erreur ! Signet non défini.],
- the unmet medical need,
- the absence of conclusive data concerning the care or life pathway,
- the absence of any demonstrated impact on the organisation of care,
- the partial response to the identified need,

SUNOSI (solriamfetol) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of SUNOSI (solriamfetol) is:

- **substantial to improve wakefulness and reduce excessive daytime sleepiness (EDS) in treatment-compliant patients with obstructive sleep apnoea (OSA) whose EDS has not been satisfactorily treated by primary OSA therapy, such as continuous positive airway pressure (CPAP) (according to article L. 165-1 of the French Social Security Code "Patient compliance is assessed over a period of 28 consecutive days. During this period, the patient must actually use his/her CPAP device for at least 112 hours", i.e., an average of 4 hours per night);**
- **insufficient to justify its funding by the French national health insurance system in non-treatment-compliant patients with obstructive sleep apnoea (OSA) whose EDS has not been satisfactorily treated by primary OSA therapy, such as continuous positive airway pressure (CPAP).**

The Committee issues a favourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use to improve wakefulness and reduce excessive daytime sleepiness (EDS) in patients with

obstructive sleep apnoea (OSA) complying with a primary OSA therapy, such as continuous positive airway pressure (CPAP), and at the MA dosages.

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 to improve wakefulness and reduce excessive daytime sleepiness (EDS) in non-treatment-compliant patients with obstructive sleep apnoea (OSA) whose EDS has not been satisfactorily treated by primary OSA therapy, such as continuous positive airway pressure (CPAP).

01.2 Clinical Added Value

1.2.1 EDS in narcolepsy

- **In patients in the event of non-response, intolerance or contraindication to the therapeutic alternatives currently available**

Considering:

- **demonstration of the superiority of solriamfetol, at the 150 mg dosage alone, versus placebo in two randomised, double-blind, phase III studies, on the MWT with a least-squares difference of 7.7 minutes (95% CI = [3.99; 11.31]), (assessment measured by the clinician) and the ESS score, with a least-squares difference of -3.8 points (95% CI = [- 5.6; -2.0] (patient-reported assessment),**
- **the relevance of these scores in this therapeutic field, with an effect size deemed to be clinically relevant versus placebo,**
- **the lack of comparative data versus an active comparator such as MODIODAL (modafinil) whereas this comparison could have been performed,**
- **the short and medium-term safety profile, marked, in particular, by the cardiovascular and psychiatric risk, mentioned in the RMP,**
- **the medical need partially met by several therapeutic alternatives already available and recommended in narcolepsy and EDS in particular,**

the Committee considers that SUNOSI (solriamfetol) provides no clinical added value (CAV V) in the current therapeutic strategy, which includes relevant comparators (see chapter Erreur ! Source du renvoi introuvable.**), to improve wakefulness and reduce excessive daytime sleepiness (EDS) in adult patients with narcolepsy (with or without cataplexy) in the event of non-response, intolerance or contraindication to the therapeutic alternatives currently available.**

- **In the other MA situations in narcolepsy**

Not applicable.

1.2.2 EDS in obstructive sleep apnoea syndrome (OSA)

- **Treatment-compliant patients whose EDS has not been satisfactorily treated by primary OSA therapy, such as continuous positive airway pressure (CPAP)**

Considering:

- **demonstration of the superiority of solriamfetol at the 150 mg, 75 mg and 37.5 mg dosages versus placebo in three randomised, double-blind, phase III studies, with, in particular, results at the 150 mg dosage on the MWT of 10.74 minutes (95% CI = [8.05; 13.44]), (assessment measured by the clinician) and the ESS score of 4.5 points (95% CI = [- 5.7; - 3.2]), (patient-reported assessment),**
- **the relevance of these scores in the assessment of EDS in OSA, with an effect size deemed to be clinically relevant versus placebo,**
- **the short and medium-term safety profile, marked, in particular, by the cardiovascular risk mentioned in the RMP in these patients already presenting cardiovascular risk factors,**
- **the unmet medical need in these patients,**

the Committee considers that SUNOSI (solriamfetol) provides a minor clinical added value (CAV IV) in the current therapeutic strategy to improve wakefulness and reduce excessive daytime sleepiness (EDS) in treatment-compliant patients with obstructive sleep apnoea (OSA) whose EDS has not been satisfactorily treated by primary OSA therapy.

- **Non-treatment-compliant patients whose EDS has not been satisfactorily treated by primary OSA therapy, such as continuous CPAP**

Not applicable.