HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
16 SEPTEMBER 2020

The legally binding text is the original French opinion version

sotalol

SOTALEX 80 mg and 160 mg scored tablets

Reevaluation

Key points

Unfavourable opinion for maintenance of reimbursement in the prevention of recurrences of supraventricular tachycardias and ventricular rhythm disorders (for more details, see MA).

Clinical benefit now insufficient to justify public funding cover (previously it was substantial) in the indications of the MA.

Role in the care pathway ?

1. Supraventricular tachycardias

- Prevention of recurrences of atrial fibrillation

Antiarrhythmic treatment may be considered as long-term therapy to maintain sinus rhythm in the event of symptomatic recurrent paroxysmal or persistent AF. It is not generally initiated from the first episode of AF. Long-term antiarrhythmic treatment is aimed at improving symptoms and preventing recurrences of symptomatic AF. It falls within the scope of specialised management with a cardiological opinion and at least annual ECG monitoring. Catheter ablation may be a first-line therapeutic alternative in specific situations or a second-line alternative in the event of failure of medicinal treatment. It requires oral anticoagulant therapy and is reserved for cardiac rhythm specialists.

Role of the medicinal product in the care pathway :

In patients with paroxysmal or persistent atrial fibrillation, the Committee considers that sotalol no longer has a role in the care pathway for the prevention of recurrences of atrial fibrillation, in view of the available alternatives, given its risk of excess mortality demonstrated in the prevention of recurrences of atrial fibrillation and its low effect size in the prevention of recurrences of atrial fibrillation compared to the control group (placebo or the absence of treatment).

In patients with permanent atrial fibrillation, the Committee reiterates that oral antiarrhythmic drugs no longer have a role in the prevention of recurrences.

- Prevention of recurrences of other supraventricular tachycardias

The therapeutic strategy for the prevention of recurrences of supraventricular rhythm disorders apart from atrial fibrillation (focal atrial tachycardias, common atrial flutter, atrioventricular nodal re-entry tachycardia (AVNRT), atrioventricular re-entry tachycardia (AVRT)) is based on catheter ablation as a first-line approach. Medicinal treatment with beta-blockers or non bradycardia-inducing calcium channel blockers is recommended pending or following refusal or failure of ablation. The use of oral antiarrhythmic drugs has become marginal.

Role of the medicinal product in the care pathway :

SOTALEX (sotalol) proprietary medicinal products no longer have a role in the care pathway for the prevention of recurrences of other supraventricular tachycardias.

2. Prevention of recurrences of ventricular rhythm disorders

With the exception of certain specific cardiac diseases, the prevention of recurrences of ventricular arrhythmias is based on an implantable cardioverter defibrillator (ICD) and, more rarely, on antiarrhythmic drugs. The decision to implant an ICD requires the opinion of a cardiac rhythm specialist. Implantation is only considered in authorised centres in patients in whom the reasonable expectancy of survival with a satisfactory functional status is more than 1 to 2 years and in patients over 30 years of age.

Beta-blockers (excluding sotalol) are recommended as first-line treatment in patients with ventricular arrhythmia.

In the event of failure of or contraindication to beta-blockers, the European guidelines indicate antiarrhythmics. Antiarrhythmic drugs are often used as an adjuvant therapy in the treatment of patients with ventricular arrhythmias. The choice of antiarrhythmic drug must take into account the causal disease and/or the associated heart condition.

Furthermore, interventional procedures are alternatives :

- The ablation of arrhythmogenic foci is considered as a second-line treatment of recurrent idiopathic ventricular tachycardias, following the failure of pharmacotherapy.
- Ablation is generally performed percutaneously (percutaneous catheter ablation), by the subepicardial route in rare cases and, in exceptional cases, surgically.
- Finally, other invasive or surgical treatments, such as myocardial revascularisation, ventricular aneurysm resection, sympathetic denervation, short-term mechanical circulatory support, heart transplant, the use of a total artificial heart device or anaesthetic sedation, represent special situations, with implementation decided upon on a case-by-case basis following a specialised opinion.

Role of the medicinal product in the care pathway :

SOTALEX (sotalol) proprietary medicinal products no longer have a role in this strategy insofar as a potential risk of excess mortality compared to placebo was identified in the SWORD study (with d-sotalol) as well as a meta-analysis conducted in the prevention of atrial fibrillation. The Committee considers that there would therefore be a potential loss of opportunity for patients in view of the alternatives, although this medicinal product is still cited in the European guidelines (ESC 2016).

◗ Special recommendations

The Committee reiterates that if it is necessary to change treatment, any overlapping of prescriptions of antiarrhythmic drugs should be avoided, since this could exacerbate their toxicity.

COMMITTEE'S CONCLUSIONS

Considering the "Reevaluation of oral antiarrhythmic drugs" assessment report and further to debate and voting, the Committee considers :

Clinical benefit

Supraventricular rhythm disorders

◗ Supraventricular rhythm disorders, primarily represented by atrial fibrillation, are serious conditions that can impair quality of life and be life-threatening for the patient, either immediately (sudden death) or following complications (heart failure, stroke).

◗ SOTALEX (sotalol) proprietary medicinal products are preventive treatments for recurrences of supraventricular rhythm disorders.

◗ The efficacy/adverse effects ratio of sotalol is insufficient in the prevention of recurrences of supraventricular tachycardias given :

- its low effect size in the prevention of recurrences of atrial fibrillation compared to the control group (placebo or the absence of treatment),
- the absence of robust new data on morbidity,
- its demonstrated risk of excess mortality in the prevention of recurrences of atrial fibrillation compared to the control group and its safety profile marked by frequent adverse effects (in particular pro-arrhythmic).

◗ There are therapeutic alternatives (see 08. Role in the care pathway).

◗ SOTALEX (sotalol) proprietary medicinal products no longer have a role in the care pathway for the prevention of recurrences of supraventricular tachycardias in view of the available alternatives.

Public health impact

Considering :

- the seriousness of supraventricular rhythm disorders,
- their high prevalence,
- the partially met medical need,
- the potentially negative impact on mortality in view of the available data, which suggested a risk of excess mortality and an efficacy only on prevention of recurrences of AF compared with placebo (with a low effect size),
- the lack of robust new data demonstrating an impact on morbidity, quality of life or the organisation of care,
- the lack of additional response to the identified need,

SOTALEX (sotalol) is likely to have a negative impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of SOTALEX (sotalol) is insufficient to justify public funding cover in view of the alternatives available in the prevention of recurrences of documented supraventricular tachycardias in the absence of uncontrolled heart failure when the need for treatment has been established.

The Committee issues an <u>unfavourable opinion</u> for maintenance of inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the indication "Prevention of recurrences of documented supraventricular tachycardias in the absence of uncontrolled heart failure when the need for treatment has been established", and at the MA dosages.

Ventricular rhythm disorders

◗ Ventricular rhythm disorders are serious diseases that can cause haemodynamic instability and sudden cardiac death in the patient.

◗ SOTALEX (sotalol) proprietary medicinal products are **preventive treatments** for recurrences of ventricular tachycardias.

◗ The efficacy/adverse effects ratio of sotalol is inadequately established in the prevention of recurrences of ventricular rhythm disorders given :
- the absence of robust new data on morbidity,
- the absence of demonstration of a benefit in terms of mortality,
- its safety profile marked by frequent adverse effects (in particular pro-arrhythmic).

◗ There are therapeutic alternatives (see chapter 05.1 Clinically relevant comparators).

◗ SOTALEX (sotalol) proprietary medicinal products no longer have a role in the care pathway for the prevention of recurrences of ventricular disorders in view of the available alternatives.

<u>Public health impact</u>

Considering :
- the seriousness of ventricular rhythm disorders,
- their prevalence,
- the partially met medical need,
- the absence of demonstration of an impact on morbidity and mortality,
- the lack of new data demonstrating an impact on quality of life or the organisation of care,
- the lack of additional response to the identified need,

SOTALEX (sotalol) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of SOTALEX (sotalol) is <u>insufficient</u> to justify its public funding cover in view of the alternatives available in the prevention of recurrences of ventricular tachycardias.

The Committee issues an <u>unfavourable opinion</u> for maintenance of inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the indication "prevention of recurrences of ventricular tachycardias", and at the MA dosages.