HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
16 SEPTEMBER 2020
The legally binding text is the original French opinion version

hydroquinidine
SERECOR 300 mg prolonged-release capsules

Reevaluation

Key points

Favourable opinion for maintenance of reimbursement only in patients with Brugada syndrome in the prevention of recurrences of rhythm disorders, and in the prevention of cardiac shocks in patients with an implantable cardioverter defibrillator (ICD).

Clinical benefit now insufficient to justify public funding cover (previously it was moderate), except in patients with Brugada syndrome.

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 hydroquinidine no longer has a role in the care pathway for the prevention of recurrences of atrial fibrillation, in view of the available alternatives, due to its low effect size on the prevention of recurrences compared to the control group, its safety profile marked by frequent adverse effects (in particular pro-arrhythmic), and the fact that its use has become marginal, as indicated in the most recent European guidelines.

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 :

The proprietary medicinal product SERECOR (hydroquinidine) no longer has a role in the care pathway for the prevention of recurrences of other supraventricular tachycardias.

2. Ventricular rhythm disorders

- Treatment of ventricular rhythm disorders

These are primarily frequent ventricular extrasystoles or symptomatic, non-sustained ventricular tachycardias in patients with left ventricular dysfunction or certain forms of arrhythmogenic cardiomyopathy.

The 2016 European guidelines indicate beta-blockers as the first-line treatment. In the event of intolerance or failure to respond to this class, oral amiodarone (off-label) with the usual precautions for use as regards its safety is indicated in the guidelines.
The ablation of arrhythmogenic foci is envisaged as an adjuvant treatment for ventricular tachycardias with underlying heart disease, in addition to the other treatments.

Role of the medicinal product in the care pathway:

The proprietary medicinal product SERECOR (hydroquinidine) no longer has a role in the care pathway for the treatment of recurrences of ventricular disorders.

- 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 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 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 :

The proprietary medicinal product SERECOR (hydroquinidine) no longer has a role in the care pathway for the prevention of recurrences of ventricular disorders except in patients with Brugada syndrome.

3. Prevention of cardiac shocks in patients with an implantable cardioverter defibrillator (ICD)

The prevention of unnecessary electric shocks and electrical storms is a major objective of treatment in patients with an ICD. Beta-blockers are recommended as first-line treatment in order to reduce appropriate and inappropriate ICD shocks.
Antiarrhythmic drugs are mentioned in the European guidelines to minimise both appropriate and inappropriate ICD interventions in patients fitted with an ICD, in particular oral amiodarone as second-line pharmacotherapy, in combination with a beta-blocker (off-label use) particularly in the presence of coronary insufficiency and/or impaired left ventricular function.

Role of the medicinal product in the care pathway :

The proprietary medicinal product SERECOR (hydroquinidine) no longer has a role in the care pathway for the prevention of recurrences of cardiac shocks except in patients with Brugada syndrome.

Special recommendations

The Committee maintains its recommendation of reserving initial prescription to cardiologists, given:
- the need for pre-treatment screening with assessment of heart function, in particular involving the performance of an ECG and, if necessary, additional cardiac imaging,
- the need to evaluate the benefit of prescription, taking into account the clinical indication, the aetiology, the patient's comorbidities and, in particular, in view of:
    - the specific safety profile of oral antiarrhythmic drugs (pro-arrhythmic effects for all drugs and extracardiac effects for amiodarone),
    - the updated efficacy profile and the Committee's new guidelines concerning the role of each drug in the care pathway.

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

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).

◗ The proprietary medicinal product SERECOR (hydroquinidine) is a preventive treatment for recurrences of supraventricular tachycardias.

◗ The efficacy/adverse effects ratio of hydroquinidine is inadequately established 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,
- 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 08. Role in the care pathway).

◗ The proprietary medicinal product SERECOR (hydroquinidine) no longer has 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 absence of demonstration of an impact on mortality in view of the available data, which suggested 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,

SERECOR (hydroquinidine) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of SERECOR (hydroquinidine) is insufficient to justify public funding cover in view of the alternatives available in the prevention of recurrences of documented supraventricular tachycardias when the need for treatment has been established and in the absence of impairment of left ventricular function.

The Committee issues an unfavourable opinion 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 when the need for treatment has been established and in the absence of impairment of left ventricular function", 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.

◗ The proprietary medicinal product SERECOR (hydroquinidine) is a curative and preventive treatment for recurrences of ventricular disorders.

◗ The efficacy/adverse effects ratio of hydroquinidine is inadequately established in the treatment and prevention of recurrences of disabling, symptomatic documented 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).

◗ In the prevention of recurrences, there are therapeutic alternatives. In the treatment of ventricular rhythm disorders, no other antiarrhythmic drug with an MA is recommended (see 08. Care pathway).

◗ The proprietary medicinal product SERECOR (hydroquinidine) no longer has a role in the care pathway, except in patients with Brugada syndrome.

Public health impact

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 robust new data demonstrating an impact on quality of life or the organisation of care,
- the lack of additional response to the identified need,

SERECOR (hydroquinidine) is unlikely to have an additional impact on public health.

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

- **moderate in the prevention of recurrences of ventricular rhythm disorders only in patients with Brugada syndrome,**
- **insufficient to justify its public funding cover in view of the available alternatives in the other MA situations, including the treatment of ventricular rhythm disorders.**

The Committee issues a favourable opinion 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 disabling, symptomatic documented ventricular rhythm disorders in the confirmed absence of impairment of left ventricular function and/or known coronary artery disease in patients with Brugada syndrome", and at the MA dosages.

The Committee issues an unfavourable opinion for maintenance of inclusion in the hospital formulary list and/or the retail formulary list of reimbursed proprietary medicinal products approved for use in the other MA situations.

Prevention of shocks in patients with an ICD

◗ Repeated cardiac shocks, either appropriate or not, impair left ventricular function and constitute an independent risk factor for mortality. They therefore adversely impact quality of life and are life-threatening.

◗ The proprietary medicinal product SERECOR (hydroquinidine) is a preventive treatment for electric cardiac shocks in patients with an ICD.

◗ The efficacy/adverse effects ratio of hydroquinidine is inadequately established in the prevention of electric cardiac shocks in certain patients with an implantable cardioverter defibrillator 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).

◗ In the prevention of shocks, there are therapeutic alternatives (see 08. Role in the care pathway).

◗ The proprietary medicinal product SERECOR (hydroquinidine) no longer has a role in the care pathway, except in patients with Brugada syndrome.

Public health impact

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,

SERECOR (hydroquinidine) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of SERECOR (hydroquinidine) is :
- **moderate in the prevention of cardiac shocks only in patients with an implantable cardioverter defibrillator and with Brugada syndrome**
- **insufficient to justify public funding cover in view of the available alternatives in the other situations for this MA indication.**

The Committee issues a favourable opinion 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 electric cardiac shocks in patients with an implantable cardioverter defibrillator with Brugada syndrome", and at the MA dosages.
The Committee issues an unfavourable opinion for maintenance of inclusion in the hospital formulary list and/or the retail formulary list of reimbursed proprietary medicinal products approved for use in the other situations.