HAUTE AUTORITÉ DE SANTÉ

**CARDIOLOGY**
**New medicinal product**
**February 2015**

**BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION**

# **BRINAVESS** (vernakalant), class I and III antiarrhythmic

**Insufficient actual benefit in the rapid conversion of recent onset atrial fibrillation to sinus rhythm in adults**

## Main points

- BRINAVESS has Marketing Authorisation as a treatment for the rapid conversion of recent onset atrial fibrillation (AF) to sinus rhythm in adult non-surgery patients (AF < 7 days duration) or post-cardiac surgery patients: AF < 3 days duration).
- The demonstration of efficacy is based on a very short-term intermediate criterion. No effect on cardiovascular morbidity or mortality has been demonstrated.
- The available data are based on a single comparative study versus placebo or amiodarone used at suboptimal doses compared with the dosages of the Marketing Authorisation and under conditions that do not permit objective evaluation of its efficacy.
- Treatment strategies involving vernakalant in the management of high-risk patients are complex, given its contraindications (in combination with class I and III intravenous antiarrhythmics) and the difficulties using it in the event of haemodynamically stable heart failure, even if it is in functional class I, since the target population is largely elderly.

## Therapeutic use

The management of patients with atrial fibrillation comprises two types of intervention: control of the arrhythmia and prevention of thromboembolic events.

- **Control of heart rate (HR) and heart rhythm:**

The treatment of arrhythmias is based on two non-exclusive options: control of the arrhythmia and/or control of the HR.
The oral pharmacological agents used as first-line treatment to control heart rate are beta blockers and bradycardic calcium channel blockers. When monotherapy is insufficient, digoxin may be used. In acute situations, in symptomatic patients in rapid atrial fibrillation, beta blockers or calcium channel inhibitors in intravenous form are recommended. In patients refractory to treatment, radiofrequency ablation of the atrioventricular node with implantation of a cardiac pacemaker allows the heart rate to be controlled.

Atrial fibrillation may be poorly tolerated by patients despite treatment to bring down the heart rate. The recommended approach in such cases is to restore and maintain sinus rhythm with an antiarrhythmic. Electrical or pharmacological cardioversion can then be considered, depending on the patient's condition.
To restore sinus rhythm, the two main active substances used in France are flecainide and amiodarone. Electrical cardioversion can likewise be considered, depending on the patient's condition.

- **Prevention of thromboembolic events:**

Antithrombotic treatments are routinely used in patients with AF if they are not contraindicated. VKAs are recommended in patients without mechanical valves at high risk of a CVA and in patients with at least one cardiovascular risk factor (target INR: 2.5). Aspirin is recommended as an alternative to VKAs in patients in whom the latter are contraindicated and in low-risk patients.

# Clinical data

In non-cardiac surgery patients with atrial fibrillation

In two studies, the results in patients with recent AF (> 3 h and ≤ 7 days) concern 220/336 of patients in the first study (145 patients treated with vernakalant and 75 treated with placebo) and 170/265 of the intention-to-treat population in the second study (86 patients treated with vernakalant and 84 treated with placebo). In these studies, the percentages of patients with recent atrial fibrillation (> 3 h and < 7 days) in sinus rhythm for at least 1 min during the 90 min immediately after the first infusion were greater in the vernakalant group (51.7% and 51.2%) than in the placebo group (4% and 3.6%), a difference of 47.7% and 47.6%, p < 0.0001.

In a third study, the percentage of patients with recent atrial fibrillation (> 3 h and < 48 h) in sinus rhythm for at least 1 min during the 90 min immediately after the first infusion was greater in the vernakalant group (51.7%) than in the injectable amiodarone group (5.2%), a difference of 46.6% [36.6; 56.5], p < 0.0001.

In patients with atrial fibrillation after cardiac surgery

In a study in patients with recent atrial fibrillation (> 3 h and < 72 h) or atrial flutter following cardiac surgery, the percentage of patients in sinus rhythm for at least 1 min during the 90 min immediately after the first infusion was greater in the vernakalant group (44.9%) than in the placebo group (14.8%), a difference of 30% [16.7; 43.4], p = 0.0002.

The serious adverse events observed in these studies were primarily cardiac in origin: hypotension, bradycardia, ventricular arrhythmia, angina, atrial thrombosis, cardiac arrest, syncope, heart failure, atrial flutter.

# Special prescribing conditions

Medicinal product reserved for hospital use

# Benefit of the medicinal product

- The actual benefit* of BRINAVESS is insufficient for reimbursement by National Health Insurance in the indication of the Marketing Authorisation.
- Does not recommend inclusion on the list of reimbursable products for hospital use.

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[i] * The actual benefit (AB) of a proprietary medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the AB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.