HAUTE AUTORITÉ DE SANTÉ

CARDIOLOGY
Focus
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BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

Proprietary medicinal products based on olmesartan, angiotensin II antagonists:
OLMETEC, ALTEIS (olmesartan)
CoOLMETEC, ALTEISDUO (olmesartan/hydrochlorothiazide)
SEVIKAR, AXELER (olmesartan/amlodipine)

Does not recommend the continuation of reimbursement, because its efficacy has been demonstrated only in terms of a reduction in blood pressure readings, no effect on morbidity and mortality has been demonstrated unlike that of certain active ingredients of the same class (except in uncomplicated essential arterial hypertension), and because of the increased risk of serious enteropathies, even though they are very rare

Main points

- Olmesartan is indicated, in monotherapy or in combination, in the treatment of essential arterial hypertension (AH).
- The efficacy of olmesartan, unlike that of the majority of other sartans, has been demonstrated only in terms of a reduction in blood pressure readings and not in terms of morbidity and mortality (except in uncomplicated essential AH).
- Unlike the other sartans that are available, olmesartan carries an increased risk of serious enteropathies, even though they are very rare (< 1/10,000).
- The results of a study by CNAMTS confirmed an increased risk of hospitalisation for intestinal malabsorption with olmesartan compared with angiotensin-converting enzyme (ACE) inhibitors, which was not found for other sartans.
- Prescription of olmesartan instead of another sartan could be a missed opportunity for patients. These proprietary medicinal products thus no longer have a role in the therapeutic strategy for patients with hypertension.

Therapeutic use

- Diet and lifestyle measures are recommended for all patients with hypertension regardless of their blood pressure level.
- In clinical trials, some thiazide diuretics, beta blockers, calcium-channel inhibitors, angiotensin-converting enzyme inhibitors and angiotensin II receptor antagonists showed a benefit in morbidity and mortality, in the prevention of cardiovascular events and in death from any cause. Diuretics, calcium-channel inhibitors, angiotensin-converting enzyme inhibitors and angiotensin II receptor antagonists are thus recommended in the first-line management of patients with uncomplicated essential hypertension. According to the guidelines, beta-blockers appear less effective than the other classes in the prevention of stroke; thus, they should be offered as second-line treatment in patients with hypertension in primary prevention.

Role of the medicinal products in the therapeutic strategy

In view of:

- the demonstration of its efficacy only in terms of a reduction of blood pressure readings (intermediate efficacy endpoint),
- the absence of a demonstration of efficacy in terms of cardiovascular morbidity and mortality and the existence of numerous alternatives for which this has been demonstrated, particularly from the same therapeutic class (sartans),
- the risk of, very rare but serious, enteropathies,

the prescription of olmesartan instead of another sartan could be a missed opportunity for patients. Consequently, these proprietary medicinal products no longer have a role in the therapeutic strategy for patients with hypertension.

Clinical data

- Several studies have reported serious cases of enteropathy on olmesartan resulting in chronic diarrhoea with weight loss, vomiting, and sometimes dehydration with impairment of renal function and hypokalaemia, which can lead to prolonged hospitalisation. The enteropathy can occur several months or several years after the start of treatment and recurrence of the symptoms has been observed after the reintroduction of olmesartan.
- An official drug safety survey has showed that the 84 cases reported in France are similar to those described in the literature. Several cases (n = 19, 22.6%) with positive readministration have been reported, which supports the causal relationship. Moreover, in cases where a control biopsy was carried out after discontinuation, the rapid regression after discontinuation of olmesartan is also a strong argument in favour of the responsibility of the medicinal product.
- The results of the complementary study carried out by CNAMTS confirm that the increased risk of hospitalisation for intestinal malabsorption, including enteropathies, is significantly higher with olmesartan compared with ACE inhibitors, and which was not found for other sartans. This relative risk on olmesartan compared with ACE inhibitors is 2.27 (95% CI [1.59; 3.23], $p < 0.001$) and increases with the duration of exposure.

Benefit of the medicinal product

- The actual benefit* of the proprietary medicinal products based on olmesartan (OLMETEC, CoOLMETEC, SEVIKAR, ALTEIS, ALTEISDUO and AXELER) is insufficient with respect to the available alternatives to justify their reimbursement by National Health Insurance.
- Does not recommend the continuation of reimbursement for supply by pharmacists and for hospital use.

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This document was created on the basis of the Transparency Committee Opinion of 29 April 2015 and is available at **www.has-sante.fr**

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* 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 by National Health Insurance.