

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

ILTRIA (acetylsalicylic acid/atorvastatin/ramipril), platelet aggregation inhibiting drug, statin and ACE inhibitor in combination

Insufficient clinical benefit in secondary prevention of stroke

Main points

- ▶ ILTRIA has Marketing Authorisation for secondary prevention of strokes as well as a substitution therapy in adults who are sufficiently controlled by the combination of acetylsalicylic acid, atorvastatin and ramipril, in the form of three components alone, at equivalent therapeutic doses.
- ▶ It has not shown its clinical benefit in terms of morbidity, mortality, adherence or quality of life. Only bioequivalence data between the fixed combination ILTRIA (100 mg acetylsalicylic acid, 20 mg atorvastatin and 10 mg ramipril) and each of its three active ingredients taken separately at the same doses are available.
- ▶ The recommended dosages of aspirin range from 75 to 160 mg/day as secondary prevention. In patients whose cholesterol level is high, the 20 mg/day dosage may be insufficient to achieve the therapeutic target in terms of LDL cholesterol. ILTRIA is therefore not suitable for treatment of all patients due to the fixed doses of acetylsalicylic acid (100 mg) and atorvastatin (20 mg) proposed.

Therapeutic use

- The management of patients as secondary prevention of cardiovascular diseases is overall and is based on:
 - managing associated cardiovascular risk factors: smoking (cessation), overweight (target BMI <25 kg/m²), diabetes (target HbA1C <7%), dyslipidaemia (target LDL-c < 100 mg/dL) and hypertension (target value <140/90 mmHg or <130/80 mmHg in diabetics and patients with renal impairment),
 - physical activity: 30 minutes per day,
 - prevention of cardiovascular complications.
- Reduction in cardiovascular events may call for several therapeutic classes (anti-hypertensive agents, beta blockers and angiotensin-converting enzyme (ACE) inhibitors, lipid-lowering agents, platelet aggregation inhibiting drugs, etc.), seeking to reduce cardiovascular risk factors and participating in the prevention of cardiovascular complications.
- In secondary prevention, low-dose acetylsalicylic acid (75 to 160 mg/day) is used as a platelet aggregation inhibiting drug in first-line. In case of major intolerance to acetylsalicylic acid, clopidogrel and ticlopidine are alternatives. Some statins have demonstrated their efficacy in secondary prevention in patients with coronary heart disease (pravastatin, simvastatin, fluvastatin).
- Long term administration of ACE inhibitors having demonstrated their efficacy in terms of morbidity and mortality is recommended in patients with coronary heart disease with left ventricular dysfunction (ejection fraction ≤ 40%), hypertension, diabetes or chronic renal failure and in patients with coronary heart disease.
- **Role of the medicinal product in the therapeutic strategy**
ILTRIA is a substitution therapy for the free combination of atorvastatin at a dosage of 20 mg/day, aspirin at 100 mg/day and ramipril at doses of 2.5 to 10 mg/day in patients treated and stabilized by each of the three components at the same doses. Its role in therapeutic use cannot be determined.

Clinical data

- One study has demonstrated bioequivalence between the fixed combination ILTRIA (100 mg acetylsalicylic acid, 20 mg atorvastatin and 10 mg ramipril) and each of its three active ingredients taken separately at the same doses.

The bioequivalence between the other dosages of ILTRIA (100 mg/20 mg/2.5 mg and 100 mg/20 mg/2.5 mg) and taking the ingredients separately at the same doses has not been studied.

- The adverse effects are those of the three active ingredients contained in ILTRIA (atorvastatin, acetylsalicylic acid and ramipril).
- The bioequivalence study does not allow the therapeutic benefit of the fixed combination to be assessed in terms of reduction of cardiovascular events, adherence or quality of life and clinical data related to the active ingredients used alone or in combination.

Benefit of the medicinal product

- The actual clinical benefit of ILTRIA is insufficient to justify reimbursement by National Health Insurance.
- Does not recommend inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.



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* The actual clinical benefit (ACB) of a 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 ACB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.

** The improvement of actual clinical benefit (IACB) describes the improvement in treatment provided by a medicinal product compared with existing treatments. The HAS Transparency Committee assesses the degree of IACB on a scale from I (major) to IV (minor). A level V IACB (equivalent of "no IACB") means "no clinical added value".