BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

LIPTRUZET (ezetimibe/atorvastatin), fixed combination of cholesterol-lowering drugs

No clinical benefit demonstrated when compared with taking its two components separately

Main points

- LIPTRUZET has a Marketing Authorisation, as adjunctive therapy to diet, in adults with hypercholesterolaemia (heterozygous or homozygous familial, or non-familial) or mixed dyslipidaemia when the ezetimibe + atorvastatin combination is indicated.
- The efficacy of the combination (free or fixed) of ezetimibe with atorvastatin has been demonstrated only on a biological criterion, the reduction of LDL cholesterol (LDL-c) levels.
- The efficacy in terms of morbidity and mortality has not been demonstrated to date.
- No clinical data studying the efficacy of the fixed combination is currently available.

Therapeutic use

Primary hypercholesterolaemia (heterozygous familial or non-familial)

- Lifestyle and dietary measures are the first strategy to implement and should be continued throughout the treatment. Treatment measures are then guided by LDL-c thresholds, set according to the patient's cardiovascular risk and the safety of the treatments. Treatment with statins at minimum dose, emphasising those that have demonstrated their efficacy in terms of morbidity and mortality (atorvastatin, fluvastatin, pravastatin, rosuvastatin and simvastatin), is recommended in the first line.
- In case of failure, lifestyle and dietary measures and treatment adherence should be strengthened. If this is not enough, a combination of cholesterol-lowering drugs may then be offered:
  - for lowering LDL-c, the combinations statin + ezetimibe (EZETROL) and statin + cholestyramine (QUESTRAN) are possible;
  - to act on triglycerides and HDL-c, the combination statin + fibrates may be offered only for patients with high cardiovascular risk.
- When a statin is poorly tolerated, the choice is made between fibrates, cholestyramine and ezetimibe. Fibrates are used in mixed dyslipidaemia with elevation of LDL-c and triglycerides and reduced HDL-c, whereas cholestyramine and ezetimibe would be used in pure hypercholesterolaemia.

Homozygous familial hypercholesterolaemia

- Statins are recommended in the first line and can, when targets are not reached, be combined with ezetimibe or cholestyramine. Apheresis of LDL-c may also be considered. Medicinal treatment must be combined with lifestyle and dietary measures.
- In adults with homozygous familial hypercholesterolaemia uncontrolled despite well-conducted lipid-lowering treatments, LOJUXTA (lomitapide) may be offered in the last line in addition to a diet low in fat and in combination with existing lipid-lowering treatments at maximum doses, with or without low-density lipoprotein apheresis.

Role of the medicinal product in the therapeutic strategy

In adults with hypercholesterolaemia not controlled by a well-conducted treatment with a statin in monotherapy, combination with ezetimibe may be offered in a free or fixed form.

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Similarly, in patients who already receive atorvastatin and ezetimibe at the same doses, LIPTRUZET can be offered as a substitution.

Clinical data

- The data available for the fixed combination of ezetimibe and atorvastatin are based on two studies that have demonstrated bioequivalence between the fixed combination ezetimibe 10 mg + atorvastatin 10 mg (and 80 mg) and the separate administration of its components. The results of these studies were extrapolated to other available doses.
- Three studies have demonstrated the efficacy of the combination of ezetimibe with atorvastatin in terms of reduction of LDL-c levels.

Benefit of the medicinal product

- The actual benefit* of LIPTRUZET is substantial.
- LIPTRUZET does not provide clinical added value** (CAV V) compared with taking the two ingredients at the same doses separately.
- Recommends inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

* 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.

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

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