INNOHEP (tinzaparin), anticoagulant

No clinical benefit demonstrated in the extended treatment of symptomatic venous thromboembolism and prevention of its recurrence in patients who have active cancer and/or are undergoing chemotherapy when compared with other anticoagulants.

Main points
- INNOHEP has Marketing Authorisation in the extended treatment of symptomatic venous thromboembolism and in the prevention of its recurrence in patients who have progressive cancer and/or who are undergoing chemotherapy.
- It has not been evaluated in this specific clinical situation. The studies of tinzaparin have a low level of evidence.
- The efficacy of prolonged treatment with tinzaparin has not been established after 3 to 6 months of treatment, but only after 12 months of treatment. This efficacy was demonstrated by comparison with treatment with unfractionated heparin (UFH) or low molecular weight heparin (LMWH) followed by an early switch to a vitamin K antagonist (VKA). No difference between the two treatments in major bleeding or mortality was demonstrated.
- No comparison with FRAGMINE is available. Demonstration of the therapeutic benefit of INNOHEP with respect to VKAs has not been solidly established.

Pre-existing indications
INNOHEP also has Marketing Authorisation for the curative treatment of established deep vein thromboses and for the curative treatment of pulmonary embolism.

This summary does not cover these indications.

Therapeutic use
- In patients with progressive cancer, whether or not they are undergoing chemotherapy, LMWHs (first-line treatment option) or a VKA are used for the treatment of venous thromboembolism or the prevention of its recurrence. In cases of severe renal impairment, the standard antithrombotic treatment is a UFH followed by an early switch to a VKA.
- The recommended duration of treatment with LMWH is 3 to 6 months. After 6 months of treatment:
  - If the cancer is still being treated and the patient is tolerating the heparin, the LMWH should be continued.
  - If the cancer is no longer being treated, or if the patient can no longer tolerate LMWH, a switch to a VKA is recommended.
- The choice between LMWH and VKA is contingent on the risk-benefit ratio (drug interactions, chemotherapy, invasive procedures, patient's general condition) and the acceptability of the treatment. According to the recommendations of the National Cancer Institute, LMWHs are preferred compared with VKAs in the situation of active cancer.
Role of the medicinal product in the therapeutic strategy

Among the LMWHs recommended in this situation, INNOHEP is an alternative to FRAGMINE (dalteparin) and LOVENOX (enoxaparin), which do not have Marketing Authorisation in this indication. Even though it has not been specifically evaluated in patients with cancer, and the level of evidence for its efficacy relative to VKAs is lower than for dalteparin (FRAGMINE), INNOHEP is a 1st-line alternative to VKAs in these patients.

Clinical data

- No studies specifically carried out with tinzaparin in patients with progressive cancer and/or who are undergoing chemotherapy are available, but only subgroup analyses of patients with cancer in studies that included such patients. In the subgroup of patients with cancer in a study that compared tinzaparin with UFH/warfarin treatment, there were only fewer recurrences of thromboembolism (primary endpoint) in the tinzaparin group than in the control group after 12 months of treatment. There was no difference after 3-6 months of treatment. No difference in major bleeding or mortality was demonstrated.
- In a meta-analysis carried out on the basis of two studies, there was no difference between the groups (INNOHEP and VKA) after 3 to 6 months of treatment in terms of recurrent venous thromboembolism. However, after 12 months of treatment, INNOHEP had reduced recurrences of venous thromboembolism more than a VKA (RR = 0.39 (95% CI [0.19-0.81]). Another meta-analysis, which looked at the results of five studies, produced similar results.

Benefit of the medicinal product

- The actual benefit* of INNOHEP is substantial.
- INNOHEP does not provide a clinical added value** (CAV V, nonexistent) in the therapeutic strategy for extended treatment of symptomatic venous thromboembolism and prevention of its recurrence in patients who have progressive cancer and/or are undergoing chemotherapy.
- Recommends inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

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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 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”.