HAUTE AUTORITÉ DE SANTÉ

CARDIOLOGY
Update
February 2019

TRANSPARENCY COMMITTEE OPINION SUMMARY

PREVISCAN (fluindione), vitamin K antagonist

Moderate clinical benefit in the marketing authorisation indications, limited exclusively to the renewal of a balanced and well-tolerated fluindione treatment

Main points

- PREVISCAN has been granted a marketing authorisation for the prevention of thromboembolic complications related to certain embologenic cardiopathies and to complicated myocardial infarction, for the treatment of deep vein thrombosis and pulmonary embolism and for the prevention of their recurrence.
- Considering the higher risk of immunoallergic reactions with fluindione compared to coumarins vitamin K antagonists (VKAs), its use is **now restricted to the renewal of treatment of patients already well-balanced by fluindione**.
- The use of VKAs is contraindicated during pregnancy, except in some extremely limited situations.

Therapeutic strategy

- In patients with embologenic cardiopathy, complicated myocardial infarction or deep vein thrombosis, one of the main therapeutic objectives is to prevent the occurrence of a thromboembolic complication.
- The anticoagulant treatment includes, according to drugs indications and the clinical situation, a VKA, a direct acting oral anticoagulant (DOAC), or parenteral fondaparinux, an unfractionated heparin (UFH), or a low molecular weight heparin (LMWH) with early VKA relay.
- There is no argument for replacing an effective, well-balanced and well-tolerated VKA treatment with a DOAC and vice versa. Any change in anticoagulant treatment exposes the patient to potentially serious haemorrhagic or thromboembolic risks.

Role of the medicinal product in the therapeutic strategy

- Initiation of treatment with PREVISCAN is no longer authorised. Its place within the therapeutic strategy is now limited to the renewal of well-balanced and well-tolerated fluindione treatment, in all its indications, considering the immunoallergic risk, particularly during the first 6 months of treatment and the existence of medicinal alternatives. The French National Agency for Medicines and Health Products Safety considered that the therapeutic effects of fluindione no longer outweigh the risks resulting from its use when initiating treatment.
- Its use, along with that of the other VKAs, is now contraindicated throughout pregnancy due to teratogenic, foetotoxic and neonatal risks, except in pregnant women with a mechanical heart valve and presenting a high risk of thromboembolism and for whom the potential benefits of PREVISCAN may outweigh the risks.

Clinical data

- A national pharmacovigilance survey confirmed that the use of fluindione is more frequently associated with the onset of immunoallergic reactions than that of other VKAs. These immunoallergic reactions are rare, but often severe, particularly renal such as tubulointerstitial nephropathy, hepatic, haematological or dermal such as DRESS syndrome . These reactions usually occur during the first 6 months of treatment. The survey shows that impaired renal function may persist in some patients (43% in the survey), with the onset of chronic kidney failure or the worsening of pre-existing chronic kidney failure. These sequelae are generally observed in cases of late diagnosis and late discontinuation of fluindione treatment.

Benefit of the medicinal product

- The actual clinical benefit* of PREVISCAN is moderate.
- Approved for continuing non-hospital pharmacy reimbursement or for hospital treatment.

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This document was drafted on the basis of the Transparency Committee opinion dated 20 February 2019 (CT-15282) available at **www.has-sante.fr**

* 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 may be high, moderate, low, or insufficient for the medicinal product to be covered by public funding.