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HAEMATOLOGY
New medicinal product
July 2016

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

OCTAPLASLG (human plasma proteins), medicinal product derived from blood

No clinical benefit demonstrated when compared with currently available normal plasmas.

Main points

- OCTAPLASLG is the first plasma with Marketing Authorisation in France in the treatment of complex coagulation factor deficiencies, substitution therapy in coagulation factor deficiencies, potentially dangerous haemorrhages during fibrinolytic therapy, therapeutic plasma exchange procedures and rapid reversal of the effects of oral anticoagulants (coumarin or indanedione).
- It is a fresh-frozen plasma (FFP) differentiated according to the blood group (A, B and O), obtained from a large mixture of donations of blood of the same group and solvent/detergent-inactivated with additional stages with a view to minimising allergic, immunological and infectious risks.
- There has been no convincing demonstration of superiority with regard to these various risks (potential risk as regards the prion risk) in comparison to normal plasma.
- Like other plasmas, it is a first-line product in its indications.

Therapeutic use

- FFPs are indicated in the management of serious haemorrhages, therapeutic plasma exchange procedures, substitution therapy in coagulation factor deficiencies (congenital deficiencies) that do not exist in stable purified form (rare diseases).
- The use of FFP in the rapid reversal of the effects of oral anticoagulants and haemorrhages during fibrinolytic therapy is exceptional owing to the existence of medicinal alternatives that do have Marketing Authorisation.

Role of the medicinal product in the therapeutic strategy

OCTAPLASLG is an alternative to currently available normal plasmas (inactivated FFP in units (Q-FFP) made from whole blood and blood inactivated by treatment with amotosalen). Like its alternatives, OCTAPLASLG has a first-line place:

- in complex coagulation factor deficiencies requiring the administration of plasma, such as coagulopathies due to severe hepatic failure or a massive transfusion,
- in therapeutic plasma exchange procedures (including thrombotic microangiopathy with an emergency background and also pre- and post-transplantation), with the exception of atypical haemolytic and uraemic syndrome exhibiting factors predictive of progression towards chronic renal failure, in which OCTAPLASLG has a place in the second line after using the first-line drug eculizumab (SOLIRIS),
- in congenital coagulation factor deficiencies: deficiencies of factor V, protein S and plasminogen, as well as factors XI and XIII, but only in emergency situations in the absence of an available purified fraction. In the other deficiencies, including FXI and FXIII, OCTAPLASLG has a place in the second line.

OCTAPLASLG has a second-line place limited to certain exceptional situations:

- In the rapid reversal of oral anticoagulants, in the event of lack of availability of a prothrombin complex concentrate (PCC) to antagonise the AVKs, in the event of severe haemorrhage or lack of availability of a PCC not containing heparin to antagonise the AVKs, in the event of a severe haemorrhage in a patient with a history of heparin-induced thrombocytopenia.
- In potentially dangerous haemorrhages during fibrinolytic therapy, OCTAPLASLG has a place limited to the exceptional situation of the unavailability of tranexamic acid.

Clinical data

- No clinical studies have been carried out specifically with OCTAPLASLG, only with OCTAPLAS, a fresh frozen plasma bioequivalent to OCTAPLASLG. By comparison with the unitary standard or quarantined FFP comparators, unmixed and non-inactivated plasmas, the efficacy of OCTAPLAS, and consequently of OCTAPLASLG, has proved similar as regards the essential biological parameters (including the INR, APTT, PT, FVIII and fibrinogen levels). On the basis of the available clinical studies, relating to small patient groups, the efficacy of OCTAPLASLG plasma or its comparators (solvent/detergent-treated normal plasma) seems overall comparable with that of standard plasma unmodified by physicochemical treatment, such as quarantined plasma. There is no available rigorous demonstration that would make it possible to assert with a high level of proof the non-inferiority of OCTAPLASLG versus its comparators.
- The data from the clinical studies have very little to contribute as regards rare and very rare risks. The global European haemovigilance experience coming from substantial exposure over a period of 22 years to OCTAPLAS in various categories of patients, gradually replaced by OCTAPLASLG, does not any particular signal.. The pharmacovigilance follow-up over 4½ years of using OCTAPLASLG in several European countries and in the United States did not reveal new safety of OCTAPLASLG in comparison to the safety profile of OCTAPLAS.
- The tolerability profile of OCTAPLASLG does include the possibility of the onset of a mild acute allergic reaction occurring, more rarely acute and occasionally severe (anaphylactic or anaphylactoid) allergic reactions. High infusion rates can in rare cases induce cardiovascular effects due to the toxicity of the citrate (fall in ionised calcium), especially in patients presenting liver function disorders. During the plasma exchange procedure, symptoms attributable to citrate toxicity (fatigue, paraesthesia, tremor and hypocalcaemia) can occur in rare cases.

Special prescribing conditions

- Medicine for hospital prescription.
- Administration should take place in a healthcare establishment or at a blood transfusion centre authorised to dispense drugs to patients treated there.

Benefit of the medicinal product

- The actual benefit* of OCTAPLASLG is substantial.
- OCTAPLASLG does not provide clinical added value** (CAV V) by comparison with the normal plasma products currently available.
- Recommends inclusion on the list of reimbursable products for hospital use.

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This document was created on the basis of the Transparency Committee Opinion of 20 July 2016 (CT-15085) and is available at **www.has-sante.fr**

* 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”.