HAUTE AUTORITÉ DE SANTÉ

ANTISEPSIS
Update
January 2019

TRANSPARENCY COMMITTEE OPINION SUMMARY

CHLORAPREP (chlorhexidine/isopropyl alcohol), antiseptics

High clinical benefit in skin antisepsis before catheter placement, but no demonstrated clinical advantage in the therapeutic strategy

Main points

- CHLORAPREP has been granted a marketing authorisation for skin disinfection prior to an invasive medical procedure. The reassessment of this medicinal product only related to skin antisepsis prior to the placement of vascular catheters (marketing authorisation sub-population).
- Its superiority over 5% alcoholic povidone-iodine has been demonstrated in terms of reduction of central catheter-related infections.
- Its impact on mortality, quality of life and care organisation has not been demonstrated.
- Uncertainties remain concerning the transposability of clinical results to French practices.
- In one study, its safety profile was marked by more frequent skin reactions than with 5% alcoholic povidone-iodine.

Therapeutic strategy

- For the skin antisepsis of adults prior to insertion of an intravascular catheter, the guidelines below should be followed:
  - use an alcoholic antiseptic solution rather than an aqueous solution,
  - use a 2% alcoholic chlorhexidine solution rather than an alcoholic povidone-iodine solution in intensive care and in all other sectors.
  - Skin cleaning with a mild soap before antisepsis is recommended only in cases of visible soiling

  These guidelines are based on the CLEAN study that included only patients requiring the placement of central, arterial or haemodialysis catheters in French intensive care units. These results were extrapolated, with no supporting clinicaldata, to all types of intravascular catheters and outside of intensive care.
  When performing technical procedures in the medical office, the use of alcoholic chlorhexidine or alcoholic povidone-iodine is recommended for procedures performed on healthy skin: placement of peripheral venous catheters, arthrocentesis, skin biopsy, central venous catheter approach, arterial puncture, locoregional anaesthesia, contraceptive implant placement, or paravertebral or epidural injection. In extremely rare cases of cumulative intolerance or allergy to povidone-iodine and to chlorhexidine, a chlorine derivative may be used for skin antisepsis. In children, depending on age, different antiseptics are recommended for skin disinfection prior to an invasive procedure.

- **Role of the medicinal product in the therapeutic strategy**

  Antiseptics in alcoholic solutions (alcoholic povidone-iodine or alcoholic chlorhexidine) should be preferred over aqueous or weakly alcoholic solutions, except in children under the age of 30 months.
  CHLORAPREP is a first-line skin antisepsis treatment prior to the placement of vascular catheters, like the other alcoholic antiseptics. The CLEAN study clinical data were obtained on the following vascular catheters: central venous, arterial and haemodialysis. No data are available for peripheral venous catheters.

Clinical data

- One French randomised, open study conducted according to a two-by-two factorial design (CLEAN study) compared the antiseptic efficacy of 2% alcoholic chlorhexidine to that of 5% alcoholic povidone-iodine, along with the efficacy of single-step skin preparation compared to that of 4-step preparation, in the prevention of catheter-associated infections in intensive care patients requiring short-term placement of an intravascular catheter (central venous catheter, arterial catheter and/or haemodialysis catheter). Patients were randomised according to a 1:1:1:1 ratio to receive 4 different skin antisepsis strategies: skin preparation with 2% alcoholic chlorhexidine applied in 1 or 4 steps with an applicator, or skin preparation with 5% alcoholic povidone-iodine applied in 1 or 4 steps without applicator.
  In total, 2,349 patients were included, for the insertion of 5,159 catheters. Catheters remained in place for a mean duration of 6 days. Nearly 47% of patients underwent placement of an arterial catheter, 42% a central venous catheter and 11% a haemodialysis catheter.
  This study demonstrated that skin disinfection with 2% alcoholic chlorhexidine significantly reduces the incidence of catheter-related infections compared to skin disinfection with 5% alcoholic povidone-iodine: 0.28 versus 1.77 for 1000 catheter-days (RR=0.15; CI95% [0.05; 0.41]).
  The patients in the alcoholic chlorhexidine group displayed a lower incidence of catheter-related bacteraemia and colonised catheters (exploratory secondary endpoints).
  The exploratory results in the various sub-groups were comparable, with the exception of central venous catheters (n=2,155), for which the antiseptic efficacy of alcoholic chlorhexidine was superior only in terms of catheter colonisation; no difference was observed in terms of catheter-related infections and catheter-related bacteraemia in this sub-group. The safety data revealed a higher frequency of severe skin reactions with alcoholic chlorhexidine than with alcoholic povidone-iodine (3% versus 1%).
- New warnings have been added to the CHLORAPREP SPC; these pertain to the risk of severe allergic reactions and of chemical burns in infants for all chlorhexidine-based alcoholic antiseptics (following the PRAC recommendations of September 2014) and the risk of burns when using an electrosurgical knife for all alcoholic antiseptics.

Benefit of the medicinal product

- The actual clinical benefit* of CHLORAPREP is high.
- CHLORAPREP does not provide any clinical added value** (CAV V) in the therapeutic strategy.
- Approved for retention as hospital treatment.

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This document was drafted on the basis of the Transparency Committee opinion dated 09 January 2019 (CT-15625) 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.

** The clinical added value (CAV) corresponds to the clinical improvement offered by a medicinal product compared to existing treatments. The HAS Transparency Committee assesses the CAV level from I, major, to IV, minor. A level V CAV (equivalent to "no clinical added value") denotes a "lack of clinical improvement".