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TRANSPARENCY COMMITTEE
Opinion
19 March 2014

BETADINE SCRUB 4%, cutaneous solution (foaming)

125 ml bottle (CIP: 34009 301 086 1 1)

Applicant: MEDA PHARMA

INN	povidone-iodine
ATC code (2013)	D08AG02 (Antiseptics)
Reason for the review	Renewal of inclusion
List concerned	National Health Insurance (French Social Security Code L.162-17)
Indications concerned	“Cleaning and adjuvant treatment of primary bacterial infections of the skin and mucosa or skin and mucosal conditions susceptible to secondary infection. Antiseptic hand-washing for healthcare staff and surgeons. Preoperative skin antisepsis.”

Cleaning and adjuvant treatment of primary bacterial infections of the skin and mucosa or skin and mucosal conditions susceptible to secondary infection.	Low actual benefit
Antiseptic hand-washing for healthcare staff and surgeons.	Low actual benefit
Preoperative skin antisepsis.	Substantial actual benefit

01 ADMINISTRATIVE AND REGULATORY INFORMATION

Marketing Authorisation (procedure)	Initial authorisation 23/04/1974, validated 17/12/1997	
Prescribing and dispensing conditions/special status	Not listed	
ATC Classification	2013 D D08 D08A D08AG D08AG02	Dermatologicals Antiseptics and disinfectants Antiseptics and disinfectants Iodine products povidone-iodine

02 BACKGROUND

Review of a proprietary medicinal product re-included on the list of medicines refundable by National Health Insurance for a 5-year period starting on 31/12/2008 (Official Gazette of 26/05/2009).

In the previous Transparency Committee opinion of 26 November 2008 for renewal of inclusion, the actual benefit allocated to BETADINE SCRUB was:

- low in the indication “cleaning and adjuvant treatment of primary bacterial infections of the skin and mucosa or skin and mucosal conditions susceptible to secondary infection”;
- moderate in the indication “antiseptic hand-washing for healthcare staff and surgeons”;
- substantial in the indication “preoperative skin antisepsis”.

03 THERAPEUTIC INDICATIONS

“Cleaning and adjuvant treatment of primary bacterial infections of the skin and mucosa or skin and mucosal conditions susceptible to secondary infection.

Antiseptic hand-washing for healthcare staff and surgeons.

Preoperative skin antisepsis.”

04 DOSAGE

See summary of product characteristics (SPC).

05 CLINICALLY RELEVANT COMPARATORS

05.1 Medicinal products

There are no other foaming solutions of povidone-iodine.

The other antiseptic foaming solutions that have at least one indication in common with BETADINE SCRUB and are refundable in retail pharmacies are:

Foaming chlorhexidine				
PLUREXID UCB Pharma SA	Aqueous chlorhexidine 1.5%	Cleaning and adjuvant treatment of primary bacterial skin and mucosal infections or skin and mucosal conditions susceptible to secondary infection	Low (26/11/2008)	National Health Insurance/hospital use
SEPTIVON 1.5% Omega Pharma France	Aqueous chlorhexidine 1.5%	Cleaning and adjuvant treatment of primary bacterial infections of the skin or skin conditions susceptible to secondary infection	Low (01/12/2010)	National Health Insurance/hospital use
Foaming chlorhexidine combination				
CYTEAL Pierre Fabre Dermatologie	Chlorhexidine 0.1% Hexamidine 0.1% Chlorocresol 0.3%	Cleaning of primary bacterial infections of the skin and mucosa or skin and mucosal conditions susceptible to secondary infection	Low (26/11/2008)	National Health Insurance/hospital use

No other antiseptic proprietary medicinal products are indicated in preoperative skin antisepsis.

Only one other proprietary medicinal product is indicated in antiseptic hand-washing; it is only included on the list of products for hospital use, and is available in retail pharmacies as a non-refundable product:

HIBISCRUB 4% Mölnlycke Healthcare SA	Aqueous chlorhexidine 4%	- Cleaning and adjuvant treatment of primary bacterial infections of the skin or skin conditions susceptible to secondary infection - Antiseptic hand-washing by healthcare staff - Surgical antisepsis: antiseptic hand-washing by surgeons	No opinion available	Hospital use (1982)
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06 ANALYSIS OF AVAILABLE DATA

06.1 Efficacy

The company has not provided any new clinical efficacy data.

06.2 Adverse effects

► The company submitted a “summary bridging report” summarising data from the periodic safety update reports covering the period from 8 October 2005 to 7 October 2010. Additions have been made concerning kidney disorders, thermal burns, cases occurring during off-label use, and cases occurring during pregnancy and breastfeeding.

► “Burns in case of maceration” was added to the Undesirable Effects section of the SPC on 18 April 2013.

► The known safety profile of this proprietary medicinal product is not affected by these data and this information.

06.3 Prescription data

According to IMS data (summer 2013 moving annual total), 312,000 prescriptions for BETADINE SCRUB are issued per year. The prescriber is a general practitioner in 52% of cases, a dermatologist in 32% of cases and a gastroenterologist in 7% of cases. Surgeons were not included among the specialisms listed.

07 THERAPEUTIC USE

07.1 Cleaning and adjuvant treatment of primary bacterial infections of the skin and mucosa or skin and mucosal conditions susceptible to secondary infection¹

“Whatever the extent of the bacterial skin infection, daily hygiene activities using ordinary soap and water must be implemented prior to any local or systemic treatment.

As there is no clinical evidence of efficacy, the use of antiseptics to treat or prevent primary or secondary bacterial skin infections is not recommended, whether the wound is clean or dirty.

If an antiseptic is used in these indications, aqueous povidone-iodine, chlorine solutions (Dakin's solution), aqueous chlorhexidine or combined chlorhexidine + quaternary ammonium (Biseptine) may be used. Strong alcohol solutions should not be used on damaged skin or mucosa.”

¹Prise en charge des plaies aux Urgences, SFMU [French Society for Emergency Medicine] 2005, http://www.sfm.org/documents/consensus/cc_plaies.pdf, accessed 25/09/2013.

07.2 Antiseptic hand-washing for healthcare staff and surgeons²

Hand hygiene:

There are three possible approaches to hand hygiene: simple hand-washing, hand-washing with an antiseptic and use of a hand rub sanitiser.

Simple hand-washing aims to eliminate dirt and reduce transient skin flora through mechanical action using “mild” soap (detergent only) and water. It is strongly recommended to use an alcohol hand rub in place of hand-washing (with mild or antiseptic soap) if there is no visible dirt on the hands.

Surgical disinfection:

Surgical disinfection using a hand rub sanitiser should be preferred to surgical hand-washing.

For reasons of efficacy and skin safety, hands should be washed on arrival in the operating theatre, at least 10 minutes before surgical disinfection using a hand rub sanitiser: wash the hands with mild soap for a total duration not exceeding one minute; do not use a brush except for the nails and for the first wash of the day; rinse very thoroughly for one minute, using a mechanical action to eliminate any soap residue; and dry hands, forearms and elbows very thoroughly with a non-sterile hand towel.

The technique for using the hand rub sanitiser itself is as follows:

- Look at the clock to identify the start time.
- Use an alcohol hand sanitiser complying with standard EN12791.
- Use enough of the product to keep the hands and forearms wet for the recommended time period, taking more if necessary.
- Rub until completely dry before putting gloves on.
- At the end of the surgical procedure, if a second operation is planned, only use a hand rub sanitiser and do not wash the hands with soap unless they are visibly dirty or powdered gloves have been used; if hand-washing is necessary, this should be done immediately after removing the gloves.

In conclusion:

According to the 2009 SFHH [French Society for Hospital Hygiene] guidelines, antiseptic soaps only play a limited role in antiseptic hand-washing for healthcare staff and surgeons, secondary to the use of alcohol hand rubs.

07.3 Preoperative skin antisepsis³

At least one preoperative shower should be taken (B3).

No recommendation can be made as to the type of soap (antiseptic or non-antiseptic) used for the preoperative shower (C2).

No recommendation can be made regarding the number of preoperative showers (C3). The product used should be packaged in a single-use container.

No recommendation can be made regarding the timing of the preoperative shower (C3). In practice, it should be taken as close to the procedure as possible.

No recommendation can be made regarding the routine use of shampoo (C3).

As with the preoperative shower, no recommendation can be made regarding the product (antiseptic or non-antiseptic) used to shampoo the hair (C3).

²SFHH. Recommandations pour l'hygiène des mains. 2009 - <http://www.sf2h.net>, accessed 18/12/2013.

³SFHH. Gestion pré-opératoire du risque infectieux. Updated Oct 2013 - <http://www.sf2h.net>, accessed 18/12/2013.

In conclusion, according to the 2013 guidelines, in preoperative skin antisepsis BETADINE SCRUB may be used on the same basis as any other foaming antiseptic proprietary medicinal product or non-antiseptic soap.

08 TRANSPARENCY COMMITTEE CONCLUSIONS

In view of all the above information, and following the debate and vote, the Committee's opinion is as follows:

08.1 Actual Benefit

08.1.1 Cleaning and adjuvant treatment of primary bacterial infections of the skin and mucosa or skin and mucosal conditions susceptible to secondary infection

- ▶ Primary bacterial infections of the skin and skin conditions susceptible to secondary infection are not serious but may lead to infectious complications that can be severe.
- ▶ This proprietary medicinal product is intended as adjuvant therapy.
- ▶ The efficacy/adverse effects ratio this medicinal product in this indication is low.
- ▶ This proprietary medicinal product has a limited role in the therapeutic strategy, which is based on daily hygiene activities using ordinary soap and water.
- ▶ There are medicinal and non-medicinal treatment alternatives.

Taking account of these points, the Committee considers that the actual benefit of BETADINE SCRUB remains low in the cleaning and adjuvant treatment of primary bacterial infections of the skin and mucosa or skin and mucosal conditions susceptible to secondary infection.

08.1.2 Antiseptic hand-washing for healthcare staff and surgeons

- ▶ Infections occurring as complications of surgery can be severe and potentially life-threatening or disabling.
- ▶ This proprietary medicinal product is intended as preventive therapy.
- ▶ The efficacy/adverse effects ratio for this medicinal product in this indication is modest.
- ▶ This medicinal product has a limited role in hand-washing, secondary to alcohol sanitisers.
- ▶ There are treatment alternatives.

Taking account of these points, the Committee considers that the actual benefit of BETADINE SCRUB is low in antiseptic hand-washing for healthcare staff and surgeons.

08.1.3 Preoperative skin antisepsis

- ▶ Infections occurring as complications of surgery can be severe and potentially life-threatening or disabling.
- ▶ This proprietary medicinal product is intended as preventive therapy.
- ▶ The efficacy/adverse effects ratio for this medicinal product in this indication is high.
- ▶ This medicinal product is a first-line therapy.
- ▶ There are treatment alternatives.

Taking account of these points, the Committee considers that the actual benefit of BETADINE SCRUB remains substantial in preoperative skin antisepsis.

The Committee recommends continued inclusion on the list of medicines refundable by National Health Insurance in the indications and at the dosages in the Marketing Authorisation.

▶ **Proposed reimbursement rate: 65%**

09 TRANSPARENCY COMMITTEE RECOMMENDATIONS

▶ **Packaging**

Single-dose packaging is required for preoperative skin antisepsis.