



Summary of investigation results

Chlorhexidine gluconate or products containing chlorhexidine hydrochloride (Prescription drugs)

October 17, 2017

Non-proprietary name

- a. chlorhexidine gluconate
- b. chlorhexidine hydrochloride/diphenhydramine salicylate/hydrocortisone acetate/benzalkonium chloride concentrated solution 50

Brand name (Marketing authorization holder)

- a. Hibitane gluconate solution 20% (Dainippon Sumitomo Pharma Co., Ltd.), Acesclean hand disinfection solution 0.2% (Nichi-Iko Pharmaceutical Co., Ltd.), Chlorhexidine gluconate EW 5% "NP" for disinfection solution (Nipro Corporation), and others (refer to the attachment below)
- b. Despakowa Oral Cream (Kowa Company, Ltd.)

Indications

- a. Refer to the attachment below.
- b. Aphthous stomatitis, solitary aphtha, decubitus ulcer, marginal periodontitis

Summary of revision

- a. chlorhexidine gluconate
 - 1. "Anaphylaxis" should be added to the precaution with regards to shock in the Important Precautions section.
 - 2. "Anaphylaxis" should be added in the Clinically Significant Adverse Reaction section with regards to shock.
- b. chlorhexidine hydrochloride/diphenhydramine salicylate/hydrocortisone acetate/benzalkonium chloride concentrated solution 50
 - 1. Precautions with regards to shock, anaphylaxis should be added in the Important Precautions section.
 - 2. The Clinically Significant Adverse Reactions section should be newly created to



add “shock, anaphylaxis.”

Background of the revision and investigation results

Regarding chlorhexidine gluconate, use on mucosal surface was prohibited based on the reexamination in 1985 and 1992 in Japan. Recently in the U.S. revision of package inserts to add a warning was requested in February 2017 about serious allergic reactions associated with over-the-counter skin antiseptic products containing chlorhexidine gluconate. Cases of anaphylaxis involving the use of products containing chlorhexidine (chlorhexidine gluconate and chlorhexidine hydrochloride) on sites other than mucosal surface have been accumulated in Japan. Following investigation results based on the opinions of expert advisors and the available evidence, the MHLW/PMDA concluded that revision of the package insert was necessary for products containing chlorhexidine gluconate or chlorhexidine hydrochloride.

The number of reported adverse reactions and fatal cases in the last 3 fiscal years in Japan (in and after FY 2014)

a. chlorhexidine gluconate

A total of 8 cases associated with anaphylaxis have been reported (including 3 cases for which a causal relationship to the product could not be ruled out). 1 fatal case has been reported (a causal relationship to the product could not be ruled out for this patient).

b. chlorhexidine hydrochloride/diphenhydramine salicylate/hydrocortisone acetate/benzalkonium chloride concentrated solution 50

No case associated with shock or anaphylaxis has been reported.



This English version is intended to be a reference material for the convenience of users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

Attachment

Brand name	Marketing authorization holder	Indications
Hibitane gluconate solution 20% and others	Dainippon Sumitomo Pharma Co., Ltd. and others	Disinfection of the hands and skin, disinfection of the skin at surgical sites (surgical fields), disinfection of wound sites of the skin, disinfection of medical devices, disinfection of operating rooms, hospital rooms, furniture, instruments, goods, etc. Cleaning/disinfection of the conjunctival sac, disinfection of skin of the external genitalia and vulva in the obstetrics/gynecology and urology clinics
Hibitane solution 5% and others	Dainippon Sumitomo Pharma Co., Ltd. and others	Disinfection of the hands and skin, disinfection of the skin at surgical sites (surgical fields), disinfection of wound sites of the skin, disinfection of medical devices, disinfection of operating rooms, hospital rooms, furniture, instruments, goods, etc.
Chlorhexidine gluconate scrub 4% "Nichi-Iko" and others	Nichi-Iko Pharmaceutical Co., Ltd. and others	Disinfection of the hands of medical professionals such as physicians and nurses at medical facilities
Wellup Hand Lotion 1% and others	Maruishi Pharmaceutical Co., Ltd. and others	Disinfection of the hands and skin
Acesclean hand disinfection solution 0.2%	Nichi-Iko Pharmaceutical Co., Ltd. and others	Disinfection of the hands
Chlorhexidine gluconate EW 0.5% "NP" for disinfection solution and others	Nipro Corporation and others	Disinfection of the skin at surgical sites (surgical fields), disinfection of medical devices
0.05% Hexizac Water R and others	Yoshida Pharmaceutical Company Limited and others	Disinfection of wound sites of the skin, disinfection of operating rooms, hospital rooms, furniture, instruments, goods, etc.



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0.05% Hexizac Water W and others	Yoshida Pharmaceutical Company Limited and others	Disinfection of wound sites of the skin, disinfection of operating rooms, hospital rooms, furniture, instruments, goods, etc. Cleaning/disinfection of the conjunctival sac, disinfection of skin of the external genitalia and vulva in the obstetrics/gynecology and urology clinics
0.02W/V% Maskin Water and others	NIKKO Pharmaceutical Co., Ltd. and others	Cleaning/disinfection of the conjunctival sac Disinfection of skin of the external genitalia and vulva in the obstetrics/gynecology and urology clinics