1. NAME OF THE MEDICINAL PRODUCT

Emxidine 7.1% w/w gel

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Chlorhexidine digluconate 7.1% w/w (equivalent to 4% w/w chlorhexidine).

Each pack contains a 3g dose containing 213 mg of chlorhexidine digluconate equivalent to 120mg chlorhexidine.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Gel.

Colourless to yellow translucent gel.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Emxidine is indicated for prophylaxis of omphalitis (infection of the umbilical cord) in newborn infants.

4.2 Posology and method of administration

Posology

The recommended dose is 3 gram applied once daily for seven days. Healthcare providers should take account of local umbilical cord care guidelines regarding single dose application (see section 5.1). The first application must occur within 24 hours of birth.

For infants born at less than 32 weeks gestation (or weighing less than 1500 grams at birth), the recommended dose is a single 3 gram applied once only in the first 24 hours after birth (see section 4.4).

For infants born at less than 32 weeks gestation (or weighing less than 1500 grams at birth), the recommended dose is once only in the first 24 hours after birth.

Method of administration

Wash your hands before and after each use with soap and clean water.
Clean the umbilical cord stump and the skin around the base of the umbilical cord with a dry cloth prior to applying Emxidine. Use enough gel to cover the freshly cut umbilical cord stump and the skin around the base of the umbilical cord within 24 hours after birth.
Do not use Emxidine in combination with any other product. Do not cover the umbilical cord stump with tight dressings.

4.3 Contraindications

For the caregiver - This product should not be handled by anyone with a known history of hypersensitivity to chlorhexidine (see section 4.4) or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

For external use only. Do not inject or swallow.

Keep out of the eyes and ears and do not use over large areas of the body. If Emxidine comes into contact with the eyes, wash out promptly and thoroughly with clean water.

This product contains chlorhexidine. There have been reports of hypersensitivity and skin irritation after topical administration of chlorhexidine, including generalised allergic reactions and anaphylactic shock. The prevalence of chlorhexidine hypersensitivity is not known, but available literature suggests this is likely to be very rare. The product should be discontinued and immediate medical help should be sought in case of any symptoms which may indicate an allergic reaction.

If skin irritation or redness occurs, prompt medical advice should be sought.

Treatment with Emxidine may be associated with the development of methaemoglobinaemia, via degradation to 4 –chloroaniline, although this has not been observed in clinical trials. This risk is likely to be increased in infants born prematurely, specifically less than 32 weeks gestation or weighing less than 1500 grams (see section 4.2). Emxidine should be discontinued if symptoms and signs associated with methaemoglobinaemia, such as cyanosis or breathlessness, are observed and immediate medical advice sought.
The use of chlorhexidine solutions, both alcohol based and aqueous, for skin antisepsis prior to invasive procedures has been associated with chemical burns in neonates. Based on available case reports and the published literature, this risk of chemical burns appears to be higher in preterm infants, especially those born before 32 weeks of gestation, and occurs within the first 2 weeks of life (see section 4.2).

4.5 Interaction with other medicinal products and other forms of interaction

None known.

4.6 Fertility, pregnancy and lactation

Not applicable for the intended patient population.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

Tabulated list of adverse reactions

Adverse reactions are classified by System Organ Class. Adverse reactions that occurred either during clinical studies or that were spontaneously reported are presented below.

Frequencies were defined as follows:

Very common ≥1/10
Common ≥1/100 to <1/10
Uncommon ≥1/1000 to <1/100
Rare ≥1/10000 to <1/1000
Very rare <1/10000
Not known (cannot be estimated from the available data)

The adverse reactions tabulated below have been associated with post-marketing data from different marketed chlorhexidine formulations (antiseptic solution, antiseptic cream and antiseptic mouthwash). No post-marketing data is available for the 7.1 % w/w gel formulation.

System organ class	Adverse reaction(s)	Frequency
Immune system disorders	Hypersensitivity and anaphylaxis	Not known
	Allergic skin reactions such as erythema and skin irritation	Not known

Description of selected adverse reactions

The most serious reported adverse reactions to medicinal products or devices containing chlorhexidine are systemic hypersensitivity/anaphylaxis, see section 4.4. Signs related to a hypersensitivity reaction include rash, urticaria, angioedema, difficulty in breathing, collapse or loss of consciousness.

4.9 Overdose

This has not been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antiseptics and disinfectants, ATC code: D08AC02

Mechanism of action

Chlorhexidine has a wide range of antimicrobial activity. Chlorhexidine is effective against a wide range of gram-negative and gram-positive vegetative bacteria, yeasts, dermatophyte fungi and lipophilic viruses. It is inactive against bacterial spores except at elevated temperatures.

Clinical efficacy and safety

Efficacy has been demonstrated in three non-GSK published community-based randomised controlled trials of 7.1% chlorhexidine digluconate solution. A meta-analysis within a Cochrane review of these studies showed 23% reduction (95% CI 6-37%) in all-cause neonatal mortality in the intervention groups compared to the control groups (dry cord care, soap/water and hand washing). The same meta-analysis showed a reduction in umbilical cord infection ranging from 27 to 56% depending on severity: 27% reduction in skin redness (95% CI 17-36%), 31% reduction in redness with pus or severe redness (95% CI 21-40%), and 56% reduction in severe redness with pus (95% CI 31-72%). A non-GSK published study of 7.1% chlorhexidine digluconate gel vs solution showed that the gel was non-inferior to the solution in terms of antimicrobial efficacy.

Single versus multiple applications: The effect of single versus multiple applications was assessed in a Cochrane review. The incidence of moderate and severe omphalitis was reduced with multiple applications, although there was no evidence of difference in overall mortality between the groups.

Antimicrobial studies: In-vitro tests to assess the antimicrobial activity and persistence of effect showed that chlorhexidine digluconate 7.1% w/w gel and solution are comparable.

5.2 Pharmacokinetic properties

Chlorhexidine is cationic in nature and binds strongly to skin. Data relating to topical administration in neonates are limited. After topical application, trace amounts of chlorhexidine may be absorbed percutaneously in preterm newborns.

In newborns and small children bathed in water treated with 4.0 % and 0.4 % chlorhexidine digluconate, respectively, the amount of chlorhexidine found in blood samples and in the faeces was extremely low.

There are no data on metabolism of chlorhexidine following topical administration.

5.3 Preclinical safety data

Information pertaining to general toxicology, reproductive toxicology, safety pharmacology and carcinogenicity available from the literature revealed no special hazard for humans relevant to acute topical use.

Skin Irritation/Sensitization: In an *in-vitro* skin irritancy study using human derived skin cells, chlorhexidine digluconate gel 7.1% w/w showed moderate irritancy.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Guar gum
Benzalkonium Chloride
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Preserve in tight container,protected from light,at temperature not more than 30°C

6.5 Nature and contents of container

3g presentation in a tube.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. SCIENTIFIC OPINION HOLDER

Emzor Pharmaceutical Industries Limited
No 13 Richfield Avenue,Ajao Estate,Lagos

8. SCIENTIFIC OPINION AUTHORISATION NUMBER(S)

B4-0593

9. DATE OF FIRST SCIENTIFIC OPINION /RENEWAL OF THE SCIENTIFIC OPINION

N/A

10. DATE OF REVISION OF THE TEXT

July 2021