ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

Medicinal product no longer authorised

1. NAME OF THE MEDICINAL PRODUCT

Umbipro 7.1% w/w gel

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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

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

Umbipro 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 a 3 gram sachet 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 sachet applied once only in the first 24 hours after birth (see section 4.4).

Method of administration

Apply Umbipro as soon as possible within 24 hours after birth. Clean the umbilical cord stump and the skin around the base of the stump with a dry cloth prior to applying Umbipro. Apply adequate content of the sachet to ensure complete coverage of the umbilical cord, from the cut surface to the base and including the immediate surrounding abdominal skin. Wash hands before and after use.

Umbipro should not be applied in combination with any other product. Occlusive dressings should not be applied to the umbilical cord stump, as doing so could increase the absorption of the product through the dermis.

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.

Medicinal product no longer authorised

Keep out of the eyes and ears and do not use over large areas of the body. If Umbipro 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 Umbipro 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). Umbipro 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.

Medicinal product no longer authorised

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.

Medicinal product no longer authorised

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
Sodium acetate trihydrate
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Store below 30°C and away from direct sunlight.

6.5 Nature and contents of container

3 g presentation in a foil laminate sachet. Pack sizes of a single sachet wallet or a 7 sachet carton.

Not all pack sizes may be marketed.

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

GlaxoSmithKline Trading Services Limited
12 Riverwalk
Citywest Business Campus
Dublin 24
Ireland.

8. SCIENTIFIC OPINION AUTHORISATION NUMBER(S)

N/A

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

Medicinal product no longer authorised

N/A

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

Medicinal product no longer authorised

Medicinal product no longer authorised

ANNEX II

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

GlaxoSmithKline Consumer Healthcare S.A. (Pty) Ltd.
39 Hawkins Ave
Epping Industria 1
Cape Town
7460
South Africa.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product not subject to medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports**

The scientific opinion holder shall submit the first periodic safety update report for this product within 90 calendar days after the data lock point of 1 June 2017. Subsequently, the scientific opinion holder shall submit periodic safety update reports for this product every year until otherwise agreed by the CHMP.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk Management Plan (RMP)**

The scientific opinion holder shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

Medicinal product no longer authorised

ANNEX III

LABELLING AND PACKAGE LEAFLET

Medicinal product no longer authorised

A. LABELLING

Medicinal product no longer authorised

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON/ENVELOPE WALLET

1. NAME OF THE MEDICINAL PRODUCT

Umbipro 7.1% w/w gel
chlorhexidine digluconate

2. STATEMENT OF ACTIVE SUBSTANCE(S)

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

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

3. LIST OF EXCIPIENTS

Also contains guar gum, sodium acetate trihydrate and purified water. See package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Gel
1 sachet.
7 sachets.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Cutaneous use only
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

For external use only.

8. EXPIRY DATE

EXP.

9. SPECIAL STORAGE CONDITIONS

Store below 30°C and away from direct sunlight.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Medicinal product no longer authorised

11. NAME AND ADDRESS OF THE SCIENTIFIC OPINION HOLDER

GlaxoSmithKline Trading Services Limited, 12 Riverwalk, Citywest Business Campus, Dublin 24, Ireland.
Glaxo Group Ltd logo

12. SCIENTIFIC OPINION AUTHORISATION NUMBER(S)

13. BATCH NUMBER<, DONATION AND PRODUCT CODES>

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

N/A – product will not be licenced in the EU

Medicinal product no longer authorised

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

FOIL SACHET

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Umbipro 7.1% w/w gel
chlorhexidine digluconate
Cutaneous use only

2. METHOD OF ADMINISTRATION

Read the package leaflet before use.

3. EXPIRY DATE

EXP

4. BATCH NUMBER<, DONATION AND PRODUCT CODES>

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

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

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

6. OTHER

For external use only.
For umbilical cord care only.
Throw away any remaining gel after use.
Store below 30°C and away from direct sunlight.

Medicinal product no longer authorised

B. PACKAGE LEAFLET

Medicinal product no longer authorised

Package leaflet: Information for the user

Umbipro 7.1% w/w gel
Chlorhexidine Digluconate

Read all of this leaflet carefully before you start applying this medicine because it contains important information for you and your baby.
Always use this medicine exactly as described in this leaflet or as your healthcare worker has told you.
- Keep this leaflet. You may need to read it again.
- Ask your healthcare worker if you need more information or advice.
- This medicine is for your baby only. Do not pass it on to others. It may harm them.
- If your baby gets any side effects, talk to your healthcare worker. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Umbipro is and what it is used for

Umbipro contains a medicine called chlorhexidine digluconate. Umbipro is an antiseptic gel. Umbipro is used to prevent umbilical cord infections and should only be used on newborn babies.

2. What you need to know before you apply Umbipro

Do not apply Umbipro
- if you are allergic to chlorhexidine digluconate or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your healthcare worker before using Umbipro.

This medicine should only be applied to the umbilical cord stump and the skin around the base of the umbilical cord.

Do not swallow this medicine. Keep out of eyes and ears.
➔ If it goes into eyes, wash out with clean water.

Umbipro can cause severe allergic reactions or redness or irritated skin around the umbilical cord. See section 4.
- ➔ **Immediately stop using Umbipro** and **seek medical advice** if your baby has any of the signs listed under severe allergic reactions, see section 4.
- ➔ **Seek medical advice immediately** if your baby has redness or skin irritation around the umbilical cord.

Umbipro can cause a condition called methaemoglobinaemia (a blood disorder).

Medicinal product no longer authorised

➔ **Immediately stop using Umbipro** and **seek medical advice** if your baby has blue nails, skin, tongue or lips.

Use carefully in babies born early (less than 32 weeks of pregnancy or weighing less than 1500 grams) because Umbipro is more likely to cause chemical skin burns or methaemoglobinaemia in babies born early.

3. How to use Umbipro

Always use this medicine exactly as your healthcare worker has told you. Check with your healthcare worker if you are not sure. Wash your hands before and after each use with soap and clean water.

You will be provided with seven sachets for seven days treatment, unless told otherwise by your healthcare worker.

Clean the umbilical cord stump and the skin around the base of the umbilical cord with a dry cloth prior to applying Umbipro. Use enough gel from the sachet to cover the freshly cut umbilical cord stump and the skin around the base of the umbilical cord within 24 hours after birth.

Repeat once daily for the first seven days of life, unless told otherwise by your healthcare worker.

Do not use Umbipro in combination with any other product. Do not cover the umbilical cord stump with tight dressings.

If your baby is born early, less than 32 weeks, (or weighing less than 1500 grams at birth) then only use for one day.

If you forget to use Umbipro
Do not apply two sachets to make up for a forgotten dose.

If you have any further questions on the use of this medicine, ask your healthcare worker.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

- Severe allergic reactions. Signs include:
    - raised and itchy rash (hives)
    - swelling sometimes of the face or mouth
    - difficulty in breathing
    - collapse or loss of consciousness

➔ **Immediately stop using Umbipro** and **seek medical advice** if your baby has any of these signs.

Redness or skin irritation around the umbilical cord.

➔ **Seek medical advice immediately** if your baby has redness or skin irritation around the umbilical cord.

The frequency of the side effects listed above is not known (cannot be estimated from the available data).

Reporting of side effects
If your baby gets any side effects not listed in this leaflet talk to your healthcare worker.

Medicinal product no longer authorised

5. How to store Umbipro

Keep this medicine out of the sight and reach of children.

Store below 30°C and keep away from direct sunlight.

Do not use this medicine after the expiry date which is stated on the sachet. The expiry date refers to the last day of that month.

Throw away any leftover gel after using the amount needed.

6. Contents of the pack and other information

What Umbipro contains
- The active substance is chlorhexidine (as digluconate). Chlorhexidine digluconate 7.1% w/w (equivalent to 4% w/w chlorhexidine).
- Each sachet contains a 3 g dose containing 213 mg of chlorhexidine digluconate equivalent to 120 mg chlorhexidine.
- The other ingredients are guar gum, sodium acetate trihydrate and purified water.

What Umbipro looks like and contents of the pack

For one day treatment dosing:
Each pack contains 1 sachet. Each sachet contains 3 grams of colourless to yellow translucent gel.

For seven days dosing:
Each pack contains 7 sachets. Each sachet contains 3 grams of colourless to yellow translucent gel.

Not all pack sizes may be marketed.

Scientific Opinion Holder and Manufacturer

GlaxoSmithKline Trading Services Limited
12 Riverwalk
Citywest Business Campus
Dublin 24
Ireland.

Manufacturer
GlaxoSmithKline Consumer Healthcare S.A. (Pty) Ltd.
39 Hawkins Ave
Epping Industria 1
Cape Town
7460
South Africa.

This leaflet was last revised in <{MM/YYYY}> <{month YYYY}>.

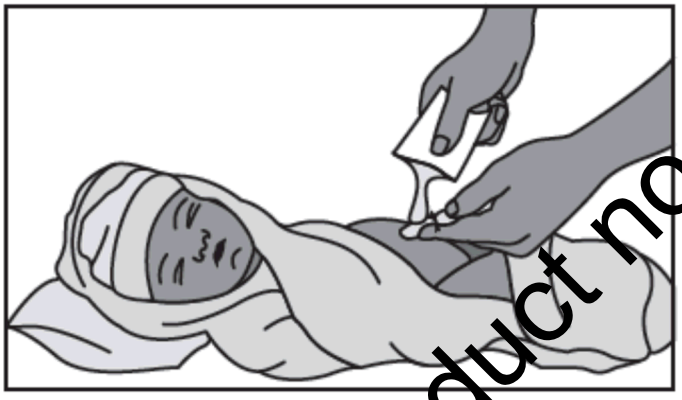
Other sources of information>

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

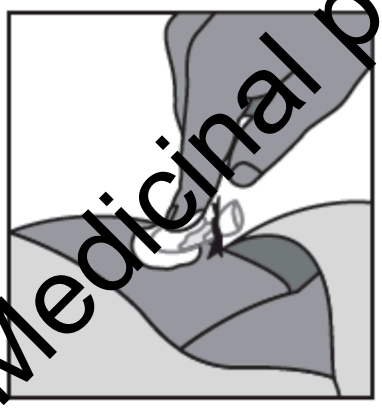
Medicinal product no longer authorised

Step by step instructions:

1. Wash your hands carefully **before and after** applying chlorhexidine gel, using soap and clean water.



2. Use enough gel from the sachet to cover the freshly cut umbilical cord stump and the skin around the base of the umbilical cord within 24 hours after birth.



3. Spread the gel on the umbilical cord stump and the skin around the base of the cord using your finger.

Medicinal product no longer authorised