SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

DICLOPLAST 140mg medicated topical patch

2 Qualitative and quantitative composition

Each 140 cm^2 (10 cm x 14 cm) of medicated patch contains a total of 180 mg of diclofenac epolamine corresponding to 140 mg of diclofenac sodium (1% w/w).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Medicated patch

White to pale yellow paste spread as a uniform layer onto unwoven support.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Dicloplast is indicated for topical treatment of rheumatic diseases, pain and on-infectious inflammation.

4.2 Posology and method of administration

Cutaneous use only

Posology
Adults and adolescents 16 years and older
1 application morning and evening (for up to 12 hours)

Duration of administration
Dicloplast is to be used for as short as possible. The duration of the treatment should not exceed 14 days.

If there is no improvement, during the recommended duration of treatment or symptoms worsen, a doctor should be consulted.

Elderly
This medication should be used with caution in elderly patients who are more prone to adverse events. See also Section 4.4.

Children and adolescents below the age of 16 years
There are insufficient data on efficacy and safety available for children and adolescents below 16 years of age (see also contraindication section 4.3).

In children aged 16 years and over, if this product is required for more than 7 days for pain relief or if the symptoms worsen, the patient/parents of the adolescents is/are advised to consult a doctor.

Patients with hepatic or renal insufficiency
For the use of Dicloplast in patients with hepatic or renal insufficiency see

section 4.4.

Method of administration
Cut the envelope containing the medicated patch as indicated. Remove one medicated patch, remove the plastic film used to protect the adhesive surface and apply it to painful joint or region. If necessary, it can be held in place with an elastic net. Carefully reseal the envelope with the sliding closure.

The patch should be used whole.

4.3 Contraindications

This medicinal product is contraindicated in the following cases:
- Hypersensitivity to diclofenac, acetylsalicylic acid or other non-steroidal anti-inflammatory drugs (NSAIDs) or any excipients of the finished medicinal product listed in section 6.1.
- Patients in whom attacks of asthma, urticaria or acute rhinitis are precipitated byacetylsalicylic acid or other non-steroidal anti-inflammatory drugs (NSAIDS)
- damaged skin, whatever the lesion involved: exudative dermatitis, eczema,infected lesion, burn or wound.
- from the beginning of the 6th month of pregnancy (see 4.6 Pregnancy andlactation).
- Patients with active peptic ulceration.
- Children and adolescents aged less than 16 years.

4.4 Special warnings and precautions for use

- The medicated patch should be applied only to intact, non-diseased skin, and not to skin wounds or open injuries, and should not be worn when bathing or showering.
- The medicated patch should not come into contact with or be applied to the mucosae or the eyes.
- Not for use with occlusive dressing.
- Discontinue the treatment immediately if a skin rash develops after applying the medicated patch.
- Do not administer concurrently, by either the topical or the systemic route, any medicinal product containing diclofenac or other NSAIDs.
- The possibility of systemic adverse events from application of topical diclofenac cannot be excluded if the preparation is used over a prolonged period (see the product information on systemic forms of Diclofenac). Although systemic effects should be low, the patch should be used with caution in patients with renal, cardiac or hepatic impairment, history of peptic ulceration or inflammatory bowel disease or bleeding diathesis. Non-steroidal anti-inflammatory drugs should be used with particular caution in elderly patients who are more prone to adverse events.
- Patients should be warned against exposure to direct and solarium sunlight in order to reduce the risk of photosensitivity.
- Bronchospasm may be precipitated in patients suffering from or with a previous history of bronchial asthma or allergenic disease or allergy to acetylsalicylic acid or other NSAID. The medicated patch should be used with caution in patients with or without chronic asthma in whom attacks of asthma, urticaria or acute rhinitis are precipitated by acetylsalicylic acid or other non-steroidal anti-

inflammatory agents (see 4.3 Contraindications). In order to minimise the occurrence of undesirable effects it is recommended to use the lowest effective dose for the shortest duration necessary to control symptoms, without exceeding the approved maximum 14 days (Please see section 4.2 and 4.8).

Fetal Toxicity

Premature Closure of Fetal Ductus Arteriosus:

- Avoid use of NSAIDs, including lornoxicam, in pregnant women at about 30 weeks gestation and later. NSAIDs, including lornoxicam, increase the risk of premature closure of the fetal ductus arteriosus at approximately this gestational age.

Oligohydramnios/Neonatal Renal Impairment:

- Use of NSAIDs, including lornoxicam, at about 20 weeks gestation or later in pregnancy may cause fetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment. These adverse outcomes are seen, on average, after days to weeks of treatment, although oligohydramnios has been infrequently reported as soon as 48 hours after NSAID initiation. Oligohydramnios is often, but not always, reversible with treatment discontinuation. Complications of prolonged oligohydramnios may, for example, include limb contractures and delayed lung maturation. In some postmarketing cases of impaired neonatal renal function, invasive procedures such as exchange transfusion or dialysis were required.
- If NSAID treatment is necessary between about 20 weeks and 30 weeks gestation, limit lornoxicam use to the lowest effective dose and shortest duration possible. Consider ultrasound monitoring of amniotic fluid if lornoxicam treatment extends beyond 48 hours. Discontinue lornoxicam if oligohydramnios occurs and follow up according to clinical practice [*see 4.6 Fertility, pregnancy and lactation*].

4.5 Interaction with other medicinal products and other forms of interaction

Since systemic absorption of diclofenac during labelled use of the medicated patchesis very low, the risk of developing clinically relevant drug-drug interactions is negligible.

4.6 Fertility, pregnancy and lactation

Pregnancy

Risk Summary

Use of NSAIDs, including Dicloplast, can cause premature closure of the fetal ductus arteriosus and fetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment. Because of these risks, limit dose and duration of Dicloplast use between about 20 and 30 weeks of gestation, and avoid Dicoplast use at about 30 weeks of gestation and later in pregnancy (see Labor and Delivery - Clinical Considerations, Data).

Premature Closure of Fetal Ductus Arteriosus

Use of NSAIDs, including Dicloplast, at about 30 weeks gestation or later in pregnancy increases the risk of premature closure of the fetal ductus arteriosus.

Oligohydramnios/Neonatal Renal Impairment

Use of NSAIDs at about 20 weeks gestation or later in pregnancy has

been associated with cases of fetal renal dysfunction leading to oligohydramnios, and in some cases, neonatal renal impairment.

The systemic concentration of diclofenac is lower after topical administration, compared to oral formulations. With reference to experience from treatment with NSAIDs with systemic uptake, the following is recommended:
Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation and gastroschisis after use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk for cardiovascular malformation was increased from less than 1%, up to approximately 1.5 %. The risk is believed to increase with dose and duration of therapy.
Data from observational studies regarding other potential embryofetal risks of NSAID use in women in the first or second trimesters of pregnancy are inconclusive. In the general U.S. population, all clinically recognized pregnancies, regardless of drug exposure, have a background rate of 2-4% for major malformations, and 15-20% for pregnancy loss.
Based on animal data, prostaglandins have been shown to have an important role in endometrial vascular permeability, blastocyst implantation, and decidualization. In animal studies, administration of a prostaglandin synthesis inhibitor such as diclofenac, resulted in increased pre- and post-implantation loss and embryo-foetal lethality.
Prostaglandins also have been shown to have an important role in fetal kidney development. In published animal studies, prostaglandin synthesis inhibitors have been reported to impair kidney development when administered at clinically relevant doses.

In addition, increased incidences of various malformations, including cardiovascular, have been reported in animals given a prostaglandin synthesis inhibitor during the organogenetic period.
During the first and second trimester of pregnancy, diclofenac should not be given unless clearly necessary. If diclofenac is used by a woman attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low andduration of treatment as short as possible.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the mother and the neonate, at the end of pregnancy, to:
- possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses.
- inhibition of uterine contractions resulting in delayed or prolonged labour.
Consequently, diclofenac is contraindicated during the third trimester of pregnancy.

Labor and Delivery

Clinical Considerations
Fetal/Neonatal Adverse Reactions
Premature Closure of Fetal Ductus Arteriosus:
Avoid use of NSAIDs in women at about 30 weeks gestation and later in pregnancy, because NSAIDs, including Dicloplast, can cause premature closure of the fetal ductus arteriosus (see Data).

Oligohydramnios/Neonatal Renal Impairment
If an NSAID is necessary at about 20 weeks gestation or later in pregnancy, limit the use to the lowest effective dose and shortest duration possible. If Dicloplast treatment extends beyond 48 hours, consider monitoring with ultrasound for oligohydramnios. If oligohydramnios occurs, discontinue Dicloplast and follow up according to clinical practice (see Data).

Data
Human Data

Premature Closure of Fetal Ductus Arteriosus:
Published literature reports that the use of NSAIDs at about 30 weeks of gestation and later in pregnancy may cause premature closure of the fetal ductus arteriosus.

Oligohydramnios/Neonatal Renal Impairment:
Published studies and post marketing reports describe maternal NSAID use at about 20 weeks gestation or later in pregnancy associated with fetal renal dysfunction leading to oligohydramnios, and in some cases, neonatal renal impairment. These adverse outcomes are seen, on average, after days to weeks of treatment, although oligohydramnios has been infrequently reported as soon as 48 hours after NSAID initiation. In many cases, but not all, the decrease in amniotic fluid was transient and reversible with cessation of the drug. There have been a limited number of case reports of maternal NSAID use and neonatal renal dysfunction without oligohydramnios, some of which were irreversible. Some cases of neonatal renal dysfunction required treatment with invasive procedures, such as exchange transfusion or dialysis.

Methodological limitations of these post marketing studies and reports include lack of a control group; limited information regarding dose, duration, and timing of drug exposure; and concomitant use of other medications. These limitations preclude establishing a reliable estimate of the risk of adverse fetal and neonatal outcomes with maternal NSAID use. Because the published safety data on neonatal outcomes involved mostly preterm infants, the generalizability of certain reported risks to the full-term infant exposed to NSAIDs through maternal use is uncertain.

Breast-feeding

Like other NSAIDs, diclofenac passes into breast milk in small amounts. However, attherapeutic doses of diclofenac medicated patch no effects on the suckling child are anticipated.
Because of a lack of controlled studies in lactating women, the product should onlybe used during lactation under advice from a healthcare professional. Under this circumstance, Dicloplast should not be applied on the breasts of nursing mothers, nor elsewhere on large areas of skin or for a prolonged period of time (seesection 4.4).

4.7 Effects on ability to drive and use machines

Diclofenac medicated patch application has no influence on the ability to drive anduse machines.

4.8 Undesirable effects

Adverse reactions (Table 1) are ranked under heading of frequency, the most frequent first, using the following convention: very common: (>1/10); common (≥1/100, <1/10); uncommon (≥1/1,000, <1/100); rare (≥1/10,000, <1/1,000); very rare (<1/10,000); Not known: cannot be estimated from the available data.

Table 1

Infections and infestations	
Very rare	Rash pustular
Immune system disorder	
Very rare	Hypersensitivity (including urticaria), angioneurotic oedema, anaphylactic type reaction
Respiratory, thoracic and mediastinal disorders	
Very rare	Asthma
Skin and subcutaneous tissue disorders *	
Common Uncommon Rare Very rare	Rash, eczema, erythema *, dermatitis (including allergic and contact dermatitis*), pruritus* petechiae * Dermatitis bullous (e.g. erythema bullosum), dry skin Photosensitivity reaction
General disorders and administration site conditions *	
Common Uncommon	Application site reactions * Feeling hot

*Adverse reactions have been reported in a clinical trial, where 1252 patients were treated with Dicloplast medicated patch and 734 with Placebo inclinical trials.

Systemic absorption of diclofenac is very low compared with plasma levels

obtained following administration of oral forms of diclofenac and the likelihood of systemic side effects reactions (like gastric, hepatic and renal disorders) occurring with topical diclofenac is very small compared with the frequency of side effects associated with oral diclofenac. However, where Dicloplast is applied to a relatively large area of skin and over a prolonged period, the possibility of systemic side effects cannot be excluded.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il

4.9 Overdose

There is no experience with overdose of diclofenac medicated patch. Should systemic side effects occur due to incorrect use or accidental overdose (e.g. in children) of this product, the general measures recommended for intoxication withnon-steroidal anti-inflammatory drugs should be taken.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anti-inflammatory preparations, non-steroids for topical use.

ATC Code: M02AA15

Diclofenac hydroxyethylpyrrolidine or diclofenac epolamine is a water soluble salt of diclofenac.

Diclofenac is a nonsteroidal anti-inflammatory drug derived from phenylacetic acid which belongs to the aryl carboxylic acid group of compounds.

In the form of a medicated patch, it has topical anti-inflammatory and analgesic activity.

5.2 Pharmacokinetic properties

Following cutaneous application of the medicated patch, diclofenac epolamine is absorbed through the skin.

The absorption kinetics at steady state show a prolonged release of the active ingredient with a maximum diclofenac plasma level (Cmax) of 17.4 ±13.5ng/ml, which is reached after about 5 hours (Tmax 5.4±3.7 hours).

Diclofenac is extensively bound to plasma protein (about 99%).

Systemic transfer in healthy volunteers when using the medicated patch, compared with oral forms of diclofenac, is of the order of 2%, as estimated from the urinary excretion of the drug and its metabolites and from a between study comparison.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans, beyond the information included in other sections of the SPC. In the rat and rabbit, diclofenac epolamine and epolamine monosubstance have caused embryotoxicity and increased embryolethality after oral use.

6 PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Supporting layer:
Unwoven polyester support.

Adhesive layer (active gel):
D-Sorbitol Solution (70%), Purified Water, 1,3 Butylene Glycol, Sodium Carboxyvinyl Polymer, Carboxymethylcellulose Sodium, Kaolin, Propylene Glycol, Gelatin (Type A), Povidone (K 90), Tartaric Acid, Titanium Oxide, Dihydroxyaluminium Aminoacetate, Polysorbate 80, Disodium Edetate, Methyl Parahydroxybenzoate, Propyl Parahydroxybenzoate, Fragrance, Polyester Unwoven Fabric, Polypropylene Film.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.
After first opening the sealed envelope: 3 months

6.4 Special precautions for storage

Do not store above 25ºC

6.5 Nature and contents of container

Sealed envelopes made of paper/polyethylene /aluminium/ethylene methacrylic acid c-opolymer contain 2 or 5 medicated patches.

Pack size: 2 or 5 medicated patches per box.

The package also contains an elastic, polyester, tabular net made of a non-woven fabric.

Not all pack size may be marketed.

6.6 Special precautions for disposal

Remaining active ingredient of the patch may pose a risk to the aquatic

environment. Do not flush used patches down the toilet. The patches shouldbe disposed of according to local requirements.

7 MANUFACTURER

IBSA INSTITUTE BIOCHIMIQUE SA, SWITZERLAND

Via Al Ponte 13, C-H6903, Lugano, Switzerland

8 LICENSE HOLDER AND IMPORTER

CTS Ltd.

4 Haharash st., Hod Hasharon, 4524075

9 MARKETING AUTHORISATION NUMBER(S)

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10 DATE OF REVISION OF THE TEXT

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