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Public Assessment Report

Diclac Long 23.2 mg/g gel (Diclofenac diethylamine)

HU/H/0745/001/DC

Marketing authorisation holder: Sandoz B.V.

Date: 05.06.2023

This module reflects the scientific discussion for the approval of *Diclac Long 20 mg/g gel.* The procedure was finalised at 09.02.2023. For information on changes after this date please refer to the module 'Update'.

CONTENT

LAY SUMMARY

After careful assessment of its quality and therapeutic benefit/risk ratio, the member states have granted the marketing authorisation of the Diclac Long 23.2 mg/g gel. The holder of the marketing authorisation in the RMS is Sandoz Hungaria Kft.

The active substance is diclofenac diethylamine.

Diclac Long 23.2 mg/g gel
Each g of gel contains 23.2 mg of diclofenac diethylamine (corresponding to 20 mg of diclofenac sodium).

The other ingredients are:

propylene glycol, oleyl alcohol, isopropyl alcohol, butylhydroxytoluene, diethylamine, paraffin light liquid, macrogol cetostearyl ether, carbomer, cocoyl caprylocaprate, perfume cream and purified water.

What Diclac Long looks like and contents of the pack

Diclac Long is a viscous white gel with a characteristic fragrance.

The gel is packed in an aluminium laminate tube with an HDPE shoulder sealed with a top seal and a polypropylene cap.
Pack sizes: tubes of 50 g, 100 g, 150 g and 180 g.

Not all pack sizes may be marketed.

What Diclac Long is and what it is used for

Diclac Long contains diclofenac.

- Diclofenac belongs to a group of medicines called non-steroidal anti-inflammatory drugs (NSAIDs).
- It relieves pain and reduces inflammation in painful conditions affecting the joints and muscles.

Diclac Long can be used to treat the following disorders:
Adults and adolescents aged 14 years and older

- muscle and joint injuries (e.g. sprains, strains, bruises, backache, sports injuries), reduces pain even in case of moderate and severe pain, improves mobility of patients and helps to return to usual everyday activities
- tendonitis (e.g. tennis elbow), swelling around the elbow and knee

Adults (18 years and older)

- mild arthritis of the knee and fingers

Patients must talk to a doctor if they do not feel better or if they feel worse after 7 days.

What patients need to know before using Diclac Long

Patients should not use Diclac Long

- if they are allergic to
  - diclofenac,
  - other medicines used to treat pain, fever or inflammation, such as ibuprofen or acetylsalicylic acid (a substance also used to prevent blood clotting) or
  - any of the other ingredients of this medicine (listed in section 6)

  Symptoms of an allergic reaction may include: wheezing or shortness of breath (asthma; bronchospasm); skin rash with blisters or hives; swelling of the face, tongue or throat; runny nose. If the patients are not sure, they should ask their doctor or pharmacist.
- on open injuries, inflammations or infections of the skin as well as on eczema (dry, itchy skin) or mucous membranes
- in the last trimester of pregnancy
- in children and adolescents below 14 years of age

Warnings and precautions

Patients should tell their doctor or pharmacist before using Diclac Long.
Patients should not use Diclac Long in larger than recommended doses and over a prolonged period unless your doctor recommends explicitly.
Patients should apply Diclac Long only to intact, not diseased or injured skin.
This medicine is only for use on the skin. It should not be swallowed.
Patients should avoid contact with eyes and mouth.
If contact with eyes happens, rinse your eyes well with clean water. See your doctor if any discomfort persists.
After applying the gel on the skin, patients can use a permeable (non-occlusive) bandage but they should allow the gel to dry on the skin for a few minutes. Patients should not use an airtight occlusive dressing.
Patients should stop using Diclac Long if they develop a skin rash.
Patients should avoid sun exposure, including solarium, when using this medicine.
Patients should prevent children from touching the area to which the gel is applied.
Patients should be careful when smoking or near open flames due to the risk of severe burns.
Diclac Long contains paraffin, which is potentially flammable if it accumulates on fabric (clothing, bedding, bandages etc.) and cannot be completely removed by washing.

Children and adolescents

- Diclac Long is not recommended for children and adolescents below 14 years of age. There are not enough data available on efficacy and safety in this age group (see section “Patients should not use Diclac Long” above).
- If in adolescents aged 14 years and older this medicine is required for more than 7 days for pain relief or if the symptoms worsen, the patient or parents are advised to consult a doctor.

Other medicines and Diclac Long

Patients should tell their doctor or pharmacist if they are taking, have recently taken or might take any other medicines.

In intended, cutaneous use of Diclac Long no interactions have become known so far.

Pregnancy and breast-feeding

If the patients are pregnant or breast-feeding, they think they may be pregnant or are planning to have a baby, they should ask their doctor or pharmacist for advice before using this medicine.

- **Pregnancy**
  Patients should not use Diclac Long during the last trimester of pregnancy as it could harm their unborn child or cause problems at delivery.
  During the first and second trimester of pregnancy, Diclac Long should be used only after consultation with their doctor.
- **Breast-feeding**
  Diclac Long should only be used under medical advice during breast-feeding as diclofenac passes into breast milk in small amounts. Patients should not apply Diclac Long on the breasts if they are a nursing mother nor elsewhere on large areas of skin or for a prolonged period of time.

Driving and using machines

Diclac Long has no or negligible influence on the ability to drive or to use machines.

Diclac Long contains butylhydroxytoluene, which may cause local skin reactions (e.g. contact dermatitis) or eye and mucus membrane irritation.

How to use Diclac Long?

Patients should always use this medicine exactly as described in the Package leaflet or as their doctor or pharmacist has told them. They should check with their doctor or pharmacist if they are not sure.

The recommended dose is:
Adults and adolescent aged 14 years and older
Diclac Long is used 2 times a day (preferably morning and evening), providing long-lasting pain relief for up to 12 hours.
Depending on the size of the affected site to be treated, a cherry to walnut sized quantity, corresponding to 2 - 4 g of gel is required. Patients should not take more than 8 g of the gel per day.

Elderly patients
No special dose adjustment is necessary. If the patients are elderly, they should pay special attention to side effects and, if necessary, consult a doctor or pharmacist.

- **Applying this medicine**
  - Before using for the first time, patients should remove the plastic seal from the tube. Patients should not use if the seal is broken.
  - Diclac Long is for cutaneous use (should only be used on the skin).

- Patients should apply the gel to the affected parts of the body thinly and rub gently into the skin.
- After use, patients should wipe their hands with a cotton cloth or absorbent paper and then wash their hands if the treated area is not their hands.

Diclac Long can be used with non-occlusive bandages but should not be used with an airtight occlusive dressing.

Duration of use
The duration of use depends on the symptoms and the underlying disease.
Patients should contact their doctor if the pain or the inflammation do not improve or become worse within 7 days.

- **Adults (18 years and older)**

Diclac Long should not be used longer than 14 days for treatment of injuries of muscles, tendons and connective tissue and 21 days for the treatment of arthritis without medical advice.

- **Adolescents (below 18 years, 14 years and older)**

Diclac Long should not be used longer than 7 days without medical advice.
Longer treatment may be recommended only by a doctor.

If more Diclac Long has been taken

- An overdose is unlikely to happen if the patients use more Diclac Long than they should, because the absorption into the blood stream is low when used on the skin.
- If the recommended dose is significantly exceeded when used on the skin, the gel should be removed and washed off with water.
- If the patients accidentally swallow this medicine, they should contact their doctor immediately.

If Diclac Long has been forgotten to take

If the patients miss a dose, they should apply it as soon as possible. Patients should not use a double dose to make up for a forgotten dose.

If the patients have any further questions on the use of this medicine, they should ask their doctor or pharmacist.

Possible side effects

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

Some rare and very rare side effects might be serious.
If the patients experience any of the following signs of allergy, they should **stop** using Diclac Long and **tell a doctor or pharmacist immediately**:

- Skin rash with blisters; hives (rare: may affect up to 1 in 1,000 people)
- Wheezing, shortness of breath or feeling of tightness in the chest (asthma) (very rare: may affect up to 1 in 10,000 people)
- Swelling of the face, lips, tongue or throat (very rare: may affect up 1 in 10,000 people)

Other side effects are possible:

Common side effects (may affect up to 1 in 10 people):
Skin rash, itching, reddening, eczema, dermatitis (inflammation of the skin) including contact dermatitis.

Very rare side effects (may affect up 1 in 10,000 people)
- Pustular rash
- Hypersensitivity reactions (including hives)
- Sensitivity to light with appearance of skin reactions after exposure to sunlight

When Diclac Long is applied to a large area of skin and over a prolonged period, the possibility of systemic side effects (e.g. renal, hepatic or gastrointestinal side effects, systemic hypersensitivity reactions) - as they occur possibly after systemic administration of diclofenac-containing medicines - cannot be completely excluded.

Reporting of side effects
If the patients get any side effects, they should talk to their doctor, pharmacist. This includes any possible side effects not listed in this leaflet. Patients can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects patients can help provide more information on the safety of this medicine.

How to store Diclac Long?

This medicine should be kept out of the sight and reach of children.

Patients should not use this medicine after the expiry date which is stated on the tube after EXP. The expiry date refers to the last day of that month.

This medicine should be stored below 25°C. This medicine should not be refrigerated or freezed.

Patients should not use this medicine if they notice visible signs of deterioration.

Patients should not throw away any medicines via wastewater or household waste. Their pharmacist should be asked how to throw away medicines they no longer use. These measures will help protect the environment.

SCIENTIFIC DISCUSSION

This module reflects the scientific discussion for the approval of Diclac Long 0,01 mg vaginal tablets.The procedure was finalised at 02. 07. 2020. For information on changes after this date please refer to the module 'Update'.

I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Member States have granted marketing authorisation for Diclac Long 20 mg/g gel.

The proposed product is a gel, containing diclofenac diethylamine as the active substance (1 g of gel contains diclofenac as 23.2 mg diclofenac diethylamine, which corresponds to 20 mg diclofenac sodium).

This is an application submitted according to Article 10(3) of Directive 2001/83/EC, as amended, this legal basis is the most appropriate for products for local use. With Hungary as the Reference Member State in this Decentralized Procedure, Sandoz Hungaria Kft. is applying for the Marketing Authorisations for Diclac Long 20 mg/g gel in BE, BG, HR, LT, LV, respectively.

The product under consideration, Diclac Long 20 mg/g gel, have Voltadol (Spain), as Reference Medicinal Product, which was authorised in Spain on 11.11.2009. The strength, the pharmaceutical form and the indication of the reference medicinal product do not differ between the RMS and the CMSs. The name of the reference product is Voltaren Emulgel Forte 20 mg/g gel in the RMS.

The product is indicated for the following conditions:
Adults and adolescent aged 14 years and older
For the relief of pain, inflammation and swelling:
- soft tissue injuries: to relieve post-traumatic inflammation of the tendons, ligaments, muscles, and joints, e.g. in case of sprains, strains and bruises, back pain (sports injuries);
- localised forms of soft-tissue rheumatism, e.g. tendonitis, tennis elbow, bursitis, shoulder-hand syndrome and periarthropathy.

Adults (18 years and older)
- treatment of mild arthritis in the joints of the knees and fingers.

A comprehensive description of the indications and posology is given in the SmPC.

II. QUALITY ASPECTS

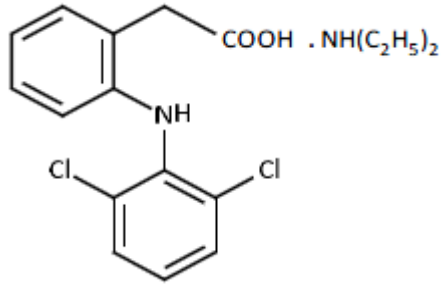
II.1 Introduction

The chemical-pharmaceutical assessment report concerns the application of Diclac Long 20 mg/g gel via a decentralized procedure according to Article 10(3) of Directive 2001/83/EC (i.e a hybrid application). The product has been developed by Kern Pharma S.L., Spain.
The reference medicinal product is Voltadol 11,6 mg/g gel (Glaxosmithkline Consumer Healthcare, S.A), which has been on the market since 2009.

II.2 Drug substance

Data on the quality and manufacture of the active substance were provided in the applicant's submission using the Active Substance Master File (ASMF) procedure. The Quality Overall Summary is adequate.

INN name: Diclofenac diethylamine
Chemical name: Diethylammonium 2-[(2,6-dichloroanilino) phenyl]acetate *[British Pharmacopoeia]*
Structure:



The active substance is white to light beige, crystalline powder. Sparingly soluble in water and in acetone, freely soluble in ethanol (96%) and in methanol, practically insoluble in 1M sodium hydroxide. Diclofenac diethylamine has no chiral centre in its structural formula. The manufacturer consistently produces the same polymorphic form.

The ASMF holder presented complete details of the manufacturing process. Description of the manufacturing process of the active pharmaceutical ingredient (API) is adequate.

Evidence of the structure has been confirmed by elemental analysis, ultraviolet spectroscopy, infrared spectroscopy, proton and carbon nuclear magnetic resonance spectrum and mass spectrometry. The impurity profile of the API contains detailed information about organic and inorganic impurities, genotoxic impurities and residual solvents.

Diclofenac diethylamine is not in the Ph.Eur. Therefore, an in-house specification has been set for the active substance, which includes the following tests: description, solubility, melting point, identification by IR, TLC, acidity or alkalinity, clarity and colour of solution, related substances, loss on drying, assay, residual solvents, particle size and microbiological purity.
The presented specification is in accordance with the Ph.Eur. general monograph on *Substances for Pharmaceutical Use* and the ICH Q6A guideline. The specifications reflect all relevant

quality attributes of the active substance and were found to be adequate to control the quality of the drug substance. The limits set are properly justified.

Testing methods not described in details in the Pharmacopoeia are adequately drawn up and sufficiently validated. Reference materials used by the active substance manufacturer and the drug product manufacturer for the control of the substance are adequately characterised.
The substance complies with the requirements of the EMA guideline on genotoxic impurities.

Batch analysis data justify the limits, indicate the good performance of testing methods and demonstrate the batch to batch consistency of the production.

Stability studies have been performed with the drug substance. According to the presented stability data the proposed re-test period is acceptable if stored in an airtight container, protected from light.

Good Manufacturing Practice (GMP) compliance of the API manufacture is demonstrated by the applicant.

II.3 Medicinal product

The aim of the development was to obtain an oil in water emulsion containing 23.2 mg Diclofenac diethylamine active substance as a hybrid to the reference medicinal product Voltadol Forte® 23.2 mg/g gel authorised in Spain by Glaxosmithkline Consumer Healthcare, S.A, which has been on the market since 2014.

A satisfactory package of data on development pharmaceutics has been presented. The qualitative and quantitative composition of the test product is as same as the reference product. The in vitro equivalence of the test and reference drug products is demonstrated by comparative release test by Franz cell model. The pharmaceutical equivalence is justified also by comparative impurity analysis. In order to confirm that the formulation is able to preserve itself from the microbiological point of view a challenge test was performed, the efficacy of antimicrobial preservation is sufficiently proved.

The compositions and the pharmaceutical tests evaluated during development of the final formulation are included in the documentation. As a result of development studies product with the following appearance and composition was obtained:
The drug product is a white gel for topic administration and it can presented in tubes 30 g, 50 g, 60 g, 100 g, 120 g, 150 g and 180 g. Each g of gel contains 23.2 mg of the active substance Diclofenac diethylamine, equivalent to 20.0 mg of Diclofenac sodium.
The used excipients are Propylene glycol, Oleyl alcohol, Isopropyl alcohol, Butylhydroxytoluene, Diethylamine, Liquid paraffin, Macrogol cetostearyl ether, Carbomer 980 F, Cocoyl caprylocaprate, Perfume cream 45399 and Purified water.
The control of excipients is in line with pharmacopoeial or in-house requirements. Declaration on compliance of Perfume cream 45399 with Cosmetic Regulation (EC) No. 1223/2009 has been provided. Testing methods not described in details in the Pharmacopoeia are adequately drawn up and sufficiently validated. Compliance of the product with the general monograph of the European Pharmacopoeia *on the Products with the risk of TSE* has been demonstrated by the Applicant.

A description and flow chart of the manufacturing method has been provided. Appropriate in-process controls are included in the manufacturing process. Satisfactory batch formula were also presented. GMP compliance of the manufacturing site has been demonstrated.

The finished product specification is satisfactory. Acceptance criteria have been justified with respect to conventional pharmaceutical requirements as prescribed in the relevant dosage form monograph of the Ph.Eur. and the ICH Q6A guideline. The test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and complied with the specification.

The packaging material consists of an aluminium laminate tube composed by several layers of polyethylene, aluminium and polyethylene (internal layer) attached to an HDPE shoulder sealed with a top seal and a polypropylene cap.

Finished product stability studies have been conducted in accordance with the current guidelines. Based on the results, a shelf-life of 2 years is approved with the following storage restriction: Store below 25°C. Do not refrigerate or freeze.

The Summary of Product Characteristics, patient Information Leaflet and label texts are pharmaceutically acceptable.

II.4 Discussion on chemical, pharmaceutical and biological aspects

Conclusion: The product has been shown to meet the current regulatory requirements with regards to its quality and content of the active substance as well as dosage-form characteristics until the end of the approved shelf-life consistently. The manufacture and the quality standards applied adequately support the safe use and efficacy of the product.

III. NON-CLINICAL ASPECTS

III.1 Introduction

Pharmacodynamic, pharmacokinetic and toxicological properties of diclofenac are well known. As diclofenac is a widely used, well-known active substance, the applicant has not provided additional studies and further studies are not required. Overview based on literature review was submitted.

III.1 Pharmacology

The animal studies with topically applied diclofenac proved its anti-inflammatory and analgesic effect. Also when compared with other topical treatments, diclofenac was better or at least equal to the other treatments tested.

III.2 Pharmacokinetics

The pharmacokinetics of diclofenac in animal species, which was studied after intravenous, intramuscular, oral and topical administrations, is characterised by a rapid elimination half-life. After topical application its systemic absorption is low; however, diclofenac is distributed to the inflammatory sites proving its ability to reach the target tissue.

III.3 Toxicology

Based on conventional studies on safety pharmacology, genotoxicity and carcinogenic potential, the pre-clinical data do not reveal any specific hazards for humans apart from those already described in the relevant sections of the SmPC. In the animal studies the chronic toxicity of diclofenac following systemic application mainly manifested as gastrointestinal lesions and ulcers. In a 2-year toxicity study, a dose-dependent increase in the incidence of thrombosis of the heart was observed in diclofenac-treated rats.

In animal studies on reproductive toxicity, systemically administered diclofenac caused inhibition of ovulation in rabbits and impairment of implantation and early embryonic development in rats. Gestation and duration of parturition were prolonged by diclofenac. The embryotoxic potential of diclofenac was investigated in three animal species (rat, mouse, rabbit). Foetal death and growth retardation occurred at materno-toxic dose levels. Based on the available non-clinical data, diclofenac is regarded as being non-teratogenic. Doses below the maternotoxic threshold had no impact on the postnatal development of the offspring.

Overall, diclofenac is a thoroughly examined drug and it can be concluded that the proposed Diclofenac diethylamine 23.2 mg/g gel formulation has a favourable safety profile in animals.

III.4 Ecotoxicity/environmental risk assessment (ERA)

The applicant submitted a detailed ERA based on the Guideline on the environmental risk assessment of medicinal products for human use (EMEA/CHMP/SWP/4447/00 corr 2). According to the Phase I and Phase II/Tier A analysis the Diclac Long 20 mg/g gel to be marketed does not represent any environmental risk.

III.5 Discussion on the non-clinical aspects

The non-clinical overview on the pre-clinical pharmacology, pharmacokinetics and toxicology is adequate. There are no objections to approval of Diclac Long 20 mg/g gel from a non-clinical point of view.

IV. CLINICAL ASPECTS

IV.1 Introduction

The Note for Guidance on the clinical requirements for locally applied, locally acting products containing known constituents (CPMP/EWP/239/95) specifies that therapeutic equivalence should be demonstrated between the test and reference topical products.

The application contains an adequate review of published clinical data and the bioequivalence has been shown.

IV.2 Pharmacokinetics

Bioequivalence study

To support the application, one confirmatory pivotal bioequivalence study with the strength of 23.2 mg/g gel was submitted. This study was a randomized, open-label, fully-replicated 4-period, 2-sequence, single-dose, cross-over bioequivalence study in healthy male and female volunteers. Based on the results of the bioequivalence study the Test Product (Diclofenac diethylamine 23.2 mg/g gel, Kern Pharma S.L., Spain) is considered bioequivalent with Reference Product (Voltadol Forte® 23.2 mg/g gel, Novartis Consumer Healthcare, Germany).

Pharmacokinetic properties

The quantity of diclofenac absorbed through the skin is proportional to the size of the treated area, and depends on both the total dose applied and the degree of skin hydration. After topical application of the 23.2 mg of diclofenac diethylamine salt/g gel two times a day to approximately 400 cm^2 of skin, the extent of systemic exposure as determined by plasma concentrations of the active substance was equivalent to diclofenac 10 mg/g gel, applied four times daily. The relative bioavailability of diclofenac for the 23.2 mg of diclofenac diethylamine salt/g gel versus tablet was 4.5% on day 7 of treatment, for equivalent diclofenac sodium doses.

Diclofenac concentrations have been measured from plasma, synovial tissue and synovial fluid after application of topical diclofenac to hand and knee joints. Maximum plasma concentrations were approximately 100 times lower than after oral administration of the same quantity of diclofenac. 99.7% of diclofenac is bound to serum proteins, mainly albumin (99.4%).

Diclofenac accumulates in the skin, which works as a depot, continuously releasing the active substance into deeper tissues. Due to its properties, diclofenac has an affinity to inflamed tissue. Diclofenac preferentially distributes and persists in deep inflamed tissues, such as the joint, where it is found in concentrations up to 20 times higher than in plasma.

Biotransformation of diclofenac involves partly glucuronidation of the intact molecule, but mainly single and multiple hydroxylation resulting in several phenolic metabolites, most of which are converted to glucuronide conjugates. Two of the phenolic metabolites are biologically active, however, to a much smaller extent than diclofenac.

The total systemic clearance of diclofenac from plasma is 263 ± 56 ml/min. The terminal plasma half-life is 1-2 hours. Four of the metabolites, including the two active ones, also have short plasma half-lives of 1-3 hours. One metabolite, 3'-hydroxy-4'-methoxy-diclofenac, has a longer half-life but is virtually inactive. Diclofenac and its metabolites are excreted mainly in the urine.

IV.3 Pharmacodynamics

The Applicant has not carried out clinical pharmacodynamic studies. An updated review of the current literature on the clinical pharmacodynamic of diclofenac administered topically was submitted. The clinical overview on the clinical pharmacology is adequate.

IV.4 Clinical efficacy

An updated review of the current literature on the clinical efficacy of diclofenac administered topically was submitted. Diclofenac was studied in several different topical formulations. The results of the published clinical studies demonstrated the efficacy of diclofenac administered locally in the treatment of inflammatory conditions when compared to control or active treatment groups. Topical diclofenac treatments provided effective pain relief for the treatment of osteoarthritis. Topical diclofenac formulations relieved the symptoms in case of inflammation and pain of traumatic or rheumatic origin.

IV.5 Clinical safety

An updated review of the current literature on the clinical safety of diclofenac administered topically was submitted. Systemic absorption following topical diclofenac is very low compared to the plasma levels of the active substance after oral administration. Therefore, the likelihood of systemic adverse reactions is very rare following topical administration of diclofenac. According to the literature data diclofenac gel for topical administration is safe and very well-tolerated across its indications, with few reported adverse effects.

IV.6 Pharmacovigilance

IV.6.1 Summary of the Pharmacovigilance System

The Applicant has submitted a signed Summary of the Applicant's Pharmacovigilance System. Provided that the Pharmacovigilance System Master File fully complies with the new legal requirements as set out in the Commission Implementing Regulation 520/2012 and as detailed in the relevant GVP module, the Summary is considered acceptable.

IV.6.2 Risk Management Plan (version 1.2 signed 25.01.2023)

Summary of safety concerns

Summary of safety concerns	
Important identified risks	None
Important potential risks	None
Missing information	None

As the active substance (diclofenac diethylamine) has been used for decades and its safety concerns are well-known so there were no safety concerns applicable for this EU RMP based on the requirement to present only the important identified or potential risks and missing information linked to further pharmacovigilance activities or additional risk minimization measures in the EU.

Pharmacovigilance plan

Routine pharmacovigilance activities are considered sufficient to manage all of the safety concerns connected to Sandoz's product containing diclofenac diethylamine.
No additional activities are proposed.

Risk Minimisation Measures

Routine risk minimisation measures (i.e. wording in SmPC, PL and classification as a prescription only medicine) are considered sufficient to manage all of the safety concerns connected to Sandoz's product containing diclofenac diethylamine.
No additional activities are proposed. For any further information on risk minimisation, please refer to the product information.

Periodic Safety Update Reports

The requirements for submission of periodic safety update reports for these medicinal products are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

IV.7 Discussion on the clinical aspects

The application contains an adequate review of published clinical data of diclofenac used topically and the bioequivalence has been shown.

One pivotal bioequivalence study was submitted. Based on the bioequivalence study the Test Product (Diclofenac diethylamine 23.2 mg/g gel, Kern Pharma S.L., Spain) is considered bioequivalent with the Reference Product (Voltadol Forte® 23.2 mg/g gel, Novartis Consumer Healthcare, Germany).

V. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

V.1 Summary

The application contains an adequate review of published non-clinical and clinical data of diclofenac used topically.

To support the application, one confirmatory pivotal bioequivalence study with the strength of 23.2 mg/g Diclofenac diethylamine gel was submitted. Based on this study it is concluded that the test product, Diclofenac diethylamine 23.2 mg/g gel developed by Kern Pharma is essentially similar to the reference product, Voltadol Forte®, authorised and marketed in the European Union by Novartis Consumer Healthcare.

Furthermore, based on the data available for this product and considering the bibliographic non-clinical and clinical efficacy and safety data, a favourable benefit-risk can be concluded for the Diclac Long 20 mg/g gel.

V.2 Classification

Diclac Long 20 mg/g gel is not subject to medical prescription.

V.3 Package Leaflet and user consultation

A user consultation with target patient groups on the package information leaflet (PIL) has been performed on the basis of a bridging report making reference to Diclofenac sodium Teva 2% w/w gel, DE/H/5493+6245+6603/001-002/DC and Voltaren Emulgel Forte 20 mg/g gel, GlaxoSmithKline-Consumer Kft., OGYI-T-5572/33+43. The bridging report submitted by the applicant has been found acceptable.

VI. UPGRADE: STEPS TAKEN AFTER THE INITIAL PROCEDURE WITH AN INFLUENCE ON THE PUBLIC ASSESSMENT REPORT

This module reflects the procedural steps and scientific information after the finalisation of the initial procedure.

Scope	Procedure number	Product information affected	Date of start of the procedure	Date of end of procedure	Approval or non approval

*Only procedure qualifier, chronological number and grouping qualifier (when applicable)