Submission to the Medicines Classification Committee

Pharmacy Only classification

140 mg diclofenac transdermal patch for topical use

Date prepared: 31 January 2014

Sponsor/Applicant: Novartis Consumer Health Australasia Pty Ltd

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Executive Summary

Topical NSAID products have had a long history of use in New Zealand and internationally, with a well-established safety profile. Topical NSAIDs currently on the market are indicated for the temporary relief of pain associated with soft tissue injuries, as well as other painful musculoskeletal conditions.

Diclofenac presented in a transdermal patch for topical use (diclofenac patch) offers consumers with a viable alternative to oral and other topical NSAID products; with features that arguably could increase consumer compliance (twice daily application, convenient dosage form).

The product is suitable for self-selection for the temporary relief of local pain in acute soft tissue injuries. Pain symptoms from these minor ailments are easily recognised and self-diagnosed by the consumer, as exhibited by Voltaren Emulgel 1.16% diclofenac diethylammonium which carries the same indication and has been classified as General Sale for over 10 years in Australia and New Zealand.

Request for Trans-Tasman harmonisation

In March 2013, the Australian Schedule 2 (Pharmacy Medicine) classification for diclofenac was amended to include 'transdermal preparations for topical use containing 140 mg or less of diclofenac'.

The Australian Advisory Committee on Medicines Scheduling (ACMS) considered that Pharmacy Medicine status was appropriate for diclofenac patch at this stage because:

- there has been no clinical/marketing experience with this novel formulation in Australia; and
- Schedule 2 Pharmacy Medicine status allows capacity to obtain professional advice from a pharmacist at the time of purchase.

In New Zealand, all preparations for external use other than for the treatment of solar keratosis are currently classified as General Sale.

This lack of harmonisation results in different labelling requirements for the same product in either country. Low volumes for New Zealand means that it is not commercially viable to launch products with specific New Zealand labelling.

This application proposes classification of diclofenac when presented in a transdermal patch for topical use containing 140 mg or less as Pharmacy Only, so as to harmonise with the Australian Schedule and thus allow common packs to be marketed in both countries.

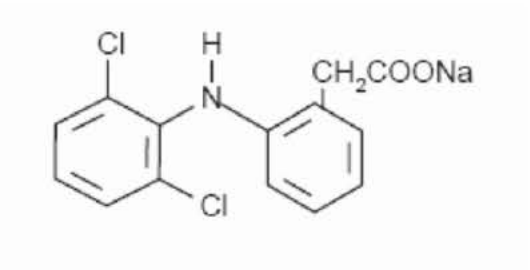
[redacted]

Part A

A.1. International Non-proprietary Name (or British Approved Name or US Adopted Name) of the medicine

Name: Diclofenac sodium

Chemical structure:



Molecular Formula: C14H11Cl2NO2

Molecular Weight: 296.15

CAS number: 15307-86-5

A.2. Proprietary name

[redacted]

A.3. Name of company/organisation/individual requesting classification

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A.4. Dose form(s) and strength(s)

Dose form: transdermal patch for topical use
Strength: 140 mg

A.5. Pack size

Proposed pack sizes: 2, 5, 10

A.6. Indications

Local symptomatic treatment of the following musculoskeletal inflammatory conditions - acute soft tissue injuries, sprains, strains, tendinitis, bursitis, contusion and sports injury

A.7. Present classification of medicine

All preparations for external use other than for the treatment of solar keratosis are currently classified as General Sale:

Classification	Conditions (if any)
General Sale	in preparations for external use other than for the treatment of solar keratosis

A.8. Classification sought

This application proposes to classify diclofenac patch as 'Pharmacy-Only', in line with the Australian Schedule 2 (Pharmacy Medicine):

Classification	Conditions (if any)
Pharmacy Only	in solid dose form in medicines containing 12.5 milligrams or less per dose form in packs containing not more than 30 tablets or capsules and with a recommended daily dose of not more than 75 milligrams; in transdermal preparations for topical use containing 140 mg or less of diclofenac
General Sale	in preparations for external use other than for the treatment of solar keratosis; except when specified elsewhere in this schedule

A.9. Classification status in other countries (especially Australia, UK, USA, Canada)

Country	Conditions (if any)
Australia	Pharmacy Medicine
UK	Pharmacy Only
Canada	Not applicable (not registered)
USA	Not applicable (not registered)

A.10. Extent of usage in New Zealand and elsewhere and dates of original consent to distribute

Diclofenac patch has not yet been registered or marketed in Australia or New Zealand.

[redacted]

A.11. Labelling or draft labelling for the proposed new presentation

See attached draft artwork in Appendices 6-8.

A.12. Proposed warning statements if applicable

See attached draft artwork in Appendices 6-8.

A.13. Other products containing the same active ingredient and which would be affected by the proposed change

To the best of our knowledge, no diclofenac patches are currently available in New Zealand thus no other product should be affected.

Part B

B.1. A statement of the benefits to both the consumer and to the public expected from the proposed change

Consumer benefit
Pharmacy Only classification allows capacity to obtain professional advice from a pharmacist at the time of purchase.

Public health benefit
Harmonisation with the Australian scheduling for diclofenac patch enables the product to be marketed in New Zealand.

Voltaren Patch provides an additional method of application of a topical NSAID to treat soft tissue injury; and thus serves as another alternative to systemic medications. With demonstrated low systemic absorption, this can be of considerable benefit, especially in the elderly.

B.2. Ease of self-diagnosis or diagnosis by a pharmacist for the condition indicated

Voltaren Patch is indicated for the temporary relief of local pain in acute soft tissue injuries, including sprains and strains (see draft labels in Appendices 6-8). Pain symptoms in these minor ailments are well-characterised, usually of limited duration, and easily identified by a consumer who currently self-select and self-medicate with non-prescription analgesics.

Further, the proposed indication is consistent with the currently available Voltaren Emulgel 1.16% diclofenac diethylammonium gel which has been available for general sale for over ten years: For the temporary relief of local pain in acute soft tissue injuries including sprains and strains (e.g. sports injuries).

Treatment using Voltaren Patch can be managed by the consumer without the need for medical intervention; and can arguably be managed more safely than a topical NSAID gel given it is provided in 'divided preparations'. However, as no patch containing an anti-inflammatory currently exists without a prescription; we acknowledge that consumers would expect the availability of a pharmacist at the point of purchase to assist in selecting and using the product appropriately in order to maximise safe use of the product.

Appropriate use of the product will be further supported by relevant warnings, precautions and directions for use on the product label (see draft labels in Appendices 6-8).

B.3. Relevant comparative data for like compounds

Topical applications, such as Voltaren Patch, are particularly beneficial for symptomatic relief of localised pain, because they are applied directly to the injured area without the risk of introducing systemic side-effects, unlike oral analgesics.

Of key importance in any topical preparation is the level of systemic exposure a patient might experience whether it is from a gel or a patch preparation. As shown in tables 1-3 below, systemic exposure to diclofenac is low for Voltaren Patch compared with topical 1% diclofenac gel and oral 25 mg diclofenac tablet.

Although bioavailability (BA) data for topically applied products is of limited relevance for efficacy purposes; with respect to safety concerns, low systemic absorption BA is favourable in demonstrating that Voltaren Patch has low potential for serious side-effects compared with oral NSAIDs for patients at risk of gastrointestinal events (gastric or duodenal ulceration, perforation or gastrointestinal bleeding); renal events (fluid retention and oedema) or cardiovascular events (hypertension).

[redacted]

[redacted]				

[redacted]

			CI	Reference
[redacted]				

[redacted]

[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

B.4. Local data or special considerations relating to New Zealand

As the product has not yet been registered or marketed in New Zealand, Novartis has not identified any local data or special considerations which could be regarded as being specific to New Zealand.

B.5. Interactions with other medicines

None known. If Voltaren Patch is used as directed, interactions observed in association with oral diclofenac are not expected to occur due to the low systemic rate transfer of the patch.

B.6. Contraindications

Voltaren Patch must not be used:

- in patients with hypersensitivity to the active substance or to any of the excipients
- of the medicinal product;
- in patients with hypersensitivity to any other analgesic and anti-inflammatory drug
- (non-steroidal anti-inflammatory drugs [NSAIDs] including acetylsalicylic acid);
- in patients who have previously experienced an asthma attack, urticaria or acute
- rhinitis when taking acetylsalicylic acid or any other NSAID;
- on open injuries, burns, skin infections or eczema;
- during the last trimester of pregnancy

B.7. Possible resistance

Not applicable.

B.8. Adverse events - nature, frequency etc.

The following frequency categories are used for reporting undesirable effects:

Very common	≥1/10
Common	≥1/100 to <1/10
Uncommon	≥1/1,000 to <1/100
Rare	≥1/10,000 to <1/1,000
Very rare	<1/10,000
Not known	cannot be estimated from the available data

Skin and subcutaneous tissue disorders

- **Common:** Local skin reactions such as skin redness, burning sensation, pruritus, erythema, skin rash, sometimes with pustules or wheals.
- **Uncommon:** Hypersensitivity reactions or local allergic reactions (contact dermatitis).
- **Frequency not known:** In patients using topical NSAIDs, there have been isolated reports of generalised skin rash, hypersensitivity reactions such as angio-oedema, anaphylactic-type reactions and photosensitisation.

The systemic absorption of topically applied diclofenac (either gel or patch) is very low compared to the blood drug concentration following oral administration of diclofenac. Therefore, the probability of undesirable systemic effects (such as gastrointestinal or renal disturbances, bronchospasm) is expected to be minimal. However, if topical preparations of diclofenac were used in large amounts over larger areas of skin for prolonged periods, the potential for systemic absorption and therefore unwanted effects cannot be ruled out.

B.9. Potential for abuse or misuse

No safety trends have been identified in the Novartis global database that would suggest a potential for misuse or abuse with diclofenac patches.

[redacted]

Based on the mechanism of action of diclofenac, a potential for abuse and dependence is not anticipated for this product. It is intended for the treatment of symptoms associated with soft-tissue injuries. Voltaren Emulgel (1.16% diclofenac diethylammonium) currently marketed in Australia is indicated for treatment of symptoms associated with soft tissue injuries as well as tissue rheumatism and nonserious arthritic conditions. This preparation has been available for general sale (unscheduled) for more than 10 years in Australia. No reports of abuse or dependence have been entered in the global safety database since first launch.

The potential for harm from inappropriate use is low as the product is presented in 'divided preparations' where the consumer receives a limited amount of diclofenac, as compared with topical NSAID gels. A warning is presented on the outer carton and pack insert that only one patch is to be used at a time, even if more than one pain site exists.

References

Supporting documentation