

PRIOR AUTHORIZATION POLICY

POLICY: Solaraze® (diclofenac sodium 3% gel – PharmaDerm, generics)

TAC APPROVAL DATE: 06/12/2019

OVERVIEW

Diclofenac sodium 3% gel (Solaraze®, generics) is a topical nonsteroidal anti-inflammatory drug (NSAID) indicated for the topical treatment of actinic keratoses (AK).¹ It is also noted in the labeling that sun avoidance is indicated during therapy. The mechanism of action of diclofenac sodium in the treatment of AK is unknown or not completely understood; however, it is hypothesized that diclofenac sodium may clear AK lesions via cell signaling mechanisms and possibly may play a part in the reduction of angiogenesis and induction of apoptosis (either directly or through a cytotoxic independent pathway).²

There are other topical NSAIDs commercially available in the US: diclofenac sodium topical 1% gel (Voltaren® Gel, generics) which is indicated for the relief of the pain of osteoarthritis (OA) of joints amenable to topical treatment, such as the knees and those of the hands; Flector® Patch (diclofenac epolamine 1.3% topical patch) which is indicated for the topical treatment of acute pain due to minor strains, sprains, and contusions; and Pennsaid® (diclofenac sodium 2% w/w topical solution) which is indicated for the treatment of the pain of OA of the knee(s).³⁻⁵

Other Uses

There are data to support the use of diclofenac sodium 3% gel for the treatment of actinic cheilitis (actinic keratosis of the lips). A report of six cases treated with diclofenac sodium 3% gel demonstrated complete response for five patients and partial response for one patient, after 6 weeks of treatment.⁶ In an open-label study involving 27 patients with actinic cheilitis who completed 30 to 180 days of therapy with diclofenac 3% in 2.5% hyaluronic acid gel, complete remission was observed in 44% of patients (n = 12/27) and a significant improvement in 56% (n = 15/27) of patients was observed.⁷ Another open-label study demonstrated efficacy with diclofenac sodium 3% gel when used for 90 days in 19 patients with actinic cheilitis.⁸

Diclofenac can also be used for the treatment of Bowen's disease, a form of squamous cell carcinoma in situ.^{9,10} There are two published case series (one involving two patients,¹⁰ another involving five patients⁹) which demonstrated clinical and histological resolution of Bowen's disease in all seven patients. In one case series, patients were treated for 90 days, while in the other case series, patients were treated for 8 weeks. Available guidelines detailing management of Bowen's disease note that evaluation of studies on the treatment of Bowen's disease can be problematic due to the varying healing and success rates with the varying locations of the lesions/patches.^{11,12} In addition, the management of Bowen's disease employs several different types of treatment and, like the management of AK, selection of therapy depends on various factors such as lesion characteristics, lesion location, etc. The main treatment options used for Bowen's disease include topical fluorouracil (5-FU), imiquimod, cryotherapy, curettage, excision, photodynamic therapy, radiotherapy, and laser.¹¹

The use of diclofenac sodium 3% gel has been studied in a small open-label study (exact formulation not specified) and in one case series for the management of patients with disseminated superficial actinic porokeratosis (DSAP).^{13,14} In the open-label study, 17 adults with DSAP initially received 12 weeks of therapy with diclofenac sodium 3% gel and could continue for an additional 12 weeks.¹³ At 12 weeks, the target area lesions (treated lesions) had a mean reduction of 4% vs. a 12% mean increase in the total body (global) lesions. For those ten patients who received 24 weeks of therapy, there was a mean increase in the

target area lesions of 10% vs. a mean increase of 19% for the total body (global) lesions at that time point. Only three of the ten patients who completed 24 weeks of therapy had a reduction in their number of lesions. In the eight patient case series, all patients received diclofenac sodium 3% gel for at least 6 months.¹⁴ All of these DSAP patients had tried at least one other therapy (mean was three previous therapies) prior to diclofenac sodium 3% gel. Only two of the eight patients (25%) had a partial response at 6 months. Three other patients received more than 6 months of treatment (7 or 13 months), but none experienced a response. As is typical of other therapies tried for the management of DSAP, results with diclofenac sodium 3% gel demonstrated limited, if not marginal, effectiveness. Most of the therapies tried for DSAP (e.g., cryotherapy, topical 5-FU, topical vitamin D₃ analogues, retinoids, keratolytics, imiquimod, laser, and photodynamic therapy) are ineffective.¹³⁻¹⁵

The benefit of topical diclofenac therapy in osteoarthritis is uncertain. There has been one small, randomized, placebo-controlled study assessing the efficacy of a topical diclofenac 3%/sodium hyaluronate 2.5% gel (Canadian formulation) applied as 2 grams four times daily (QID) to one joint for 2 weeks in patients (n = 119) with uncontrolled OA pain despite chronic (≥ 1 month) oral NSAID use.¹⁶ The addition of topical diclofenac 3%/sodium hyaluronate to oral NSAID therapy resulted in only marginally greater analgesic effect than NSAID alone. Other topical agents are indicated for this use.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of diclofenac sodium 3% gel. All approvals are provided for the duration stated below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of diclofenac sodium 3% gel is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Actinic Keratoses.** Approve for 6 months.

Other Uses with Supportive Evidence

2. **Actinic Cheilitis (Actinic Keratoses of the Lip[s]).** Approve for 6 months.
3. **Bowen's Disease.** Approve for 6 months after a trial of at least one other therapy used for the management of Bowen's disease (e.g., topical 5-fluorouracil [5-FU], imiquimod, cryotherapy, photodynamic therapy, curettage, excision, laser, or radiotherapy).
4. **Disseminated Superficial Actinic Porokeratosis (DSAP).** Approve for 6 months after a trial of at least two other therapies used for the management of DSAP (e.g., topical 5-fluorouracil [5-FU], imiquimod, topical corticosteroids, topical vitamin D₃ analogues, topical or oral retinoids, cryotherapy, photodynamic therapy, and laser).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Diclofenac sodium 3% gel has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Osteoarthritis (OA).**
2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Solaraze® gel [prescribing information]. Melville, NY: PharmaDerm®, a division of Fougere Pharmaceuticals, Inc.; April 2016.
2. Stockfleth E, Ferrandiz C, Grob JJ, et al for the European Skin Academy. Development of a treatment algorithm for actinic keratoses: a European Consensus. *Eur J Dermatol.* 2008;18(6):651-659.
3. Voltaren® Gel [prescribing information]. Princeton, NJ: Sandoz; May 2016.
4. Flector® Patch [prescribing information]. New York, NY: Pfizer; August 2018.
5. Pennsaid® topical solution [prescribing information]. Lake Forest, IL: Horizon Pharma; May 2016.
6. Ulrich C, Forschner T, Ulrich M, et al. Management of actinic cheilitis using diclofenac 3% gel: a report of six cases. *Br J Dermatol.* 2007;556(Suppl 3):43-46.
7. Lima Gda S, da Silva GF, Gomes AP, et al. Diclofenac in hyaluronic acid gel: an alternative treatment for actinic cheilitis. *J Appl Oral Sci.* 2010;18(5):533-537.
8. Nelson CG, Spencer J, Nelson CG Jr. A single-arm, open-label efficacy and tolerability study of diclofenac sodium 3% gel for the treatment of actinic keratosis of the upper and lower lip. *J Drugs Dermatol.* 2007;6(7):712-717.
9. Patel MJ, Stockfleth E. Does progression from actinic keratosis and Bowen's disease end with treatment: diclofenac 3% gel, an old drug in a new environment? *Br J Dermatol.* 2007;156(Suppl 3):53-56.
10. Dawe SA, Salisbury JR, Higgins E. Two cases of Bowen's disease successfully treated topically with 3% diclofenac in 2.5% hyaluronan gel. *Clin Exp Dermatol.* 2005;30(6):712-713.
11. Morton CA, Birnie AJ, Eedy DJ. British Association of Dermatologists' guidelines for the management of squamous cell carcinoma *in situ* (Bowen's disease) 2014. *Br J Dermatol.* 2014;170:245-260.
12. Braathen LR, Szeimies R-M, Basset-Sequin N, et al. Guidelines on the use of photodynamic therapy for nonmelanoma skin cancer: an international consensus. *J Am Acad Dermatol.* 2007;56(1):125-143.
13. Marks S, Varma R, Cantrell W, et al. Diclofenac sodium 3% gel as a potential treatment for disseminated superficial actinic porokeratosis. *J Eur Acad Dermatol Venereol.* 2009;23(1):42-45.
14. Vlachou C, Kanelleuse AI, Martin-Clavijo A, Berth-Jones J. Treatment of disseminated superficial actinic porokeratosis with topical diclofenac gel: a case series. *J Eur Acad Dermatol Venereol.* 2008;22(11):1343-1345.
15. American Osteopathic College of Dermatology. Disseminated superficial actinic porokeratosis. Available at: http://www.aocd.org/skin/dermatologic_diseases/dsap.html. Accessed on June 7, 2019.
16. Roth SH. A controlled clinical investigation of 3% diclofenac/2.5% sodium hyaluronate topical gel in the treatment of uncontrolled pain in chronic oral NSAID users with osteoarthritis. *Int J Tissue React.* 1995;17(4):129-132.

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
Annual revision	No criteria changes	06/08/2016
Annual revision	No criteria changes	06/07/2017
Annual revision	No criteria changes	06/13/2018
Annual revision		06/12/2019

*For a further summary of criteria changes, refer to respective TAC minutes available at: <http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx>; TAC – Therapeutic Assessment Committee.