Highlights of a publication on efficacy and safety of diclofenac sodium gel (DSG 1%) in knee osteoarthritis

HALEON

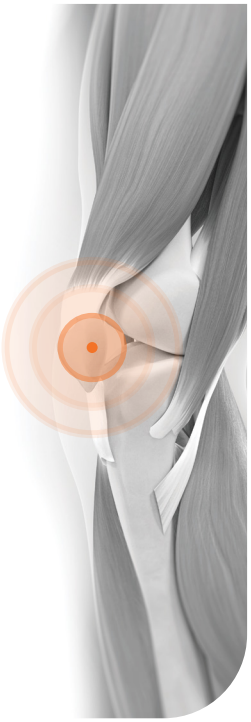
Randomized controlled trial of diclofenac sodium gel in knee osteoarthritis[1]

Barthel HR, Haselwood D, Longley III S, Gold MS, Altman RD.
Semin Arthritis Rheum. 2009;39(3):203-212.

Voltaren
The joy of movement

Background

Osteoarthritis (OA) currently affects approximately 300 million people worldwide.[2] The pain associated with OA commonly presents as a flare that requires use of acute pain-management treatments.



- Oral NSAIDs (nonsteroidal anti-inflammatory drugs) are widely recommended; however, dose-related risks of gastrointestinal, cardiovascular, and hepatotoxicity effects should be considered before use.
- Topical NSAIDs can be recommended prior to oral NSAIDs due to their proven safety and tolerability profile, as well as low systemic exposure.
- The American College of Rheumatology (ACR) guidelines suggested topical NSAIDs are an appropriate first choice for some patients with more limited disease and when medication is required.[3,4]
- ACR and the Osteoarthritis Research Society International (OARSI) guidelines strongly recommend topical NSAIDs for patients with knee OA who don't have comorbidities due to their clinical efficacy and safety profile.[3,4]

DSG 1% is currently the only topical NSAID approved for use in the United States.

Study objective and methodology

A 12-week, randomized, double-blind, vehicle-controlled, parallel-group, multicenter study to assess the efficacy and safety of topical DSG 1% in mild to moderate symptomatic knee osteoarthritis.

Eligibility criteria	• Ambulatory men and women ≥35 years • Diagnosis of OA in 1 or both knees • Symptom onset ≥6 months before screening • Radiograph of the target knee within the previous year graded 1, 2, or 3 on the Kellgren-Lawrence disease severity scale • Baseline pain-on-movement score of ≥50 mm on a 100-mm visual analog scale (VAS) and a baseline Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain subscale score of ≥9 on a 20-point scale
DSG 1% (n=254)	• 4 g 4 times daily
Vehicle (n=238)	• 4 g 4 times daily

Primary outcomes

- WOMAC pain and physical function scores at Week 12
- Global rating of disease at Week 12
- Pain on movement at Week 4

Secondary outcomes

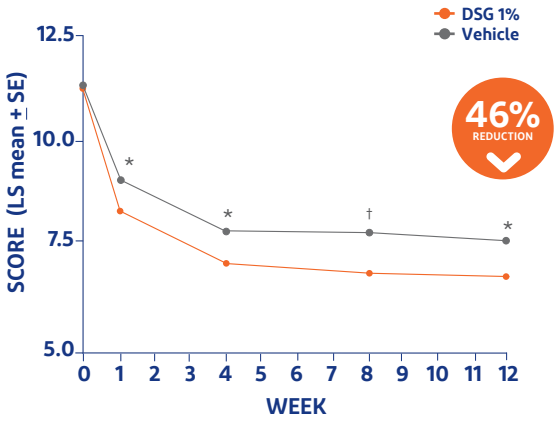
- WOMAC pain and physical function scores and global rating of disease assessment at Weeks 1, 4, and 8
- Pain-on-movement assessment at Weeks 1, 8, and 12
- OARSI response assessed in 2 ways: with the WOMAC pain index or with pain on movement as the pain measure
- Rescue medication use
- Global evaluation of treatment

Results

Efficacy

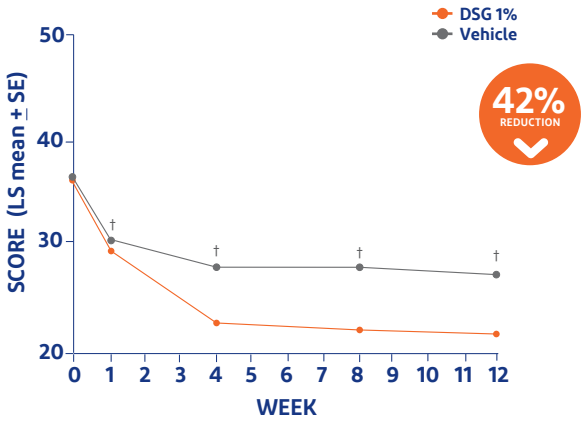
Patients treated with DSG 1% exhibited significant improvement in mean WOMAC pain index, mean WOMAC physical function, mean global rating of disease, and reductions in pain on movement at Week 4 compared to vehicle and baseline.

Pain index



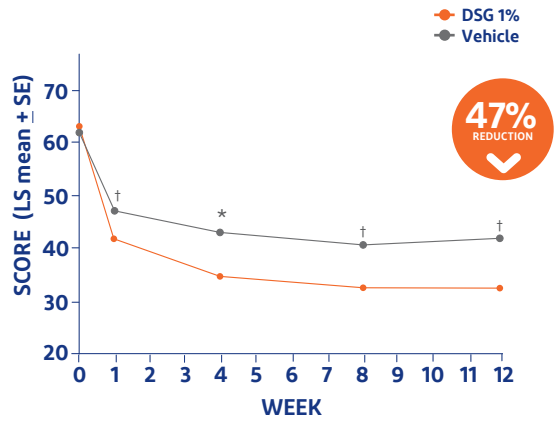
Patients treated with DSG 1% exhibited greater decrease in **WOMAC pain index** (-5.0 versus -4.0; *P*=0.01) relative to baseline

Physical function



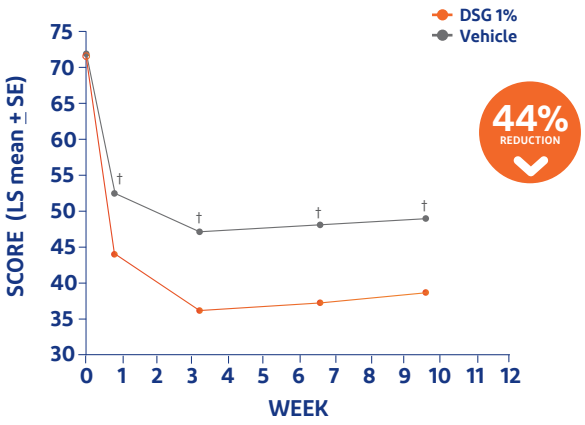
Patients treated with DSG 1% exhibited greater decrease in **WOMAC physical function** (-15.0 versus -10.9; *P*=0.001) relative to baseline

Global rating of disease



Patients treated with DSG 1% exhibited greater mean decrease in **patients' global rating of disease** (-27.0 versus -18.2; *P*<0.001)

Pain on movement



Reductions in **pain on movement at Week 4** were significantly greater with DSG 1% than with vehicle (-27.7 versus -20.1 mm; *P*<0.002)

*$P \leq 0.01$; †$P \leq 0.001$.

Application of DSG 1% leads to greater improvement in pain relief and mobility; up to 43% from baseline–a 10% greater improvement compared to placebo.

Safety

- Adverse events (AEs) in both DSG 1% and vehicle were mild or moderate in severity.
- Gastrointestinal AEs were infrequent and no specific gastrointestinal AE occurred in 3% of patients; the incidence of gastrointestinal disorders was 5.9% with DSG 1% and 5.0% with vehicle.
- Application-site reactions were the most frequent treatment-related AE (5.1% and 2.5% in the DSG 1% and vehicle groups, respectively).
- 82% of patients in the DSG 1% group and 75% of the vehicle group completed treatment. Discontinuation due to AEs was low and similar for both DSG 1% (5.1%) and vehicle (3.8%).

Study strengths

- All endpoints have been widely accepted as meaningful clinical measures of the therapeutic efficacy of a drug.
- Assessment methods were fully validated to measure the clinical efficacy of therapies in patients with OA.

Study limitations

- Only patients with unilateral symptoms were studied; the symptoms of knee OA are often bilateral.
- Duration of study was 12 weeks; OA is a chronic disease and average treatment is likely to be longer.

Conclusions

- DSG 1% in patients with primary OA of the knee achieved statistically and clinically significant improvements of pain and improved measures of physical function compared with vehicle over 12 weeks.
- DSG 1% is an efficacious, first-line treatment option with a proven safety profile, low systemic exposure, and favorable tolerability.
- DSG 1% may be a good treatment option for mild-to-moderate OA of the knee in patients who have contraindications to other OA treatments, or who prefer not to take systemic therapy.

EASE OF USE CERTIFIED
Arthritis Foundation

DSG 1% is indicated for use over-the-counter (OTC) up to 21 days without consulting a physician, so it is appropriate for flares of acute pain.

References

1. Barthel HR, Haselwood D, Longley III S, Gold MS, Altman RD. Randomized controlled trial of diclofenac sodium gel in knee osteoarthritis. *Semin Arthritis Rheum*. 2009;39(3):203-212. **2.** Boer CG, Hatzikotoulas K, Southam L, et al. *Cell*. 2021;184(18):4784-4818. **3.** Kolasinski SL, Neogi T, Hochberg MC, et al. *Arthritis Rheumatol*. 2020;72(2):220-233. **4.** Bannuru RR, Osani MC, Vaysbrot EE, et al. *Osteoarthritis Cartilage*. 2019;27(11):1578-1589.