Zilretta®
triamcinolone acetonide extended release injectable suspension 32 mg

AAOS GUIDELINE UPDATE

ZILRETTA CAN IMPROVE PATIENT OUTCOMES OVER IMMEDIATE-RELEASE CORTICOSTEROIDS

AAOS
American Academy of Orthopaedic Surgeons

Intra-articular (IA) corticosteroids could provide short-term relief for patients with symptomatic osteoarthritis of the knee.[1]

Strength of Recommendation: Moderate ★★★☆

Evidence from two or more "Moderate" quality studies with consistent findings, or evidence from a single "High" quality study for recommending for or against the intervention. Also requires no or only minor concerns addressed in the EtD framework.

Rationale

Our search found 19 high (Campos 2017, Cai 2019, Abou-Raya 2014, Erturk 2016, de Campos 2013, Shrestha 2018, Mendes 2019, Yilmaz 2019, Chao 2010, Raynauld 2003, McAlindon 2017, Henrikson 2015, Neilsen 2018, Riis 2017, Arden 2014, Delgado-Enciso 2019, Smith 2003, Soriano-Maldonado 2016) and 6 moderate quality studies (Conaghan 2018, Langworthy 2019, Gaffney 1995, Yavuz 2012, Yilmaz 2019, Jones 1996) comparing intra-articular corticosteroids to control to treat knee osteoarthritis. Overall pain and function improved with intra-articular corticosteroids; however, it is important to note that such effect lasted only up to 3 months. When we differentiated intra-articular corticosteroids extended versus immediate release (one high, two moderate quality studies) (Bodick 2015, Conaghan 2018 and Langworthy 2019), our analyses demonstrated that, extended release IA steroids can be used over immediate release to improve patient outcomes (Moderate strength recommendation).

The Intra-Articular Corticosteroids recommendation has been downgraded one level because of potential risk in accelerating osteoarthritis from injections.

ZILRETTA is the only available extended-release intra-articular corticosteroid

Evidence Based

Based on a systematic review of 25 high and moderate quality studies, AAOS updated the evidence-based clinical practice guideline on management of osteoarthritis of the knee (OAK) in August 2021—for the first time since 2013.

Differentiated Benefit

Three key publications (Bodick 2015, Conaghan 2018, and Langworthy 2019) supported the differential analysis indicating benefit of extended-release intra-articular steroids (IAS) over immediate-release corticosteroids to improve patient outcomes.[1-4]

Evidence-based review highlights the potential of ZILRETTA to improve outcomes in patients with OA knee pain.

INDICATION AND SELECT IMPORTANT SAFETY INFORMATION

Indication

ZILRETTA is an extended-release synthetic corticosteroid indicated as an intra-articular injection for the management of osteoarthritis pain of the knee.

Limitation of Use: The efficacy and safety of repeat administration of ZILRETTA have not been demonstrated.

Contraindication

ZILRETTA is contraindicated in patients who are hypersensitive to triamcinolone acetonide, corticosteroids, or any components of the product.

Please see Important Safety Information on the reverse of this page and full Prescribing Information.

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Warnings and Precautions

- **Intra-articular Use Only:** ZILRETTA has not been evaluated and should not be administered by epidural, intrathecal, intravenous, intraocular, intramuscular, intradermal, or subcutaneous routes. Serious events have been reported with epidural and intrathecal administration of corticosteroids and none are approved for this use. ZILRETTA should not be considered safe for epidural or intrathecal administration.
- **Hypersensitivity Reactions:** Rare instances of anaphylaxis, including serious cases, have occurred in patients with hypersensitivity to corticosteroids.
- **Joint Infection and Damage:** A marked increase in pain accompanied by local swelling, restriction of joint motion, fever, and malaise are suggestive of septic arthritis. Examine joint fluid to exclude a septic process. If diagnosis is confirmed, institute appropriate antimicrobial therapy. Avoid injecting corticosteroids into a previously infected or unstable joint. Intra-articular administration may result in damage to joint tissues.
- **Increased Risk of Infections:** Infection with any pathogen in any location of the body may be associated with corticosteroid use. Corticosteroids may increase the susceptibility to new infection and decrease resistance and the ability to localize infection.
- **Alterations in Endocrine Function:** Corticosteroids can produce reversible hypothalamic-pituitary-adrenal axis suppression, with potential for adrenal insufficiency after withdrawal of treatment, which may persist for months. In situations of stress during that period, institute corticosteroid replacement therapy.
- **Cardiovascular and Renal Effects:** Corticosteroids can cause blood pressure elevation, salt and water retention, and increased potassium excretion. Monitor patients with congestive heart failure, hypertension, and renal insufficiency for edema, weight gain, and electrolyte imbalance. Dietary salt restriction and potassium supplementation may be needed.
- **Increased Intraocular Pressure:** Corticosteroid use may be associated with increased intraocular pressure. Monitor patients with elevated intraocular pressure for potential treatment adjustment.
- **Gastrointestinal Perforation:** Corticosteroid administration may increase risk of gastrointestinal perforation in patients with certain GI disorders and fresh intestinal anastomoses. Avoid corticosteroids in these patients.
- **Alterations in Bone Density:** Corticosteroids decrease bone formation and increase bone resorption. Special consideration should be given to patients with or at increased risk of osteoporosis prior to treatment.
- **Behavior and Mood Disturbances:** Corticosteroids may cause adverse psychiatric reactions. Prior to treatment, special consideration should be given to patients with previous or current emotional instability or psychiatric illness. Advise patients to immediately report any behavior or mood disturbances.

Adverse Reactions

The most commonly reported adverse reactions (incidence ≥1%) in clinical studies included sinusitis, cough, and contusions.

Please see full Prescribing Information.

References: 1. American Academy of Orthopaedic Surgeons Management of Osteoarthritis of the Knee (Non-Arthroplasty) Evidence-Based Clinical Practice Guideline. https://www.aaos.org/OAK3CPG. Published August 30, 2021. **2.** Bodick N, Lufkin J, Willwerth C, et al. An intra-articular, extended-release formulation of triamcinolone acetonide prolongs and amplifies analgesic effect in patients with osteoarthritis of the knee: a randomized clinical trial. *J Bone Joint Surg Am.* 2015;97(11):877-888. **3.** Conaghan PG, Hunter DJ, Cohen SB, et al. Effects of a single intra-articular injection of a microsphere formulation of triamcinolone acetonide on knee osteoarthritis pain: a double-blinded, randomized, placebo-controlled, multinational study. *J Bone Joint Surg Am.* 2018;100(8):666-677. **4.** Langworthy MJ, Conaghan PG, Ruane JJ, et al. Efficacy of triamcinolone acetonide extended-release in participants with unilateral knee osteoarthritis: a post hoc analysis. *Adv Ther.* 2019;36(6):1398-1411.

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