### Epidural Steroid Injections for Back Pain

#### Summary

Epidural steroid injections (ESIs) are a treatment for back pain that has not responded to conservative measures. Local steroid injections may improve pain by reducing inflammation, thus relieving pressure on nerve roots or other structures that may be the origin of pain.

The evidence for ESIs in patients who have lumbar or cervical radiculopathy includes many small randomized controlled trials (RCTs) and a number of systematic reviews of these RCTs. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, medication use, and treatment-related morbidity. The evidence base lacks large-scale, high-quality trials and has a high degree of variability among the available trials in terms of patient populations, techniques of epidural injections, and comparison treatments. The results of individual trials are mixed, with some reporting significant benefits for the ESI group and others reporting no benefit. Most systematic reviews do not perform pooled analyses due to heterogeneity of trials. In the 2 reviews that reported quantitative results, short-term pain relief at up to 6 months follow-up was superior in patients treated with epidural steroids. None of the analyses reported long-term benefits for treatment with ESIs. Adverse events are generally mild, but were not well reported in these trials. Serious adverse events (SAEs) can occur, but the rate of SAEs is unknown. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

The evidence for ESIs in patients who have spinal stenosis includes 1 moderately large RCT, a few small RCTs, and systematic reviews of these RCTs. Relevant outcomes include symptoms, functional outcomes, health status measures, quality of life, medication use, and treatment-related morbidity. The largest RCT and the majority of smaller trials do not report a benefit for ESIs. The evidence is sufficient to determine qualitatively that the technology is unlikely to improve the net health outcome.

The evidence for ESIs in patients who have nonspecific low back pain includes a number of small RCTs and systematic reviews of these RCTs. Relevant outcomes include symptoms, functional outcomes, health status measures, quality of life, medication use, and treatment-related morbidity. The majority of trials are of low quality and do not report a benefit for ESIs. The evidence is insufficient to determine the effects of the technology on health outcomes.

#### Related Policies

7.01.87  Artificial Intervertebral Disc: Lumbar Spine
Epidural steroid injections performed with fluoroscopic guidance may be considered medically necessary for the treatment of back pain when the following criteria are met:

- Lumbar or cervical radiculopathy (sciatica) that is not responsive to at least 4 weeks of conservative management (see Policy Guidelines section); AND
- Persistent pain is present of at least moderate-severe intensity; AND
- Short-term relief of pain is the anticipated outcome;

Repeat treatment of persistent pain due to radiculopathy/sciatica may be considered medically necessary under the following conditions:

- Previous epidural steroid injections were successful at relieving pain; AND
- At least 30 days have elapsed since the prior injection (see Policy Guidelines for maximum number of injections); AND
- No more than 6 injections given over a 12 month period.

Repeat treatment is considered not medically necessary if the initial treatment did not result in substantial pain relief.

Simultaneous treatment of two vertebral levels may be considered medically necessary if criteria are met at each level.

Simultaneous treatment of more than two vertebral levels is considered not medically necessary.

Epidural steroid injections are considered investigational in all other situations, including but not limited to treatment of spinal stenosis and nonspecific low back pain.

The use of fluorography (imaging of the epidural space) as a component of epidural steroid injections is considered investigational.

Policy Guidelines

The diagnosis of lumbar radiculopathy is typically made by a combination of suggestive signs and symptoms in conjunction with imaging that demonstrates compression of a spinal nerve root. Symptoms are due to irritation of the spinal nerve root at L4, L5, or S1, and may include posterior leg pain that extends past the knee, a loss of sensation in a dermatomal pattern, and/or loss of deep
tendon reflexes. However, all of these symptoms may not be present. On exam, provocative tests such as the straight leg maneuver are positive. Magnetic resonance imaging (MRI) is the most useful imaging modality and can confirm or exclude the presence of nerve root compression, most commonly due to herniated disc.

There are several aspects of epidural steroid injection therapy that are not standardized. Expert opinion was sought through clinical vetting on the following issues:

- The optimal time for assessing a response to epidural steroid injections. Expert opinion supports that response can be assessed anytime from immediately to several weeks after the procedure, with the most popular time to assess response being 1 to 2 weeks after injection.
- The definition of a clinically significant response to injections. Expert opinion supports that a reasonable definition of response is at least a 20-point improvement on a 0-100 VAS scale, or an improvement of at least 50% in functional status, when measured using a validated scale.
- The maximum number of injections in 1 year. There is not agreement on the maximum number of injections that should be given in one year. Some experts agree that no more than 3 injections should be given in 1 year, but other experts believe that more than 3 per year can be used safely. None of the expert opinion supported more than 6 injections given over a 12 month period.

Conservative nonsurgical therapy for at least 4 weeks should include the following:

- Use of prescription strength analgesics for several weeks at a dose sufficient to induce a therapeutic response
  - Analgesics should include anti-inflammatory medications with or without adjunctive medications such as nerve membrane stabilizers or muscle relaxants AND
- Participation in at least 4 weeks of physical therapy (including active exercise) or documentation of why the patient could not tolerate physical therapy, AND
- Evaluation and appropriate management of associated cognitive and behavioral issues

Background

Back pain is an extremely common condition. Most episodes are self-limited and will resolve within 1 month, but a small percentage will persist and become chronic. Patients with chronic back pain may suffer from serious disability and may use a high volume of medical services. Despite high utilization, many patients with chronic back pain do not improve with available treatments including surgical interventions. Therefore, there is a high unmet need to determine the efficacy of different treatments for chronic back pain and to determine specific patient populations who may benefit from specific interventions. Along with this unmet need for efficacious treatments in patients with chronic back pain, there has been a proliferation of new technologies, and large increases in the number of patients treated and in the intensity of treatment. Therefore, there is a concern for overtreatment of patients who may not benefit from interventions for back pain.

Back pain can result from a variety of underlying causes. Sciatica is a subset of low back pain that is associated with irritation of 1 or more lumbar spinal nerve roots, which results in symptoms of
radiculopathy. Symptoms of radiculopathy include pain that radiates down the leg to below the knee, numbness, muscle weakness, and lack of reflexes in a dermatomal distribution. Most patients with sciatica respond to conservative care with resolution of their symptoms between several weeks and several months following onset. In a subset of patients, symptoms and signs of progressive muscle weakness prompt a more aggressive intervention to prevent permanent dysfunction. In other patients, symptoms persist, despite conservative management, without progression of neurologic signs, and further treatment options are sought for pain relief.

Spinal stenosis is another common source of back pain. Spinal stenosis is caused by narrowing of the spinal canal due to degenerative changes, leading to impingement of the spinal cord and the spinal nerve roots. Symptoms of spinal stenosis can include back pain, leg pain with exertion (neurogenic claudication), muscle weakness, and sensory deficits. Definitive treatment for spinal stenosis is surgery, which includes decompression of the spinal canal with or without spinal fusion. Epidural steroids may reduce inflammation from pressure on the spinal cord, and thus reduce symptoms of compression.

Nonspecific low back pain, sometimes called mechanical low back pain, is diagnosed when no specific etiology of pain can be identified. While the origin of nonspecific low back pain is not certain, many experts feel that the pain is of discogenic origin or due to painful movement of the vertebrae. In these instances, epidural steroid injections may reduce swelling of the vertebral disc and/or surrounding structures, leading to pain relief.

Regardless of specific etiology, conservative management is the first-line treatment for most patients with back pain. Nonsteroidal anti-inflammatory drugs (NSAIDs) or other analgesics are used for symptom relief. These agents should be used at a sufficient dose to induce a therapeutic response for at least several weeks. Modification of activity in conjunction with some form of exercise therapy, often involving a physical therapist, is usually also prescribed early in the course of symptoms. For patients with persistent nonradicular back pain, current guidelines recommend interdisciplinary rehabilitation, which is defined as an integrated approach using physical rehabilitation in conjunction with a psychological or psychosocial intervention.

For patients who fail conservative therapy, there are a number of interventional techniques available, ranging from minimally invasive procedures such as injections to major surgeries such as spinal decompression with fusion. Injections can be given in different locations (soft tissues, intraspinal, SI joints, etc.) and can use different therapeutic agents (eg, botulinum toxin, steroids, proteolytic enzymes). Other interventional techniques include radiofrequency ablation, prolotherapy, and chemonucleolysis. Most of these nonsurgical interventions do not have high-quality evidence demonstrating efficacy. Numerous different surgical interventions are available, such as discectomy and spinal fusion, each of which can be performed by a variety of different techniques. The decision to undertake surgery is best made in the setting of shared decision making between the patient and surgeon, with thorough considerations of the risks and benefits of surgery.

Epidural Steroid Injections

Epidural injection therapy is one of several second-line therapies available for patients who fail conservative treatment and is one of the most common modalities used for patients who fail initial
Epidural injections are performed by inserting a needle into the space between the dura and ligamentum flavum and injecting a steroid preparation. There is considerable variability in the technical aspects of epidural injections. There are several different approaches possible for entering the epidural space (translaminar, transforaminal, caudal). In addition, the procedure may be performed with or without fluoroscopic guidance. A national survey published in 2002 reported that 30% of academic institutions and 77% of private practices use fluoroscopy. Other authors have estimated that lack of correct needle position in the epidural space may occur in 25% of more of injections. Further variability of technique may involve factors such as the depth of injection into the epidural space, volume of injectate, and the filling patterns of the injectate.

Treatment is generally given as 1 to 3 injections, each performed at least 1 month apart. Treatment is generally limited to no more than 3 injections in a 12-month period, owing to concerns about the AEs of chronic steroid administration, both locally and systemically.

### Regulatory Status

Steroids are not U.S. Food and Drug Administration (FDA)–approved for use as epidural injections, such use represents off-label use of an FDA-approved medication. The specific preparations used for epidural injections are steroids added to a sterile saline solution, which are prepared by a compounding pharmacy.

### Rationale

Assessment of efficacy for therapeutic intervention involves a determination of whether the intervention improves health outcomes. The optimal study design for this purpose is a randomized controlled trial (RCT) that includes clinically relevant measures of health outcomes. Intermediate outcome measures, also known as surrogate outcome measures, may also be adequate if there is an established link between the intermediate outcome and true health outcomes. Nonrandomized comparative studies and uncontrolled studies can sometimes provide useful information on health outcomes but are prone to biases such as noncomparability of treatment groups, placebo effect, and variable natural history of the condition.

The evidence base on the efficacy of epidural steroid injections for back pain is large, with many RCTs published. In addition to the RCTs, there have been numerous systematic reviews of RCTs published. This literature review will therefore concentrate on a representative sample of the available systematic reviews of RCTs, emphasizing the most recently published systematic reviews.

### Sciatica/Radiculopathy

#### Lumbar Radiculopathy/Sciatica

A systematic review of epidural injections for sciatica was published by Pinto et al in 2012. This review included RCTs that included information on at least 1 of the outcomes of overall pain, leg pain, back pain, or disability status. There were a total of 25 publications included in the review, representing 23 unique trials. The sample size in the trials ranged from 23 to 325, with most studies enrolling fewer than
100 patients. Using the GRADE classification, the level of quality was determined to be high for each outcome.

Pooled results for each of the outcomes are summarized in Table 1. The magnitude of the between-group differences is small, and statistically significant only for the outcomes of short-term leg pain and short-term disability. The greatest magnitude of difference was 6.2 units on a 0 to 100 visual analog scale (VAS) for short-term leg pain. This magnitude of difference is below the minimally important difference for a 0 to 100 pain scale, which is generally considered to be in the range of 10 to 30 units.7

Table 1. Pooled Results From Pinto et al3 Systematic Review

<table>
<thead>
<tr>
<th>Outcome (0-100 Scale)</th>
<th>Weighted Mean Difference Between Groups (95% CI)</th>
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<tbody>
<tr>
<td></td>
<td>Short Term</td>
</tr>
<tr>
<td>Leg pain</td>
<td>-6.2 (-9.0 to -3.0)</td>
</tr>
<tr>
<td>Back pain</td>
<td>0.5 (-3.9 to 4.8)</td>
</tr>
<tr>
<td>Disability</td>
<td>-3.1 (-5.0 to -1.2)</td>
</tr>
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</table>

CI: confidence interval. ESI: epidural steroid injection.

Benyamin et al published a systematic review that included RCTs and non-RCTs of epidural injections in patients with low back pain and/or leg pain.2 There were 19 studies that met the inclusion criteria. Most of these trials (13/19) compared epidural steroids with an active control and 5 of 19 used a placebo control. A qualitative summary of studies was performed, without any quantitative meta-analysis. Subgroup analysis was performed on studies that included patients with disc herniation and radiculopathy. The authors also separated the intervention into studies that used fluoroscopic guidance. Of the 8 studies that used fluoroscopic guidance, all reported short-term results that favored epidural steroid injections. Among 4 trials that reported longer term follow-up at 1 year, 2 were positive and 2 were negative.

Chou et al included epidural steroid injection for low back pain with radiculopathy as part of their systematic review of nonsurgical interventional therapies for low back pain.4 These authors identified 17 RCTs reporting on short-term benefit, and 4 RCTs reporting on longer term benefit. For short-term benefits, the results were mixed. A total of 10 of 17 trials reported no benefit, and 7 of 17 reported a statistically significant benefit. Of the 7 trials that were rated higher quality, 4 of 7 reported a benefit and 3 of 7 reported no benefit. Subgroup analysis by type of placebo control (epidural or soft tissue injection) revealed that most trials using a soft tissue control injection (5/6) reported a benefit, while most of these trials using an epidural control injection (9/11) reported no benefit. Other subgroup analyses based on duration of symptoms, use of imaging to confirm prolapsed disc, and study quality did not show any significant differences.

A systematic review by Manchikanti et al identified 13 RCTs that evaluated epidural steroid injections for the treatment of lumbar radiculopathy.5 Two of these trials compared epidural steroids with placebo and the remaining compared epidural steroids with an active control. No pooled analysis was performed. The authors reported that most of the trials reported positive effects for both short-term and long-term pain relief.
An earlier systematic review and meta-analysis was published in 1995 by Watts and Silagy. This review included 11 trials of epidural steroids that were judged to be of good quality, enrolling a total of 907 patients. The odds of pain relief (defined as at least 75% reduction in pain scores) at 60 days posttreatment for the epidural steroid group compared with control was 2.61 (95% CI, 1.90 to 3.77). At 12-month follow-up, there was also a statistically significant improvement in the odds of pain relief (odds ratio [OR] = 1.87; 95% CI, 1.31 to 2.68).

Several individual RCTs have been completed since publication of the most recent systematic reviews. These trials have corroborated the results of previous research, generally reporting a small benefit for treatment with ESI. The largest of these trials was a double-blind, sham-controlled study that compared ESI with gabapentin in 145 patients with lumbar radiculopathy. There were no differences between groups for the primary outcome of change in pain scores. At 1 month, the change in pain scores in the ESI group was -2.2 (SD=2.4) versus -1.7 (SD=2.6) in the gabapentin group (p=0.25); at 3 months, the change in pain scores were -2.0 (SD=2.6) in the ESI group versus -1.6 (SD=2.7) in the gabapentin group (p=0.43). ESI was superior to gabapentin on some secondary outcomes at 1 month (eg, percent successful outcome, 66% in ESI group vs 46% in gabapentin group; p=0.02); however, at 3 months, these differences were no longer significant.

In the RCT with the longest follow-up of 2 years, 120 patients were randomized to ESI or sham control. Primary outcome measures were at least 50% improvement on the Oswestry Disability Index and the numeric pain rating scale. There were no differences between groups reporting a good response, with 57% in the ESI group and 65% in the sham group reporting at least 50% improvement at 2 years (p=NS). Another RCT randomized 63 patients from general medical practices in the Netherlands to usual care or usual care plus 1 injection of ESI. The main outcomes were change in numeric pain scores and the Roland-Morris Disability Questionnaire (RMDQ) score. A small, statistically significant difference was found in favor of the ESI group on both outcomes, but was considered too small to be clinically relevant.

Cervical Radiculopathy

There are a smaller number of published trials on the use of epidural steroids for cervical radiculopathy. Two systematic reviews were identified that summarized the literature on cervical epidural injections for cervical radiculopathy.

Benyamin et al included studies of epidural injections for neck pain that was present for more than 3 months, with or without radiculopathy. The authors identified 3 RCTs that met their inclusion criteria, all of which treated patients with cervical radiculopathy, but only 1 of which compared epidural steroids with a control condition. One of the other trials compared 2 different preparations of steroids, and the third trial compared steroids plus morphine with steroids alone. In the single trial comparing steroids with control, 42 patients were randomized to epidural steroid injections (n=24) or to steroid injections in the adjacent neck muscle. One week after the last epidural injection, more patients in the epidural group reported good pain relief compared with control (76% vs 36%, p not reported), and at 1-year follow-up, the difference in the percent of patients reporting good pain improvement persisted in favor of the epidural steroid group (68% vs 12%, p not reported).

Diwan et al performed a systematic review of epidural steroid injections for chronic neck and upper extremity pain and reported separately on the evidence for cervical radiculopathy. This analysis
included 4 RCTs, 3 of which were included in the Benyamin 2009 review. The fourth RCT, which was the largest (n=120) and rated the highest in quality, randomized patients to epidural steroid plus local anesthetic versus local anesthetic alone, and reported on pain relief at 6 months and 12 months. At 6 months, the percent of patients experiencing pain relief was 82% for the steroid group versus 73% for the control group, a difference that was not statistically significant. At 12 months, outcomes were also not different between groups, with 72% of patients in the steroid group reporting pain relief compared with 68% in the control group.

Since the time these systematic reviews were published, Cohen et al reported the results of an RCT in 2014, which compared ESI, conservative treatment, or a combination of both for patients with cervical radiculopathy.14 A total of 169 patients were randomized to conservative care (physical therapy plus medications), ESIs, or a combination of both treatments. The primary outcomes were neck and arm pain measured at 1 and 3 months posttreatment. There were no differences noted between ESI and conservative care on any of the outcome measures. The group receiving combination therapy had a greater reduction in arm pain at 1 month compared with the 2 individual treatments, and had a greater success rate at 3 months (56.9% vs 26.8%, p=0.006).

**Section Summary**

There are a large number of small RCTs that evaluate epidural steroid injections for lumbar radiculopathy/sciatica, and numerous systematic reviews that summarize these trials. For short-term pain relief, the direction of benefit in virtually all trials is in favor of epidural injections, and the differences between groups reached statistical significance in some trials but not others. Most systematic reviews do not perform quantitative meta-analysis, thus limiting the ability to examine these small trials with increased power. In 1 meta-analysis that reported pooled results, there was a statistically significant improvement in pain at 6 months, but the mean difference was less than the minimally important clinical difference for a 0 to 100 VAS pain scale. For long-term pain relief at 1 year or beyond, most trials report negative results, and no pooled analysis reports significant differences.

**Spinal Stenosis**

In the Benyamin 2012 systematic review,2 there were 6 RCTs identified that treated patients with spinal stenosis, 5 of which compared steroid injections with a local anesthetic alone. Two of the trials reported group differences in favor of the steroid group, 3 reported significant improvement in pain for the steroid group but did not report between-group differences, and the final trial reported no significant improvement for the steroid group.

The systematic review by Chou et al4 identified 3 small placebo controlled trials on treatment of spinal stenosis, but in 2 of these studies only a subset of treated patients had spinal stenosis. The authors rated the quality of this evidence poor and concluded that it was not possible to determine whether epidural steroids offer a benefit for spinal stenosis.

Manchikanti et al identified 4 RCTs of epidural steroid injections for treatment of lumbar spinal stenosis.5 Two of these trials compared epidural steroids with control and reported on pain relief and/or disability. Neither of the 2 included trials reported that pain relief with epidural steroids was superior to control, either short term or long term.
The systematic review by Diwan et al identified 1 RCT of 60 patients that treated cervical spinal stenosis. In this trial, there were no significant differences in the percent of patients reporting pain relief in the epidural group compared with control at 6 months (87% vs 80%) or at 12 months (73% vs 70%).

Since the publication of the systematic reviews, an additional moderately large-sized RCT of epidural steroid injections for spinal stenosis was published in 2014. This trial randomized 400 patients with lumbar central spinal stenosis and at least moderate to severe leg pain (≥4 on 0-10 VAS) or disability (≥7 on Roland Morris Disability Questionnaire, 0-24 scale) due to spinal stenosis to either epidural steroid injections plus lidocaine or lidocaine alone. One repeat injection could be given at 3 weeks at the discretion of the patient and treating physician. Both patients and treating physicians were blinded to treatment assignment. The primary outcomes were the patient’s rating of buttocks, hip or leg pain at 6 weeks following initial treatment, and the Roland Morris Disability Questionnaire score at 6 weeks. Secondary outcomes included the same outcome measures at 3 weeks posttreatment, measures of back pain, percent responders (defined either as ≥30% reduction in pain, or ≥50% reduction in pain), and scores on several quality-of-life scales.

At 6-week follow-up, there were no significant differences in the primary outcomes. The change in pain on the 0-10 VAS for the steroid group was -2.8 for the steroid group compared with -2.6 for the control group (adjusted between-group mean difference, -0.2 points; 95% CI, -0.8 to 0.4; p=0.48), and the change in the disability score was -4.2 points for the steroid group versus -3.1 points for the control group (adjusted between group mean difference, -1.0 points; 95% CI, -2.1 to 0.1; p=0.07). There were small, statistically significant differences in measures of pain and disability at 3 weeks, but these were less than the minimal clinical difference for the scales, and differences did not persist at 6 weeks. On the secondary outcomes at 6 weeks, there were generally no between-group differences except for 2 subscales of the QOL measures (symptoms of depression on PHQ-8 scale, and satisfaction on SSSQ scale).

Section Summary

There are only a few RCTs that evaluate epidural steroids for spinal stenosis, and the published systematic reviews do not perform pooled analysis of the available trials. Most published trials do not report significant benefit for epidural steroids, including a moderately large sized RCT published in 2014. This evidence does not support that epidural steroids improve outcomes for patients with spinal stenosis.

Nonspecific Low Back Pain

A Cochrane review was published in 2008 on injection therapy for subacute and chronic low back pain. This review included RCTs that enrolled patients with low back pain for at least 1 month and reported pain outcomes. A total of 18 studies met the inclusion criteria, 10 of which were considered to be at low risk for bias. Due to high levels of heterogeneity, pooled analysis was not performed. Of the 18 included studies, 5 reported a benefit for treatment with epidural steroids. There were 2 placebo-controlled studies of short-term outcomes of leg pain. Neither of these studies reported a significant improvement of pain associated with epidural injections. Three studies compared epidural steroids with
nonsteroidal anti-inflammatory drug (NSAIDs), and none of these reported significant improvements for patients treated with epidural steroids.

The systematic review by Benyamin et al.\(^2\) identified 3 trials of epidural steroid injections for nonspecific low back pain, 1 randomized and 2 nonrandomized. The randomized trial reported a greater percentage of patients with pain relief following epidural steroid injection compared with local anesthetic alone (83% vs 73%), but this between-group difference was not statistically significant. The 2 nonrandomized studies reported improvements for patients treated with epidural steroids, but no between-group comparisons were done.

Manchikanti et al. addressed the indication of nonspecific low back pain (axial low back pain) in their systematic review.\(^5\) However, there were no RCTs identified that met their inclusion criteria, and only 3 nonrandomized studies were included. This evidence was insufficient to form conclusions on the efficacy of epidural steroids for nonspecific low back pain.

**Section Summary**

The evidence on epidural steroid injections for nonspecific low back pain is limited. Small RCTs have been published, but these have generally been judged to be of low quality, and most studies do not report significant improvements for the epidural steroid group. This evidence is not sufficient to determine whether epidural steroids improve outcomes for the treatment of nonspecific low back pain.

**Mixed Indications**

A systematic review by Choi et al published in 2012 included trials of epidural steroids for back pain, regardless of specific indication.\(^17\) There were a total of 29 studies included in the review, of which 23 of 29 met at least 5 of 11 quality criteria. The authors noted evidence for noncomparability of groups (selection bias) at baseline, particularly for the baseline pain levels. For pain outcomes, combined analysis revealed a statistically significant difference in favor of epidural steroids at 6 months (weighted mean difference, -0.41; 95% CI, -0.66 to -0.16) but a nonsignificant result at 12 months. For disability level, there were no statistically significant differences between groups at either 6- or 12-month follow-up. There was also no difference reported in the need for future surgery for patients receiving epidural steroid injections.

**Safety**

Potential adverse effects (AEs) of epidural steroid injections can include complications of the injection itself, such as inadvertent puncture of the dura, bleeding, and infections. Additional complications may be related to the administration of steroids, including suppression of the hypothalamic-pituitary axis and the immune system.

The adverse effects (AEs) of epidural steroid injections are not well-reported in the treatment trials. In 1 systematic review, only 4 of 15 included trials reported on adverse events.\(^18\) In addition to the lack of systematic reporting of AEs, the available trials are generally small and therefore not adequate for determining rates of uncommon AEs. A consensus panel convened in part by the U.S. Food and Drug Administration (FDA) reviewed the literature on serious neurologic complications following ESI.\(^19\) The
evidence was restricted to case reports and reports of malpractice claims. Reports included direct needle injury to the spinal cord, arterial injury, swelling of an unrecognized epidural lesion, and paraplegia/stroke. Based on the pattern of reports, the report concluded that stroke and paraplegia were likely caused by intraarticular injection of particulate steroids. Therefore, the rate of AEs is mostly uncertain.

In the systematic review by Chou et al, it was noted that while there were case reports of serious adverse events (SAEs) such as paralysis and infection due to epidural injections in the literature, SAEs were rarely reported in the clinical trials. Of the 17 trials included in the treatment of low back pain with radiculopathy, 10 of 17 did not report AEs at all, and the AEs reported in the other trials were generally transient and mild. In 1 high-quality trial with systematic reporting of AEs, 3.3% of patients (4/120) experienced a postinjection headache, 0.8% (1/120) experienced postdural puncture headache, 1.7% (2/120) experienced postinjection nausea, and 4.2% (5/120) experienced other AEs.

In 2014, FDA issued a drug safety communication on rare but serious neurologic problems associated with epidural steroid injections. This communication stated that the safety of epidural injections has not been established and that FDA has not approved corticosteroids for this use. Potential serious adverse neurologic events include loss of vision, stroke, paralysis, and death.

The FDA subsequently assembled an expert panel that issued a report in 2015. This report included a series of recommendations regarding the ESI technique, including clinically relevant issues related to its performance, such as the use of particulate steroids, use of contrast, and use of sedation.

Epidural steroids are generally compounded medications, ie, the specific preparations for clinical use are prepared at a pharmacy rather than by the manufacturer of the drug. In 2012, there were several hundred patients who developed fungal meningitis complications due to contaminated medication obtained from a single pharmacy. CDC obtained preliminary data on 137 patients. Of those, 12 of 137 patients (9%) died, 3 of 137 (2%) had stroke, and 3 of 137 (2%) had osteomyelitis or epidural abscess. The contamination was attributed to faulty sterilization procedures at the pharmacy that compounded the medications.

Section Summary

AEs, both minor and serious, can occur following ESIs. For serious neurologic events, the evidence consists of case reports and as a result, the rate of SAEs is uncertain. Few SAEs have been reported in the RCTs, but there is also a lack of systematic reporting in the available trials. Minor AEs that are self-limited (eg, headache) are more common, but the evidence is not sufficient to determine the actual rate of such events. Further research is needed to determine the true rate of AEs attributable to ESIs. The FDA consensus panel has issued guidelines for the technical performance of ESI with the goal of reducing potential serious neurologic events.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in Table 2.
Table 2. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
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<tbody>
<tr>
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<tr>
<td>NCT01934868</td>
<td>A Comparison of the Long Term Outcomes of Prolotherapy Versus Interlaminar Epidural Steroid Injections (ESI) for Lumbar Pain Radiating to the Leg</td>
<td>160</td>
<td>May 2017</td>
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<tr>
<td><strong>Unpublished</strong></td>
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<tr>
<td>NCT02196883</td>
<td>A Prospective, Randomized, Single Blind Study Comparing Transforaminal Epidural Steroid Injections at the Level of MRI Pathology vs Clinical Symptoms</td>
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<td>NCT01495923</td>
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</table>

NCT: national clinical trial.

Summary of Evidence

The evidence for epidural steroid injections (ESIs) in patients who have lumbar or cervical radiculopathy includes many small randomized controlled trials (RCTs) and a number of systematic reviews of these RCTs. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, medication use, and treatment-related morbidity. The evidence base lacks large-scale, high-quality trials and has a high degree of variability among the available trials in terms of patient populations, techniques of epidural injections, and comparison treatments. The results of individual trials are mixed, with some reporting significant benefits for the ESI group and others reporting no benefit. Most systematic reviews do not perform pooled analyses due to heterogeneity of trials. In the 2 reviews that reported quantitative results, short-term pain relief at up to 6 months follow-up was superior in patients treated with epidural steroids. None of the analyses reported long-term benefits for treatment with ESIs. Adverse events are generally mild, but were not well reported in these trials. Serious adverse events (SAEs) can occur, but the rate of SAEs is unknown. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

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The evidence for ESIs in patients who have nonspecific low back pain includes a number of small RCTs and systematic reviews of these RCTs. Relevant outcomes include symptoms, functional outcomes, health status measures, quality of life, medication use, and treatment-related morbidity. The majority of trials are of low quality and do not report a benefit for ESIs. The evidence is insufficient to determine the effects of the technology on health outcomes.
Practice Guidelines and Position Statements

The 2014 update of the guidelines for the performance of fusion procedures for degenerative disease of the lumbar spine from the American Association of Neurological Surgeons\textsuperscript{22} states that lumbar epidural steroid injections are an option for short-term relief of chronic low back pain without radiculopathy in patients with degenerative disease of the lumbar spine. (Level III evidence.) Caudal epidural steroid injections are an option for reducing low back pain without radiculopathy of greater than 6 weeks’ duration in patients with degenerative disease of the lumbar spine. (Level III evidence).

The Agency for Healthcare Research and Quality issued an evidence-based practice center systematic review protocol in 2014. Project title: Pain management injection therapies for low back pain\textsuperscript{23} stated that between 1994 and 2001, the use of epidural injections increased by 271 percent and facet joint injections increased by 231 percent among Medicare beneficiaries. Despite these dramatic increases, use of injection therapies for low back pain remains controversial. Systematic reviews of injection therapies have come to conflicting conclusions regarding the benefits of injection therapies, and clinical practice guidelines provide discordant recommendations regarding their use. Important challenges in conducting a review of this topic include sparse data from randomized trials for most injection therapies (with the exception of epidural steroids), inconsistency of results across trials, as well as variability across studies in the methods used to select patients for inclusion, the specific techniques used, the comparisons evaluated, and the outcomes assessed.\textsuperscript{17}

The 2012 North American Spine Society clinical guidelines for multidisciplinary spine care diagnosis and treatment of lumbar disc herniation with radiculopathy\textsuperscript{24} stated there were no studies available which directly addressed the role of epidural steroid injections or selective nerve root blocks in the diagnosis of patient selection for subsequent surgical treatment of a lumbar disc herniation with radiculopathy.

In 2011, the North American Spine Society revised their clinical guidelines for multidisciplinary spine care diagnosis and treatment of degenerative lumbar spinal stenosis.\textsuperscript{25} They made the following recommendation: a multiple injection regimen of radiographically-guided transforaminal epidural steroid injection or caudal injections is suggested to produce medium-term (3-36 months) relief of pain in patients with radiculopathy or neurogenic intermittent claudication from lumbar spinal stenosis. Grade C recommendation

The North American Spine Society issued 2010 clinical guidelines for multidisciplinary spine care diagnosis and treatment of cervical radiculopathy from degenerative disorders.\textsuperscript{26} The following grade C recommendation was made: Transforaminal epidural steroid injections using fluoroscopic or CT guidance may be considered when developing a medical/interventional treatment plan for patients with cervical radiculopathy from degenerative disorders. Due consideration should be given to the potential complications.

The 2013 North American Spine Society issued a review and recommendation statement for lumbar transforaminal epidural steroid injections (LTFESI).\textsuperscript{272} The following recommendations were made:
• Transforaminal epidural steroid injections using fluoroscopic or CT guidance may be considered when developing a medical/interventional treatment plan for patients with cervical radiculopathy from degenerative disorders. Due consideration should be given to the potential complications. Level of evidence III

• Patients with lumbar scoliotic stenosis and radiculopathy experience significantly higher success rates if their symptoms were present for less than three months. Level of evidence IV

• There is no significant difference between EMG-positive and -negative groups in terms of pain difference, but a mild functional improvement in an EMG positive patient undergoing LTFESI. Level of evidence V

The 2011 North American Spine Society issued a review and recommendation statement for cervical epidural steroid injections. The following recommendation was made: Both transforaminal and interlaminar epidural steroid injections may be considered to provide short- and long-term relief of cervical radiculitis. Recommendation level C

The 2010 guidelines on chronic pain management from the American Society of Anesthesiologists state that transforaminal epidural injections should be performed with appropriate image guidance to confirm correct needle position and spread of contrast before injecting therapeutic substances. Image guidance may be considered for interlaminar epidural injections to confirm correct needle position and spread of contrast before injecting therapeutic substance.

The American College of Physicians issued a 2008 guideline for the diagnosis and treatment of low back pain that stated: Patients with persistent low back pain and signs and symptoms of radiculopathy or spinal stenosis should be evaluated with MRI (preferred) or CT only if they are potential candidates for surgery or epidural steroid injection. (Strong recommendation, moderate-quality evidence)

The American Pain Society published guidelines on the use of interventional therapies for low back pain in 2009, based on a systematic review of the evidence published in the same year. These guidelines made the following recommendations regarding epidural steroid injections:

• In patients with persistent radiculopathy due to herniated lumbar disc, it is recommended that clinicians discuss risks and benefits of epidural steroid injections as an option (weak recommendation, moderate quality evidence). It is recommended that shared decision making regarding epidural steroid injection include a specific discussion about inconsistent evidence showing moderate short-term benefits, and lack of long-term benefits.

• There is insufficient evidence to adequately evaluate benefits and harms of epidural steroid injection for spinal stenosis.

• There is insufficient evidence to adequately evaluate benefits of local injections, botulinum toxin injection, epidural steroid injection, intradiscal electrothermal therapy, therapeutic medial branch block, radiofrequency denervation, sacroiliac joint steroid injection, or intrathecal therapy with opioids or other medications for nonradicular back pain.
The American Society of Interventional Pain Physicians published updated guidelines for interventional techniques in chronic spinal pain. The following recommendations were made regarding epidural steroid injections of the lumbar spine:

- The evidence is good in managing disc herniation or radiculitis for caudal, interlaminar, and transforaminal epidural injections;
- The evidence is fair for axial or discogenic pain without disc herniation, radiculitis or facet joint pain with caudal, and interlaminar epidural injections, and limited for transforaminal epidural injections;
- The evidence is fair for spinal stenosis with caudal, interlaminar, and transforaminal epidural injections;
- The evidence is fair for postsurgery syndrome with caudal epidural injections and limited with transforaminal epidural injections.

The following recommendations were made regarding epidural steroid injections of the cervical spine:

- The evidence is good for cervical interlaminar epidural injections for cervical disc herniation or radiculitis.
- The evidence is fair for axial or discogenic pain, spinal stenosis, and postsurgery syndrome.

The American Academy of Neurology published guidelines in 2007 on the use of epidural steroids for lumbosacral radiculopathy. These guidelines made the following recommendations:

- Epidural steroid injections may result in some improvement in radicular lumbosacral pain when determined between two and six weeks following the injection, compared to control treatment (Level C, Class I-III). The average magnitude of effect is small, and the generalizability of the observation is limited by the small number of studies, limited to highly selected patient populations, the few techniques and doses studied, and variable comparison treatments.
- In general, epidural steroid injections for radicular lumbosacral pain have shown no impact on average impairment of function, on need for surgery, or on long-term pain relief beyond three months. Their routine use for these indications is not recommended (Level B, Class I-III).
- Data on the use of epidural steroid injections to treat cervical radicular pain are inadequate to make any recommendation (Level U).

**U.S. Preventive Services Task Force Recommendations**

Epidural steroid injection is not a preventive service.

**Medicare National Coverage**

No national coverage determination (NCD) for epidural steroid injections was found. In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.
References


### Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Reason</th>
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<tbody>
<tr>
<td>December 2014</td>
<td>New Policy</td>
<td>Policy created with literature review. Epidural steroid injections are medically necessary for treatment of lumbar sciatica/radiculopathy when criteria are met, not medically necessary if previous epidural injections were not successful, and investigational for all other situations.</td>
</tr>
<tr>
<td>June 2016</td>
<td>Update Policy</td>
<td>Policy updated with literature review through October 15, 2015; references 9-11, 14, and 19 added. Minor editorial changes to the policy statement with the intent unchanged.</td>
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This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 24, 2016 and is effective July 15, 2016.

Deborah M. Smith, MD, MPH