



Preserving the integrity of competition. Inspiring true sport. Protecting the rights of athletes.

ATHLETES & PRESCRIBING PHYSICIANS PLEASE READ

USADA can grant a Therapeutic Use Exemption (TUE) in compliance with the World Anti-Doping Agency International Standard for TUEs. The TUE application process is thorough and designed to balance the need to provide athletes access to critical medication while protecting the rights of clean athletes to compete on a level playing field.

Included in this document is a checklist of items necessary for a complete TUE Application and the WADA Guidelines used to evaluate TUE Applications for your specific condition. (Please be aware that the TUE Committee may ask for additional information while evaluating TUE Applications). It is important that the TUE Application include all the documentation outlined in the checklist below. Please reference the included guidelines for details related to types of diagnoses, specific laboratory tests, and more.

TUE APPLICATION CHECKLIST – MUSCULOSKELETAL CONDITIONS

- Complete and legible TUE Application form
- Copies of all relevant examinations and clinical notes from the original diagnosis through present
 - If the athlete received surgery for the injury, a surgical summary should be included
 - The intended duration of the medication regimen should be specified (2 weeks, long term, etc.)
- Copies of all laboratory results/reports related to the diagnosis
- A statement from the physician explaining why the Prohibited Substance is needed
 - Why other treatments (with either permitted or prohibited substances/methods) failed or are not appropriated for treating the condition.

U.S. Anti-Doping Agency

5555 Tech Center Drive, Suite 200, Colorado Springs, CO 80919 | Tel: 719.785.2000 | Fax: 719.785.2001
usada@usada.org | www.usada.org

MUSCULOSKELETAL CONDITIONS

1. Medical Condition

Musculoskeletal conditions including those arising from injuries are common in sport. In this setting of sport, we traditionally classify injury according to a mechanism of acute macrotrauma or repetitive overuse ranging from minor injuries to muscle, tendon and other “soft tissues” to more serious fractures, dislocations and spinal cord trauma. However, athletes may also suffer from arthropathies with familial or degenerative aetiologies such as osteoarthritis, rheumatological or autoimmune diseases.

The management of musculoskeletal conditions requires some understanding of the inflammatory response and the biochemistry of pain production. Potent anti-inflammatory agents, powerful analgesics and “disease-modifying agents” are amongst the agents used to treat musculoskeletal conditions. This is especially so for conditions such as rheumatoid arthritis, systemic lupus erythematosus and ankylosing spondylitis which may require long-term or intermittent administration of medications. Consequently, the use of such pharmacological agents and hence, the need for a therapeutic use exemption (TUE), will vary. Non-steroidal anti-inflammatory drugs (NSAIDs) are most commonly used for treatment of musculoskeletal conditions and do not require a TUE.

Relevant to the TUE process, there are two classes of prohibited substances commonly used in the management of musculoskeletal conditions. These are glucocorticoids (GCs) and narcotics, both of which are only prohibited “in-competition”. Therefore, a TUE is required only when these substances are necessary during a defined in-competition period and, in the case of GCs, if they are administered via oral, rectal, intramuscular or intravenous routes.

GCs may be used to manage musculoskeletal injuries and conditions because of their potency as anti-inflammatory agents. However, in some instances, their use in competitive sport has become excessive and inappropriate with little regard for potential side effects. The scientific and clinical evidence supporting the liberal use of systemic GCs in sports injuries remains contentious and a conservative approach to their use is recommended.

2. Diagnosis

All musculoskeletal conditions demand an accurate diagnosis invariably involving a complete history and thorough physical examination. In addition, appropriate investigations including imaging modalities such as MRI, CT, nuclear medicine and

ultrasonography plus laboratory tests may be necessary to confirm a diagnosis and rule out any relevant co-morbidity.

The results of appropriate imaging and other investigations should accompany the history and physical examination in the TUE application. The opinion of a specialist in musculoskeletal medicine will strengthen the application.

NOTE: Particular care should be invested in the diagnosis of musculoskeletal conditions affecting the young athlete where premature degeneration or impeded skeletal development may result from inadequate management.

3. Good Medical Practice

A. Classes of the Prohibited Substances

1. Glucocorticoids
2. Narcotics

Indications

1. Glucocorticoids

There is little, if any, evidence to indicate that GCs favorably alter the outcome of the majority of musculoskeletal injuries. While GCs have potent anti-inflammatory effects that may be beneficial in the treatment of selected conditions, the most commonly accepted indications for short-term use are conditions associated with nerve compression such as a herniated intervertebral disc or transient neuropraxia. However, it should be noted again that the use of GCs invokes the TUE process only when these agents are administered via oral, rectal, intramuscular or intravenous routes and are taken just prior to or during a competition. GC administration via all other routes is permitted without a TUE at all times.

For rheumatological and autoimmune conditions, GCs may be necessary to control inflammatory symptoms on an ongoing basis, with transient increase in dosage from time to time during exacerbations of the disease.

2. Narcotics

Narcotics are usually indicated for short-term pain relief following acute injury or post-surgery (typically between 1-7 days). They are seldom prescribed beyond seven days however, this may depend on circumstances including the complexity

of a surgical procedure. The use of narcotic analgesics administered through any route is only prohibited in-competition.

NOTE: Refer to the TUE Physician Guidelines on Neuropathic Pain for further discussion on narcotics as well as the use of cannabinoids.

B. Typical Dosage, Frequency and Duration of Treatment

1. Glucocorticoids

GCs may be administered as a single dose via intramuscular, intra-articular, intrabursal or epidural routes, followed by a sufficient period of time for monitoring and clinical re-evaluation (usually a minimum of seven days). Administration of further doses is determined by the effectiveness of the initial treatment and the severity of the condition. The use of GCs for the treatment of most musculoskeletal conditions via these application routes rarely exceeds three doses.

When GCs are administered orally, they are generally prescribed over a short course of 3-5 days. In a request for the use of oral GCs in the treatment of an acute disc injury, the permitted alternatives of an epidural or a nerve sleeve injection need to be demonstrated as being inappropriate or ineffective.

For chronic inflammatory musculoskeletal diseases (e.g. rheumatoid arthritis), a low maintenance dose of oral GCs may be indicated with transiently increased dosage for exacerbations. The use of a disease activity score and laboratory markers help to guide the use and dosage of GCs in these conditions. Intra-articular GCs may also be administered and do not require a TUE. However, these conditions are not commonly seen in elite athletes.

2. Narcotics

Narcotics are administered in a dosage and frequency sufficient to control severe pain during the acute phases of injury or surgery and during the period of post-operative convalescence. However, it would be highly unlikely that an athlete requiring narcotics for an acute injury would be competing in elite sport. Narcotics may be prescribed, rarely, for chronic pain, typically in disability sport, and usually under the supervision of a specialist (See TUE Physician Guidelines on Neuropathic Pain for more details).

4. Alternative Non-Prohibited Treatments

The accepted management of acute musculoskeletal injuries begins with the simple modalities of rest, ice, compression and elevation. Initial medication may include NSAIDs, non-narcotics and/or muscle relaxants. Other treatment options include modalities such as heat, cryotherapy, traction, ultrasound, electrical stimulation, manual therapy, bracing and therapeutic exercises.

In rheumatological and autoimmune diseases, other immunosuppressive drugs referred to as disease-modifying anti-rheumatic medications may be added as necessary to control the progression of disease. These may include anti-malarials, cytostatics (e.g. methotrexate, azathioprine), TNF-binding proteins (e.g. adalimumab) which are not prohibited and therefore do NOT require a TUE.

5. Consequences to Health if Treatment is Withheld

The consequences of not treating a musculoskeletal condition are continued pain and possible reduced function. GCs are known to have a powerful anti-inflammatory effect, thereby providing relief of pain and swelling in selected conditions. GCs have not been shown to accelerate or promote better healing in musculoskeletal tissues (ligament, tendon, hyaline cartilage, bone, muscle).

6. Monitoring Treatment

The pain and swelling of acute inflammation and the loss of movement typically associated with acute musculoskeletal injuries and conditions are usually short-lived, typically less than one week. While there are certain conditions that require prolonged treatment, these are much less common. The continued use of GCs and/or narcotics may adversely affect the general health and sport performance of the athlete. Systemic GCs use, for example in the management of chronic rheumatological disease, is usually titrated according to disease activity.

7. TUE Validity and Recommended Review Process

The indications, dosage and duration of the use of GCs and narcotics are dependent on the specific musculoskeletal condition or injury. Typically, neither of these medications is administered for longer than one week. If it becomes necessary to extend the use of these agents, the athlete deserves a full review and diagnostic reassessment. This is of particular importance in the management of pre-adolescent and adolescent athletes, and for chronic inflammatory musculoskeletal conditions which may require long-term or recurrent GCs.

Well-documented medical conditions requiring intermittent or recurrent courses of oral glucocorticoids (GCS) could be granted TUEs for up to 12 months. In such cases, conditions should be attached to the TUE approval certificate, requesting either:

1. A notification in writing to the TUEC at the time, or soon after, the GCS are used throughout the 12 month period, or;
2. A written summary of use, from the treating doctor, at the end of the 12-month period.

Note: the TUEC should also reserve the right to request relevant medical records during the time of approval.

These documents are to ensure that systemic GCs are not used around the time of competition, without good medical reason, and will then be used by the TUEC to determine if subsequent approvals for long-term use of GCs will be approved in future.

It is recommended that a more cautious approach should be used with athletes from sports with a higher risk of GC abuse, as longer term approvals may not be appropriate for these groups.

8. Appropriate Cautionary Matters

The prolonged use of GCs, even at low dosages, has the potential for a number of serious side-effects such as Cushingoid features, avascular necrosis of the hip or suppression of the hypothalamic/pituitary/adrenal axis resulting in secondary adrenal insufficiency. Particular attention should be paid to the treatment of young athletes who may be more susceptible to the effects of GCs due to ongoing musculoskeletal development.

Where there is little or no scientific evidence of its effectiveness, or is not usual clinical practice for the use of oral GCs, such as in musculoskeletal injuries, a TUE should generally not be granted. However, each application should be managed on an individual basis.

The potential hazards of the prolonged use of narcotics are that of drug tolerance and dependency.

While the use of narcotics may be acceptable from a medical and TUE perspective, the relevant sport association may decide that in certain situations, their use poses an unacceptable safety risk to the athlete and/or other competitors. Sport safety issues are outside the realm of anti-doping.

9. References

1. Patel DR, Baker RJ. Musculoskeletal injuries in sports. *Prim Care*. 2006 Jun; 33(2): 545-79
2. Selected issues for the adolescent athlete and the team physician: a consensus statement. *Med Sci Sports Exerc*. 2008 Nov; 40(11): 1997-2012. Doi: 10.1249/MSS.ObO13e31818acdc (No authors listed)
3. Barnsley L, Lord SM, Wallis BJ, Bogduk N. Lack of effect of intraarticular corticosteroids for chronic pain in the zygapophyseal joints. 1994 April 14; *N Eng J Med* 330(15): 1047-50
4. Maffulli N, Baxter-Jones AD Common skeletal injuries in young athletes. *Sports Med* 1995; 19: 137–49.
5. Maffulli N, Longo UG, Gougoulis N et al. Long-term health outcomes of youth sports injuries. *Br J Sports Med* 2010; 44: 21-25 doi: 10.1136/bjsm.2009.069526
6. Dvorak J, Feddermann N, Grimm K. Glucocorticosteroids in football: use and misuse. *Br J Sports Med*. 2006 July; 40(Suppl 1): i48-154
7. Nichols A W. Complications associated with the use of corticosteroids in the treatment of athletic injuries. *Clin J Sport Med* 2005. 15370–375.375.
8. Harmon K G, Hawley C. Physician prescribing patterns of oral corticosteroids for musculoskeletal injuries. *J Am Board Fam Pract* 2003. 16209–212.212.