

Pain Management in Sport

Prohibited Substance: Narcotics and cannabinoids

For Glucocorticoids, please refer to the Musculoskeletal Conditions Guidelines.

1. Introduction

As described in the International Olympic Committee <u>Consensus Statement</u> on pain management in elite athletes, pain can be classified as nociceptive, neuropathic or nociplastic. These terms are clinical descriptions, and not diagnoses.

- Nociceptive pain refers to pain associated with tissue damage or inflammation, and thus is the most common type of pain associated with sport injury.
- Neuropathic pain is defined as pain that results from a lesion or disease in the somatosensory system. Neuropathic pain is frequently difficult to treat, and commonly interferes with everyday activities and participation in sport. Athletes with underlying neurological conditions have a higher incidence of neuropathic pain.
- Nociplastic pain is chronic pain in which a specific aetiology cannot be identified, but clinical
 and psychophysical findings such as hypersensitivity suggest altered nociceptive function.
 Nociplastic pain may result from sport injury, and like neuropathic pain, it is difficult to treat
 and commonly interferes with everyday activities and participation in sport.

For the purposes of clinical management, pain can be divided into acute and chronic causes. The successful management of pain requires an inter-disciplinary approach utilizing non-pharmacologic management, and pharmacologic treatment when warranted, that are grounded in the biopsychosocial medical model.

2. Diagnosis

a. Acute pain

Acute pain can occur in a number of settings, and will most often be nociceptive: for example, muscular injury or inflammation, trauma, fractures, dental conditions, and post-surgery. In sport, all conditions demand an accurate diagnosis involving a complete history and thorough physical examination. In addition, appropriate investigations including imaging modalities such as x-ray, MRI, CT, nuclear medicine and ultrasonography plus laboratory tests may be necessary to confirm a diagnosis and rule out any relevant comorbidity. If applicable, the results of appropriate imaging and other investigations should accompany the TUE application.



b. Chronic pain

Chronic pain may be:

- i) neuropathic (examples include spinal cord injury, peripheral nerve trauma (including radiculopathy related to recurrent or persistent disc herniation), stroke, traumatic brain injury, and complex regional pain syndrome, type 2 and
- ii) nociplastic (examples include fibromyalgia, myofascial pain, chronic low back pain, and complex regional pain syndrome, type 1.)

Due to the complexity of chronic pain, a TUE application for the use of a prohibited substance should include a thorough history, including symptomatology; physical examination findings, including a full neurological examination; and results of relevant investigations when needed to establish or confirm diagnosis (e.g., CT, MRI, electromyography (EMG), and nerve conduction studies (NCS). The description or presumed origin of the pain as well as the opinion of an appropriate medical specialist could be helpful.

3. Treatment

a. Acute Pain

The management of acute pain usually begins with appropriate non-pharmacologic measures which could include rest, appropriate loading for the stage of injury, ice, compression, elevation, and dietary measures in the case of dental conditions. Initial medication may include nonsteroidal anti-inflammatory drugs (NSAIDs), non-narcotic analgesics or skeletal muscle relaxants. Other treatment options include modalities such as heat, cryotherapy, traction, ultrasound, electrical stimulation, manual therapy, bracing and therapeutic exercises. In some cases of severe acute pain (e.g., some dental conditions, fractures, post-surgery), it may be appropriate to move directly to narcotic analgesics.

b. Chronic Pain

First line treatment for chronic pain should include non-pharmacologic strategies which address contributory factors from biological, psychosocial, and contextual domains, such as physical therapy, cognitive behavioral therapy, and the optimization of sleep and nutrition.

Pharmacologic strategies include the following first-line strategies:

- 1) Non-narcotic analgesics and NSAIDS on an "as needed" basis if not frequently required; persistent use not recommended given potential side effects
- 2) Antidepressants such as tricyclic amines (e.g., amitriptyline, nortriptyline) and dual reuptake inhibitors of serotonin and norepinephrine (e.g., duloxetine, venlafaxine)
- Anticonvulsants such as gabapentin and pregabalin

Second line medications include:

- 1) Capsaicin 8% patches
- 2) Lidocaine patches



4. Prohibited substances

1) Narcotics

NOTE: The use of narcotics administered by any route is only prohibited in-competition.

2) Cannabinoids

NOTE: The use of cannabinoids administered by any route is only prohibited in-competition.

3) Glucocorticoids (GCs)

NOTE: The use of glucocorticoids administered by any route is only prohibited incompetition.

Please see the WADA <u>TUE Physician Guidelines on Musculoskeletal Conditions</u> and the Glucocorticoids and Therapeutic Use Exemptions available on the WADA website

Narcotics and cannabinoids are prohibited in-competition only. However, an in-competition urine sample may show levels above the established laboratory reporting levels even though use occurred out-of-competition. In accordance with the Code, a resulting positive doping test, known as an adverse analytical finding (AAF), could render the athlete liable to a sanction under the concept of Strict Liability. However, as per ISTUE Article 4.1e, the athlete is permitted to apply retroactively for a TUE if there is an in-competition AAF from out-of-competition use. It is therefore important that the athlete have a medical file, detailing the diagnosis and rationale for narcotic or cannabinoid use, prepared to submit to their ADO if necessary.

a. Indications

1. Narcotics

Narcotics are usually indicated for short-term pain relief following acute injury, acute dental condition or post-surgery (typically between 1-7 days). They are seldom indicated beyond seven days; however, this may depend on circumstances including the complexity of a surgical procedure. *NOTE: The use of narcotic analgesics administered through any route is only prohibited in-competition*

With chronic pain, the clinical landscape has shifted considerably in the past several years. Whereas narcotics had been recommended for chronic non-cancer pain, emerging evidence tells us that such an approach has been generally unsuccessful, with more complications and side-effects than benefits long-term. Thus, narcotics are not generally considered as appropriate treatment for long-term management of chronic pain, although TUECs need to evaluate each case on its own merits.

Note that the mixed opioids (tramadol) and codeine may be utilized in specific situations; however, there are no clear indications for utilizing codeine as treatment for neuropathic and nociplastic pain. Codeine is not included in the Prohibited List. It should be noted that S7. Narcotics is a "closed" section meaning that only those substances specifically listed are prohibited.



Cannabinoids

The most well-studied medical use of cannabinoids is for the management of chronic pain conditions, predominantly neuropathic pain. There is evidence that cannabinoids have a modest analgesic effect for some pain conditions, such as refractory neuropathic pain. Due consideration and precaution should be exercised in the prescription of cannabinoids, especially for an athlete with a history of substance abuse, psychosis, poorly controlled mood or anxiety disorder. The literature for utilizing cannabinoids for the management of acute or nociplastic pain is less robust, and therefore the athlete must present clear and sufficient justification for use. There is emerging data on the use of cannabidiol (or CBD, the non-psychoactive component of cannabis) in the treatment of chronic pain. CBD is not prohibited, but if a non-synthetic CBD is used, there may be a risk of contamination with tetrahydracannabinol (THC, the psychoactive component of cannabis). The risk is quite low, but there remains a possibility that the THC level will be sufficiently high to trigger an Adverse Analytic Finding (AAF) on testing.

3. Glucocorticoids (GCs)

Please see the WADA <u>TUE Physician Guidelines on Musculoskeletal Conditions</u> and the <u>Glucocorticoids and Therapeutic Use Exemptions</u> available on the WADA website

b. Typical dosage, route, frequency and duration

1. Narcotics

Narcotics are usually taken orally, but they may also be administered intramuscularly, intravenously, transdermally or via a targeted, intrathecal delivery system.

2. Cannabinoids

Cannabinoids are available in a variety of formulations depending on country; prescription cannabinoids include dronabinol, nabilone and nabiximols. Herbal cannabis preparations are also legally available in some jurisdictions. Cannabinoids can be taken orally, inhaled through a vaporizer or by smoking. Herbal cannabis may contain widely varying levels of active cannabinoids (THC and CBD), so the dosage and frequency of administration of cannabinoids depends on the product used and need of the individual. *All cannabinoids are prohibited with the exception of CBD*.

For narcotics and cannabinoids, the dosages and duration of treatment are individualized, and may be indefinite in the case of neuropathic pain due to a chronic injury to the somatosensory system. Regular clinical review by a specialist with expertise in pain management for satisfactory analgesic and functional outcomes is considered to be the accepted practice to regulate use of pain medications.

5. Consequences to health if treatment is withheld

Chronic untreated pain carries the potential to impair a range of activities of daily living from minor to significant, depending on factors including the severity and location of pain, the individual's coping skills and their desired activity level.



6. Monitoring treatment

For all pain types, treatment monitoring is primarily clinical. The use of narcotics or cannabinoids should be at their lowest effective dose to preserve the functional status of the athlete while minimizing side effects.

7. TUE duration

The indications, dosage, and duration of the use of GCs and narcotics in the management of acute pain are dependent on the specific condition or injury. Athletes with severe acute pain requiring narcotics are unlikely to be competing. In most cases, neither of these medications are 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.

In the management of chronic pain, when narcotics and cannabinoids are administered long-term, a TUE may be granted for periods of 1 to 4 years. An annual review of the status of the athlete-patient by a relevant specialist is recommended to ensure that on-going treatment remains appropriate.

8. Appropriate precautionary matters

It is recognized that while narcotics and cannabinoids may substantially improve an individual's ability to accomplish everyday activities, they may also have a negative (ergolytic) impact on the ability to participate effectively in sports requiring dexterity and rapid coordination.

Side effects of narcotics range from drowsiness and lethargy to dependency, addiction and even death from accidental or intentional overdose. Cannabinoids carry the potential for unpredictable mood, altered affect, increased anxiety, and diminished concentration, reaction time, alertness, coordination and balance, and judgement. Chronic cannabis smoking has also been shown to be associated with chronic bronchitis. The benefits and risks from a medical perspective are for consideration by the athlete and their physician and are not part of the TUE decision process.

It may be noted that although the use of narcotic analgesics and cannabinoids may be acceptable from a medical and TUE perspective, the relevant sporting association may decide that in certain situations, the use of narcotics and cannabinoids are an unacceptable safety risk to the athlete and/or other competitors. Sport safety issues are outside the realm of TUEs and anti-doping.

It is important to note that anti-doping authorities do not carry the authority to grant athletes legal rights to possess and carry illegal and/or controlled substances, including narcotics and cannabinoids across jurisdictional / international borders. It is the responsibility of the athlete to be aware of the law in the countries or jurisdictions in which they may be travelling.

To be clear, having a TUE granted by an ADO will not supersede any laws that prohibit possession, importation or usage of a drug that exist in some jurisdictions.



References

- 1. Chong MS, Brandner B. Neuropathic agents and pain. New Strategies. *Biomedicine & Pharmacotherapy*. 60(7): 318-322. 2006.
- 2. Collier R. Most Paralympians inspire, but others cheat. CMAJ. 179(6): 524. 2008.
- 3. Davis MP. What's new in neuropathic pain? Support Care Cancer. 15: 363-372. 2007.
- 4. Jongen J, Hans G. Neuropathic pain and pharmacological treatment. Pain Pract. 2013.
- 5. Saarto T, Wiffen PJ. Antidepressants for neuropathic pain. *Cochrane database of systematic reviews (1469-493X)*, (4), p. CD005454. 2007.
- 6. https://www.wada-ama.org/en/prohibited-list
- 7. Dworkin RH, et al. Recommendations for the pharmacological management of neuropathic pain: An overview and literature update. *Mayo Clin Proc.* 85(3) (suppl):S3-S14. 2010.
- 8. Haanpaa M, Treede RD. Diagnosis and classification of neuropathic pain. *Pain: Clinical Updates*. Vol XVIII, Issue 7. 2010.
- 9. Cruccu G, Truini A. Tools for assessing neuropathic pain. *PLoS Med* 6(4): e1000045. doi: 10.1371/journal.pmed.1000045. 2009.
- 10. Marilyn A. Huestis, Irene Mazzoni, Olivier Rabin. Cannabis in sport. *Sports Med.* November 1; 41(11): 949–966.2013. doi:10.2165/11591430-000000000-00000.
- DE Moulin, AJ Clark, I Gilron, et al. Pharmacological management of chronic neuropathic pain Consensus statement and guidelines from the Canadian Pain Society. Pain Res Manage 2007;12(1):13-21.
- 12. Attal N, Cruccu G, Baron R, Haanpaa M, Hansson P, Jensen TS, Nurmikko T. EFNS guidelines on the pharmacological treatment of neuropathic pain: 2010 revision. Eur J Neurol 2010; 17:1113-e88.
- 13. National Institute of Health and Care Excellence. Neuropathic pain pharmacological treatment. NICE Clinical Guideline 173. 2013.
- 14. Ko GD, Bober SL, Mindra S, Moreau JM. Medical cannabis the Canadian perspective. J Pain Res. 2016 Sep 30;9:735-744.
- 15. Hainline B, Derman W, Vernec A et al. International Olympic Committee Consensus on pain management in elite athletes. Br J Sports Med 2017; 51: 1245-1258.
- 16. Hainline B et al. Pain in elite athletes -- neurophysiological, biomechanical and psychosocial considerations: a narrative review. Br J Sports Med 2017;51:1259-1264.
- 17. Moseley GL, Baranoff J, Rio E, et al. Nonpharmacological management of persistent pain in elite athletes: rationale and recommendations. Clin J Sports Med 2018;5:472-479.
- 18. Ware MA, Jensen D, Barrette A, et al. Cannabis and the health and performance of the elite athlete. Clin J Sports Med 2018;5:480-484.