

NEUROPATHIC PAIN

1. Medical Condition

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.

The successful management of neuropathic pain requires an inter-disciplinary approach comprising pharmacologic and non-pharmacologic treatment options via a biopsychosocial medical model. The primary goal of successfully managing neuropathic pain is to improve function and to alleviate pain.

Relevant to the TUE process, there are two classes of prohibited substances frequently prescribed to manage neuropathic pain. Both classes are prohibited only in-competition. They are:

- a. Narcotics (“opioids”);
- b. Cannabinoids.

The use of narcotics and cannabinoids in the management of neuropathic pain is often long-term and necessitates regular monitoring. In certain countries where cannabinoids and/or narcotics remain illegal substances, there is no recourse to these drugs in clinical settings; in some cases, simple possession represents a criminal offence.

2. Diagnosis

A. Medical History

Individuals with neuropathic pain typically have a history of disease or injury to the central or peripheral nervous system. Examples include spinal cord injury and peripheral nerve trauma. Some individuals with stroke or traumatic brain injury may experience central neuropathic pain. Individuals with amputations may experience either stump pain or “phantom limb” pain. Neuropathic pain may also manifest in complex regional pain syndrome. Neuropathic pain is independent of nociceptive input and is often described as a hypersensitive burning pain with associated numbness, tingling, “shooting” pain, hot and cold sensations, and an “electrical” shock. Neuropathic pain is a clinical description and not a diagnosis.

B. Diagnostic criteria

A specific diagnostic tool for neuropathic pain does not exist, so a grading system of definite, probable, and possible neuropathic pain has been proposed. Additionally, nociceptive pain and neuropathic pain have different yet overlapping etiologies. Various questionnaires are available to attempt to distinguish or screen neuropathic pain from other pain disorders. Examples include the DN4 (>4/10) (Douleur Neuropathique en 4 Questions) and the Freynhagen Pain Detect Questionnaire. Quantitative sensory testing, which analyses perception in response to external stimuli, is largely subjective and does not provide conclusive proof of neuropathic pain.

Due to the complexity of neuropathic 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; results of relevant investigations when needed to establish or confirm diagnosis (e.g. CT, MRI, electromyography (EMG), and nerve conduction studies (NCS). The opinion of an appropriate medical specialist could be helpful.

3. **Non-Prohibited Treatments**

First line treatment should include non-pharmacologic strategies, which address contributory factors from biological, psychosocial and contextual domains, such as physical therapy, cognitive behavioural therapy, and addressing sleep and nutrition.

Pharmacologic strategies include the following first-line strategies:

- a. Antidepressants such as tricyclic amines (e.g., amitriptyline, nortriptyline) and dual reuptake inhibitors of serotonin and norepinephrine (e.g. duloxetine, venlafaxine);
- b. Anticonvulsants such as gabapentin and pregabalin.

Second line medications include:

- a. Capsaicin 8% patches;
- b. Lidocaine patches;
- c. Tramadol, which is a mixed opiate-serotonergic drug.

4. **Prohibited Substances**

A. Classes of prohibited substances that may be utilized in the treatment of neuropathic pain:

1. Narcotics
2. Cannabinoids

Indications:

1. Narcotics

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 now rarely considered as justifiable treatment for long-term management of neuropathic pain. Note that the mixed opioids (tramadol) and codeine are not included in the Prohibited List, and may be utilized in specific situations; however, there are no clear indications for utilizing codeine as treatment for neuropathic pain. It should be noted that Narcotics (Section 7) is a “closed” section meaning that only those substances specifically listed are prohibited.

2. Cannabinoids

The most well studied medical use of cannabinoids is for the management of chronic pain conditions, predominantly neuropathic pain. There is good 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.

B. Typical Dosage, Route, Frequency

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. Where possible, vaporizing appears to be a safer option to smoking, and reduces odor and inconvenience to others.

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.

C. Recommended Duration of Treatment

The duration of treatment is 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 neuropathic 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 his/her desired activity level.

6. Treatment Monitoring

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 Validity and Recommended Review Process

In situations including the management of acute pain or in post-operative care, narcotic analgesics may be administered for a period of days. However, in the management of chronic neuropathic pain, narcotics and cannabinoids are typically administered long-term. Therefore 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. Any Appropriate Cautionary Matters

It is recognized that while these medications 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 and even death if they are abused. Cannabinoids carry the potential for unpredictable mood, altered affect, increased anxiety, and diminished concentration, reaction time, alertness, coordination, and judgement. Chronic cannabis smoking has also been shown to be associated with chronic bronchitis.

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

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safety risk to the athlete and/or other competitors. Sport safety issues are outside the realm of anti-doping.

It is very important to note that 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.

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