

Image: Constraint of the stateImage: Constraint of the stat

by Shikha Tandon, Larry D. Bowers, PhD & Matthew N. Fedoruk, PhD

USADA has developed an online educational tutorial to provide health professionals with information on anti-doping specific rules and resources.



Shikha Tandon (above), Larry D. Bowers, PhD & Matthew N. Fedoruk, PhD, are with the United States Anti-Doping Agency Colorado Springs, Col. *Contact: standon@usada.org*

Abstract

Physicians and health professionals are a vital component in preserving the integrity of competition and the core principles of true sport. When treating an athlete, health professionals need to be cognizant of the anti-doping rules of the relevant sport organization. This review aims to provide an overview of the World **Anti-Doping Agency Prohibited** List, Therapeutic Use Exemptions, roles and responsibilities of the health professional, as well as provide resources that will guide their work with athletes.

Introduction

In sport, the second place is often viewed as the 'first loser'.1 Athletes, and their coaches, are sometimes willing to make sacrifices and take risks, in an attempt to gain a competitive edge. Performance enhancement, with a 'win-at-all-costs' attitude, can be achieved by utilizing various physiological, mechanical, and pharmacological doping techniques.1 Athletes and support personnel depend on the knowledge and expertise of health professionals to help guide them in making good medical decisions. Health professionals that work with athletes are often the

first line of contact and it is important that they understand and comply with anti-doping policies and rules. Understanding the anti-doping rules can be challenging, but it is essential to ensuring success in program compliance, and avoiding potentially negative consequences - such as a positive anti-doping test or an adverse health event. Health professionals that fail to comply with anti-doping rules, run the risk of an anti-doping rule violation, which could lead to a possible period of ineligibility or lifetime ban from sport, for both the athlete and health professional.²

The U.S. Anti-Doping Agency and the World Anti-Doping Code

The U.S. Anti-Doping Agency (USADA) is the independent antidoping agency for the Olympic and Paralympic movement in the United States.³ USADA has the authority to execute a national anti-doping program encompassing testing, adjudication, education, and research; and to develop programs, policies, and procedures in each of these areas. USADA is a signatory to the World Anti-Doping Code (WADC) and is compliant with the WADC and all the accompanying WADC International Standards - The Prohibited List, International Standard for Testing,

International Standard for Therapeutic Use Exemptions, International Standard for Laboratories, and International Standard for Protection of Privacy and Personal Information.³ In addition to the athlete, the actions of health professionals, in sport, are governed by the WADC and also by sport-specific anti-doping program rules.²

The World Anti-Doping Agency Prohibited List

The World Anti-Doping Agency (WADA) Prohibited List is a document that serves as the international harmonizing document and lists the substances and methods that are prohibited in Olympic sport.⁴ The list is divided in to different categories and identifies which classes of substances and methods are prohibited at all times (in- and out-of-competition), in-competition only, as well as those substances that are prohibited in specific sports. WADA convenes an independent panel of international experts to consider the composition of the Prohibited List on an annual basis.⁴

A substance or method is considered for the Prohibited List if it meets any two of the following three criteria.⁴

- It has the potential to enhance sport performance;
- It represents an actual or potential health risk to the athlete;
- It violates the spirit of sport.

After the Prohibited List is revised each year by the WADA List Expert Group, it is sent to stakeholders for comment and finally approved by the WADA Executive Committee.⁴ The revised list is approved and released each October for implementation the following January 1 to give opportunity to educate stakeholders on the revisions. For new substance additions, this may require changing a medication to non-prohibited alternatives or apply for a Therapeutic Use Exemption (TUE). While beta-blockers may be used in treating intraocular hypertension,⁵ they also have the potential to steady nerves in competition.⁶ Diuretics can be misused by athletes to rapidly excrete water from the body in order to meet weight categories, and also be used as a masking agent to dilute the urine such that lower concentrations of the prohibited substance is excreted from the body.⁷ Stimulants can enhance performance by increasing energy and focus.⁸ It is important to examine performance-enhancement broadly to consider the potential enhancement of not only speed, strength, and energy utilization, but also to include the enhancement of recovery, time to exhaustion, concentration and focus, pain tolerance, weight loss and maintaining optimal weight, thermoregulatory capacity, and confidence. Sidebar 1 outlines a case study on the use of thyroid hormone for performance enhancement.

The prohibited classes of substances that are prohibited at all times include non-approved substances (S0), anabolic agents (S1), peptide

> hormones, growth factors, related substances and mimetics (S2), beta-2 agonists (S3), hormone and metabolic modulators (S4), diuretics and masking agents (S5). Stimulants (S6), narcotics (S7), cannabinoids (S8), and glucocorticoids (S9) are prohibited in-competition only. Alcohol (P1) and betablockers (P2) are substances that are prohibited, in-competition only, in some sports. Methods that are prohibited at all times

Sidebar 1 Thyroid Hormone Case Study

A Tour de France cyclist admitted doping after having an adverse analytical finding. Among the prohibited substances he admitted using, were IV insulin, growth hormone, EPO. He also admitted using thyroxine. The reason that he gave for the use of thyroid hormone was:

- A. Enhance muscle growth
- B. Recover faster from training
- C. Weight loss
- D. Increased heart rate
- E. Increased ventilation rate

Answer: C.

He claimed that the few additional kilograms that he lost, improved his climbing performance.

include manipulation of blood and blood components (M1), chemical and physical manipulation (M2), and gene doping (M3).9 Substances, such as Tetrahydrogestrinone (THG), while not been proven through controlled studies to enhance athletic performance, are still prohibited. This is because these substances have the potential to cause adverse health effects due to their structural similarity with other anabolic agents. Oftentimes, it may not be ethical practice to conduct studies to test for human athletic performance enhancement using these unapproved substances. Table 1 lists examples of substances on the WADA Prohibited List for common medical diagnoses.

It must be noted that the WADA prohibited list is an open list as it

provides examples of prohibited substances and also prohibits any substances with similar biological effects. Agencies such as the National Collegiate Athletic Association (NCAA)¹⁰ and Major League Baseball (MLB)¹¹ follow their own prohibited lists. Physicians should be aware of the competition status of the athlete, and consult the appropriate prohibited list, prior to prescribing any medication.

USADA's Global Drug Reference Online (GlobalDRO) resource provides athletes and support personnel with information regarding the prohibited status of medication as per the current WADA Prohibited List.¹² The user can search for specific pharmaceutical products as well as some over-the-counter medications that are sold in the United States, United Kingdom, Japan, and Canada. GlobalDRO does not provide information on dietary supplements or homeopathic medications. The USADA Wallet Card also provides a handy, quick reference summary guide to the common prohibited and permitted substances and medications under the WADA Prohibited List.13 These resources can be accessed by athletes and health professionals via the USADA website.

Table 1

Examples of substances on the WADA Prohibited List for common medical diagnoses. The WADA prohibited class is listed in parenthesis for each substance.

Medical Diagnosis	Examples of substances that are prohibited by WADA
Attention Deficit Hyperactivity Disorder	Methylphenidate (S6), Amphetamine (S6)
Asthma	Albuterol (S3), Salmeterol (S3), Formoterol (S3)
Androgen Deficiency/Male Hypogonadism	Testosterone (S1)
Arterial Hypertension	Hydrochlorothiazide (S5)
Diabetes Mellitus	Insulin (S4)
Post Infectious Cough	Pseudoephedrine (S6), Prednisone (S9)
Sinusitis/Rhinosinusitis	Pseudoephedrine (S6), Prednisone (S9)
Musculoskeletal Injuries	Methylprednisolone (S9), Oxycodone (S7)
Vitamin Deficiency	Intravenous infusion of vitamins (M2)
Allergies	Prednisone (S9)
Surgery	Oxycodone (S7)
Pain Management	Marijuana (S8)

Therapeutic Use Exemptions (TUEs)

In some situations, an athlete may have an illness or medical condition that requires the legitimate use of a substance that is listed on the WADA Prohibited List. In such situations, an athlete may be granted a Therapeutic Use Exemption (TUE).¹⁴ USADA can grant a TUE for athletes, in compliance with the World Anti-Doping Agency International Standard for Therapeutic Use Exemptions (ISTUE).¹⁵ The ISTUE document is a global standard and it should be noted that while some prescription of medication and treatment may be within the standard of care or common medical practice in the U.S., it may not be the normal standard within the international community. There are well established criteria, set by WADA, that need to be adhered to prior to approving a TUE¹⁶ and a committee of experts reviews the diagnostic work-up much like an insurance review. These criteria are available in the ISTUE and have been designed to balance providing an unfair advantage with the need to provide athletes access to critical medication.¹⁴ While the criteria for granting a TUE are listed in the ISTUE, it is the responsibility of the anti-doping organization to

appoint a team of qualified physicians that will serve as the TUE Committee (TUEC) and review each TUE application on an individual basis.¹⁶ Physicians that are treating the athlete are responsible for providing and reporting accurate and complete medical information in the TUE application. The effectiveness of an alternative that is not prohibited should be evaluated, documented, and reported. A complete TUE file enables the TUEC to follow the diagnostic work-up process without ever seeing the athlete in-person and provide a thorough evaluation of the application.

The criteria for granting a TUE, as outlined in the WADA ISTUE, is as follows:¹⁶

- The Athlete would experience a significant impairment to health if the prohibited substance or prohibited method were to be withheld in the course of treating an acute or chronic medical condition.
- The therapeutic use of a prohibited substance or prohibited method would produce no additional enhancement of performance other than that which might be anticipated by a return to a state of normal health following the treatment of a legitimate medical condition. The use of any prohibited substance or prohibited method to increase 'low-normal' levels of any endogenous hormone is not considered an acceptable therapeutic intervention.

- There is no reasonable therapeutic alternative to the use of the otherwise prohibited substance or prohibited method.
- The necessity for the use of the otherwise prohibited substance or prohibited method cannot be a consequence, wholly or in part, of the prior use, without a TUE, of a substance or method which was prohibited at the time of use.

As part of the TUE application process, the athlete is required to provide complete, and comprehensive medical documents and notes to support the diagnosis. There are WADA guideline documents,¹⁷ written by physicians, available for Attention Deficit Hyperactivity Disorder (ADHD), adrenal insufficiency, anaphylaxis, androgen deficiency, arterial hypertension, asthma, diabetes mellitus, female to male transsexual athletes, growth hormone deficiency (childhood and adult), infertility and polycystic ovarian syndrome, inflammatory bowel disease, intravenous infusion, intrinsic sleep disorders, musculoskeletal injuries, post infectious cough, renal transplantation, and sinusitis and rhinosinusitis.¹⁷ These documents are available on the USADA website and provide the treating physician with relevant information as well as lists out documentation that is required to support a TUE application. A TUE application that does not provide supporting medical documentation is returned to the athlete as incomplete and will not be



processed. Figure 1 lists the number of TUEs approved by USADA in 2013.

It is important to keep in mind that the WADA TUE process may not be adopted by all sports organizations. For example, the National Collegiate Athletic Administration (NCAA), the organization responsible for overseeing anti-doping in college level sports, reviews the Medical Exception for Banned Substances application, for some substances, retroactively if the athlete has an adverse test result.¹⁸ USADA considers retroactive TUEs only in emergency circumstances, and generally requires 28 days of processing time for a TUE application.¹⁵ When preparing for a surgery, the USADA website provides a to-do surgery checklist that covers anti-doping information that can be used by the athlete and the physician.¹⁵

Roles and Responsibilities of the Physician in Sport

Due to their focus on performance, athletes sometimes present their physicians with unique situations when compared to what is seen in the general population. Non-athletes are often motivated by the goal of prolonging a healthy life and seek reduced suffering and pain in an attempt to maintain long-term function.¹⁹ Athlete patients, on the other hand, are performance driven and sometimes achievement, or the ability to compete, may take precedence in their mind over long term health.¹⁹ Post injury or illness, the main priority of an athlete is recovery such that they may return to competition and training at the earliest moment. This may cause them to be motivated to push the

Sidebar 2 Intravenous Infusions Case Study

Case:

An athlete that you are treating is competing in an upcoming event and must adhere to USADA anti-doping rules. There is some concern that on competition day the weather will be hot and humid, greatly increasing the chances of dehydration among the athletes. If there is a situation where the athlete is dehydrated and comes to you, as a health professional, and inquires about fluid replacement by IV for quick rehydration so that he/she may recover more quickly after the event. As a health professional, what would be your course of action?

Answer:

Intravenous infusions (IV) and/or injections of more than 50 mL per 6 hour period are prohibited, except for those legitimately received in the course of hospital admissions, surgical procedures or clinical investigations. The literature supports the position that drinking appropriate fluids may correct mild dehydration after exercise. IV infusions to aid in recovery are only warranted in severe cases of dehydration and gastrointestinal upset. When treating dehydration, if the athlete receives IV with saline and dextrose solution above 50 mL over 6 hours, the athlete/physician is required to apply to USADA for an emergency Therapeutic Use Exemption (TUE) by providing all relevant medical documentation and a complete TUE application form.

Table 2

Anti-Doping specific resources that a	re available to the health	professional.
---------------------------------------	----------------------------	---------------

USADA Resources	Description	Weblink
GlobalDRO	Check the WADA status of medications by ingredient or brand name.	http://www.globaldro.com/us-en/
Wallet Card	List of medicines that are not prohibited by WADA in sport.	http://www.usada.org/substances/tue/
WADA Prohibited List	List of substances and methods that are prohibited in sport.	http://www.usada.org/substances/prohibited-list/
Supplement 411	Information on Dietary Supplements including a High- Risk List.	http://www.supplement411.org/supplement411/
Drug Reference Line	Speak to an expert to understand the Prohibited List, TUEs, and Dietary Supplements.	http://www.usada.org/substances/drug-reference-phone-line/
Ask the Scientist	Ask USADA's scientists and experts questions related to anti-doping science.	http://www.usada.org/science/ask-the-scientists/
Surgery Checklist	Information on anti-doping considerations in preparation for surgery.	http://www.usada.org/substances/tue/
HealthPro Advantage	Online anti-doping educational tutorial, specific to health professionals.	http://www.usada.org/resources/healthpro/
Athlete Express	Information on the basics of drug-testing.	http://www.usada.org/athletes/
Play Clean Tip Center	Anonymously report doping in sport.	http://www.usada.org/athletes/playclean/

limits of their rehabilitation program. In some cases, the physician is responsible for making recommendations about when an athlete may resume certain activities. It is important that the physician is mindful of their obligations towards an athlete, or a sports team, and should carefully evaluate the motivation behind their actions. Sidebar 2 outlines a case study on intravenous infusions in sport.

As an example, as outlined in the College of Physicians and Surgeons of British Columbia, Professional Standards and Guidelines document, some of the responsibilities of a physician that is prescribing drugs to an athlete in sport, is as follows.²⁰

- The physician should exercise caution when prescribing medications to athletes. The first responsibility of the physician is the health and safety of the patient.
- The physician should be mindful of the use of performance enhancing drugs (PEDs) in all levels of sport, be it high school or at an elite level. The physician should be knowledgeable about the possible dangers of PEDs and communicate directly with patients in an attempt to educate those that are engaging in these practices.
- The physician should not prescribe or advise patients about access to substances and services for the deliberate purpose of enhancing their sporting performance.
- The physician should not prescribe or administer any prohibited substance or assist with any method of doping, or succumb to pressure from patients, coaches or others to do so. The physician should be up to date in his knowledge on the WADA Prohibited List and consult it, and other anti-doping resources.
- The physician should prescribe to athletes and administer only those drugs which are medically indicated for established and bona fide medical conditions, in accordance with relevant clinical guidelines and the medical standard of care. The physician should also

be aware of the TUE process and comply with the specific provisions contained in the ISTUE to provide only medically necessary drug treatment.

The WADA Code addresses the roles and responsibilities of athlete support personnel, who are defined as 'Any coach, trainer, manager, agent, team staff, official, medical, paramedical personnel, parent, or any other person working with, treating, or assisting an athlete participating in or preparing for sports competition'.² The Code has evolved to recognize the actions of athlete support personnel and also lists out possible sanctions for involvement with managing or participating in a doping program.

Resources for the Health Professional

USADA has developed a portal on their website which offers health professionals various anti-doping specific resources and documents, as listed in Table 2. HealthPro Advantage, USADA's online education tutorial, caters to health and medical professionals.²¹ The goal of this 90-minute tutorial is to deliver practical, valuable, and directly applicable knowledge, specific to a health professional, who works with high-performance athletes. The tutorial features lessons on topics such as: Anti-Doping Roles and Responsibilities of Health Professionals, the WADA Prohibited List, the Sample Collection Process, Dietary Supplements, and the Therapeutic Use Exemption (TUE) process. Some of the benefits of completing the tutorial include:

- Learning to avoid errors which could contribute to an athlete testing positive and a possible anti-doping rule violation.
- Information on accessing various drug reference and educational resources.
- Determining the status of medication, including distinguishing substances prohibited at all times or only in-competition, or only in particular sports.
- Understanding the notification, sample collection, and anti-doping results management process.

- Understanding the roles and responsibilities of the athlete and team medical staff in the doping control process.
- Understanding the process for filing a TUE.
- Understanding Olympic Games and other major games specific anti-doping rules.
- Understanding and explaining the risks of dietary supplement use.

Conclusion

Physicians and health professionals that are treating athletes have an important role within the sporting community. Knowledge and understanding ensures that medical treatment provided to the athlete is in compliance with the anti-doping rules. Prior to prescribing any medication to the athlete, it is important to verify the prohibited status, in sport, of the medication. Therapeutic Use Exemption (TUE) procedures must be followed if the prohibited substance or method is medically necessary for the athlete. To enable a thorough evaluation of the TUE by the TUEC, it is important that the medical information provided by the health professional is detailed and accurate. The WADA Code states that those persons that are involved in doping of athletes, or covering up doping, should be subject to sanctions which are more severe than those given to athletes that test positive in a drug test. USADA has developed an online educational tutorial to provide health professionals with information on anti-doping specific rules and resources.

References

1. Baron DA, Martin DM, Magd SA. Doping in sports and its spread to at-risk populations: an international review. World Psychiatry. 2007; 6:118-123.

2. The World Anti-Doping Agency. 2015 World Anti-Doping Code. Available at: https://www.wada-ama.org/en/resources/the-code/2015world-anti-doping-code#.VCWsVfldWAU. Accessed September 25, 2014.

3. The United States Anti-Doping Agency. About United States Anti-Doping Agency Page. Available at: http://www.usada.org/about/. Accessed September 25, 2014.

4. The World Anti-Doping Agency. World Anti-Doping Agency Prohibited List Page. Available at: http://list.wada-ama.org/. Accessed September 25, 2014.

5. Noecker RJ. The management of glaucoma and intraocular hypertension: current approaches and recent advances. Ther Clin Risk

Manag. 2006; 2(2):193-206.

6. Lardon MT. Performance-enhancing drugs: where should the line be drawn and by whom? Psychiatry (Edgmont). 2008; 5(7):58-61.
7. Cadwallader AB, de la Torre X, Tieri A, Botrè F. The abuse of diuretics as performance-enhancing drugs and masking agents in sport doping: pharmacology, toxicology and analysis. Br J Pharmacol. 2010; 16(1):1-16.

 Docherty JR. Pharmacology of stimulants prohibited by the World anti-Doping Agency (WADA). Br J Pharmacol. 2008; 154(3):606-622.
 The World Anti-Doping Agency. The 2015 Prohibited List International Standard. Available at: https://wada-main-prod. s3.amazonaws.com/resources/files/wada-2015-prohibited-list-en.pdf. Accessed October 01, 2014.

The National Collegiate Athletic Association. 2013-2014 NCAA
 Banned Drugs. Available at: http://www.ncaa.org/health-and-safety/
 policy/2013-14-ncaa-banned-drugs. Accessed September 25, 2014.
 Major League Baseball. MLB Players Association Joint Drug
 Agreement Page. Available at: http://mlbplayers.mlb.com/pa/info/cba.
 jsp. Accessed September 25, 2014.

12. The United States Anti-Doping Agency. USADA Global Drug Reference Online Page. Available at: http://www.globaldro.com/us-en/. Accessed September 25, 2014.

13. The United States Anti-Doping Agency. USADA Publications and Policies Page. Available at: http://www.usada.org/resources/publications-and-policies/. Accessed September 25, 2014.

14. Green GA. Doping control for the team physician – A review of drug testing procedures in sport. Am J Sports Med. 2006; 34:1690–1698.

15. The United States Anti-Doping Agency. USADA Therapeutic Use Exemptions Page. Available at: http://www.usada.org/substances/tue/. Accessed March 25, 2015.

16. The World Anti-Doping Agency. WADC International Standard for Therapeutic Use Exemptions 2011. Available at: https://www. wada-ama.org/en/resources/science-medicine/international-standardfor-therapeutic-use-exemptions-istue#.VCT-G_ldWAU. Accessed September 25, 2014.

17. The World Anti-Doping Agency. WADA Resources List
Page. Available at: https://www.wada-ama.org/en/resources/
search?f[0]=field_topic%3A24. Accessed September 25, 2014.
18. The National Collegiate Athletic Association. 2014 NCAA Drug
Policies Brochure. Available at: http://www.ncaa.org/sites/default/files/
Drug%20Policies%202014-15%2094256.pdf. Accessed September 25, 2014.

19. Murthy AM, Dwyer J, Bosco JA. Ethics in sports medicine. Bull NYU Hosp Jt Dis. 2012; 70(1):56-59.

20. College of Physicians and Surgeons of British Columbia. 2011 Professional Standards and Guidelines – Physician prescribing of performance enhancing drugs in sport. Available at: https://www.cpsbc. ca/files/pdf/PSG-Physician-Prescribing-of-Performance-Enhancing-Drugs-in-Sport.pdf. Accessed September 25, 2014.

21. The United States Anti-Doping Agency. USADA Health Professional Resources Page. Available at: http://www.usada.org/resources/healthpro/. Accessed September 25, 2014.

Disclosure

None reported.