Intravenous infusions and/or injections

1. Introduction

Intravenous (IV) infusions have been included on the WADA List of Prohibited Substances and Methods under section *M2. Prohibited Methods; Chemical and Physical Manipulation* since 2005[1]. An IV infusion or injection is the supply of fluid and/or prescribed medication by drip or push directly into a vein.

The wording in the Prohibited List (section M2.2) states that the following is prohibited: *Intravenous infusions and/or injections of more than a total of 100 ml per 12-hour period except for those legitimately received in the course of hospital treatments, surgical procedures or clinical diagnostic investigations*[1]*.* However, it should be noted that a TUE is required for any Prohibited Substance included in the intravenous infusion even if given "*in the course of hospital treatments, surgical procedures or clinical diagnostic investigations".*

To reiterate: Infusions or injections of more than 100 ml within a 12-hour period are prohibited, unless the infused/injected substance is administered during a 1) hospital treatment, 2) surgical procedure or 3) clinical diagnostic investigation. Therefore, athletes should always apply for a TUE if they receive an intravenous treatment of more than 100 ml within a 12-hour period if the three exemptions do not apply. For example:

a) medical practitioner's office, hotel room, in a home, tent or vehicle
b) event organizers' medical facility, tent, first aid station or start-finish line facility
c) IV clinics or any clinic/treatment room or center outside of a hospital facility unless a clinical diagnostic investigation or surgical procedure has been performed

Please note that these are guiding examples and not an exhaustive list of settings where infusions would normally require a TUE.

The tables in the Appendix contain more details on the principles and examples of when IV infusion/injections with or without a prohibited substance are permitted or prohibited.

The key messages are:

1. If a non-prohibited substance is infused or injected without being part of a hospital treatment, surgical procedure or clinical diagnostic investigation, a TUE must be submitted for the prohibited method if more than 100 ml of fluid is used within a 12-hour period.

2. If a prohibited substance is administered via IV infusion or injection, a TUE application must be submitted for the prohibited substance regardless of whether the infusion is less than 100 ml or the setting/circumstances under which it is administered.

3. In situations of medical emergency or under clinical time-constraints, an athlete may apply for a retroactive TUE as per the International Standard for Therapeutic Use Exemptions.

2. Diagnosis

a. Medical history

A summary of the athlete's history and the findings of a physical examination should confirm the diagnosis and/or the clinical condition that resulted in the need for an IV infusion. A description of the clinical situation, including signs and symptoms of the illness that preceded the treatment and specific medical indication for the IV infusion, must be included in the TUE application.

Even though an IV infusion or injection given as part of a hospital treatment, surgical procedure, or clinical diagnostic investigation is not prohibited, the athlete is advised to obtain and keep a copy of the medical records from the intervention or procedure. Of course, if a prohibited substance is administered in those settings, one would need to apply for a TUE for that substance.

b. Diagnostic criteria

A clearly defined diagnosis or clinical condition should be established in accordance with the International Classification of Diseases standards of the World Health Organization (ICD-11). In some instances, particularly when the infusion is used in an emergency situation, a diagnosis may not be clearly established (see section 5). Hence, the athlete's clinical condition and situation should be explained as well as relevant objective findings to the extent possible.

c. Relevant medical information

A detailed description of the substance infused, the rate of infusion and any other relevant clinical information from the treating physician should be included. It must be explained why an alternative permitted therapy, for example oral rehydration in case of dehydration, is not a valid option. Any existing co-morbidities that would influence the decision for granting a TUE should also be included.

3. Treatment

Legitimate medical indications for IV infusions are well-established and are commonly associated with either medical emergencies or in-patient hospital treatment. If an athlete receives an IV treatment, the details should be documented in medical records and then submitted if a TUE application is required.

When an IV infusion is administered to an athlete, the following criteria should be fulfilled:

a) a well-described diagnosis and/or clinical condition
b) it was not medically reasonable to try a permitted alternative treatment
c) the treatment was ordered by a physician and administered by qualified medical personnel
d) adequate medical records of the treatment are available

The use of IV infusions in sport is commonly linked with rehydration after exhaustive effort and this situation is arguably the major cause of debate on the need for and efficacy of various rehydration methods. It must be understood that the use of IV fluid replacement following exercise and/or acute weight reduction to correct mild to moderate dehydration is not clinically indicated nor substantiated by the medical literature. There is a well-established body of scientific evidence to confirm that oral rehydration is the preferred therapeutic choice, potentially even more effective than IV infusion. [3-15]

Another common cause of dehydration is infectious diarrhea, particularly frequent when travelling in foreign environments. Also, in such clinical situations, oral rehydration is the preferred and most effective method of rehydration unless the medical condition justifies the choice of IV treatment.[19] It is understood that athletes may, in some situations, have difficulty ingesting and retaining oral fluids. This should be described in the clinical notes.

a. Name of prohibited method

Intravenous infusion or injection of >100 ml within a 12-hour period unless legitimately received in the course of hospital treatments, surgical procedures or clinical investigations.

b. Recommended duration

It depends upon the diagnosis and the particular clinical condition or situation. If the infusion is a single intervention, the TUE duration should be related to the specific occurrence and valid for a relatively short duration.

4. Other non-prohibited alternative treatments

Where clinically appropriate, oral delivery of fluids and/or medications should be considered before intravenous administration is performed.

5. Consequences to health if treatment is withheld

These will be dependent on the clinical condition and situation. However, in case of a medical emergency, a possible consequence of withholding IV treatment could result in serious harm to health or even death. Medical personnel may in certain emergency situations open an IV access line to monitor the athlete before a full clinical evaluation is completed. This is up to the medical personnel at the site to decide. The setting where the infusion takes place will determine whether or not a retroactive TUE is needed.

Therefore, the health and well-being of the athlete must always remain the priority. Consequently, when an IV infusion is considered by medical personnel as a treatment option, an athlete's medical needs should be assessed in the same way as any other patient. If an athlete is judged by medical personnel to be clinically unstable and/or in an emergency situation, treatment with IV fluids **should never be withheld** on grounds that the method is on the List of Prohibited Substances and Methods.

6. Treatment monitoring

Continuous evaluation by a treating physician or someone acting on his/her behalf should be performed until the desired treatment effect has been achieved.

7. TUE duration and recommended review process

The duration of the TUE should be limited to the time needed to treat the clinical condition or perform the medical intervention. Longer lasting and more frequent usage of an IV infusion would typically occur in a hospital setting and would therefore not require a TUE.

8. Any appropriate cautionary matters

It is the responsibility of the treating physician to evaluate the clinical indication for an IV infusion or injection. However, it is the responsibility of the athlete to inform the treating physician that according to WADA rules, an intravenous infusion of more than 100 ml of fluid within a 12-hour period is prohibited in non-emergency situations. It is also the responsibility of the athlete to initiate and complete a subsequent TUE application, if and when needed.

It should be emphasized that the health and well-being of the athlete must always remain the priority during medical investigations and treatments.

References

1. World Anti-Doping Agency, WADA Prohibited List: https://www.wada-ama.org/en/prohibited-list

2. World Anti-Doping Agency, International Standard for Therapeutic Use Exemptions: https://www.wada-ama.org/en/resources/world-anti-doping-program/international-standard-therapeutic-use-exemptions-istue

3. Arbitral Award, CAS 2002/A/389-393.

4. Arbitral Award, CAS 2006/A/1102 & 1146

5. Canadian Academy of Sports Medicine: A brief overview about intravenous hydration in athletics. Casa DJ, Maresh CM, Armstrong LE et al. Intravenous versus oral rehydration during a brief period: responses to subsequent exercise in the heat. *Med. Sci. Sports Exerc.* 2000 Jan; 32(1): 124-133.

6. Webster S, Rutt R, Weltmann, A. Physiological effects of a weight loss regimen practiced by college wrestler. *Med. Sci. Sports Exerc.* 1990 Apr; 22(2): 229-34.

7. Naghii, MR. The Significance of Water in Sport and Weight Control. *Nutr. Health.* 2000;14(2), 127-132.

8. Sawka, MN. Physiological consequences of hypohydration: exercise performance and thermoregulation. *Med. Sci. Sports Exerc.* 1992 Jun; 24(6):657-70.

9. Maresh CM, Herrera-Soto JA, Armstrong LE, et al. Perceptual responses in the heat after intravenous versus oral rehydration. *Med. Sci. Sports Exerc.* 2001 Jun; 33(6):1039-1045.

10. Castellani JW, Maresh CM, Armstrong LE, et al. Endocrine responses during exercise-heat stress: effects of prior isotonic and hypotonic intravenous rehydration. Eur. *J. Appl. Physiol. Occup. Physiol.* 1998 Feb; 77(3): 242-248.

11. Kraemer WJ, Fry AC, Rubin MR, Triplett-McBride T, et al. Physiology and performance responses to tournament wrestling. *Med. Sci. Sports Exerc.* 2001 Aug; 33(8):1367-78.

12. Mudambo SM, Reynolds N. Body fluid shifts in soldiers after a jogging/walking exercise in the heat. *Centr. Afr. J. Med.* 2001 Sept-Oct; 47(9-10): 220-225.

13. Landers DM, Arent SM, Lutz RS. Affect and cognitive performance in high school wrestlers undergoing rapid weight loss. *J. Sport Exerc. Psychol.* 2001 Dec; 23(4): 307-316.

14. Riebe D, Maresh CM, Armstrong LE, Kenefick RW, et al. Effects of oral and intravenous rehydration on ratings of perceived exertion and thirst. *Med. Sci. Sports Exerc.* 1997 Jan; 29(1): 117-124.

15. Rogers IR, Hook G, Stuempfle KJ, et al. An Intervention Study of Oral Versus Intravenous Hypertonic Saline Administration in Ultramarathon Runners with Exercise-Associated Hyponatremia: A Preliminary Randomized Trial. *Clin. J. Sport Med.* 2011 May; 21(3); 200-3.

16. Casa DJ, Ganio MS, Lopez RM et al. Intravenous versus oral Rehydration: Physiological, Performance, and Legal Considerations. *Curr. Sports Med. Rep.* 2008: 7 (4); S41-49.

17. Vandenbos F, et al. Relevance and complications of intravenous infusion at the emergency unit at Nice University Hospital. *J. Infect.* 2003 Apr; 46(3): 173-6.

18. ASOIF Medical Consultative Group: Minutes of the meeting 7th May 2006.

19. Binder HJ, Brown I, Ramakrishna BS, Young GP. Oral rehydration therapy in the second decade of the twenty-first century. Curr Gastroenterol Rep. 2014;16(3):376. doi:10.1007/s11894-014-0376-2.

Appendix

Below are three tables which illustrate the possible four combinations of a method and a substance that may be either permitted or prohibited during the administration of an IV infusion.

Table 1

In principle, four possibilities exist when both the substance and the method may be either permitted or prohibited

Method is Prohibited Substance is Prohibited	Method is Permitted Substance is Prohibited
Method is Prohibited Substance is Permitted	Method is Permitted Substance is Permitted

Table 2

Requirements for a TUE when the infusion is **not** given during a hospital treatment, surgical procedure, or clinical diagnostic investigation. The prohibited and permitted substance names are used as examples.

Prohibited Method: IV infusion of >100 ml within a 12-hour period Prohibited Substance: furosemide **Need TUE for substance** **Need TUE for method**	Permitted Method: Infusion of ≤100 ml within a 12-hour period Prohibited Substance: Insulin **Need TUE for substance**
Prohibited Method: IV infusion of >100 ml within a 12-hour period Permitted Substance: Dextrose **Need TUE for method**	Permitted Method: Infusion of ≤100 ml within a 12-hour period Permitted Substance: iron sucrose **NO need for TUE**

Table 3

Requirements for a TUE when infusion **is** given during a hospital treatment, surgical procedure, or clinical diagnostic investigation. The prohibited and permitted substance names are used as examples.

Prohibited Method: IV infusion of >100 ml within a 12-hour period Prohibited Substance: furosemide **Need TUE for substance**	Permitted Method: Infusion of ≤100 ml within a 12-hour period Prohibited Substance: Insulin **Need TUE for substance**
Prohibited Method: IV infusion of >100 ml within a 12-hour period Permitted Substance: Dextrose **NO need for TUE**	Permitted Method: Infusion of ≤100 ml within a 12-hour period Permitted Substance: ondansetron **NO need for TUE**