S9. Glucocorticoids

All injectable routes of administration are now included as prohibited routes of administration for glucocorticoids during the In-Competition period. As proposed in the draft 2021 *Prohibited List* circulated for consultation to stakeholders in May 2020, *WADA's* Executive Committee approved, at its 14-15 September 2020 meeting, prohibiting all injectable routes of administration of glucocorticoids during the *In-Competition* period. Examples of injectable routes of administration include: intravenous, intramuscular, periarticular, intra-articular, peritendinous, intratendinous, epidural, intrathecal, intrabursal, intralesional (e.g. intrakeloid), intradermal, and subcutaneous. However, in order to thoroughly and widely communicate the rule changes and to allow sufficient time for information and education, the Executive Committee decided to introduce the prohibition of all injectable glucocorticoid routes and the implementation of the new rules on 1 January 2022. This period will allow, for example, *Athletes* and medical personnel to get a better understanding of the practical implementation of the washout periods, Laboratories to update their procedures to incorporate the revised and substance-specific new reporting values, and sports authorities to develop educational tools for *Athletes*, medical and support personnel, addressing the safe use of glucocorticoids for clinical purposes in anti-doping.

For clarification, oral administration of glucocorticoids also includes oromucosal, buccal, gingival and sublingual routes. Dental intracanal application is not prohibited.

• Oral, intramuscular, rectal and intravenous routes have been prohibited for some time because there is clear evidence of systemic effects which could potentially enhance performance and be harmful to health. There are now also sufficient data available to show that the same systemic concentrations as existing prohibited routes can be achieved after administration by local injection (including periarticular, intra-articular, peritendinous and intratendinous) at licensed therapeutic doses.

• The systemic plasma and hence urinary concentrations of glucocorticoids that are reached after administration by local injection using normal licensed therapeutic doses were demonstrated to reach levels consistent with doses that were shown to have the potential to improve performance in clinical studies. These levels are similar to, and even higher than, those obtained after other existing prohibited routes of administration of the same drug. The systemic effect of glucocorticoids following local injectable routes of administration may therefore present a significant potential to both improve performance and cause harm to health.

Glucocorticoids include naturally occurring hormones and synthetic analogues and possess a wide range of potencies and pharmacokinetic properties. The body naturally produces a daily output of the endogenous glucocorticoid (cortisol). However, administering glucocorticoid drugs can result in a total glucocorticoid exposure to the body that is much greater than the highest levels of normal physiological cortisol production, which could potentially be performance enhancing.

• The administration of glucocorticoid medications by topical routes, in accordance with the manufacturer's approved regimen, such as inhaled, intranasal, ophthalmological, dental-intracanal, perianal and dermal, are unlikely to reach systemic concentrations which may be performance enhancing.

• However, for other routes of administration (for example, oral), studies involving commonly used glucocorticoids at the normal therapeutic dose range indicated a performance-enhancing effect. These doses can be expressed in terms of cortisol-equivalents and thereby the dose which may be

potentially performance enhancing for any glucocorticoid and route of administration can be determined using this approach.

• This systematic approach was applied to determine the glucocorticoid routes of administration that are either prohibited, or not prohibited in sport. Consequently, revised and substance-specific laboratory reporting levels based on excretion studies are introduced to better reflect the proposed approach. To note, the revised reporting levels will be increased or will remain unchanged for all glucocorticoids except triamcinolone acetonide, which was revised to a lower reporting level. Overall, these changes should reduce the number of Adverse Analytical Findings reported by laboratories.

Washout periods following administration of glucocorticoids

• Any injection of glucocorticoids is prohibited In-Competition. Given the widespread availability and the common use of glucocorticoids in sports medicine, Athletes and their Support Personnel should be advised of the following:

1. Use of a glucocorticoid by injection during the In-Competition period requires a Therapeutic Use Exemption; otherwise, an alternative permitted medication in consultation with a physician shall be used.

2. After administration of glucocorticoids, urinary reporting levels which would result in an Adverse Analytical Finding can be reached for different periods of time after administration (ranging from days to weeks), depending on the glucocorticoid administered and the dose. To reduce the risk of an Adverse Analytical Finding, Athletes should follow the minimum washout periods*, expressed from the time of the administration to the start of the In- Competition period (i.e. beginning at 11:59 p.m. on the day before a Competition in which the Athlete is scheduled to participate, unless a different period was approved by WADA for a given sport). These washout periods are based on the use of these medications according to the maximum manufacturer's licensed doses:

Washout period *refers to the time from the last administered dose to the time of the start of the In-Competition period (i.e. beginning at 11:59 p.m. on the day before a Competition in which the Athlete is scheduled to participate, unless a different period was approved by WADA for a given sport). This is to allow elimination of the glucocorticoid to below the reporting level.*

** *Oral routes also include oromucosal, buccal, gingival and sublingual.* If the glucocorticoid needs to be administered via a prohibited route within these washout time periods, a Therapeutic Use Exemption (TUE) may be required. Physicians administering local injections of glucocorticoids should be aware that periarticular or intra-articular injection may sometimes inadvertently result in intramuscular administration. If intramuscular administration is suspected, the washout periods for the intramuscular route should be observed, or a TUE application sought.

4. Please note that as per Article 4.1e of the International Standard for TUEs, an Athlete may apply retroactively for a TUE if the Athlete Used Out-of-Competition, for therapeutic reasons, a Prohibited Substance that is only prohibited In-Competition. Athletes are strongly advised to have a medical file prepared and ready to demonstrate their satisfaction of the TUE conditions set out at Article 4.2, in case an application for a retroactive TUE is necessary following Sample collection.

• For additional information including the revised reporting levels, please consult the recently published article with details of the process that lead to these changes:

Glucocorticoid		**Washout period***
Oral**	All glucocorticoids;	3 days
	Except: triamcinolone acetonide	30 days
Intramuscular	Betamethasone; dexamethasone; methylprednisolone	5 days
	Prednisolone; prednisone	10 days
	Triamcinolone acetonide	60 days
Local injections (including periarticular, intra-articular, peritendinous and intratendinous)	All glucocorticoids;	3 days
	Except: triamcinolone acetonide; prednisolone; prednisone	10 days