



Preserving the integrity of competition. Inspiring true sport. Protecting the rights of athletes.

ATHLETES & PRESCRIBING PHYSICIANS PLEASE READ

USADA can grant a Therapeutic Use Exemption (TUE) in compliance with the World Anti-Doping Agency International Standard for TUEs. The TUE application process is thorough and designed to balance the need to provide athletes access to critical medication while protecting the rights of clean athletes to compete on a level playing field.

Included in this document is a checklist of items necessary for a complete TUE Application and the WADA Guidelines used to evaluate TUE Applications for your specific condition. (Please be aware that the TUE Committee may ask for additional information while evaluating TUE Applications). It is important that the TUE Application include all the documentation outlined in the checklist below. Please reference the included guidelines for details related to types of diagnoses, specific laboratory tests, and more.

TUE APPLICATION CHECKLIST – SINUSITIS, RHINOSINUSITIS

- Complete and legible TUE Application form
- Copies of all relevant examinations and clinical notes from the original diagnosis through present
 - The physician should specify the type of sinusitis (acute bacterial or chronic), the symptoms experienced, and the symptom duration.
- Copies of all laboratory results/reports related to the diagnosis, if applicable
- A statement from the physician explaining why the Prohibited Substance is needed
 - Why other treatments (with either permitted or prohibited substances/methods) failed or are not appropriated for treating the condition.

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SINUSITIS/RHINOSINUSITIS

1. Medical Condition

Sinusitis refers to inflammation of the sinuses only while the more clinically relevant term should be Rhinosinusitis which is the inflammation of both the sinus and the nasal mucosa. Rhinosinusitis is a frequently occurring disease, with significant impact on athletic performance in both competition and training. There are two types of rhinosinusitis: acute bacterial rhinosinusitis (ABRS) and chronic rhinosinusitis (CRS).

2. Diagnosis

A. Medical History

ABRS is a clinical diagnosis with upper respiratory tract infection (URTI) signs and symptoms of more than 7 days duration without improvement or improvement followed by worsening. The two main causative agents of ABRS are *Streptococcus pneumoniae* and *Haemophilus influenzae*. CRS is an inflammatory disease involving the nasal mucosa and paranasal sinuses. Symptoms of CRS are usually of lesser intensity than those of ABRS, but their duration exceeds the 4 weeks commonly used as the upper limit for the diagnosis of ABRS. The main causative agents of CRS are *Streptococcus pneumoniae*, *Haemophilus influenzae* and anaerobes. A diagnosis of CRS is probable if 2 or more major symptoms are present for at least 8 to 12 weeks along with documented inflammation of the paranasal sinuses or nasal mucosa.

B. Diagnosis Criteria

ABRS Symptom Table

Facial **P**ain/pressure/fullness
Nasal **O**bstruction
Nasal purulence/discolored postnasal **D**ischarge
Smell: Hyposmia/anosmia

The diagnosis of ABRS requires the presence of ≥ 2 PODS symptoms, one of which must be O or D, and symptom duration of >7 days without improvement (Desrosiers et al, 2011).

The diagnosis is based on history and physical examination. Nasal culture and sinus aspirates are not necessary. Radiological imaging is not required for uncomplicated ABRS.

Chronic Rhinosinusitis (CRS)

CRS is diagnosed on clinical grounds but must be confirmed with at least 1 objective finding on endoscopy or computed tomography (CT) scan.

CRS Symptom Control

Facial **C**ongestion/fullness

Facial **P**ain/pressure/fullness

Nasal **O**bstruction

Nasal purulence/discolored postnasal **D**ischarge

Smell: Hyposmia/anosmia

A diagnosis requires at least 2 CPODS present for 8-12 weeks, plus documented inflammation of the paranasal sinuses or nasal mucosa. CRS is a clinical diagnosis and must be confirmed with at least 1 objective finding such as nasal purulent nasal polyposis, on endoscopy or sinus opacification on CT scan. Objective testing is necessary to rule out the differential diagnosis of migraine, dental abscesses, allergic rhinitis and atypical facial pain syndromes.

3. Good Medical Practice

A. Name of Prohibited Substance:

Oral decongestant (pseudoephedrine) (PSE) and 1st generation (sedating) anti-histamine combination (if available). The use of PSE is mainly reserved for bouts of acute exacerbations of sinusitis. An athlete with well-managed CRS should not have a regular need for the administration of PSE. Please note that PSE is effectively prohibited "in-competition" ONLY (see Caution below). A TUE is not required for out of competition use.

- Route: Oral
- Frequency: As indicated on the manufacturer's label.
- Antihistamine preparations are not prohibited
- Although each case must be judged individually, it would be highly unlikely for a TUE to ever be granted for suprathreshold dosages of PSE as other reasonable treatment alternative exist.
- Recommended duration: Up to 8 weeks as needed for symptom control.

CAUTION: Pseudoephedrine is prohibited in-competition at a urinary concentration above the threshold of 150µg/mL (as of January 1, 2010). The threshold level has been established based on the intake of therapeutic doses of PSE, defined as a maximum daily dose of 240mg PSE taken either as:

- 4 daily administrations (one every 4-6 hours) of a 60mg pill (or 2x30mg pills), or

- 2 daily administrations (one every 12 hours) of a 120mg pill (extended release), or
- 1 daily administration of a 240mg pill (extended release). The TUE application should demonstrate the presence of the condition as evidenced by history and physical examination in addition to failed trials of other non-prohibited substances.

Although rare, it is possible that the established threshold level may be reached by some individuals taking therapeutic dosages, particularly 6-20 hours after the extended release pill. **Therefore WADA advises that athletes stop taking PSE pills 24 hours before the in-competition period.**

B. Name of Prohibited Substance:

Systemic Glucocorticoids (GCs)

A short course of oral preparations of GCs: (eg. prednisone 30-40 mg) may be necessary in chronic rhinosinusitis (with or without polyps) either for initial control and early disease management, or for the treatment of recurrences or exacerbations. Ongoing treatment with systemic GCs is rare unless complicated nasal polyposis is present. Oral GCs are prohibited in-competition only.

- Route: Oral
- Frequency: OD
- Recommended duration: short finite period of time such as 4-5 days.
- TUE requirements: A TUE is required for use of oral glucocorticoids in-competition. The application should demonstrate a clear diagnosis of chronic rhinosinusitis.

It is quite rare that intravenous glucocorticoids may be used for the treatment of sinusitis. Although the use of an intravenous infusion is not prohibited in the course of hospital admissions, it would still be necessary to acquire a TUE for any prohibited substance that may be delivered via the intravenous route. Systemic glucocorticoids are prohibited only during the in-competition period.

4. Other Non-Prohibited Alternative Treatments

- Ensure adequate hydration.
- Antibiotics such as amoxicillin / clavulanate. Second line fluoroquinolones may be useful in cases of bacterial resistance or complication. Anaerobe coverage in CRS is recommended.
- Topical intranasal glucocorticoids may help improve resolution rates and improve symptoms.

- Analgesics such as acetaminophen or non-steroidal anti-inflammatories may provide symptom relief.
- Saline irrigation and topical nasal decongestant spray or drops (e.g. Xylometazoline) may provide symptom relief.
- Mucolytics, anti-histamines and leukotriene modifiers may be helpful in CRS
- Referral to a specialist should occur if nasal polyps are present.
- Surgery may be beneficial and indicated for athletes who have failed medical therapy
- Allergy testing may be indicated for those athletes with CRS who may have an atopic component.

5. Consequences to Health if not treated

Failure to treat sinusitis or a failed response to treatment can lead to chronic cough, orbital complications or intracranial neurological complications including blindness, ophthalmitis, meningitis, brain abscess, or osteomyelitis.

6. Treatment Monitoring

Treatment is monitored by the treating physician to ensure efficacy of the treatment regimen.

7. TUE Validity and Recommended Review Process

A TUE is required for the use of pseudoephedrine and for oral glucocorticoids in competition only. As treatment of sinusitis tends to be short term, the TUE duration is also short in duration.

8. Any Appropriate Cautionary Matters

An athlete that fails to respond to therapy or with severe symptoms should be referred to a otolaryngologist specialist for investigation of other underlying conditions. Warning symptoms and signs include:

- Unusual severe symptoms
- Systemic toxicity
- Altered mental status
- Severe headache
- Swelling of the orbit or change in visual acuity

9. References

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