

## FSG 1900-01 MEDICATIONS AND AIRCREW

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**References:**

- A. B-GA-100-001/AA-000 National Defence Flying Orders
- B. CF Drug Benefit List
- C. FSG 1400-01 Mental Health Disorders
- D. FSG 300-01 Temporary Flying Restrictions
- E. FSG 1400-04 Fatigue Management in the Royal Canadian Air Force
- F. FSG 900-01 Diabetes in Aircrew
- G. FSG 600-01 Aircrew Cardiovascular Risk Screening

**Record of Amendments approved by AUMB**

Date yyyy-mm-dd	Change/Reason
2016-12-05	Page 5/Para 12/Antibiotics Grounding period for antibiotics standardized at 4 days. Harmonized for short or long-term use.
2016-12-05	Page 6/Para 22/NSAIDs Celecoxib approved for aircrew for short or long-term use. Previous concerns about adverse cardiovascular effects recently clarified.
2016-12-05	Page 8/Paras 33-36/Sedatives/Hypnotics Guidelines for operational use clarified and harmonized with FSG 1400-03. Grounding period for zopiclone increased to 12 hrs

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<p>2016-12-05</p>	<p>Page 8/Para 38/Hypertension</p> <p>Recommendation for thiazide diuretics changed to long-acting preparations such as chlorthalidone. Recent data shows limited efficacy for short-acting preparations such as hydrochlorothiazide.</p>
<p>2023-03-09</p>	<p><u>General</u></p> <p>Contact information for CFEME Medical Consult Services updated.  Medication are grouped by medical specialty area and moved to an Annex  Medications listed in other policies or orders have been added.  Clarification of grounding/ungrounding recommendations made for some previously approved medications where prior wording was ambiguous.  Section on Health Supplements and Complementary or Alternative Medicine added.</p> <p><u>New Additions</u></p> <p>Antihistamines: Rupatidine (Rupall); Bilastine (Blexten)  Sublingual Immunotherapy Standardized Allergen Extracts: White Birch (Itulatek);  Grass Pollen (Oralair)  Contraceptives: hormonal subdermal implants included in permissible options  Emergency contraception: Ulipristal acetate (Ella)  HIV PrEP: Emtricitabine/tenofovir disoproxil fumarate (Truvada)  Topical and systemic decongestant: grounding guidance added</p>
<p>2024-06</p>	<p><u>Updated recommendations</u></p> <p>Diabetes medication section updated to reflect changes to FSG 900-01 as per 2024 revision approved at March 2024 AUMB</p> <p>Asthma medication section updated to provide additional clarification to investigations and flight restrictions</p> <p><u>New additions</u></p> <p>Disease Modifying Anti-Rheumatic Drugs (DMARDs) section updated with more detailed recommendations regarding the use of methotrexate  Section on Biologic Medication and Biosimilars added.  Creatine monohydrate powder added to Health Supplements Section</p>

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## GENERAL INFORMATION

1. These Guidelines have been developed to assist Flight Surgeons and Basic Aviation Medicine Providers (BAvMed) in determining the aeromedically acceptable use of medications for RCAF aircrew. Each prescribing situation is unique in terms of the illness, the individual, and the drug, and it is difficult to legislate the sensible use of medications in aircrew. Determining whether a medication may be used in aircrew on flying duties and what restrictions may be appropriate should be based on a sound knowledge of the drug actions and pharmacokinetics, adverse effects, and the operational environment including possible contingency situations. Aircrew are prohibited from self-medication under ref A Vol 1, Chap 9, pp 2-4.
2. These Guidelines are revised periodically and are reviewed and approved by the Aerospace and Undersea Medical Board (AUMB). The Guidelines are interfaced with the CF P&T Committee through the RCAF Surgeon/AMA. Aircrew should be prescribed medications available within the CAF Formulary (ref B) whenever possible. These guidelines do not constitute a drug benefit list.
3. When determining appropriate flying restrictions, the Flight Surgeon/BAvMed Provider should consider whether he/she would be comfortable flying on the various missions that the aircrew member will be serving on while taking the prescribed medication, and that all possible risk mitigation actions to minimize the risk have been initiated.
4. If in doubt about prescribing any medication for aircrew, Flight Surgeons and BAvMed Providers should obtain advice from Aeromedical Standards (ASCS) at the Air Division Surgeon's office or from the Military Medicine Section at Canadian Forces Environmental Medicine Establishment (CFEME).
5. One of the functions of the Flight Surgeon is to brief their squadron aircrew and ground crew on the appropriate use and precautions in the use of drugs, including over-the-counter (OTC) medications and herbal preparations, which aircrew may not consider as "drugs". These guidelines may be helpful in the preparation of such briefings.
6. Aircrew may also be prescribed medications from sources other than their Flight Surgeon (e.g. by Dental Officers or Consultants) and aircrew should be briefed on the requirement to consult their Flight Surgeon/BAvMed Provider prior to returning to flying duties while taking medication prescribed from any source.

## DRUGS, DISEASES AND FLIGHT SAFETY

7. In prescribing any medication for aircrew, the Flight Surgeon/BAvMed Provider should consider both the nature of the disease process and the medication. Sometimes, the disease or medical problem itself will preclude flying rather than the potential side-effects of the medication. A simple example is the use of topical nasal steroids in allergic rhinitis. It's not the medication, but rather the degree of upper respiratory congestion and systemic

atopic symptoms that are the determining factors. For example, inability to clear the ears on descent can cause considerable pain during a very critical portion of the flight and be a greater concern than the side-effects of a topical nasal steroid.

8. Any medication may have effects of concern in the aviation environment. The possibility of an idiosyncratic reaction must be kept in mind when introducing any medication for aircrew. Adverse effects that may be merely annoying on the ground can produce serious aeromedical consequences in air operations.
9. When prescribing a medication for aircrew, physicians should be familiar with the product monograph including pharmacokinetics and published adverse effects. For drugs with CNS or other side-effects of aeromedical concern, aircrew should not return to flight duties until at least five-half lives have passed after stopping the medication. With respect to adverse effects, the following possibilities should be considered:
  - a. **Acute incapacitation** – Is there any possibility that this drug, in this situation, might cause incapacitation; anaphylaxis, acute vertigo, hypotension, arrhythmias, diplopia, etc.; and,
  - b. **Performance decrements** – Performance decrements may occur through a direct effect on the CNS or through a non-CNS adverse effect (e.g. GI upset, which can be distracting enough to cause a critical lapse of attention). Drugs with obvious CNS side-effects (e.g. minor tranquilizers) are obvious exclusions for aircrew duty, but subtle side-effects from other medications may also cause serious flight safety problems. For example, gastrointestinal upset from erythromycin which caused mild nausea and resulted in anxiety, hyperventilation and an air emergency for a student pilot at 2 CFFTS in Moose Jaw.
10. When considering the potential safety implications of both drugs and illness, there are three major areas of concern:
  - a. **Flight Safety** – Does the medication or the illness have the potential to compromise flight safety? If so, the aircrew must be grounded.
  - b. **Mission** – In military air operations, successful completion of the mission may be of utmost importance, whether it is a tactical fighter sortie during hostilities or a helicopter search and rescue mission to a sinking freighter in peacetime. Flight mission completion is a top operational priority that must be considered when prescribing medications to aircrew.
  - c. **Individual Health Compromise** – The third major concern is the potential effects of continuing flight duties while taking the medication on the health and well-being of the individual aircrew member. For example, a pilot with early ankylosing spondylitis

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would be better to be restricted from rotary wing operations where back discomfort due to posture and vibration is a very common problem, than to continue flying in the environment with a medication even though aeromedically acceptable. Special consideration must also be taken with pregnant or nursing female aircrew members.

## **ANNEX A – MEDICATION CONSIDERATIONS AND RECOMMENDATIONS**

The following sections provide general guidelines for specific drug groups listed by specialty area. Comments on health vitamins, supplements and alternative medicines are found at the end of the list.

It is impossible to cover every drug available. If you have any doubts or concerns regarding a particular prescribing situation be sure to discuss the problem with one of the physicians on staff at ASCS or CFEME. It is imperative that medication not previously cleared for use in RCAF aircrew not be used prior to obtaining clearance.

NOTE: the term aircrew unless otherwise specified refers to all RCAF aircrew. Exceptions where ground based aircrew may use the medication without duty restriction (such as in a live controlling position) will be stated.

### **II. ALLERGY MEDICINE**

#### **A. ANTIHISTAMINES**

- i) The anticholinergic and sedative effects of the older generation anti-histamines (eg chlorpheniramine) make them unsuitable for use in aircrew. The sedative interactive effects with alcohol are potentiating and potentially dangerous.
- ii) The following second generation H1 antagonist antihistamines have not been demonstrated to have anticholinergic or CNS effects:
  - (1) loratadine (Claritin)
  - (2) desloratadine (Aerius)
  - (3) fexofenadine (Allegra)
  - (4) rupatadine (Rupall) and
  - (5) bilastine (Blexten)

They may be used in aircrew with the following provisions:

- (1) An initial 3 day grounding period;
  - (2) Review with flight surgeon to assess for adverse effects prior to return to flight duty;
  - (3) No alcohol consumption within a 24 hour period prior to use of the antihistamine.
  - (4) After the initial assessment, grounding is not required for recurrent intermittent use.
- ii) Clemastine (Tavist) and cetirizine (Reactine) may produce drowsiness and CNS side-effects and are not recommended as first line antihistamines for aircrew, but may be considered as an exceptional use after a failed trial of loratadine, desloratadine, or fexodenadine with the following provisions:

- (1) An initial 8 day grounding period;
  - (2) Review with flight surgeon to assess for adverse effects prior to return to flight duty;
  - (3) No alcohol consumption within a 24 hour period prior to use of the antihistamine.
  - (4) After the initial assessment, grounding is not required for recurrent intermittent use.
- iii) Topical antihistamine sprays for allergic rhinitis do not require a flying restriction
- iv) Topical antihistamine drops for allergic conjunctivitis do not require a flying restriction

## **B. ALLERGY DESENSITIZATION**

### **1. SUBCUTANEOUS IMMUNOTHERAPY (SCIT)**

- (1) Aircrew require a 12 hour grounding following initiation of desensitization therapy and following each administration of an escalating dose. Return to flying duties without restriction follows only if there are no adverse systemic effects. Four hour grounding is required following all maintenance doses of desensitization therapy with return to flying duties only if there are no side effects (as per FSG 300-01 Temporary Flying Restrictions).

Note: This is not to be confused with subcutaneous immunoglobulin therapy (SCIG) which is generally disqualifying due to the side effect profile and the underlying condition.

### **2. SUBLINGUAL IMMUNOTHERAPY (SLIT)**

- (1) Oral allergy immunotherapy (SLIT) is an alternate approach for some allergens to injection therapy. The risk of serious systemic reactions is lower than SCIT and doses can be self-administered. Mild to moderate local reactions are common, but generally occur within 10 minutes of ingestion and abate within 1 hour.
- (2) The following Standardized Allergen Extracts have been reviewed for use in aircrew:

- (a) Standardized Allergen Extract, White Birch (Itulatek); and
- (b) Grass Pollen Allergen Extract (Oralair)

They may be used in aircrew with the following requirements:

- (a) An initial 7 day grounding period after the first dose;

- (b) If no moderate or severe reactions or side effects, may be returned to flight duty providing:
  - (i) Epi-pen must be carried on their person while engaged in aircrew duties;
  - (ii) At least 1 hour between routine dose and flight;
  - (iii) Each dose escalation requires a 4 hour grounding period

### III. ANESTHESIA AND PAIN MEDICINE

#### A. ORAL ANALGESICS

- i) For simple analgesia (e.g. relief of musculoskeletal aches, headache, etc), acetaminophen is preferable for use by aircrew and requires no flying restriction.

##### 1. NSAIDS

- (1) ASA and other non-steroidal anti-inflammatory drugs (NSAIDs), which inhibit prostaglandin synthesis, all have potentially serious side-effects on both the GI tract and the CNS. CNS effects include sedation, headaches, and decreased vigilance. Indomethacin generally produces the most pronounced CNS effects. Hypersensitivity reactions (e.g. acute bronchospasm) may occur with any of the NSAIDs in sensitive persons. Increases in hepatic transaminases progressing to frank hepatitis may also occur.
- (2) GI effects are common and vary from non-specific, distracting GI upset to gastritis progressing to ulceration. For aircrew requiring other than brief NSAID treatment (up to 1 week), concurrent GI protection with a proton-pump inhibitor or use of the COX-2 NSAID celecoxib is recommended.
- (3) Aircrew should be briefed on the potential GI side-effects of ASA and NSAIDs and be cautioned on self- medicating with OTC ASA/NSAIDs.
  - (a) This medication class can be used by all aircrew with the following provisions:
    - (i) The condition for which the medication is being used does not cause interference with the safe performance of duties;
    - (ii) The first week of use should be taken after duty shift is complete and at least 10 hours prior to the next;
    - (iii) If no side effects are experienced after the first week of use, then no restriction for aircrew duty is required for occasional intermittent or ongoing use;
    - (iv) If aircrew require NSAIDs for prolonged periods (longer than two weeks), NSAIDs should be prescribed with appropriate GI protection with a proton pump inhibitor such as pantoprazole or with misoprostol.

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- (v) Oxicams and celecoxib are acceptable therapeutic choices for either short or long term use.

### 2. MUSCLE RELAXANTS

- (1) Muscle relaxants (e.g. Norflex) must not be used by any aircrew on flying duties. Muscle relaxants may have long half-lives, and aircrew may require continued grounding for several days (i.e. at least five half-lives) after being prescribed such medication.

### 3. NARCOTICS

- (1) The use of any drug containing a narcotic requires a grounding period sufficient to ensure the drug is fully metabolized based upon the elimination half-life.

## B. REGIONAL AND GENERAL ANESTHETICS (as per FSG 300-01)

- i) Grounding for longer than listed below may be necessary after regional or general anaesthetic due to the medical reasons for administration of the anaesthetic, or type and extent of surgery. If there are side effects from the anaesthetic then an aviation medicine provider should make an individualised decision on flight restriction. Administration of the anaesthetic itself requires grounding, for:
  - (1) General, spinal or epidural anaesthetic. Minimum three days grounding and then may return to flying duties if no adverse effects;
  - (2) Major peripheral nerve blocks. Minimum 48 hrs grounding and then may return to flying duties if no adverse effects;
  - (3) Short-acting IV sedative (e.g., midazolam, ketamine, fentanyl, etc). Minimum 72 hr grounding and then may return to flying duties if no side effects; and
  - (4) Local or regional anaesthetic for minor procedures including dental. Minimum 12 hr grounding and then may return to flying duties if no adverse effects.

## IV. CARDIOLOGY

### A. ANTI-HYPERTENSIVES

- i) The initiation of pharmacologic therapy for hypertension requires that aircrew be grounded until the blood pressure is reasonably controlled and the adverse effects of treatment assessed. This will generally require a grounding of 2-4 weeks. Addition of new medications will require an additional grounding period of equivalent length.

- ii) For aircrew routinely exposed to a high G environment (2.5 + Gz or higher) an operational flying evaluation with a standards officer to assess G tolerance within the aircraft operational envelope may be required prior to resumption of unrestricted flight duty.
- iii) The introduction of antihypertensive medications for RCAF aircrew is recommended as follows:

1.     Thiazides

Thiazide diuretics have the longest track-record as antihypertensive medications in aircrew and are recommended as initial treatment of hypertension in most aircrew. Based on data showing improved blood pressure control over shorter acting agents a long-acting thiazide such as chlorthalidone is recommended. Thiazides may induce undesirable metabolic adverse effects including hypokalemia, hyperuricemia, hyperlipidemia, and glucose intolerance. These potential adverse effects must be closely monitored. Extending thiazide dosage beyond 25 mg daily of chlorthalidone or 50 mg of hydrochlorothiazide is not recommended because it does not increase therapeutic efficacy, and may increase adverse effects.

- (a) This medication class is approved for use in all aircrew both alone and in combination with other approved anti-hypertensives without flight restriction after the initial grounding period. Complete acclimation to an antihypertensive medication may take 2-4 weeks. Ungrounding can occur after 2 weeks, provided:
  - (i) The blood pressure is adequately controlled
  - (ii) The aircrew is not experiencing any side effects
  - (iii) Orthostatic vital signs are within normal limits

2.     ACE inhibitors/Angiotensin receptor blockers

Angiotensin converting enzyme inhibitors or angiotensin receptor blockers may be used as initial monotherapy for hypertension. With a vasodilator action, ACEi/ARBs may reduce G-tolerance, so a G tolerance assessment is necessary for aircrew routinely exposed to a high G environment. ACEi/ARBs may be used in RCAF aircrew for the treatment of hypertension without requiring an operational flying restriction. Dual therapy with ACEi or ARB plus thiazide is also permitted without requiring a flying restriction.

- (a) This medication class is approved for use in aircraft control, transport, and rotary wing aircrew both alone and in combination with other approved anti-hypertensives without flight restriction after the initial grounding period of 2-4 weeks. Ungrounding can occur after 2 weeks, provided:
  - (i) The blood pressure is adequately controlled
  - (ii) The aircrew is not experiencing any side effects

(iii) Orthostatic vital signs are within normal limits

(b) This medication class is approved for use in aircrew regularly exposed to flying in a high G environment (exposure to 2.5 + Gz or higher) both alone and in combination with other approved anti-hypertensives without flight restriction after the initial grounding period of 2-4 weeks, provided:

(i) The blood pressure is adequately controlled

(ii) The aircrew is not experiencing any side effects

(iii) Orthostatic vital signs are within normal limits

(iv) Repeat G-tolerance assessment has been carried out successfully.

### 3. Calcium channel blockers

For aircrew, long acting dihydropyridine calcium channel blockers (e.g. amlodipine, felodipine, nifedipine) may be used alone or in combination therapy with a thiazide or ACE inhibitor without requiring an operational flying restriction. CCBs have not been evaluated for effects on G-tolerance, and because of their vasodilatory effect, they should not be used as first line agents for aircrew exposed to a high G environment.

(a) This medication class is approved for use in aircraft control, transport, and rotary wing aircrew both alone and in combination with other approved anti-hypertensives without flight restriction after the initial grounding period of 2-4 weeks. Ungrounding can occur after 2 weeks, provided:

(i) The blood pressure is adequately controlled

(ii) The aircrew is not experiencing any side effects

(iii) Orthostatic vital signs are within normal limits

(b) This medication class is approved for use in aircrew regularly exposed to flying in a high G environment (exposure to 2.5 + Gz or higher) both alone and in combination with other approved anti-hypertensives without flight restriction after the initial grounding period of 2-4 weeks, provided:

(i) The blood pressure is adequately controlled

(ii) The aircrew is not experiencing any side effects

(iii) Orthostatic vital signs are within normal limits

(iv) Repeat G-tolerance assessment has been carried out successfully.

### 4. Beta-blockers

Beta-blockers may be indicated if clinical assessment suggests a significant adrenergic input to the hypertension. Because of their central beta- blocking effect and potential effect on performance, a beta-1 selective agent such as atenolol or acebutalol is preferred.

- (c) This medication class is approved for use in non-pilot aircrew both alone and in combination with other approved anti-hypertensives without flight restriction after the initial grounding period. Complete acclimation to an antihypertensive medication may take 2-4 weeks. Ungrounding can occur after 2 weeks, provided:
  - (i) The blood pressure is adequately controlled
  - (ii) The aircrew is not experiencing any side effects
  - (iii) Orthostatic vital signs are within normal limits
  
- (d) Pilots treated with beta-blockers must be assigned an A3, restricted from solo tactical fighter and tactical helicopter operation. Ungrounding and return to flight with the A3 restriction can occur after 2 weeks, provided:
  - (i) The blood pressure is adequately controlled
  - (ii) The aircrew is not experiencing any side effects
  - (iii) Orthostatic vital signs are within normal limits

## B. DYSLIPIDEMIA MANAGEMENT

- i) Updated guidelines for cardiovascular risk screening are promulgated as Flight Surgeon Guideline 600-01 Aircrew Cardiovascular Risk Screening and 900-01 Metabolic Syndrome and Diabetes in Aircrew and should be followed for aircrew.
  - 1. Statins  
If medication is required for dyslipidemia, treatment with an HMG CoA reductase inhibitor (statin) is recommended. This medication class can be used in all aircrew without flight restriction after a grounding period of one week.
  
  - 2. Fibrates  
  
Fibrates are no longer recommended for the prevention of atherosclerotic cardiovascular disease but are recommended for the treatment of hypertriglyceridemia. This medication class can be used in all aircrew without flight restriction after a grounding period of one week.
  
  - 3. Ezetimibe (Ezetrol)  
  
Inhibits cholesterol absorption and works synergistically with statins to reduce LDL cholesterol. Ezetimibe is generally well tolerated, with GI symptoms such as flatulence being the most common side-effect. Occasionally severe diarrhea, pancreatitis, myalgias may occur. This medication can be used in all aircrew without flight restriction after a grounding period of one week.

4. Niacin

A recent large trial failed to confirm efficacy in reducing cardiovascular events, and because of this, along with troublesome adverse effects, niacin is not recommended for dyslipidemia treatment in aircrew

5. PCSK9

Inhibitors such as evolocumab (Repatha) may be considered for aircrew who do not tolerate statins or fail to reach targets with statin and ezetimibe. The medication can be used after a grounding period of two weeks.

**V. DERMATOLOGY**

**A. HAIR GROWTH STIMULANTS**

1. Topical Minoxidil (Rogaine)

Rogaine (minoxidil) is not supplied by the CF.

- (a) Aircrew other than pilots may use Rogaine after a 7 day grounding period to ascertain any potential side-effects without a flying restriction.
- (b) Pilots in transport and rotary wing environment who obtain topical minoxidil require a 7 day grounding period with Flight Surgeon/BAvMed Provider review before returning to flight duties.
- (c) Pilots flying in high G environment (fighter/fast jet, Harvard II trainer) will require a repeat G- tolerance assessment following the initial grounding period

2. Finasteride (Propecia)

Finasteride is being promoted as another agent to regenerate hair growth and aircrew may approach the Flight Surgeon about its use. It is not supplied by the CF. Aircrew using this medication should initially be grounded for 7 days for observation.

**B. ACNE and ROSACEA TREATMENTS**

1. Tetracyclines Other Than Minocyclin

Low dose antibiotics - can be used in all aircrew after an initial 4 day grounding period without flight restriction.

2. Minocycline

Should be avoided in aircrew due to the high incidence of vestibular side effects

3. Accutane

All aircrew using isotretinoin must remain under the close supervision of the Flight Surgeon in consultation with a dermatologist (temporary G4 required). Caution should be used in prescribing isotretinoin therapy for aircrew that use facemasks routinely while flying

(2) Aircrew other than pilot may use isotretinoin without restriction after a 7 day initial period of grounding.

(3) During the period of treatment, pilots using isotretinoin must be given a temporary A3 category, restricted to fly with or as copilot after a 7 day initial period of grounding.

C. ANTIFUNGAL AGENTS FOR ONYCHOMYCOSIS

i) Terbinafine (Lamasil), fluconazole (Diflucan), and itraconazole (Sporonox) may be used to treat fungal infections of the nails in aircrew. Pulsed dosage is the preferred regimen. GI upset is the most common side-effect. Aircrew should be grounded for 48 hours on the initiation of treatment and with each pulse.

**VI. ENDOCRINOLOGY**

A. THYROID TREATMENT

i) Hyperthyroid - Patients with hyperthyroidism must be grounded on diagnosis of hyperthyroidism. If thyroid suppression treatment with propylthiouracil or methimazole is undertaken, aircrew must remain grounded until a euthyroid state has been re-established.

(1) Aircrew other than pilot may be returned to flying duties under the close supervision of the Flight Surgeon, but require a geographic limitation from deployments greater than 8 weeks to allow appropriate follow-up.

(2) Pilots of tactical fighter and tactical helicopter aircraft must remain grounded during the full course of anti-thyroid suppression. I<sup>131</sup> therapy may be preferred therapy. Aircrew must remain grounded during therapy and until clinically and biochemically euthyroid following treatment.

ii) Hypothyroid - Patients may be returned to flying duties while using thyroid replacement hormones once a state of clinical and biochemical euthyroidism has been established (i.e. TSH normal, no signs or symptoms)

B. DIABETES MEDICATIONS

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- i) Detailed directions about the investigation and management of diabetes in aircrew are provided in Ref F.
- ii) The following table excerpt from Annex A of Ref F outlines the recommended stepwise approach to initiating medications in diabetic aircrew, with the preliminary grounding period.

Lifestyle management	Diet, Exercise, Education	No grounding (provided HbA1c < 8)
Add Biguanide	Metformin	14 days
Add DPP4i	Linagliptin, Saxagliptin, Sitagliptin	30 days
Add SGLT2i	Canagliflozin, Dapagliflozin, Empagliflozin	30 days
Discontinue DPP4i Add GLP1a	Semaglutide, Liraglutide	30 days
Add Basal Insulin	Glargine, detemir	Minimum 90 days review by ASCS -specialist consult mandatory
Add Bolus Insulin (eg prandial/sliding scale)	Lispro, Aspart	Generally disqualifying -Minimum 180 days -review by ASCS -specialist consult mandatory

**C. STEROIDS**

- i) In general, systemic corticosteroids are not compatible with flight duties for any aircrew.
- ii) Inhaled and topical intranasal corticosteroids are acceptable without requiring an operational flying restriction.
- iii) Anabolic steroids (eg testosterone) prescribed for deficiency syndromes are acceptable for unrestricted flying duties, after an initial grounding period appropriate to the pharmacokinetics of the formulation used, and monitoring to ensure levels in therapeutic range are not exceeded.
- iv) Anabolic steroid use for other than deficiency syndromes (e.g. body building) is not permitted in aircrew.

**VII. GASTROENTEROLOGY**

**A. ACID SUPPRESSION THERAPY**

- i) Active GI ulcer disease requires grounding. Aircrew suspected of having active ulcers should undergo endoscopy to include biopsy for *H. pylori*. Active ulcers should be treated with a proton-pump inhibitor such as pantoprazole which produces the most rapid healing and, where *H. pylori* has been demonstrated, eradication should be undertaken with appropriate combined therapy. If due to *H. pylori*, successful eradication should be confirmed with urea breath testing or *H. pylori* stool antigen before returning aircrew to flight duties.
- ii) For dyspeptic symptoms without a demonstrable ulcer, for reflux symptoms, and for "maintenance" therapy after ulcer healing, high potency antacids (e.g. Maalox TC; Mylanta II), sulcralfate, ranitidine in an HS dosage regimen or a proton pump inhibitor may be used by aircrew.
- iii) For gastro-esophageal reflux disease (GERD), PPIs such as pantoprazole are most efficacious and may be used for aircrew with no grounding requirement.

**B. ANTI-MOTION SICKNESS DRUGS**

- i) Airsickness is common during training, but remits in most trainees as they become familiar with the flight environment. In some, symptoms persist and additional desensitization is required, through a formal airsickness management program, which may include the use of anti-motion sickness medications, ground based desensitization training and/or habituation flights. For aircrew in training, including student pilots, Flight Surgeons may include short term use of anti-motion sickness

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medications (e.g. promethazine and dextroamphetamine) as part of the desensitization program.

- ii) Antihistamines such as dimenhydrinate (Gravol) have mild to moderate efficacy against motion sickness. They cause sedation and a performance decrement lasting several hours and are not approved for aircrew actively performing aircrew duties.
- iii) Scopolamine may produce significant side-effects including drowsiness and other CNS symptoms, and may cause visual problems with impairment of accommodation. Absorption of transdermal scopolamine is variable from person to person, and even in the same person under different conditions, so side-effects may be variable and unpredictable. It is not approved for use in aircrew.
- iv) Promethazine is more efficacious than dimenhydrinate, but causes more significant and prolonged drowsiness and performance decrements. This can be prevented by the concurrent administration of dextroamphetamine 10mg. Dextroamphetamine also has anti-motion sickness properties, so for most aircrew, the combination of promethazine 25mg orally plus dexamphetamine 10mg taken two hours before flight is efficacious without producing sedation during the flight.
- v) Currently, no anti-motion sickness medications are considered safe enough for ongoing routine use by flight deck aircrew during flight duties. Some operational flying environments are particularly provocative (eg tactical Aurora non-flight deck positions), and motion sickness may be a chronic problem requiring medication for non-flight deck aircrew.
- vi) For deployed maritime helicopter aircrew in whom sea-sickness is a problem, the use of dimenhydrinate or promethazine 25mg with or without amphetamine 10mg may also be used with an 8 hour window to flight duty.
- vii) Non-flight deck aircrew other than SAR techs may use approved anti-motion sickness medications under the direct supervision of their Flight Surgeon after discussion with ASCS at 1 CAD Winnipeg.

### C. ANTI-DIARRHEAL AGENTS

- i) Imodium may be used for mild diarrheal symptoms in transport aircrew without a flight restriction.

## VIII. GENDER, SEXUALITY AND REPRODUCTIVE HEALTH

### A. CONTRACEPTIVES

- i) Hormonal based contraception choices should be selected based on medical suitability, patient preference, and consideration of aircrew operational factors. Changing time zones frequently may interfere with maintaining regular dosing;

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personal protective equipment and operational demands may impact use of patch; and longer term deployments or operations may mean that complete menstrual suppression is preferred. Discussion of health risks related to venous thromboembolism for example, may also be impacted by increased VTE risk due to the flight environment.

(1) Hormonal contraception options including oral formulations, skin patches, subdermal implants and vaginal ring: are approved for use in aircrew with the following requirements:

- (a) Aircrew should be grounded for 7 days on initiation of medication; and
- (b) Grounded for 3 days on a change of dosage or product.

(2) Intrauterine devices require a 7 day grounding period post insertion.

(3) Depo-Provera can be considered on a case-by-case basis after discussion with ASCS.

ii) Emergency contraception options:

(1) Levonorgestrel 1.5 mg (Plan B): for use within 74 h of unprotected intercourse; requires a 24 to 48 hour grounding period based upon side effects experienced

(2) Ulipristal acetate (Ella): for use within 5 days of unprotected intercourse; requires a 24 to 48 hour grounding period based upon side effects experienced

### B. HORMONE REPLACEMENT THERAPY

i) When clinically recommended or prescribed by an endocrinologist or OB/GYN, hormone replacement therapy is acceptable for female aircrew with seven day grounding on initiation of therapy.

### C. VAGINAL HEALTH

i) Uncomplicated Vaginal Candidiasis - Oral fluconazole (Diflucan) as a single oral dose provides an effective treatment for vaginal candidiasis. A 24 hour period of non-aircrew duties is required

### D. ERECTILE DYSFUNCTION

i) Pilots and other active duty aircrew using the PDE5 inhibitors sildenafil (Viagra) or vardenafil (Levitra) should be grounded for 48 hours after each use (partly because of concerns over effects on colour vision).

## NOT CONTROLLED WHEN PRINTED

- ii) The use of tadalafil (Cialis) with its longer-half-life (18 hrs) is not recommended in aircrew actively flying

### E. HSV TREATMENT AND SUPPRESSION

- i) For aircrew with frequently recurring herpes infections, long-term suppression or treatment of an acute outbreak by the administration of an oral antiviral agent is approved with an initial 4 day grounding period. If no side effects are experienced, then no grounding is required for intermittent or long term use.

### F. BENIGN PROSTATIC HYPERTROPHY

- i) Medications may be recommended by urological consultants for aircrew who develop obstructive symptoms associated with benign prostatic hypertrophy.
- ii) 5 alpha reductase inhibitors – finasteride (Proscar) or dutasteride (Avodart). These block conversion of testosterone to dihydrotestosterone which is required for development and maintenance of BPH.
- iii) Alpha blockers –alfuzosin, doxazocin, tamsulosin, and terazocin cause relaxation of smooth muscle tone in the bladder neck, capsule and prostate. Adverse effects may include dizziness, orthostatic hypertension and rarely, syncope. Aircrew must be grounded during the first two weeks of treatment with alpha blockers. If there are no adverse effects, non-pilot aircrew may be returned to usual duties. Pilots require a restriction to fly with or as copilot, unfit fast jets, while taking alpha blockers for BPH

### G. HIV PRE-EXPOSURE PROPHYLAXIS

- i) Guidance for medications in this section refers only to the indicated use for HIV pre-exposure prophylaxis (PrEP) and does not apply to the use of medication for treatment of HIV infection. Assessment of aeromedical fitness for trained aircrew with HIV infection is carried out on a case-by-case basis with review at ASCS
- ii) Regular follow-up and monitoring is required for aircrew receiving PrEP and a geographic factor limitation is recommended in order to permit monitoring requirements to be met.
- iii) Emtricitabine/tenofovir disoproxil fumarate (Truvada) for HIV PrEP is approved for use in all aircrew with the following requirements:
  - (1) Aircrew must be grounded for 14 days upon initiation of the medication;
  - (2) Review with flight surgeon to assess for adverse effects prior to return to flight duty;
  - (3) Monitoring:

## NOT CONTROLLED WHEN PRINTED

- (a) Every 3 months: assess for adherence, side effects, HIV test
- (b) Every 6 months: serum creatinine

### **IX. HEMATOLOGY**

- a) None yet assigned

### **X. INFECTIOUS DISEASE AND IMMUNOLOGY**

#### **A. ANTIBIOTICS, ANTIFUNGALS, AND ANTIVIRALS**

- i) Most serious adverse events occur in the first 48 hours. A minimum grounding period of 4 days is recommended prior to returning to aircrew duties.
- ii) Aircrew must be grounded on initiation of treatment and must be seen by a Flight Surgeon or B Av Med Provider to be ungrounded. FS/BAvMed Providers should clarify that the acute infectious illness has resolved and there are no drug side-effects. Be aware of possible hypersensitivity reactions, or GI disturbances effects which may not be disabling, but may be significantly distracting.
- iii) Minocycline is particularly to be avoided because of its high incidence of vestibular side-effects, but other antibiotics such as TMP-SMX can also cause vestibular side-effects, and aircrew should be carefully questioned about any sensations of unsteadiness before returning to flight duties.
- iv) Topical antibiotics do not normally require a grounding period.
- v) Routine antibiotic prophylaxis for travelers' diarrhea in aircrew is not recommended (ref D) but broad spectrum treatment (e.g. with ciprofloxacin or azithromycin) may be useful to hasten recovery and return to flying duties.
- vi) Oral fluconazole (Diflucan) as a single oral dose provides an effective treatment for vaginal candidiasis. A 24 hour period of non-aircrew duties is required
- vii) Antiviral prophylaxis for seasonal influenza may be considered under some restricted circumstances (e.g., CFHS Advisory 6636-35). Oral or inhaled antiviral agents side effects and reactions may be expected in the first 24 hours.
  - (1) Aircrew require a minimum 24 hour grounding and then may return to full flying/controlling duties if no adverse effects and if no acute infectious illness is apparent.

#### **B. MALARIA CHEMOPROPHYLAXIS**

- i) Flight Surgeons/BAvMed Providers responsible for aircrew being deployed to or through malarial areas should consult with the Directorate of Force Health Protection

## NOT CONTROLLED WHEN PRINTED

(DFHP) for the most current recommendations. Messages from DFHP regarding malaria chemoprophylaxis for new deployments should normally include a separate paragraph regarding aircrew.

- ii) Malarone is preferred for chloroquine resistant areas. Malarone and primaquine have both been demonstrated to be free of performance side-effects, and may be used in aircrew. Doxycycline is also acceptable.
- iii) mefloquine is not recommended for prophylaxis in aircrew because of the potential neurocognitive effects.
- iv) All CAF members require normal G6PD tests prior to use of primaquine.
- v) 24 hour grounding following the first dose of any of these anti-malarials is recommended, but grounding is not required for further preventive doses.

### C. LTBI TREATMENT

- i) INH for TB converters (grounding for 1 week on initiation of therapy, Flight Surgeon review before return to flying, G4 (T6) – Medication requiring regular laboratory and physician services no less often than 4-weekly.

Note: active TB infection must be excluded before starting treatment.

### D. IMMUNIZATION

- i) Most vaccines are safe to administer and cause only minor side effects, including mild fever.
  - (1) Aircrew require a 12 hour initial grounding after routine immunization (including influenza, Yellow Fever, and Japanese Encephalitis) and then may continue to fly without restriction if there are no adverse effects. Immunizations reactions other than local redness, swelling, and tenderness require an assessment by an aviation medicine provider prior to return to flight.
  - (2) COVID-19 vaccination requires a 48-hr grounding period (and 72 hr no-diving period). Similar to grounding-by-policy for other vaccinations, aircrew may return to flight duties without restriction (or assessment by an aviation medicine provider) at 48 hrs post-vaccination provided they are no longer experiencing adverse effects related to the vaccine.
    - (a) Given the frequency of potential adverse effects lasting up to 72 hours following COVID-19 vaccination (more prevalent following the second dose), aircrew are to remain grounded until all adverse effects have resolved when present.

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- (b) If symptoms persist beyond 72 hrs, or they are either severe or atypical, aircrew shall report to an aviation medicine provider who will determine if further restriction from flying is required.
- ii) No aircrew restriction is needed for traveler's diarrhea prophylaxis (although oral antibiotic or oral cholera vaccination prophylaxis is not routinely recommended).
- iii) Immune globulin Injection (SC or IM) for passive immunization may cause local reactions at the administration site, but grounding is not routinely required. Intravenous immune globulin (IVIG) is more likely to produce a systemic reaction (20-50% of individuals, although most reactions are mild) so an aviation medicine provider should be consulted before return to flight duties.
- iv) Aircrew must be observed for 15 minutes in the health care clinic after receiving a tuberculin skin test (TST).

### **XI. NEUROLOGY**

- a) Not yet assigned

### **XII. RESPIROLOGY**

#### **A. ASTHMA**

- i) Asthma in general is not compatible with aircrew duties, and is disqualifying for aircrew selection per AMA 100-01.
- ii) Asthma is of aeromedical concern due to the risk for acute incapacitation, increased susceptibility to hypoxia, and increased risk of acceleration atelectasis – reducing G tolerance and affecting the ability to tolerate the use of pressure breathing devices.
- iii) Trained aircrew who develop asthmatic symptoms should have a thorough pulmonary review with a detailed history to assess causes of adult onset asthma including occupational factors, and:
  - (1) Respiriologist consult
  - (2) Pulmonary function tests before and after bronchodilator,
  - (3) Bronchoprovocation testing/methacholine challenge may also be required in consultation with ASCS.
- iv) Mild asthma that is well controlled on inhaled corticosteroids (ICS) or combination ICS/long acting beta agonists (LABA) and/or oral leukotrienes may be considered for a return to flight provided: spirometry results carried out on typical treatment regimen show FEV1/FVC ratio at or above predicted range for the patient, FEV1 is greater than 80% predicted and the use of rescue inhaler/short-acting beta agonist is not

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required more than 3 times per year. Cases with abnormal spirometry results despite treatment optimization should be discussed with ASCS.

- (1) Pilots, ACSO, and flight surgeons with mild, well controlled asthma may fly as A3 – unfit pressure breathing; no flight profiles greater than 5Gz; must carry self-administered medication on person when flying.
  - (2) SAR with mild, well controlled asthma will require review by both ASCS and CDSM for return to modified duties. An A3 - unfit diving; must carry self-administered medication on person when flying may be considered provided there are no concerns regarding exacerbation of symptoms with environmental exposures.
  - (3) Other aircrew trades with asthma well controlled with ICS or ICS/LABA combinations ± leukotriene inhibitor may be considered for unrestricted aircrew duties.
- v) More severe asthma will generally require grounding and accompanying significant MELs.
- vi) Oral bronchodilators including theophyllines are not permitted,
- vii) Long-acting muscarinic agents for COPD/asthma are not permitted for use in flying but may be considered for use in aircrew carrying out ground based duties.

### **XIII. OPHTHALMOLOGY**

#### **A. GLAUCOMA**

- i) Topical adrenergic agents, topical beta-blockers, and prostaglandin analogues (Xalatan) may be used without an Air Factor restriction after a 7 day grounding period

#### **B. CYCLOPLEGIC REFRACTION**

- i) Aircrew require 24 hour grounding after a cycloplegic refraction/dilated funduscopy. The dilating effect of the anticholinergic cyclopentolate in particular may last up to 24 hours.

### **XIV. OPERATIONAL MEDICINE**

#### **A. CHEMICAL WARFARE**

## NOT CONTROLLED WHEN PRINTED

- i) Pyridostigmine – may be used in time of a chemical warfare threat as a routine prophylactic countermeasure after tolerance pre-testing under the supervision of a Flight Surgeon, without an operational flying restriction;
- ii) Atropine (HI-6 injection) – may be carried by aircrew for use only in the event of a suspected direct chemical warfare attack and only if actual symptoms are experienced in flight;
- iii) Diazepam, edrophonium and pralidoxime will not be used in flight
- iv) CS gas - Aircrew require two hour grounding and then may return to flying duties without restriction if there are no adverse effects following exposure to "Gas Hut" training exposure to CS gas. Aircrew member must shower and change all clothing items worn in the gas hut before returning to flight duties.
- v) Non-training CS gas exposures or exposures without protective equipment requires aviation medicine provider assessment. Exposure to any other CBRN agent requires aviation medicine provider assessment.

### B. ALERTNESS

- i) Guidance on the operational management of fatigue and alertness is provided in FSG 1400-03 in detail.
  - (1) Operational use of caffeine as part of an authorized fatigue risk management system is to be in accordance with FSG 1400-03.
  - (2) Moderate use of caffeine products is permitted for aircrew provided the maximum safe recommended daily intake of 400 mg is not exceeded.
- ii) The use of modafanil and dextroamphetamine is not approved for CAF aircrew.

### XV. OTOLARYNGOLOGY

- a) Aircrew with upper respiratory infections or allergy-related congestion should be grounded until normal Eustachian tube function has returned, confirmed by examination.
- b) Topical and systemic decongestants are adrenergic agonists. Cold preparations often additionally contain older generation antihistamines. Topical decongestants are generally safer than systemic preparations, although even the topical sympathomimetic sprays are absorbed to a certain extent and can produce adrenergic effects including arrhythmias. The rebound effect of topical sympathomimetic sprays (e.g. Dristan) can start after as short a time as 48 hours of repetitive use. These medications also reduce ciliary activity and so reduce mucus clearance.

## NOT CONTROLLED WHEN PRINTED

- i) Decongestant nasal sprays (topical adrenergics) should not be used for more than three days consecutively.
  - (1) Aircrew who use decongestant spray for symptomatic management of URTI congestion should not return to flight unless at least 12 hours from the last dose.
  - (2) Aircrew recovering from URTI who return to flight prematurely may use a decongestant spray as an emergency “get me down” aid.
- ii) The use of systemic decongestants (eg pseudoephedrine) is not recommended in aircrew.
  - (1) Aircrew who do elect to use over the counter systemic formulations for symptomatic management of URTI should not return to flight:
    - (a) For 12 hours following last dose of a daytime/nondrowsy immediate release formulation; or
    - (b) For 24 hours following last dose of nighttime/drowsy immediate release formulation.
  - iii) Since many compounds of this type are available over-the-counter, Flight Surgeons and BAvMed Providers should regularly brief aircrew on the potential hazards of these compounds, including the potential arrhythmogenic potential of pseudoephedrine.
- c) Topical corticosteroids and sodium cromoglycate for allergic rhinitis produce no significant systemic effects and can be used for aircrew without restrictions.
- d) Saline rinses do not require a flying restriction.

## **XVI. PSYCHIATRY**

### **A. SEDATIVES/HYPNOTICS (See also Ref E)**

- i) In general, this class of drug is not compatible with flying duties. Specific guidelines for the use of sedatives/hypnotics to facilitate off-nominal sleep during phase shifted flight operations or during circadian transitions are outlined in FSG 1400-03 Fatigue Management in Aircrew.
- ii) Zopiclone (Imovane), temazepam (Restoril), zolpidem (Sublinox), and melatonin SR are approved for Flight-Surgeon-supervised use in aircrew to facilitate sleep in operational settings requiring off-nominal sleep or during circadian shifting. The half-life, dosages and required grounding periods are shown in para 35.
- iii) Table of sleep medications approved for aircrew

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Medication	Trade Name	Half-life (hr)	Dosage	Grounding Required (hrs)
temazepam	Restoril	8-9	7.5/15	12
zopiclone	Imovane	5	3.75/5/7.5	12
zolpidem	Sublinox	2-3	5	6
Melatonin SR			1 to 3mg SR	Not required

- iv) As per FSG 1400-03, before prescribing for operational use, the medication must be ground tested by the individual, with completion of FSG 1400-03 Annex F. Ground testing should begin with the smallest dosage, with titration upwards (and repeat ground testing) only if required to achieve adequate sleep. The smallest effective dose to achieve adequate sleep should be prescribed, maximum quantity 7.
- v) Other drugs such as antihistamines or other benzodiazepines must not be used to facilitate sleep. Triazolam (Halcion) must not be used in aircrew because of the reports of hallucinations after use.

**B. ANTI-DEPRESSANTS**

- i) The management of aircrew with mental health disorders must be carried out in accordance with FSG 1400-01 Mental Health Disorders.
- ii) Drug monotherapy is the preferred therapeutic approach for aircrew with mental health disorders.
- iii) Based on pharmacological properties including half-life, adverse effect profiles and specific aeromedical performance evaluations, the following four antidepressants are approved and preferred for use in aircrew:
  - (1) Sertraline (Zoloft)
  - (2) Citalopram (Celexa)
  - (3) Escitalopram (Cipralex)
  - (4) Bupropion (Wellbutrin)

All aircrew are to be assigned an A7 – unfit aircrew duties until condition clinically stable on the same treatment regimen for a minimum of two months or longer. Following which reassessment for return to flight duty may be considered following the protocol outlined in FSG 1400-01.

- iv) If in the opinion of the treating Psychiatrist, the preferred medications are not clinically suitable, the following additional medications may be used as second line options:

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- (1) Duloxetine (Cymbalta)
- (2) Desvenlafaxine (Pristiq)
- (3) Vortioxetine (Trintellix)

All aircrew are to be assigned an A7 – unfit aircrew duties until condition clinically stable on the same treatment regimen for a minimum of two months or longer. Following which reassessment for return to flight duty may be considered following the protocol outlined in FSG 1400-01.

- v) The following antidepressant medications are NOT approved for use in aircrew due to their potential for discontinuation effects with missed doses and short half-life:

- (1) Venlafaxine (Effexor)
- (2) Paroxetine (Paxil)

C. STIMULANTS

- i) The use of prescription stimulant medication for the treatment of ADHD, sleep-wake disorders or for maintenance of alertness is not approved for aircrew.
- ii) The authorized use of caffeine supplementation to promote wakefulness is outlined in Ref E.

D. ANTIPSYCHOTICS

- i) First and second-generation antipsychotics are not approved for aircrew.

E. MOOD STABILIZERS

- i) Mood stabilizers are not approved for aircrew.

F. SMOKING CESSATION AIDS

- i) Smoking cessation medications may be used by RCAF aircrew, within the guidelines of CF H Svcs Instruction 4200-55 Provision of Smoking Cessation Medications to Eligible CAF Personnel and DSG 03/10- Use of Zyban and Champix During Deployment
- ii) Nicotine replacement therapy– Aircrew including pilots may use nicotine gum or transdermal nicotine patches as an aid to smoking cessation without requiring an operational flying restriction. Patches must be used under the guidance of a Flight Surgeon or BAvMed Provider.

- (1) Aircrew should not fly for the first 2 days of initiating treatment and must be reviewed before returning to flying duties and at regular intervals to confirm that the individual has stopped smoking, and that there are no significant side-effects.
- iii) Zyban (bupropion) – Zyban may be used as a smoking cessation aid by RCAF aircrew consistent with CF policy. Because of potential neurocognitive side-effects and remote risk for a seizure, bupropion must be used with extreme caution and under close supervision in aircrew.
- (1) Non-pilot aircrew may be returned to flying duties after a two-week period of grounding, after being cleared by the Flight Surgeon (only).
  - (2) Pilots are restricted to fly with or as copilot during treatment.
  - (3) For all aircrew weekly visits with the Flight Surgeon are required throughout treatment to monitor for side-effects and reinforce the smoking cessation objective. Medication should be supplied in weekly aliquots, and weekly visits documented in the CFHIS.
- iv) Champix (varenicline) – In placebo-controlled trials, varenicline has superior efficacy in promoting smoking cessation compared with placebo, nicotine replacement, and bupropion. The most common adverse effects are gastrointestinal, and sleep disturbance. Serious neuropsychiatric adverse effects have been reported in post-marketing surveillance including depression, suicide and personality changes, but it is not clear to what extent these reflect the effects of nicotine withdrawal per se. Serious AEs appear to be more common in individuals with previous psychiatric conditions. Champix may be prescribed for aircrew with similar limitations as Zyban, criteria include:
- (1) Use under the supervision of a Flight Surgeon (only);
  - (2) Non-pilot aircrew may be returned to flying duties after a two-week period of grounding, after being cleared by the Flight Surgeon (only).
  - (3) Pilots are restricted to fly with or as copilot during treatment.
  - (4) For all aircrew weekly visits with the Flight Surgeon are required throughout treatment to monitor for side-effects and reinforce the smoking cessation objective. Medication should be supplied in weekly aliquots, and weekly visits documented in the CFHIS.

## **XVII. RHEUMATOLOGY**

### **A. GOUT**

- i) Allopurinol is currently approved for prophylaxis of gout. Allopurinol is indicated for prophylaxis after recurrent episodes of gout. Because of the risk of precipitating an episode of gout during initiation of allopurinol therapy (which should generally be done with colchicine coverage), aircrew must be grounded for the first 14 days of allopurinol therapy.

B. DISEASE MODIFYING ANTIRHEUMATIC DRUGS (DMARDs)

- i) DMARDs include antimalarials (chloroquine), sulfasalazine, methotrexate and biologic agents that modulate immune response. Increasingly, DMARDs are being clinically recommended for early disease suppression in rheumatoid arthritis, with a parallel application for plaque psoriasis.
- ii) These diseases are disqualifying for aircrew selection but sometimes manifest in trained aircrew.
- iii) Methotrexate (MTX): MTX is a folate anti-metabolite that inhibits DNA synthesis, repair, and cellular replication. It is used as an anti-neoplastic agent at higher doses and is used at lower doses (7.5mg to 25mg weekly) to treat rheumatoid arthritis and a number of other systemic inflammatory diseases via immunosuppression. MTX has potential for toxicity to several organ systems and has frequent monitoring and follow-up requirements that will require geographic limitations for specialist follow-up.

Common side effects of aeromedical concern include headache, fatigue, impaired concentration and 'brain fog', nausea, and fever. CNS side effects and nausea tend to occur within the first two days of each weekly dose and may or may not abate with time.

Severe adverse effects including hepatotoxicity, pulmonary toxicity, myelosuppression, increased infection risk, increased risk of lymphoproliferative disorders and nephrotoxicity.

Pulmonary toxicity is of particular concern in the operational aviation environment as it has both acute and chronic presentations and can present rapidly at any phase of treatment, although most commonly in the first year. Pneumonitis is not always reversible and fatalities have been reported.

- (1) All aircrew prescribed MTX must be restricted from flight and controlling duties and placed on an initial A7 TCAT with appropriate G and O restrictions during initiation and stabilization of treatment.
- (2) Concomitant folate prescription to reduce adverse effects should be prescribed.
- (3) Baseline and ongoing monitoring investigations are required and results must be maintained in the health record:
  - (a) Baseline CXR;
  - (b) Bloodwork: monthly x 3 months; then every 12 weeks: CBC and differential; LFTs, albumin, Creatinine and
  - (c) Baseline PFT
- (4) Monthly assessment x 3 months with the aviation medicine provider to assess for side effects: fatigue, headache, concentration problems, stomatitis, alopecia,

- diarrhea, nausea/vomiting, flu-like symptoms, shortness of breath, symptoms of myelosuppression, hepatotoxicity, infection, lymph node swelling.
- (5) A return to modified flight/controlling duties can be considered no sooner than 3 months after treatment initiation following a review with ASCS.
- (a) Pilots will be restricted to flying with or as a copilot qualified on type
  - (b) AEC and AC Op will require a restriction from AWACs
  - (c) All aircrew will require permanent G and O factor limitations as per D Med Pol, typically a G4 will be required due to lab follow-up needs.

## **XVIII. BIOLOGIC AGENTS**

Biologic agents and biosimilars are therapeutic agents that are used to treat systemic inflammatory conditions associated with autoimmunity. These therapies most commonly enact their effect by interfering with cytokine projection, interfering with T-cell activation signals, or causing B cell depletion. The clinical effectiveness of these agents seen across a broad range of conditions means that requests to consider their use in RCAF personnel are becoming more frequent.

The range of potential serious adverse effects, requirement for regular medical follow-up and cold-chain requirements will generally result in geographic and occupational restrictions that may have career impacts for military personnel in addition to their air factor.

Medications not listed in this section or listed medications being requested for use with a different clinical indication may be considered on a case-by-case basis in trained aircrew after consultation with ASCS; AUMB review may be required.

### **A. TNF-alpha INHIBITORS**

- i) TNF-alpha inhibitors are important treatment options for inflammatory conditions including rheumatoid arthritis, spondylo-arthritis, psoriasis and inflammatory bowel disease.
- ii) While they are well tolerated in many patients, there are multiple adverse effects that can occur and may be of aeromedical importance, including: injection site reactions, infusion reactions, neutropenia, infections, demyelinating disease, heart failure (HF), cutaneous reactions, malignancy and autoimmune disease.
- iii) The adverse effect profile of anti-TNF-alpha inhibitors will differ depending upon the condition being treated: for example psoriasis patients experience more side effects related to the skin and hepatobiliary system while rheumatoid patients have higher rates of infections, infusion reactions, and cardiac and respiratory side effects.

NOT CONTROLLED WHEN PRINTED

- iv) There are currently five inhibitors of TNF alpha that are widely available for the treatment of rheumatoid arthritis, psoriasis, psoriatic arthritis and inflammatory bowel disease:
  - (1) adalimumab and biosimilars;
  - (2) infliximab and biosimilars;
  - (3) etanercept and biosimilars;
  - (4) golimumab; and
  - (5) certolizumab pegol.
  
- v) Medications in this class have been approved for use in trained aircrew on a case-by-case basis. Most cases have been approved for modified flight or controlling duties, but depending upon clinical circumstances and occupation a return to an unrestricted air factor with the maintenance of appropriate G and O factors may be possible.
  
- vi) All cases of trained aircrew who are pursuing treatment with TNF alpha inhibitors are to be referred to ASCS for disposition recommendations at initiation of treatment. ASCS retains disposition authority for return to flight and controlling duties for trained aircrew seeking treatment with biologic agents, but the general management for aircrew patients on these medications is outlined as follows:
  - (1) All aircrew will require an initial 6 month TCAT with G and O restrictions during initialization and stabilization of treatment.
  - (2) Restrictions from grounding and control duties are first determined by the clinical severity of the condition being treated. In order to be considered for either modified or restricted flight duties, the medical condition must not have active symptoms that could interfere with the safe performance of duties or present a risk of sudden or unpredictable flare of symptoms.
  - (3) Baseline and ongoing monitoring investigations are required and results must be maintained in the health record:
    - (a) Baseline:
      - (i) Evaluate for the presence of malignancy including skin cancer and for the presence of latent infections;
      - (ii) CBC with differential, complete metabolic panel, pregnancy test, C-reactive protein
    - (b) Monitoring:
      - (i) Evaluate for presence of malignancy including skin cancer, lymphadenopathy, infections/infection risks, congestive heart failure, or neurological symptoms; hypersensitivity reaction, lupus-like syndrome, injection-site reactions;
      - (ii) CBC, LFTs at 4 and 12 months, then every 3 to 6 months
  - (4) A return to modified flight or controlling duties can be considered for medically stable patients with normal monitoring investigations as follows after consultation with ASCS:
    - (a) Initial grounding after the first dose

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(b) Follow-up with the aviation medicine provider to review for side effects. If there are no significant side effects, then the disposition as follows:

(i) Pilots:

1. A3T6 fit to fly with or as copilot qualified on type
2. 48 hour self-grounding after each dose
3. Domestic flying only; no seagoing deployments
4. Monthly follow-up with aviation medicine provider x 3 months then as clinically indicated or as needed to review monitoring requirements
5. Consideration can be made for a return to A1 status after the initial TCAT with appropriate G and O restrictions by submitting to ASCS for case by case review.

(ii) AEC:

1. A3T6 fit live controlling; unfit AWACs;
2. 48 hour self-grounding required after each dose
3. Monthly follow-up with aviation medicine provider x 3 months then as clinically indicated or as needed to review monitoring requirements
4. Consideration can be made for a return to A4 status after the initial TCAT with appropriate G and O restrictions by submitting to ASCS for case by case review.

(iii) All other aircrew:

1. A3T6 fit to fly for domestic flying only
2. Monthly follow-up with aviation medicine provider x 3 months then as clinically indicated or as needed to review monitoring requirements
3. Consideration can be made for a return to A2 or A4 status after the initial TCAT with appropriate G and O restrictions by submitting to ASCS for case by case review.

## B. INTERLEUKIN INHIBITORS

- i) Interleukins are a group of at least 40 cytokines that modulate growth, differentiation, and activation during inflammatory and immune responses. The use of monoclonal antibodies to inhibit specific interleukins to treat a broad range of inflammatory and autoimmune conditions is increasing.
- ii) All medications in this class carry a significant increase in the risk of infections, usually respiratory; injection site reactions are also a class wide concern. Other adverse effects of aeromedical concern do occur but vary significantly depending upon the particular medication and medical conditions being treated.
- iii) Due to the variability of the side effect profile, stabilization, and monitoring requirements, approval for ongoing flight and control duties for trained aircrew treated with this class of medications will remain as a case-by-case review with ASCS.

- (1) All cases should be referred to ASCS for review at initiation of treatment for anticipated follow-up and disposition requirements specific to the condition and biologic agent
- (2) Restrictions from grounding and control duties are first determined by the clinical severity of the condition being treated. In order to be considered for either modified or restricted flight duties, the medical condition must not have active symptoms that could interfere with the safe performance of duties or present a risk of sudden or unpredictable flare of symptoms.
- (3) All aircrew will require an initial 6 month TCAT with G and O restrictions during initialization and stabilization of treatment
- (4) Baseline and ongoing monitoring will be required as appropriate for the clinical condition and the biologic agent.

### C. B CELL DEPLETION AND INHIBITION

- i) Biologic agents that deplete or inhibit activation of B cells are used in the treatment of autoimmune disorders, lymphoproliferative disorders, and inflammatory disorders. Current agents available in this class include rituximab, belimumab, and anifrolumab. Belimumab and anifrolumab have labelled indications for the treatment of systemic lupus erythematosus.
- ii) The use of these medications for rheumatic diseases is generally second line use for those who have not responded to other biologic agents.
- iii) Many of the treatment uses for these agents are off-label and optimal treatment plans have not been established. There is potential for serious adverse effects to occur including infections, malignancy, and neuropsychiatric disturbances. In many cases the medical condition being treated with these agents would prevent safe return to flight or controlling duties.
- iv) These agents have not been approved for use while in flight or controlling duties.

## **XIX. HEALTH SUPPLEMENTS AND COMPLEMENTARY OR ALTERNATIVE MEDICINE**

There are a wide range of non-prescription traditional and nontraditional substances intended for health purposes available. In order to assess their safety or suitability for use by aircrew, consideration must be given to the type of preparation being consumed, its intended purpose and potential side effects, and whether or not there is a risk for unknown or undeclared components to be present. In Canada, only health supplements with a Drug Identification Number (DIN) have been assessed for safety and approved by Health Canada.

NOT CONTROLLED WHEN PRINTED

- i) Health supplements are nonmedical dietary or herbal preparations taken on a daily basis for the purposes of promoting wellbeing or enhancing performance.
- ii) Complementary or alternative medicines are herbal or dietary agents that are nontraditional by Western medical standards and are being taken to treat an illness or physical symptom.

While both health supplement and complementary medicines can present an aeromedical risk, complementary medicines require scrutiny not only for the safety of the substance but to ensure that the underlying medical condition is being managed safely.

A. HEALTH SUPPLEMENTS

- i) COLD-FX™ is a patented extract from North American ginseng (*panax quinquefolium*). In animal studies, it has been shown to modulate the immune response. Placebo-controlled clinical trials have shown a slight decrease in the number of colds contracted over periods up to four months (decrease of 0.25 cold/person), fewer cold symptoms, but no difference in duration.
  - (1) Ginseng may cause mild side effects including insomnia and GI upset. More serious side effects that have been reported with ginseng (but not specifically COLD-FX™) include Steven's-Johnson syndrome, mania, cerebral arteritis, and hypertension. COLD-FX™ is not included in the CF Drug Benefit List.
  - (2) COLD-FX™ now offers several branded formulations:
    - (a) Daily Support: 200 mg ginseng extract;
    - (b) Extra Strength: 300 mg ginseng extract;
    - (c) First Signs – 5 mg Zinc, 70 mg Andrographis (Green Chiretta); 125 mg echinacea; and 200 mg ginseng extract
    - (d) First Signs Nighttime- 125 mg Ginger, 100 mg Andrographis, 5 mg Melatonin; and 200 mg ginseng extract
  - (3) If CF aircrew choose to use COLD-FX™, a 7 day grounding period is recommended on initiation.
- ii) EPHEDRA ALKALOIDS/EPHEDRINE are often combined with caffeine and marketed as weight loss or performance enhancement supplements. Ephedra has serious side effects including hypertension, arrhythmia, stroke, MI, and seizures. Fatalities have occurred.

Ephedra/Ephedrine containing health supplements are not approved for use by aircrew.

NOT CONTROLLED WHEN PRINTED

- (a) Health Canada has only authorized the use of ephedrine in nasal decongestants but dietary supplements are under-regulated. Supplements without a DIN may contain Ephedra/Ephedrine
  - (b) Ephedra/Ephedrine content may be labeled under alternative names: hedra/Ephedrine content concealed under many possible alternative names such as: Cao Mahuang, Desert Herb, Ephedrae herba, Ephedra sinensis, Joint Fir, Ma Huang, Ma-Huang, Mahuang, Mahuanggen (ma huang root), Muzei Mahuang, Sea Grape, Yellow Astringent, Yellow Horse, Zhong Mahuang, Ephedra sinica, Ephedra intermedia, Ephedra equisetina, Ephedra distachya, Ephedra gerardiana, Ephedra shennungiana, Chinese Ephedra, Ma huang extract, Ephedra extract, Ephedra herb powder, epitonin and sida cordifolia
  - (c) Ma-Huang is the term for an *Ephedra sinica* based traditional Chinese medicine
- iii) CREATINE is a commonly used health supplement that aids in increased adenosine triphosphate resynthesis in between bouts of short duration high intensity exercise, improving performance and recovery. It is most commonly available as a powder. It should not be used if there is any history of kidney disease or renal dysfunction.
- (1) Creatine monohydrate powder in doses not to exceed 5 g/day may be used by aircrew without restriction or grounding requirement

**B. COMPLEMENTARY OR ALTERNATIVE MEDICINES**

- i) The following herbal remedies are often promoted as a means of managing mental health and anxiety symptoms. There are no clinical trials showing effective results and serious side effects are possible. They are not approved for use by aircrew on flying duty:
  - (1) St-John's Wort;
  - (2) Valerian; and/or
  - (3) Kava
- ii) Glucosamine – no restriction or grounding is required