

Guidance material on how to assess medications in pilots and ATCOs
February 2017
Olivier MANEN, MD, Prof.

Background :

After some discussions between the members of the Advisory Board Committee of ESAM, it was chosen to produce a paper for practitioners/AME and a leaflet for pilots/ATCOs and practitioners/AME.

This paper is structured as following (also presented in the ABC):

- As far as 18 basic principles were previously exposed, we developed each one and decided to put together some of them because leading to a same idea, with practical examples when possible.
- The second step was to differentiate 4 practical situations as a summary.
- Finally, “10 gold rules” were produced as a conclusion.

Introduction

The objective of this paper is to produce guidance for the GMP and specialists (also called “practitioners”) who are in charge of medical problems of pilots/ATCOs (also called “aircrews”) because they are not so familiar with the management of medications in a professional or private context of flying activities, and yet they have to give regular advices to their patients.

This paper may also be useful for the aeromedical examiners (AME) to make them improve in the decision-making process in case of simple or complex therapeutics, because they have to be able to take an appropriate decision whatever the medical situation is.

Due to the very high number of medications and the rapid evolution of therapeutics in general, it would be a bad idea to make a list of medications or molecule classes. On the contrary, it is more interesting to develop the main principles applying to medications in aviation medicine, giving practical but not limitative examples, so that one situation may be useful to apply to another, and all situations put together may make the stakeholders be more sensitive to the relation between medications and flight safety.

Medications and aviation medicine: the main principles

1. All medications may be problematic for aircrews. Every prescription of a drug depends on a ratio benefit/risk; this iatrogenic risk may be very low or quite high, but no one drug intake should be considered as insignificant. In case of a common situation (e.g. sore throat, headache, back pain), the ratio is expected to be high, and yet there are significant adverse effects for painkillers, anti-histaminic, anti-inflammatory or anti-tussive drugs... In case of a severe disease (e.g. spondylarthropathy, inflammatory bowel disease, chronic myeloid leukaemia), the ratio may be lower with an acceptance of more serious side effects. The choice to use such a drug by the medical team for an aircrew must not be interpreted as an

acceptable aeronautical risk but shall need a specific assessment due to the cockpit environment.

2. Considering the first point, ideally a pilot/ATCO taking medication should not fly or work. However, this objective would be impossible to reach and would not be justified in many cases as far as the flying/working activity may be practiced by taking safety instructions. Because of the commercial pressure of professional pilots/ATCOs and the strong motivation of private pilots, to adopt a strict position against medications may lead to the opposite expected effect on aircrews who may take various molecules with a prescription or by self-medication without saying anything to their AME. A more useful attitude is to arouse practitioners and aircrews to question about a possible in-flight risk and if necessary to call the AME or AeMC for information.

3. When an aircrew is using a medication, the aeromedical assessment should not take into account the adverse effects on vigilance and cognitive functions only but all possible side effects. Other situations in which the flight safety is jeopardized may be particularly due to cardiovascular or neurosensory symptoms: palpitations (flecainide and flutter 1/1), hypotension (anti-hypertensive drug), dizziness, vision or hearing impairment... However, some minor adverse effects with no consequence on the ground may distract the pilot/ATCO during operational duties: fatigue (betablockers), insomnia (corticosteroids), nausea, diarrhoea, flatulence (metformine), arthralgia, headaches... Some studies carried out in aircrews about medications by questionnaires have shown that pilots can easily quote medications with neurological or psychological impact as possibly incompatible with flying activities; but other iatrogenic effects seem to be badly known and need specific information and education.

4. Some rare and severe adverse effects of a medical treatment may appear during the fourth stage in a large population. In the same time, the real efficiency of these drugs is observed in the conditions of the “real life”, very far from those of laboratory tests. After several months or years, the ratio benefit/risk may be questioned and may lead to a stop of prescriptions and if necessary to the end of marketing. For instance, many drugs prescribed to help losing weight have been taken off the market. Some anti-histaminic drugs have also been stopped due to a risk of severe ventricular arrhythmias, and common drugs used for ENT infections in relation to brain haemorrhage episodes. For oral anti-diabetic medication, many studies about DPP4-inhibitors were necessary to prove the concept of glucose-dependent insulin-secretion by incretin hormones and so the absence of hypoglycaemia risk. On the contrary, the glitazone class is no more prescribed in France or Europe (depending on the molecule) because of a higher risk of cardiovascular disease or cancer, what is somewhat illogical in regard to the initial objective of such a treatment. Consequently, practitioners and AME should pay particular attention to new molecules and new therapeutic classes, not only for the short-term risk when piloting/controlling (e.g. a new anti-histaminic drug and its sedative effect) but also for the long-term risk.

5. This attention of AME shall not prevent aircrews from the potential benefits of a new therapeutic approach or medication for fear of unfitness, particularly in case of a severe disease. Chronic C hepatitis was the typical example of a disease with no significant symptom (except for asthenia) and so a fit decision was possible in most cases; when a medical treatment with interferon was decided, the well-known side effects including depression and suicidal behaviour led to a long period of grounding. Some pilots decided to give up or to delay the treatment when medically justified, because they couldn't afford to stop their flying/working activities, and they accepted the significant risk of cirrhosis and cancer of the

liver. In type 2 diabetes, the control of the disease requires initially oral anti-diabetics with few side effects, then multiple medication including sulfonylurea and insulin with a high risk of hypoglycaemic episodes leading to unfitness; a few pilots would take the risk to be badly controlled at an advanced stage so that their treatment may be acceptable for the fitness assessment, even if there is a long-term risk of complications involving the heart and life expectancy. In another situation of a required valve replacement for aortic valvulopathy, some pilots would choose tissue valve instead of mechanical prosthesis for fear of future potential problems due to unstable anticoagulation, and so they will need other surgery at an older age. In case of a chronic leukaemia, therapeutic protocols are improving regularly; pilots/ATCOs should have the chance to take benefits of this continuous progress. All these situations emphasize the fact that AME should always talk about the health first then about the aeromedical fitness, and they should set medical and ethical arguments above professional and leisure consideration. There are also a few situations in which AME may advise alternative medication than the one prescribed but considered as “forbidden” in aviation medicine, as far as it may be as efficient and compatible with flying/working activities (e.g. subcutaneous GLP-1 agonists instead of oral sulfonylurea drugs).

6. Many molecules are taken without any prescription; others are used because they are present in the family medicine cupboard. Several studies have shown that self-medication is a real problem in aircrews: for instance in France many of them (50-60%) use medication before consulting their GMP in case of a health problem, attitude actually depending on the age (the more you are getting old, the more you decide to have a consultation); few of them (< 50%) explain their job to the chemists when they ask for advice; and finally most of them (70%) continue their flying activities when on medication, including if sedative drug and/or if they think there is a significant risk. This may be due to professional constraints and commercial pressure, but also to a lack of knowledge about the potential risks which obviously are underestimated. Consequently, one of the multiple roles of AME is to provide information to make aircrews become more sensitive to the in-flight risk of self-medication.

7. To do so, every practitioner and AME should keep in mind that in professional and private aviation there have been famous and unknown examples of crashes for which a medical cause has played a role including possible side effects of a treatment. Moreover, all aircraft accidents have not been explained with satisfactory arguments, and so a drug-induced cause may be considered. During aeromedical examinations, AME should remind aircrews that their responsibility in case of a new situation involving a medication is clearly questioned and mentioned on the European medical certificate they are issued:

“MED.A.020 Decrease in medical fitness

Licence holders shall not exercise the privileges of their licence and related ratings or certificates at any time when they take or use any prescribed or non-prescribed medication which is likely to interfere with the safe exercise of the privileges of the applicable licence; In addition, licence holders shall, without undue delay, seek aero-medical advice when they have commenced the regular use of any medication.”

8. There are various sources of information about medication that may be used by practitioners or read by pilots/ATCOs. Aircrews should be careful of non official sources found on the internet including forums as far as such a help may be imprecise, incomplete or misunderstood. This information may be more appropriate for patients to be convinced of the usefulness of their treatment than for aircrews to decide whether they can fly/work or not. Practitioners may be helped by the official summary of a drug’s characteristics, particularly

by reading the paragraphs *Side effects*, *Special warning and safety instructions* and *Effects on the ability to drive vehicles and to use machines*. Elements to consider about adverse effects are the type of effects, the frequency, the period of high risk and the association with other side effects: all molecules of a same class have not the same risk (e.g. anti-histaminic drugs, betablockers, diuretics); practitioners should pay attention to multiple expected side effects of a drug, also to very frequent ($\geq 10\%$ of patients) and frequent (1 - 10%) side effects; clearly many drugs are dangerous at the very beginning of their introduction.

9. In frequent situations, aircrews would take benefits to have oral discussion with their practitioner or ideally with their AME. If necessary a dialogue between practitioner(s) and AME should be encouraged because GMP and specialists are more focused on the efficiency even if they think about the ratio benefit/risk, so that information from the medical team and the AME is complementary. Finally, practitioners should keep in mind that the general acceptance of a medication in aviation medicine does not mean that an individual pilot taking this medication is fit to fly: in many cases a decision shall be taken by the licensing medical Authority, a specificity which is badly known and may not be understood by the medical team (e.g. anti-diabetics, anticoagulants, anti-arrhythmia drugs, corticosteroids, immune-modulating drugs). This major role of AME shall be recognized by aircrews if they trust them, so that they will call them for advice.

10. The aeromedical decision for a pilot/ATCO taking a medication should not be considered alone but in a global approach in which the pathology/situation may be unacceptable or may have stronger consequences than the treatment itself. For instance diabetic pilots taking other medications than metformin, alpha-glucosidase inhibitor and DPP4-inhibitors do present an advanced stage of their disease, and so arguments for the absence of coronary artery disease are particularly required, taking into account the lower negative predictive value of ischemic tests. Aircrews with inflammatory bowel disease and immune-modulating drugs shall be considered as highly dependent of their treatment otherwise symptomatic and at higher risk of complications, as well as aircrews with spondylarthropathy. Anticoagulation shall question the AME about the underlying pathology which should not be considered equally in the following situations: past medical history of deep venous thrombotic events; pulmonary embolism episodes; atrial fibrillation; aortic valve replacement.

11. The medical stakeholders shall not find in the Acceptance Means of Compliance (AMC) of the European regulations explanations about how to accept medications but for anticoagulation. For this whole treatment a simple rule was decided in the situation of regular biological tests required, which means for vitamin-K antagonists: a 6-month delay with 5 INR and 4 in the target range. This “6 - 5 - 4 rule” may be dangerous if basically applied without thinking of the following points: a/ the rule is described in the AMC for all situations except for the more difficult of them: atrial fibrillation (AF); b/ some patients may have had difficulties to be well-controlled at the very beginning of their treatment but with good results in the 2-3 last months, and so a general vision of the 6-month INR is necessary; and c/ values of INR that are not in the common [2-3] target should not be considered equally: 1.9 and 3.3 vs 1.2 and 4.1... For aircrews taking oral direct anticoagulants (ODA), AME should pay attention of the other following elements: d/ these medications are recognized as efficient as vitamin-K antagonists, with a lower risk of cerebral haemorrhage events in the general population including people who are badly controlled; e/ such an evidence is uncertain in comparison to a population with excellent INR control who is at very low annual risk; f/ a pilot/ATCO may be at higher or lower haemorrhagic risk when on ODA because of individual susceptibility; g/ there is no way to be sure that a pilot/ATCO on ODA is a good observant,

even if the health and fitness are jeopardized, particularly because coagulation tests may be normal, depending on the molecule; and h/ the consequences in case of a low observance shall not be the same in individuals with chronic AF and CHA₂DS₂-VASC score at 1, and individuals with paroxysmal AF and a score at 4.

12. In case of a short intake of medication (e.g. during viral or bacterial infection, renal colic or low back pain episode), a period of grounding during several days or few weeks is justified by the disease and so the question of drugs is a false problem. On the contrary, medication may be required whereas pilots/ATCOs are feeling better, with a total duration of their treatment of several weeks or months (e.g. deep venous thrombotic event, depressive episode, sleep disorder, inflammatory colitis or arrhythmia episode) and so medication shall be part of the discussion. Finally, a medical treatment may be prescribed for the long-term or during all life (e.g. chronic hepatitis, high blood pressure, type 2 diabetes, recurrent atrial fibrillation, spondylarthropathy, chronic myeloid leukaemia or organ replacements) and so the medication shall be the main problem for the aeromedical decision.

13. All iatrogenic risk of medication should be considered in the real professional environment of pilots/ATCOs. The flying/working activities should be described because they may have an impact on the final decision: pilot vs ATCO; monopilot activity vs multipilot cockpit environment; exposure to jet lag / night work / sudden missions; offshore activity far from a medical environment; a flying job in a country with bad sanitary hygiene; very specific conditions (helicopter assistance in mountain environment, instruction activity in a school of aviation with novice pilots...) Practitioners and AME should be aware that there are situations in which a pilot has not had any aviation job yet, and may ask for several kinds of flying job including those with a high aeronautical risk. On the one hand, some drugs shall be acceptable in a multipilot cockpit environment only, because in case of a medical event in relation to a drug, the situation should be more comfortable to exclude the pilot from commands and to manage the medical and aeronautical situation. On the other hand, in case of a bad management leading to a crash, this aeronautical catastrophic event is expected to be more developed in the media in relation to the very high number of victims.

14. In most of long-term treatment situations, a period of grounding shall be observed in aircrews, not only to check for the tolerance but also the efficiency of the treatment (e.g. high blood pressure, diabetes, essential thrombocytosis). This period of grounding is usually understood by pilots/ATCOs and so it may be well accepted. The real question is to decide how long the required optimal duration should be: this duration shall be a case-by-case decision taking into account data about the disease, the treatment and the flying/working conditions. Any change in the dosage of a medication that was previously accepted in the flying/working environment should also make pilots/ATCOs and practitioners question about the new risk and the aeromedical fitness, and so it should lead them to call AME again.

15. Finally, every AME should accept the fact that some medications have no place in a cockpit environment or that some situations are not defensible, even if the pilot/ATCO is doomed to lose his/her job. In these situations, the AME has to prepare the precise argumentation and should expose it to the pilot/ATCO with technical aspects by also in a very human approach. This impossibility may be due to unacceptable risk of the treatment itself including in a multipilot cockpit environment (e.g. multiple anti-arrhythmia drugs, psychotropic drug with too sedative effect, anti-diabetics with a bad tolerance or a significant risk of hypoglycaemia). It may be due to a monopilot flying activity that cannot be changed,

particularly for rescue team helicopter pilots (e.g. requiring anticoagulation). It may also be due to ethical considerations if the health of a pilot/ATCO is expected to worsen in relation to the acceptance of the treatment with “aeromedical conditions” (e.g. insulin in cockpit and “safety target” of HbA1C). Above all and even if rarely, practitioners and AME should keep in mind that a pilot/ATCO may prefer not to take the risk of flying and yet it would be aeromedically acceptable after assessment and a decision of the licensing medical Authority: such an aircrew should be reinforced in his/her choice by the information delivered by the medical team and the AME, but he/she should not be influenced by the AME for the final choice (e.g. every pilot requiring long-term anticoagulation does not want to continue their flying/working job even if theoretically possible).

In summary: the practical situations in the real life

During the career of pilots/ATCOs, four different circumstances of a medication intake should be differentiated with consequences on the management mode:

1. Acute medical problem in where a treatment is prescribed for a short period: usually the symptoms themselves require the aircrew to be temporary grounded and so there is no real discussion about medication.

Typical examples: antibiotics, anti-inflammatory drugs, pain killers, hypnotics.

2. Medical context in which the pilot/ATCO is prescribed a treatment for a long duration, usually while initial period of a sick-leave due to the disease: the aircrew should ideally call the AME or at least ask for advice the practitioner; a longer period of grounding may be firstly required specifically due to the treatment; a return to flying/working duties may be possible with no limitation.

Typical examples: anti-hypertensive treatment, 5-ASA drugs, thyroid hormones.

3. Medical context for which the treatment refers to a severe disease and so to impossibility for a pilot/ATCO to fly/work without a consultation with the AME: the medication may be compatible with fitness, but usually after a decision of the licensing aeromedical Authority; limitation(s) may be required, first of all a multipilot activity; specific tests may punctually be asked by the AME, particularly the Maintenance of Wakefulness Test to check vigilance; the aeromedical licensing Authority may also confirm the incompatibility between the treatment and the flying/working activities.

Typical examples: anti-diabetics, anticoagulants, anti-arrhythmia drugs, oral corticosteroids, long-duration inhaled beta 2-agonists, immune-modulating agents, anti-virus agents for CVH or HIV, anti-epileptics, anti-depressive drugs.

4. Chronic disease for which a medical treatment has been prescribed previously and accepted by the AME and/or the aeromedical licensing Authority, but with a change in the intake (new dosage, re-using after a therapeutic window, new molecule as a switch, new molecule added): sometimes the aircrew may manage alone his/her fitness, all the more than this situation has been previously anticipated and discussed with the AME.

Typical examples: anti-hypertensive treatment, corticosteroids, thyroid hormones.

In conclusion: the “ten gold rules” for medication in aircrews

1. Do not make any medication seem ordinary but do not dramatize.
2. Make the aircrews be sensitive to the dangers of self-medication.
3. Remind aircrews of their responsibility in case of a drug intake with no authorized advice.
4. Imagine the possible impact of side effects in a cockpit or control tower environment.
5. Do not deprive aircrews of a justified treatment but inform them about the possible options.
6. Find some help in the official summary of a drug’s characteristics.
7. Consider the real conditions of flying/working.
8. Integrate the drug assessment into a global approach including the underlying disease.
9. Think about initial period of grounding at the beginning of a new medical treatment.
10. Do accept some therapeutic drugs as being incompatible and find arguments to explain.