

## 1 **Appendix**

### 2 **Supplemental methods:**

#### 3 *Second step*

#### 4 *Literature reviews and semi-structured interviews*

5 The literature review was conducted by using the following major medical databases:  
6 Cochrane Library, MEDLINE, Embase, and Google Scholar. The reviews were then  
7 completed by using other resources, such as Micromedex, UpToDate, Thériaque, and Swiss  
8 Agency for Therapeutic Products, and by following the recommendations of major European  
9 and North American scientific societies and regulatory agencies including the United States  
10 Food and Drug Administration, the European Medicines Administration, the Ministère de la  
11 Santé et des Services Sociaux du Québec, the National Institute for Health and Care  
12 Excellence (UK), the French National Authority for Health, and the Swiss Federal Office of  
13 Public Health. The recommendations were weighted according to their level of evidence  
14 (systematic reviews and meta-analyses of randomised controlled trials > randomised  
15 controlled trials > non-randomised intervention studies > non-experimental studies > expert  
16 opinion) and date of publication to provide physicians with the most accurate and the  
17 strongest recommendations.<sup>1</sup>

#### 18 *Semi-structured interview topics*

Domains	Subdomains
Cardiology	Acute coronary syndrome, Atrial fibrillation and Rhythm disorders, Heart failure, High blood pressure, Stable ischemic heart disease, Dyslipidaemia, Stroke and Transient ischaemic attack
Angiology/haemostasis	Deep vein thrombosis (acute & previous), Pulmonary embolism (acute & previous), Venous thromboembolism (acute & previous)
Pneumology	Chronic respiratory disease, Asthma, COPD, Cystic fibrosis, Sleep apnea
Nephrology	Benign prostatic hyperplasia, Renal failure (acute & chronic)
Gastroenterology	Constipation, Diarrhoea and Clostridium difficile diarrhoea Gastroduodenal ulcers, Hepatic impairment and cirrhosis
Rheumatology	Gout (acute & chronic), Osteoporosis, Polymyalgia rheumatic, Rheumatoid arthritis
Neurology	Myasthenia gravis, Parkinson's disease, Seizures
Psychiatry	Bipolar disorders, Depression, Schizophrenia, Sleep disorders

Pain and Analgesia	Acute pain, Migraine (attack & chronic), Neuropathic pain
Infectiology	Abdominal infections, Antimicrobial, Pneumocystis, and Toxoplasmosis prophylaxis, Bone and joint infections, Bronchopulmonary infections and Tuberculosis, Endocarditis, hepatitis B virus, hepatitis C virus, Human Immunodeficiency Virus, Probabilistic antibiotic therapy, Proper use of antibiotics, Urinary tract infections
Endocrinology	Contraception, Thyroid disorders (hypo/ hyperthyroidism), Diabete mellitus (type 1 and 2)
Ophthalmology	Glaucoma
Dependencies	Addiction, Alcoholism, Benzodiazepine dependence, Opioid use disorder, Tobacco addiction
Obesity	Proper use of drugs in the case of obesity
Pharmacology and Toxicology	Allergy, Drug-drug interactions, Extrapyrimalal syndrome G6PD deficiency, Hematotoxicity, Long QT, Serotonin syndrome
Transplants	Bone marrow transplant, Immunosuppression, Organ transplant
Vaccinations	Influenza, Pneumococcal infections, Vaccination

19

20 *Third step: Delphi study*

21 *Experts' recruitment*

22 Potential participants were nominated by word of mouth from people in the professional  
23 networks of the research group members. Two inclusion criteria were used: participants had  
24 to have (1) expertise in internal medicine and (2) the ability to complete each Delphi round  
25 within a specified period. Experts were invited to participate in the Delphi rounds and to  
26 recruit a colleague (internist had to recruit a pharmacist and vice versa) working in the same  
27 hospital. To avoid a high drop-out rate, we limited the survey to 2 rounds. Each expert  
28 disclosed his or her conflicts of interest; none of the experts had any commercial associations  
29 or financial interests that posed a conflict of interest in association with the study.

30 *Delphi rounds*

31 Before the first round, a tutorial explaining how to rate statements using the SurveyMonkey  
32 website and a document summarising all the statements included in the draft version. In this  
33 document, the following evidenced-based support for each statement was provided: the  
34 rationale for the statement, relevant data, and references (in the form of web links). The  
35 experts were not required to read all of the references but rather were instructed to refer to  
36 them whenever supporting evidence for a particular statement was needed. One week before  
37 the second round, a personalized feedback report was emailed to each expert. It included their

own first-round ratings, as well as the median panel rating for each statement. Any statement modifications were highlighted in red.

Before the deadline, experts who had not yet completed the survey were sent 2 email reminders. For experts who missed the deadline, 2 personal email reminders were sent during the 2 weeks after the deadline, and a telephone reminder was provided 3 weeks after the deadline.

#### *Integration of experts' propositions*

Propositions were presented to 3 members of the research group who were involved in the initial selection of statements, before the Delphi survey: 1 internist, 1 clinical pharmacist, and 1 clinical pharmacologist. These individuals had to indicate independently whether they wanted to integrate each proposition submitted by the experts. If all 3 members decided to integrate an expert's proposition regarding a retained statement, the principal investigator modified the retained statements accordingly. If differences persisted among the 3 members, the principal investigator discussed the arguments anonymously to all members of the triangulation group until a consensus was reached. After the second round, the same triangulation process was used, but only propositions specifying the statement were included. Propositions that would have changed the meaning of a statement were excluded, as they would have required new validation by the Delphi panel.

1. Harbour R, Miller J. A new system for grading recommendations in evidence based guidelines. *BMJ* 2001;323:334-6.