Supplemental Table 2: Additional data validated by the expert panel for inclusion in PIM-Check

PIM-Check additional data: Potentially Inappropriate Medications for Patients in Internal Medicine checklist

This supplemental table includes PIM-check statements' additional data.
It includes statements' rational and references and when appropriate recommendations, remarks, and useful links.
This tool was validated using a 2-round Delphi method including 40 international experts from Belgium, France, Quebec and Switzerland. Their median level of agreement and useful rating during the second round are indicated for each statement.
This is not a replacement for a clinical and biological evaluation by a clinician. The proposals are only applicable in the event there is no patient-specific contraindication.
Some drugs listed may not be available in each country.
A glossary of all abbreviations used in this tool is available at the end of the table.
The *, **, *** symbols refer to information contained in table 3.

CARDIOLOGY

HEART FAILURE

1 UP	**Rational**	Reduced risk of hospitalisation for heart failure and reduced risk of premature death.	
	Recommendations	Suggested dosing regimens: Titration up to effective doses or up to the maximum tolerated dose, while monitoring renal function. Maximum suggested dosing regimens: ACEI: captopril 50 mg TID, enalapril 10–20 mg BID, fosinopril 40 mg QD, lisinopril 20–40 mg QD, perindopril 8–16 mg QD, quinapril 20 mg BID, ramipril 5 mg BID, trandolapril 4 mg QD ARB: candesartan 32 mg QD, valsartan 160 mg BID, losartan 50–150 mg QD	
	References	ESC 2012: Acute and Chronic Heart Failure: http://eurheartj.oxfordjournals.org/content/33/14/1787.full.pdf?bcsi_scan_628cd39dca2568d2=xWJ7tj2YrRFrO5fphQuC5p247toBAAAAd3H7AA==&bcsi_scan_filename=1787.full.pdf ACCF/AHA 2013: Guideline for the Management of Heart Failure: http://circ.ahajournals.org/content/128/16/e240.full.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 100 % % of experts rating items useful or very useful: 97.4 %
2 UP	**Rational**	Reduced risk of hospitalisation for HF and reduced risk of premature death.	
	Recommendations	**Beta-blockers recommended in case of HF: bisoprolol, carvedilol, metoprolol or nebivolol. Maximum suggested dosing regimens: titration up to the effective doses or up to the maximum tolerated dose. Bisoprolol 10 mg QD, carvedilol 25–50 mg BID, metoprolol succinate 200 mg QD, nebivolol 10 mg QD (unlike the other 3, nebivolol does not reduce mortality for all causes combined and cardiovascular mortality).	
	References	ESC 2012: Acute and Chronic Heart Failure: http://eurheartj.oxfordjournals.org/content/33/14/1787.full.pdf?bcsi_scan_628cd39dca2568d2=xWJ7tj2YrRFrO5fphQuC5p247toBAAAAd3H7AA==&bcsi_scan_filename=1787.full.pdf ACCF/AHA 2013: Guideline for the Management of Heart Failure: http://circ.ahajournals.org/content/128/16/e240.full.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 100 % % of experts rating items useful or very useful: 92.3 %
3 UP	**Rational**	Reduced risk of hospitalisation for HF and reduced risk of premature death.	
	Remarks	Monitor renal function and kalaemia. Only in heart failure patients with a CrCl > 30 ml/min/1.73 m2 and a kalaemia < 5 mEq/L.	
	Recommendation	Suggested dosing regimens**:** Spironolactone 25–50 QD, eplerenone 50 mg QD.	
	References	ESC 2012: Acute and Chronic Heart Failure: http://eurheartj.oxfordjournals.org/content/33/14/1787.full.pdf?bcsi_scan_628cd39dca2568d2=xWJ7tj2YrRFrO5fphQuC5p247toBAAAAd3H7AA==&bcsi_scan_filename=1787.full.pdf ACCF/AHA 2013: Guideline for the Management of Heart Failure: http://circ.ahajournals.org/content/128/16/e240.full.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 97.9 %
4	**Rational**	Risk of sodium and water retention, HF exacerbation, increased risk of hospitalisation for HF	

OP		and sudden death.	
	Remarks	*Non-exhaustive list of drugs that may exacerbate HF: NSAIDs (except low-dose aspirin) and COX2-inhibitor: by hydro-sodium retention, antiarrhythmic drugs (except digoxin and amiodarone), tricyclic antidepressants, carbamazepine, corticosteroids (oral or inhaled), glitazones, and calcium inhibitors (except amlodipine and felodipine): by negative inotropic effects, moxonidine, and sotalol. ** Non-exhaustive list of sodium-rich drugs: sodium alginate, bicarbonate, diphosphate, effervescent drugs, fosfomycin, penicillins, phosphate, piperacillin, salicylate.	
	References	ESC 2012: Acute and Chronic Heart Failure: http://eurheartj.oxfordjournals.org/content/33/14/1787.full.pdf?bcsi_scan_628cd39dca2568d2=xWJ7tj2YrRFrO5fphQuC5p247toBAAAAd3H7AA==&bcsi_scan_filename=1787.full.pdf ACCF/AHA 2013: Guideline for the Management of Heart Failure: http://circ.ahajournals.org/content/128/16/e240.full.pdf George J, et al. Association between cardiovascular events and sodium containing effervescent, dispersible, and soluble drugs: nested case-control study. BMJ 2013: http://www.bmj.com/content/347/bmj.f6954	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 87.2 %
	DYSLIPIDAEMIA and HYPOLIPIDEMICS		
5 UP	**Rational**	Primary and secondary prevention of heart disease.	
	Recommendations	*Therapeutic objectives targeted based on the cardiovascular risk: Very high cardiovascular risk: Heart disease, T2DM, T1DM with organ impairment, moderate to severe renal impairment or HeartScore ≥ 10%: lifestyle and dietary rules and intensive statin treatment (reduction ≥ 50% of the initial LDLc level). High cardiovascular risk: 1 pronounced risk factor or HeartScore ≥ 5 and < 10%: lifestyle and dietary rules +/- moderate statin treatment. Low to moderate risk: HeartScore greater than 1 - < 5%: lifestyle and dietary rules. It is possible to estimate the cardiovascular risk using different scores**.	
	**Useful links	HeartScore: http://www.heartscore.org/Pages/welcome.aspx Framingham score: http://cvdrisk.nhlbi.nih.gov/calculator.asp Framingham score adapted to patients with HIV: http://www.hivpv.org/Home/Tools/tabid/91/ctl/ExamView/mid/500/eid/0/lid/0/Default.aspx ASCVD score: http://tools.cardiosource.org/ASCVD-Risk-Estimator/	
	References	ACC/AHA 2013: Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults: http://www.joslin.org/docs/2013-ACC-AHA-Guideline-Treatment-of-Blood-Cholestero-_to-Reduce-Atherosclerotic-Cardiovascular-Risk-in-Adults.pdf ESC/EAS 2012: Guidelines on cardiovascular disease prevention in clinical practice: http://eurheartj.oxfordjournals.org/content/33/13/1635.full.pdf?bcsi_scan_628cd39dca2568d2=jXT1M9P0KMth/PmrbO8RUB5K0p4BAAAAUFolAA==&bcsi_scan_filename=1635.full.pdf CCSG 2012: Diagnosis and Treatment of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adult: http://ac.els-cdn.com/S0828282X12015103/1-s2.0-S0828282X12015103-main.pdf?_tid=4ea0bcbe-e12e-11e3-991f-00000aab0f01&acdnat=1400707655_cbb12eab76ca6fd802ca29d6de6a284d	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 89.7 %
6 UP	**Rational**	Prevention of heart disease. Allows a decrease in the LDL-c and triglycerides and an increase in the HDL-c.	
	Recommendation	Suggested dosing regimen: maximum tolerated dose making it possible to achieve the target LDL-c level, based on the cardiovascular risk (*see item 5).	
	References	CCSG 2012: Diagnosis and Treatment of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adult: http://ac.els-cdn.com/S0828282X12015103/1-s2.0-S0828282X12015103-main.pdf?_tid=4ea0bcbe-e12e-11e3-991f-00000aab0f01&acdnat=1400707655_cbb12eab76ca6fd802ca29d6de6a284d ACC/AHA 2013: Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults: http://www.joslin.org/docs/2013-ACC-AHA-Guideline-Treatment-of-Blood-Cholestero-_to-Reduce-Atherosclerotic-Cardiovascular-Risk-in-Adults.pdf ESC 2011: Dyslipidaemias (Management of): http://www.escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/Dyslipidaemias-2011.aspx	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 84.6 %
7 DDI	**Rational**	Most statins undergo a hepatic metabolisation involving the CYP (except pravastatin, rosuvastatin and pitavastatin).	

		Risk of DDIs with CYP inhibitors and inducers*.	
	Remark	**Non-exhaustive list of molecules interacting with statins (see reference, page 12): www.escardio.org/static_file/Escardio/Guidelines/publications/DYSLIPguidelines-dyslipidemias-addenda.pdf	
	Reference	ESC 2011: Dyslipidaemias (Management of): http://www.escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/Dyslipidaemias-2011.aspx	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 89.7 %
8 OP	**Rational**	Increased risk of myopathy.	
	Remark	In case of combination, monitor side effects and muscle pain.	
	Reference	ESC 2011: Dyslipidaemias (Management of): http://www.escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/Dyslipidaemias-2011.aspx	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 92.3 % % of experts rating items useful or very useful: 82.1 %
STABLE ISCHAEMIC HEART DISEASE			
9 UP	**Rational**	Prevention of acute cardiovascular events.	
	Remarks	Favour a cardioselective beta-blocker*. *Non-exhaustive list of cardioselective molecules: acebutolol, atenolol, bevantolol (+ alpha-agonist), bisoprolol, celiprolol (+ alpha-blocker), esmolol, metoprolol, pafenolol, practolol, tolamolol, xamoterol. Potential contraindications: exacerbation of occlusive arterial disease of the lower limbs (stage 3–4), obstructive respiratory problems, history of major hypoglycaemia, etc.	
	Reference	ACCF/AHA/ACP/AATS/PCNA/SCAI/STS 2012: Management of Patients With Stable Ischemic Heart Disease: http://circ.ahajournals.org/content/126/25/e354.full.pdf?bcsi_scan_43167910db6ab4d9=NWTT1eR30/ndif8NPwwEGhAlIEIBAAAAjrwrAA==&bcsi_scan_filename=e354.full.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 92.3 %
10 UP	**Rational**	Prevention of acute cardiovascular events.	
	Recommendations	Suggested dosing regimen: 75 to 160 mg QD. *In case of contraindication for aspirin: treatment using clopidogrel 75 mg QD may be considered.	
	References	ACCF/AHA/ACP/AATS/PCNA/SCAI/STS 2012: Management of Patients With Stable Ischemic Heart Disease: http://circ.ahajournals.org/content/126/25/e354.full.pdf?bcsi_scan_43167910db6ab4d9=NWTT1eR30/ndif8NPwwEGhAlIEIBAAAAjrwrAA==&bcsi_scan_filename=e354.full.pdf Valgimigli M, et al. Short- versus long-term duration of dual-antiplatelet therapy after coronary stenting: a randomized multicenter trial. Circulation 2012: http://circ.ahajournals.org/content/early/2012/03/16/CIRCULATIONAHA.111.071589.full.pdf Varenhorst C, et al. Duration of dual antiplatelet treatment with clopidogrel and aspirin in patients with acute coronary syndrome. Eur Heart J 2013 [abstract]: http://eurheartj.oxfordjournals.org/content/early/2013/10/10/eurheartj.eht438.abstract	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 100 % % of experts rating items useful or very useful: 97.4 %
11 UP	**Rational**	Management of cardiovascular risk factors.	
	Recommendations	As 1st line treatment: medium to high dose statins combined with lifestyle and dietary measures. In case of intolerance: cholesterol reducer, alone or in combination with a biliary acid or nicotinic acid sequestering agent. Therapeutic goals: LDLc < 1.8 mmol/l or reduction ≥ 50% of the initial LDL-c level.	
	References	ACC/AHA 2013: Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults: http://www.joslin.org/docs/2013-ACC-AHA-Guideline-Treatment-of-Blood-Cholestero-_to-Reduce-Atherosclerotic-Cardiovascular-Risk-in-Adults.pdf ACCF/AHA/ACP/AATS/PCNA/SCAI/STS 2012: Management of Patients With Stable Ischemic Heart Disease: http://circ.ahajournals.org/content/126/25/e354.full.pdf?bcsi_scan_43167910db6ab4d9=NWTT1eR30/ndif8NPwwEGhAlIEIBAAAAjrwrAA==&bcsi_scan_filename=e354.full.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 92.3 %
SECONDARY PREVENTION OF ACUTE STEMI OR NSTEMI			

12 Other	**Rational**	Secondary prevention of an acute cardiovascular event.
	References	ACCF/AHA 2013: Guideline for the Management of ST-Elevation Myocardial Infarction: https://circ.ahajournals.org/content/127/4/e362.full.pdf ESC 2012: Acute Myocardial Infarction in patients presenting with ST-segment elevation (Management of): http://www.escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/AMI-STEMI.aspx ESC 2011: Acute Coronary Syndromes (ACS) in patients presenting without persistent ST-segment elevation (Management of): http://www.escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/ACS-2011.aspx
	Strength of recommendation	Experts median agreement: strongly agree — % of experts agree or strongly agree: 97.4 % Median usefulness rating: useful — % of experts rating items useful or very useful: 84.6 %
13 UP	**Rational**	Secondary prevention of an acute cardiovascular event.
	Recommendations	As 1st line treatment: cardioselective beta-blockers* are preferred, with the goal of a heart rate < 70/min. Alternative: in patients with beta-blockers intolerance, verapamil or diltiazem may be offered (Only in patients without HF, or decreased LVEF). Monitor DDI and adapt treatment before starting these molecules.
	Remarks	*Non-exhaustive list of cardioselective beta-blockers: acebutolol, atenolol, bevantolol (+ alpha-agonist), bisoprolol, celiprolol (+ alpha-blocker), esmolol, metoprolol, pafenolol, practolol, tolamolol, xamoterol.
	References	ACCF/AHA 2013: Guideline for the Management of ST-Elevation Myocardial Infarction: https://circ.ahajournals.org/content/127/4/e362.full.pdf ESC 2012: Acute Myocardial Infarction in patients presenting with ST-segment elevation (Management of): http://www.escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/AMI-STEMI.aspx ESC 2011: Acute Coronary Syndromes (ACS) in patients presenting without persistent ST-segment elevation (Management of): http://www.escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/ACS-2011.aspx
	Strength of recommendation	Experts median agreement: strongly agree — % of experts agree or strongly agree: 100 % Median usefulness rating: very useful — % of experts rating items useful or very useful: 94.9 %
14 UP	**Rational**	Secondary prevention of an acute cardiovascular event.
	Recommendations	Suggested regimen: double antiplatelet therapy for 1 month if a bare stent has been placed, 6 months if an impregnated stent has been placed, (duration between 1 and 12 months depending on risk factors and the type of endoprosthesis), then low-dose aspirin, alone, for life (75–160 mg QD) Re-evaluate the duration of the double antiplatelet therapy on a case-by-case basis and in collaboration with a cardiologist in the event a stent is placed (based on the risk of thrombosis on the endoprosthesis, haemorrhage risk, presence of an anticoagulant, etc.). As 2nd line: long-term clopidogrel (75 mg QD), prasugrel (10 mg QD), ticagrelor (90 mg BID).
	References	ACCF/AHA 2013: Guideline for the Management of ST-Elevation Myocardial Infarction: https://circ.ahajournals.org/content/127/4/e362.full.pdf ESC 2013: Aspirin, still first-line in secondary prevention of cardiovascular complications in peripheral artery disease: http://www.escardio.org/communities/councils/ccp/e-journal/volume11/Pages/Aspirin-peripheral-arterial-occlusive-disease.aspx#.UtHeLtJFVWI ACCP 2012: Antiplatelet Drugs. American College of Chest Physicians Evidence Based Clinical Practice Guidelines (9th Edition): http://journal.publications.chestnet.org/data/Journals/CHEST/23443/112293.pdf ACCF/AHA 2012: Focused Update Incorporated Into the ACCF/AHA 2007 Guidelines for the Management of Patients With Unstable Angina/Non−ST-Elevation Myocardial Infarction: http://circ.ahajournals.org/content/127/23/e663.full.pdf ESC 2012: Acute Myocardial Infarction in patients presenting with ST-segment elevation (Management of): http://www.escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/AMI-STEMI.aspx ESC 2011: Acute Coronary Syndromes (ACS) in patients presenting without persistent ST-segment elevation (Management of): http://www.escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/ACS-2011.aspx
	Strength of recommendation	Experts median agreement: strongly agree — % of experts agree or strongly agree: 100 % Median usefulness rating: very useful — % of experts rating items useful or very useful: 94.9 %
15 UP	**Rational**	Management of cardiovascular risk factors.
	Recommendations	As 1st line treatment: medium or high dose statins combined with lifestyle and dietary measures. In case of intolerance: cholesterol reducer, alone or in combination with a biliary acid or

		nicotinic acid sequestering agent. Therapeutic goals: LDLc < 1.8 mmol/l or reduction ≥ 50% of the initial LDL-c level.
	References	ACC/AHA 2013: Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults: http://circ.ahajournals.org/content/early/2013/11/11/01.cir.0000437738.63853.7a.full.pdf ACCF/AHA 2013: Guideline for the Management of ST-Elevation Myocardial Infarction: https://circ.ahajournals.org/content/127/4/e362.full.pdf ESC 2012: Acute Myocardial Infarction in patients presenting with ST-segment elevation (Management of): http://www.escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/AMI-STEMI.aspx ESC 2011: Acute Coronary Syndromes (ACS) in patients presenting without persistent ST-segment elevation (Management of): http://www.escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/ACS-2011.aspx
	Strength of recommendation	Experts median agreement: strongly agree — % of experts agree or strongly agree: 97.4 % Median usefulness rating: very useful — % of experts rating items useful or very useful: 94.9 %
16 UP	**Rational**	Low, but significant reduction of 30 days mortality. Modest long-term efficacy in patients with no associated pathology.
	Recommendations	Monitor renal function and kalaemia. *Non-exhaustive list of exacerbating factors: presence of HF, reduced LVEF, diabetes, prior myocardial infarction, high blood pressure or renal impairment. Alternatives: in case of ACEI intolerance, an ARB (preferably valsartan) can be prescribed.
	References	ACCF/AHA 2013: Guideline for the Management of ST-Elevation Myocardial Infarction: https://circ.ahajournals.org/content/127/4/e362.full.pdf ESC 2012: Acute Myocardial Infarction in patients presenting with ST-segment elevation (Management of): http://www.escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/AMI-STEMI.aspx ESC 2011: Acute Coronary Syndromes (ACS) in patients presenting without persistent ST-segment elevation (Management of): http://www.escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/ACS-2011.aspx
	Strength of recommendation	Experts median agreement: strongly agree — % of experts agree or strongly agree: 100 % Median usefulness rating: very useful — % of experts rating items useful or very useful: 92.3 %
	HIGH BLOOD PRESSURE	
17 UP	**Rational**	Management of cardiovascular risk factors and decreased mortality.
	Recommendations	Systolic BP (sBP) < 140 mmHg: diabetes, chronic kidney failure (CKF), history of stroke or transient ischaemic attack, patients with cardiovascular risk, or heart disease. sBP 140–150 mmHg: patient > 65 years (except in case of orthostatic hypotension). Diastolic BP (dBP) < 90 mmHg: for all patients (optionally in case of diabetes: dBP < 85 mmHg).
	Remarks	*First-line drugs to treat HBP: thiazide diuretics (chlorthalidone, hydrochlorothiazide, indapamide), ACEI, ARB, calcium inhibitors. Beta-blockers are no longer recommended by the Joint National Committee (JNC 8) as 1st line to treat HBP in the non-black general population. In case of bi-therapy, fixed combinations should be favoured in order to improve patient observance. **Pharmacological measures are recommended in adults < 60 years when the BP is > 140/90 mmHg) subject to the quality of the diagnosis in a hospitalisation context for acute affection. ***Lifestyle and diet modifications: decrease salt consumption (5–6 g/day), decrease alcohol consumption, increase fruit and vegetable intake, engage in regular physical activity (30 minutes/day, 5 to 7 days/week), counselling/assistance to quit tobacco use, weight loss and decreased waist size (body mass index < 25 kg/m², waist size < 102 cm in men and < 88 cm in women).
	References	Joint National Committee (JNC 8) 2014: Management of High Blood Pressure in Adults: http://jama.jamanetwork.com/article.aspx?articleid=1791497 ESH/ESC 2013: Arterial Hypertension (Management of): http://eurheartj.oxfordjournals.org/content/34/28/2159.full.pdf PECH 2014 : Programme Éducatif Canadien sur l'Hypertension : http://www.hypertension.ca/images/CHEP_2014/2014_CompleteCHEPRecommendations_FR_HCP1009.pdf
	Strength of recommendation	Experts median agreement: strongly agree — % of experts agree or strongly agree: 100 % Median usefulness rating: very useful — % of experts rating items useful or very useful: 97.4 %
18 Other	**Rational**	Nephroprotective effect, improved prognosis in HF and many clinical trials conducted for these indications.
	References	Joint National Committee (JNC 8) 2014: Management of High Blood Pressure in Adults: http://jama.jamanetwork.com/article.aspx?articleid=1791497

		ESH/ESC 2013: Arterial Hypertension (Management of): http://eurheartj.oxfordjournals.org/content/34/28/2159.full.pdf PECH 2014 : Programme Éducatif Canadien sur l'Hypertension : http://www.hypertension.ca/images/CHEP_2014/2014_CompleteCHEPRecommendations_FR_HCP1009.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 100 % % of experts rating items useful or very useful: 100 %
19 UP	**Rational**	Management of cardiovascular risk factors and HBP complications.	
	Remarks	*Aldosterone antagonists: spironolactone or eplerenone. Monitoring of kalaemia is recommended in case of combination with an ACEI or ARB. Monitor risk of orthostatic hypotension with alpha-1-blockers. **A resistant HBP is defined by a BP > 140–90 mmHg, despite appropriate lifestyle and dietary measures, combined with treatment with a diuretic + two other antihypertensive agents belonging to different classes, at appropriate doses and with good drug observance.	
	References	ESH/ESC 2013: Arterial Hypertension (Management of): http://eurheartj.oxfordjournals.org/content/34/28/2159.full.pdf Vaclavik J, et al. Addition of spironolactone in patients with resistant arterial hypertension (ASPIRANT): a randomized, double blind, placebo-controlled trial. Hypertension 2011: http://hyper.ahajournals.org/content/57/6/1069.full.pdf	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 89.7 % % of experts rating items useful or very useful: 79.5 %
20 OP	**Rational**	Risk of BP destabilization.	
	Recommendation	Favour a therapeutic alternative when available or reinforce blood pressure monitoring if use is necessary in these patients.	
	Remarks	*Non-exhaustive list of drugs that may increase the blood pressure: ACTH, NSAIDs and COX2-inhibitor, anti-calcineurins (cyclosporine, tacrolimus), bromocriptine, buspirone, some antidepressants (venlafaxine, duloxetine, atomoxetine, MAOIs), carbamazepine, clonidine, clozapine, corticosteroids, ergot derivatives, desflurane, erythropoietin, ketamine, metoclopramide, oestrogens (oral oestrogen contraceptives), paracetamol/acetaminophen, sibutramine, sympathomimetics (ex: ephedrine, naphazoline, phenylephrine, phenylpropanolamine, pseudoephedrine, synephrine), triptans. **Non-exhaustive list of sodium-rich drugs: sodium alginate, bicarbonate, biphosphate, citrate, effervescent drugs, fosfomycin, phosphate, salicylate, sulphate.	
	References	NIH/ NHLBI 2004: The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: http://www.nhlbi.nih.gov/guidelines/hypertension/jnc7full.pdf AHA 2007: Use of Nonsteroidal Antiinflammatory Drugs: http://circ.ahajournals.org/content/115/12/1634.full.pdf BMJ 2013: cardiovascular events and sodium containing effervescent, dispersible, and soluble drugs: http://www.bmj.com/highwire/filestream/674373/field_highwire_article_pdf/0/bmj.f6954 Prescrire le Guide. Éviter les effets indésirables par interactions médicamenteuses – Comprendre et décider (Janvier 2013)	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 92.3 % % of experts rating items useful or very useful: 76.9 %
21 OP	**Rational**	Indicated in the treatment of oedemas of cardiac, renal, hepatic origin, not related to venous insufficiency.	
	Remark	Loop diuretics may potentially replace other types of antihypertensive diuretics in case of chronic kidney disease with CrCl < 30 ml/min.	
	References	JNC8 2014: Management of High Blood Pressure in Adults: http://jama.jamanetwork.com/article.aspx?articleid=1791497 ESH/ESC 2013: Arterial Hypertension (Management of): http://eurheartj.oxfordjournals.org/content/34/28/2159.full.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 92.3 % % of experts rating items useful or very useful: 87.2 %
NON-CARDIOEMBOLIC STROKE and TRANSIENT ISCHAEMIC ATTACKS			
22 UP	**Rational**	Patients with the risk of cerebrovascular and cardiovascular recurrence.	
	References	AHA/ASA 2013: Early Management of Patients With Acute Ischemic Stroke: http://stroke.ahajournals.org/content/early/2013/01/31/STR.0b013e318284056a.full.pdf AHA/ASA 2011: Prevention of Stroke in Patients With Stroke or Transient Ischemic Attack: https://stroke.ahajournals.org/content/42/1/227.full.pdf ESC 2011: Dyslipidaemias (Management of): http://www.escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/Dyslipidaemias-2011.aspx	

	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 97.4 %
23 UP	**Rational**	Patients with the risk of cerebrovascular and cardiovascular recurrence.	
	Recommendation	*Non-exhaustive list of recommended antiplatelet therapy: low-dose aspirin (75–160 mg QD) or clopidogrel (75 mg QD).	
	Reference	ACCP 2012: Antithrombotic and Thrombolytic Therapy for Ischemic Stroke: http://journal.publications.chestnet.org/data/Journals/CHEST/23443/112302.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 100 % % of experts rating items useful or very useful: 97.4 %
ARRHYTHMIAS, ATRIAL FIBRILLATION and ANTIARRHYTHMICS			
24 Other	**Rational**	Drugs with a narrow therapeutic window. Risk of toxicity in case of overdose. Digoxin toxicity increased by a decline in renal function.	
	Recommendations	Monitor the occurrence of rhythm disorders (ventricular arrhythmia, atrioventricular blocks, etc.). Suggested dose: 125 µg QD (62.5 µg QD in elderly patients), do not to exceed 250 µg QD. The digoxinemia should be < 1 ng/ml (< 1.3 nmol/l). In case of digitalis poisoning or signs of poisoning (ex: fever, nausea/vomiting, colour distortion, etc.) temporarily discontinue digitalis +/- administer an anti-digitalis antibody, depending on the serum digoxin level and cardiac/haemodynamic manifestations.	
	Remark	Non-exhaustive list of molecules that may interact with digoxin: see item 25.	
	References	ESC 2012: Acute and Chronic Heart Failure: http://eurheartj.oxfordjournals.org/content/33/14/1787.full.pdf?bcsi_scan_628cd39dca2568d2=xWJ7tj2YrRFrO5fphQuC5p247toBAAAAd3H7AA==&bcsi_scan_filename=1787.full.pdf HFSA 2010: Comprehensive Heart Failure Practice Guideline: http://www.heartfailureguideline.org/_assets/document/Guidelines.pdf ACC/AHA/ESC 2006: Management of Patients With Ventricular Arrhythmias: http://content.onlinejacc.org/article.aspx?articleid=1137887	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 92.3 %
25 DDI	**Rational**	Drug with narrow therapeutic window, substrate of P-glycoprotein. Risk of overdose and toxicity.	
	Recommendations	Monitor the serum digoxin level and signs of overdose*. *In case of digitalis poisoning or signs of poisoning (ex: fever, nausea/vomiting, colour distortion, etc.) temporarily discontinue digitalis +/- administer an anti-digitalis antibody, depending on the serum digoxin level and cardiac/haemodynamic manifestations.	
	Remark	Non-exhaustive list of molecules that may inhibit Pgp: amiodarone, atorvastatin, certain ARVs, cyclosporine, ketoconazole, macrolides (clarithromycin+++), nalmefene, quinidine, verapamil.	
	Useful link	HUG 2014: Drug interactions, cytochromes P450 and P-glycoprotein (Pgp): http://www.hug-ge.ch/sites/interhug/files/structures/pharmacologie_et_toxicologie_cliniques/documents/interactions_medicamenteuses_et_cyp450.pdf	
	References	Akhtar N, et al. The emerging role of P-glycoprotein inhibitors in drug delivery: a patent review Expert Opin. Ther. Patents 2011 [abstract]: http://informahealthcare.com/doi/abs/10.1517/13543776.2011.561784 DuBuske L. The Role of P-Glycoprotein and Organic Anion-Transporting Polypeptides in Drug Interactions. Drug Safety 2005 [abstract]: http://link.springer.com/article/10.2165/00002018-200528090-00004	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 89.7 %
26 UP	**Rational**	Prevention of thromboembolic events and risk of stroke. Target INR = 2.5: VKA optimal safe/effective intensity in nonvalvular AF (the average of the last 5 INRs should ideally be 2.5).	
	Recommendations	*Select an oral anticoagulant from among: VKA, dabigatran, rivaroxaban and apixaban, depending on the patient's risk factors (age, weight, renal function, anticipated observance quality, patient's preferences after appropriate information, price, tolerance, potential drug interactions and clinical characteristics). Take potential contraindications into account, specificities of the patient, and in particular haemorrhage risk (HAS-BLED score***) into account.	

	Remarks	**Calculation of the CHA2DS2-VASc score: heart failure or decreased ejection fraction (1 pt), high blood pressure (1 pt), age ≥ 75 (2 pts), diabetes mellitus (1 pt), stroke (2 pts), vascular disease (1 pt), age 65–74 (1 pt), female (1 pt). Women suffering from AF, under the age of 65 years with no other risk factors, are categorized as low risk and do not require antithrombotic therapy (CHA2DS2VASc = 1 due to gender). It is possible to use the CHADS2 score: in this case, prescribe or continue an oral anticoagulant treatment if CHADS ≥ 1 and aspirin if CHADS2 = 0 in patients ≥ 65 years or older or in women with vascular pathology. ***Calculation of the HAS-BLED score: HBP (sBP > 160 mmHg) (1pt), Abnormal renal function (serum creatinine ≥ 200 µmol/L) or/and Abnormal liver function (Cirrhosis, bilirubin > 2x UNL with AST/ALT/AP > 3x UNL) (1 or 2 pts), Stroke history (1pt), Bleeding (Bleeding history or predisposition (anemia)) (1pt), Labile INR (Therapeutic time in range < 60%) (1pt), Elderly (Greater than 65 years old) (1pt), Drugs or alcohol (Drugs - other antiplatelet agents or NSAIDs, Alcohol - more than 8 drinks per week) (1 or 2 pts).
	References	AHA/ASA 2012: Oral Antithrombotic Agents for the Prevention of Stroke in Nonvalvular Atrial Fibrillation: http://stroke.ahajournals.org/content/43/12/3442.full.pdf ESC 2012: Atrial Fibrillation (Management of) 2010 and Focused Update (2012): http://eurheartj.oxfordjournals.org/content/33/21/2719.full.pdf CCS 2012: Atrial Fibrillation Guidelines: Recommendations for Stroke Prevention and Rate/Rhythm Control: http://www.onlinecjc.ca/article/S0828-282X(12)00046-3/fulltext ACCP 2012: Antithrombotic Therapy for Atrial Fibrillation: http://journal.publications.chestnet.org/data/Journals/CHEST/23443/112304.pdf
	Strength of recommendation	Experts median agreement: strongly agree — % of experts agree or strongly agree: 100 % Median usefulness rating: very useful — % of experts rating items useful or very useful: 97.4 %

ANGIOLOGY/HAEMOSTASIS

ORAL ANTICOAGULANTS

27 Other	**Rational**	Prevent side effects of oral anticoagulant treatments and improve observance.
	Reference	EHRA 2013: use of new oral anticoagulants in patients with non-valvular atrial fibrillation: http://www.escardio.org/communities/EHRA/publications/novel-oral-anticoagulants-for-atrial-fibrillation/Documents/EHRA-NOAC-Practical-ExecSumm-EHJ-2013.pdf
	Strength of recommendation	Experts median agreement: strongly agree — % of experts agree or strongly agree: 97.4 % Median usefulness rating: very useful — % of experts rating items useful or very useful: 87.2 %
28 Other	**Rational**	Prevention of risks of haemorrhagic and thromboembolic events.
	Recommendations	VKA: once QD, in the evening (except acenocoumarol in certain countries: QD or BID), doses must be adapted based on the INR objective. Dabigatran: 75, 110 or 150 mg QD to BID with or without meal. Rivaroxaban: 2.5, 10, 15 or 20 mg QD to BID with food. Apixaban: 2.5 or 5 mg, BID with or without meal.
	Remarks	Monitor renal function: the doses must be adapted based on the patient's renal function. Caution should be exercised in patients with a CrCl < 30 ml/min. Apixaban and rivaroxaban: not advised if CrCl < 15 ml/min. Dabigatran: contraindicated if CrCl < 30 ml/min. The dosing regimen may be adapted based on the patients' genetic polymorphism.
	Reference	ESC 2012: Atrial Fibrillation (Management of) 2010 and Focused Update (2012): http://eurheartj.oxfordjournals.org/content/33/21/2719.full.pdf
	Strength of recommendation	Experts median agreement: strongly agree — % of experts agree or strongly agree: 94.9 % Median usefulness rating: very useful — % of experts rating items useful or very useful: 84.6 %
29 Other	**Rational**	Intravenous route: produce similar reductions in the INR value at 24 h as oral route and has a higher anaphylactic risk. Subcutaneous route: less effective than OR. Intramuscular route: contraindicated because of bleeding risks. At 24 h, 5 mg and 1 mg of oral vitamin K 1 produce similar effects on the INR.
	Recommendations	**For supra-therapeutic INR without bleeding but requiring a quick return to a normal INR value or in case of minor bleeding, favour low doses of vitamin K 1 (1 to 5 mg). In case of trauma or major bleeding, favour higher doses 5 to 10 mg +/- prothrombotic complex concentrate.

	Remarks	*Favour the OR unless it is not available or in case of suspected malabsorption: cholestasis, absorption disorders, etc.	
	References	ACCP 2012: Antithrombotic Therapy and Prevention of Thrombosis: http://journal.publications.chestnet.org/data/Journals/CHEST/23443/112292.pdf HAS 2008 : Recommendations professionnelles Prise en charge des surdosages en antivitamines K : http://www.has-sante.fr/portail/upload/docs/application/pdf/2008-10/jlestv-20-32-s300.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 97.4 %
30 OP	**Rational**	Therapeutic alternative to VKA. DOACs can be considered to newly anticoagulated patients. Effective and well-tolerated VKA treatment should not systematically be replaced by a DOAC.	
	Recommendations	In case of altered renal function or CrCl < 30 ml/min, favour VKA. Caution should be exercised in patients with a CrCl < 30 ml/min. Apixaban and rivaroxaban: not advised if CrCl < 15 ml/min. Dabigatran: contraindicated if CrCl < 30 ml/min.	
	Reference	HAS 2013 : place pour les anticoagulants oraux non antivitamine K : http://www.has-sante.fr/portail/upload/docs/application/pdf/2013-07/fs_bum_naco_v5.pdf	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 92.3 % % of experts rating items useful or very useful: 84.6 %
31 Other	**Rational**	Dosing regimen should be adapted in case of renal impairment.	
	Recommendation	*Annual evaluation of renal function if the CrCl is > 50 ml/min and 2 to 3 times/year if CrCl < 50 ml/min or as needed if there is a factor that may alter the renal function.	
	Remarks	Exercise caution in all patients with a CrCl < 30 ml/min. Apixaban and rivaroxaban: not advised if CrCl < 15 ml/min. Dabigatran: contraindicated if CrCl < 30 ml/min.	
	Reference	ESC 2012: Atrial Fibrillation (Management of) 2010 and Focused Update (2012): http://eurheartj.oxfordjournals.org/content/33/21/2719.full.pdf?bcsi_scan_628cd39dca2568d2=eM0DtjTKfWNaBCsl4e4u+KGG4dEBAAAA/TR0BQ==&bcsi_scan_filename=2719.full.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 94.9 %
32 DDI	**Rational**	Risks of bleeding or thrombosis in case of unbalanced anticoagulant treatment.	
	Recommendations	Monitor INR for VKA, adapt dosing regimen, monitor side effects, etc.	
	Remarks	*Non-exhaustive list of interactions: Common: antiplatelet drugs, NSAIDs, COX2-inhibitor, heparins, anticoagulants with each other, rifampicin, ketoconazole. With VKA: CYP450 inducers, inhibitors (the cytochromes involved in the metabolism differ based on the molecule), antibiotics (major: ciprofloxacin, cotrimoxazole, erythromycin, metronidazole, isoniazid, ribavirin), antifungal azoles (major: fluconazole, vaginal miconazole, voriconazole), amiodarone, propafenone, diltiazem, propranolol, SSRIs, paracetamol/acetaminophen, fluvastatin, simvastatin, atorvastatin, clofibrate, fenofibrate, gemfibrozil. With dabigatran: clarithromycin, Pgp inhibitors** (amiodarone, quinidine, verapamil), drugs increasing gastric pH (antacids, pantoprazole). With rivaroxaban: CYP450 and P-glycoprotein inducers, inhibitors**, certain anti-epileptics (phenytoin, carbamazepine, phenobarbital, azole antifungals (itraconazole, voriconazole, posaconazole), ritonavir. With apixaban: common interactions with anticoagulants, CYP450 and P-glycoprotein inducers, inhibitors**.	
	Useful link	**HUG 2014: Drug interactions, cytochromes P450 and P-glycoprotein (Pgp): http://www.hug-ge.ch/sites/interhug/files/structures/pharmacologie_et_toxicologie_cliniques/documents/interactions_medicamenteuses_et_cyp450.pdf	
	References	Juurlink D. Drug interactions with warfarin: what clinicians need to know. CMAJ 2007: http://www.cmaj.ca/content/177/4/369.full.pdf Schelleman H, et al. Fibrate/Statin Initiation in Warfarin Users and Gastrointestinal Bleeding Risk. Am Journal of Med 2010: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2813204/pdf/nihms149616.pdf	

		Nutescu E, et al. Drug and dietary interactions of warfarin and novel oral anticoagulants: an update. J Thromb Thrombolysis 2011: ftp://mtr26-1-82-239-144-183.fbx.proxad.net/bibli/-%20Revue%20Articles%20FB/Biblio%20110316%20rout%E9e/74.1104-Drug%20and%20dietary%20interactions%20of%20warfarin%20and%20novel%20oral%20anticoagulants.%20An%20update_Nutescu,%20JTT.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 92.3 %
DEEP VEIN THROMBOSIS, PULMONARY EMBOLISM, VENUS THROMBOEMBOLISM			
33 UP	**Rational**	Prevention of relapses. Target INR = 2.5: VKA optimal safe/effective intensity in DVT and PE (the average of the last 5 INRs should ideally be 2.5).	
	Recommendations	Adjust the treatment duration based on the gravity: - DVT or PE caused by a temporary risk factor = 3 months. - Idiopathic DVT or PE, combined with cancer or in case of second episode: treatment > 3 months, or long-term treatment. In case of heparin/VKA relay, the INR should be located, 2 consecutive times, within the desired values before stopping heparin. Recommended molecules: Heparin, VKA, and DOAC.	
	References	ACCP 2012: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: http://journal.publications.chestnet.org/data/Journals/CHEST/23443/chest_141_2_suppl_e419S.pdf AFSSAPS 2009 : Prévention et traitement de la maladie thromboembolique veineuse en médecine : http://www.sfmu.org/documents/consensus/RBP_thrombose.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 100 % % of experts rating items useful or very useful: 92.3 %
34 UP	**Rational**	High risk of relapse. Target INR = 2.5: VKA optimal safe/effective intensity in VTE (the average of the last 5 INRs should ideally be 2.5).	
	Recommendation	Long-term treatment with annual re-evaluation.	
	Remarks	*Non-exhaustive list of major risk factors: extended immobilisation, active cancers, hereditary coagulation disorder (anti-thrombin deficiency, S protein deficiency, C protein deficiency, etc.).	
	References	ACCP 2012: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: http://journal.publications.chestnet.org/data/Journals/CHEST/23443/chest_141_2_suppl_e419S.pdf AFSSAPS 2009 : Prévention et traitement de la maladie thromboembolique veineuse en médecine : http://www.sfmu.org/documents/consensus/RBP_thrombose.pdf Kearon C, et al. Management of patients with hereditary Hypercoagulable disorders. Annu Rev Med 2000 [abstract]: http://www.annualreviews.org/doi/abs/10.1146/annurev.med.51.1.169?journalCode=med	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 94.9 %
35 UP	**Rational**	Prevention of thromboembolic events.	
	Recommendations	*Molecules with the indication: In case of hospitalisation for acute medical affection: fondaparinux, heparins with a low molecular weight (dalteparin, enoxaparin), non-fractionated heparin subcutaneously. The duration of the thromboprophylaxis should not exceed the patient's immobilisation period or the hospitalisation duration in the event of hospitalisation for acute medical affection. In case of hospitalisation for major orthopaedic surgery: fondaparinux, heparins with a low molecular weight (dalteparin, enoxaparin, tinzaparin), subcutaneous non-fractionated heparin, apixaban, dabigatran, or rivaroxaban (for total hip or knee prosthesis), anti-vitamin K, aspirin or intermittent pneumatic compression device for at least 10 to 14 days. In case of hospitalisation for non-orthopaedic surgery: adapt the treatment based on the thrombosis risk factors and the type of surgery. It is not recommended to introduce thromboprophylactic treatment in patients with a low risk of thrombosis, hospitalised for acute medical affection or for a non-orthopaedic surgical procedure.	
	Remark	**Non-exhaustive list of acute medical affections and increased thrombosis risks: cardiac or acute respiratory decompensation, severe infection, acute inflammatory rheumatological	

		affection, intestinal inflammatory affection, when they are combined with a VTE risk factor, in particular: age > 75 years, cancer, history of venous thromboembolism, hormone treatment, heart failure or chronic respiratory failure, myeloproliferative syndrome.	
	References	ACCP 2012: Prevention of VTE in Nonsurgical Patients: http://journal.publications.chestnet.org/data/Journals/CHEST/23443/chest_141_2_suppl_e195S.pdf ACCP 2012: Prevention of VTE in Nonorthopedic Surgical Patients: http://journal.publications.chestnet.org/data/Journals/CHEST/23443/112297.pdf ACCP 2012: Prevention of VTE in Orthopedic Surgery Patients: http://journal.publications.chestnet.org/data/Journals/CHEST/23443/112404.pdf ACCP 2012: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: http://journal.publications.chestnet.org/pdfaccess.ashx?ResourceID=3137556&PDFSource=13 AFSSAPS 2009 : Prévention et traitement de la maladie thromboembolique veineuse en médecine : http://www.sfmu.org/documents/consensus/RBP_thrombose.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 92.3 %
PNEUMOLOGY			
CHRONIC RESPIRATORY DISEASES			
36 Other	**Rational**	Many therapeutic failures related to inappropriate use of inhaler devices.	
	Reference	NHLBI/NIH 2007: Guidelines for the Diagnosis and Management of Asthma: http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf?bcsi_scan_43167910db6ab4d9=0&bcsi_scan_filename=asthgdln.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 100 % % of experts rating items useful or very useful: 89.7 %
37 Other	**Rational**	Improvement of the intrapulmonary deposit and of the efficacy of treatments.	
	Reference	NHLBI/NIH 2007: Guidelines for the Diagnosis and Management of Asthma: http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf?bcsi_scan_43167910db6ab4d9=0&bcsi_scan_filename=asthgdln.pdf	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 89.7 %
38 Other	**Rational**	Reduced risk of dysphonia and oropharyngeal candidiasis by decreasing stagnation of ICS.	
	Reference	Lee MK, et al. The Efficacy of Immediate Diet for Reducing Local Adverse Events of Inhaled Corticosteroid: A Pilot Study. Tuberc Respir Dis 2012: http://synapse.koreamed.org/Synapse/Data/PDFData/0003TRD/trd-73-93.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 87.2 %
39 Other	**Rational**	Worsening or possible induction of a bronchoconstriction. Monitoring of asthmatic patients' comorbidities is necessary to prevent the risk of exacerbation.	
	Recommendation	Favour alternatives when available or perform close monitoring of the respiratory functions, including with ocular beta blockers.	
	Remark	*Non-exhaustive list of cardioselective molecules: acebutolol, atenolol, bevantolol (+ alpha agonist), bisoprolol, celiprolol (+ alpha-blocker), esmolol, metoprolol, pafenolol, practolol, tolamolol, xamoterol.	
	References	NHLBI/NIH 2007: Guidelines for the Diagnosis and Management of Asthma: http://www.nhlbi.nih.gov/guidelines/asthma/asthsumm.pdf GINA 2012: Global Strategy for Asthma Management and Prevention: http://www.ginasthma.org/local/uploads/files/GINA_Report_March13.pdf GOLD 2013: diagnosis, management and prevention of COPD: http://www.goldcopd.org/uploads/users/files/GOLD_Report_2013_Feb20.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 92.3 % % of experts rating items useful or very useful: 92.3 %
ASTHMA			
40 UP	**Rational**	Inhaled corticosteroids are the most effective anti-asthmatics in monotherapy for this indication.	
	Remark	* Mild persistent asthma: nighttime symptoms 3 to 4 times/month, use of short-acting β2 mimetics > 2 times/week, < once QD, FEV1 > 80%.	
	References	NHLBI/NIH 2007: Guidelines for the Diagnosis and Management of Asthma: http://www.nhlbi.nih.gov/guidelines/asthma/asthsumm.pdf GINA 2012: Global Strategy for Asthma Management and Prevention: http://www.ginasthma.org/local/uploads/files/GINA_Report_March13.pdf	

	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 92.3 %
41 OP	**Rational**	Hides the symptoms without treating the inflammation. Risk of respiratory arrest.	
	Recommendation	Prescribe a first line inhaled corticosteroids and optionally combine it with a long-acting β2-mimetic.	
	References	NHLBI/NIH 2007: Guidelines for the Diagnosis and Management of Asthma: http://www.nhlbi.nih.gov/guidelines/asthma/asthsumm.pdf GINA 2012: Global Strategy for Asthma Management and Prevention: http://www.ginasthma.org/local/uploads/files/GINA_Report_March13.pdf	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 87.4 %
42 UP	**Rational**	This combination allows improved pulmonary function and symptoms and reduces needs for a short-acting β2-mimetic.	
	References	NHLBI/NIH 2007: Guidelines for the Diagnosis and Management of Asthma: http://www.nhlbi.nih.gov/guidelines/asthma/asthsumm.pdf GINA 2012: Global Strategy for Asthma Management and Prevention: http://www.ginasthma.org/local/uploads/files/GINA_Report_March13.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 92.3 %
	CHRONIC OBSTRUCTIVE PULMONARY DISORDER		
43 UP	**Rational**	Prevention or reduction of the symptoms of COPD.	
	Recommendations	The choice of a short- or long-acting β2-mimetic or anticholinergic +/- combined with each other or with an inhaled corticosteroid is made based on the stage of the COPD. It is possible to combine them.	
	Reference	GOLD 2013: diagnosis, management and prevention of COPD: http://www.goldcopd.org/uploads/users/files/GOLD_Report_2013_Feb20.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 92.3 % % of experts rating items useful or very useful: 87.2 %
44 OP	**Rational**	The first-line treatment for COPD is based on inhaled bronchodilators (β2-mimetic or anticholinergic). Inhaled corticosteroids are only used in the event of severe COPD with exacerbation, combined with bronchodilators. Increased risk of pneumonia in COPD patients receiving inhaled corticosteroids.	
	Remark	Inhaled corticosteroids are recommended for GOLD 3-4 stage patients (patient category C-D).	
	Reference	GOLD 2013: diagnosis, management and prevention of COPD: http://www.goldcopd.org/uploads/users/files/GOLD_Report_2013_Feb20.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 97.4 %
	NEPHROLOGY		
	RENAL FAILURE		
45 Other	**Rational**	Risk of overdose and toxicity.	
	Recommendation	See a nephrologist, pharmacist or pharmacologist, or follow the adaptation suggested in the product evaluation report, the data from the literature, etc.	
	Remark	*Non-exhaustive list of drugs requiring an adaptation or a monitoring in case of moderate to severe renal failure: acarbose, allopurinol, tranexamic acid, aminoglycosides, antalgics (ex: opiates derivatives, paracetamol/acetaminophen), antialdosterones, certain antibiotics (ex: aminoglycosides, amoxicillin, cephalosporins, quinolones, trimethoprim, vancomycin), anti-calcineurins, certain anti-epileptics (ex: primidone, vigabatrin), some H1-antihistamines (ex: ebastine, fexofenadine), H2-antihistamines, some antivirals (ex: aciclovir, famciclovir, ganciclovir, tenofovir, valaciclovir), hydrophilic β-blockers (ex: atenolol, nadolol, sotalol), colchicine, digoxin, diuretics, fibrates, direct renin inhibitors, ACEI/ARB (especially in case of severe renal failure), insulin and insulin analogues, lithium, metformin, nitrofurantoin, paroxetine, some statins (ex: simvastatin, rosuvastatin), long-acting hypoglycaemic sulfamides.	
	Useful link	*SiteGPR: optimizing the proper use of medicines: http://www.sitegpr.com/index.php?lang=en	

	Reference	KDIGO 2012: Evaluation and Management of Chronic Kidney Disease: http://www.kdigo.org/clinical_practice_guidelines/pdf/CKD/KDIGO_2012_CKD_GL.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 97.4 %
46 OP	**Rational**	Risk of renal failure exacerbation or of treatment side effect.	
	Recommendations	Favour a therapeutic alternative when available or adjust doses, monitor renal function closely and propose therapeutic drug concentration monitoring if needed. If there is a change in the renal parameters, stop taking the medication if possible.	
	Remark	*Non-exhaustive list of nephrotoxic drugs: NSAIDs, allopurinol, amphotericin B, certain antibiotics (aminoglycosides, cephalosporins, penicillins, quinolones, sulfamides, vancomycin), certain antivirals (aciclovir, ganciclovir, foscarnet), anti-aldosterones, anti-calcineurins, diuretics, direct renin inhibitors, lithium, methotrexate.	
	References	KDIGO 2012: Evaluation and Management of Chronic Kidney Disease: http://www.kdigo.org/clinical_practice_guidelines/pdf/CKD/KDIGO_2012_CKD_GL.pdf Lord A, et al. La néphrotoxicité médicamenteuse. Le Médecin du Québec, 2002 : http://www.fmoq.org/Lists/FMOQDocumentLibrary/fr/Le%20M%C3%A9decin%20du%20Qu%C3%A9bec/Archives/2000%20-%202009/055-059Lord-II0602.pdf Fored M, et al. Acetaminophen, aspirin and chronic renal failure. NEJM 2001: http://www.nejm.org/doi/pdf/10.1056/NEJMoa010323 Perneger TV, et al. Risk of kidney disease associated with the use or acetaminophen, aspirin and nonsteroidal antiinflammatory drugs. NEJM 1994: http://www.nejm.org/doi/pdf/10.1056/NEJM199412223312502	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 92.3 % % of experts rating items useful or very useful: 89.7 %
47 UP	**Rational**	Erythropoiesis stimulation causes increased iron needs.	
	Recommendations	*Sufficient iron supplement = making it possible to maintain a ferritin level between 100 and 500 ng/ml and a transferrin saturation between 20 and 30%. Intravenous supplements will be favoured, particularly in patients receiving haemodialysis.	
	Remark	In case of IV supplement, patients should be carefully monitored so as to detect any side effects and any signs or symptoms of hypersensitivity reactions during and after each administration (monitoring for at least 30 minutes). It is only administered when personnel trained to assess and provide care for anaphylactic reactions are immediately available, in an environment having the necessary means to provide resuscitation.	
	Reference	KDIGO 2012: Evaluation and Management of Chronic Kidney Disease: http://www.kdigo.org/clinical_practice_guidelines/pdf/CKD/KDIGO_2012_CKD_GL.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 97.4 %
48 UP	**Rational**	In CKD subjects, untreated anaemia may cause cardiac, cognitive and mental deterioration and debilitating symptoms. Little benefit and increased risk of thrombosis, vascular issues and death for Hb levels > 13 g/dl.	
	Recommendations	Initial dosing regimen suggested: 50 to 100 IU/kg/week. The target Hb level should generally be comprised between 11 and 12.	
	References	KDIGO 2012: Evaluation and Management of Chronic Kidney Disease: http://www.kdigo.org/clinical_practice_guidelines/pdf/CKD/KDIGO_2012_CKD_GL.pdf KDOQI 2007: Recommendations for anemia in chronic kidney disease. Update of hemoglobin target: http://www.therenalnetwork.org/qi/resources/KDOQIAnemiaCKD2007Update.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 87.2 %
49 UP	**Rational**	Prevention of calcium and phosphates disorders and of renal osteodystrophy disorders in CKD. Phosphate-binding afents bind the dietary phosphate contained in the digestive tract.	
	Remark	A calcium and phosphates evaluation makes it possible to adapt doses.	
	Reference	KDIGO 2009: Chronic Kidney Disease–Mineral and Bone Disorder: http://www.kdigo.org/pdf/KDIGO%20CKD-MBD%20GL%20KI%20Suppl%20113.pdf	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 89.7 %
50 UP	**Rational**	ACEI and ARB have nephroprotective effects.	

	Remarks	*Albuminuria: > 300 mg/24h, **microalbuminuria: 30 to 300 mg/24h. The ACEI or ARB may be suspended temporarily if renal failure worsens.	
	Reference	KDIGO 2012: Evaluation and Management of Chronic Kidney Disease: http://www.kdigo.org/clinical_practice_guidelines/pdf/CKD/KDIGO_2012_CKD_GL.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 100 % % of experts rating items useful or very useful: 100 %
BENIGN PROSTATIC HYPERPLASIA			
	Rational	Risk of urine retention and prostate obstruction.	
51 OP	**Remark**	*Non-exhaustive list of anticholinergic drugs: tricyclic antidepressants, antihistamines, antimuscarinics, some anti-Parkinson medications, antipsychotics, antispasmodics, colchicine associated with opium and tiemonium methylsulfate, muscle relaxers.	
	Reference	Mebarki S, et al. Échelles d'évaluation de l'effet anticholinergique des médicaments. NPG 2012 : http://gerontoprevention.free.fr/articles/Anticholinergiques.pdf	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 100 % % of experts rating items useful or very useful: 92.3 %
GASTROENTEROLOGY			
PEPTIC ULCER DISEASE and PROTON PUMP INHIBITORS			
	Rational	Avoid long-term treatments with no indication. Potential risk of pneumopathy, *Clostridium difficile* infection, malabsorption, osteoporosis, interstitial nephritis and rebound effect upon stopping PPI.	
52 OP	**Recommendations**	Only a small number of indications justify long-term PPI prescription and should be subjected to a specialist opinion. Non-exhaustive list of justified indications: -Ulcer associated with a factor slowing scarring (e.g.: tobacco use, large ulcer size: ≥ 10 mm, gastrotoxic drug use: primarily NSAIDs), -Long-term NSAIDs use in patients with risk of digestive bleeding: > 65 years, history of gastroduodenal ulcer, combination with a antiplatelet drug: particularly low-dose aspirin or clopidogrel and/or corticoids and/or an anticoagulant (these combinations must be avoided as much as possible), -Zollinger Ellison syndrome, -Gastrooesophageal reflux with frequent or early relapse upon stopping PPI, -Severe oesophagitis, peptic stenosis, symptomatic Barrett's oesophagus or Barrett's oesophagus associated with oesophagitis. In the other indications, gradually stopping the PPI may be suggested in order to avoid rebound acidity in case of abrupt stop.	
	References	FDA Drug Safety Communication 2012: Clostridium difficile-associated diarrhea can be associated with stomach acid drugs known as proton pump inhibitors (PPIs): http://www.fda.gov/Drugs/DrugSafety/ucm290510.htm HAS 2009 : Médicaments inhibiteurs de la pompe à protons chez l'adulte : réévaluation : http://www.has-sante.fr/portail/upload/docs/application/pdf/2009-04/argumentaire_ipp_2009-04-27_14-15-18_458.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 97.4 %
	Rational	Avoid long-term treatments with no indication. Potential risk of pneumopathy, *Clostridium difficile* infection, osteoporosis and rebound effect upon stopping PPIs.	
53 OP	**Recommendation**	Gradual stopping of PPIs may be suggested in order to avoid rebound acidity in case of abrupt stop, if the treatment has been extended.	
	Reference	HAS 2009 : Médicaments inhibiteurs de la pompe à protons chez l'adulte : réévaluation : http://www.has-sante.fr/portail/upload/docs/application/pdf/2009-04/argumentaire_ipp_2009-04-27_14-15-18_458.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 100 % % of experts rating items useful or very useful: 97.4 %
	Rational	Half-doses of PPI are recommended*: in the prevention of gastroduodenal ulcers in at-risk patients, in case of gastrooesophageal reflux without oesophagitis. Avoid long-term treatments with no indication. Potential risk of pneumopathy, infection with *Clostridium difficile*, osteoporosis and rebound effect upon stopping PPIs	
54 OP	**Recommendations**	* Suggested dosing regimen: Half-dose for gastrooesophageal reflux without oesophagitis and prevention of lesions caused	

		by NSAIDs in at-risk patients: omeprazole: 10 or 20 mg QD, lansoprazole: 15 mg QD, pantoprazole: 20 mg QD, rabeprozole: 10 mg QD, esomeprazole: 20 mg QD. Full dose for gastrooesophageal reflux with oesophagitis. In the prevention of stress ulcers in intensive care, follow local recommendations. Re-evaluate treatment if it was started before hospitalisation.
	References	Katz P, et al. Guidelines for the Diagnosis and Management of Gastroesophageal Reflux Disease. Am J Gastroenterol 2013: http://d2j7fjepcxuj0a.cloudfront.net/wp-content/uploads/2013/10/ACG_Guideline_GERD_March_2013_plus_corrigendum.pdf ASGE 2010: The role of endoscopy in the management of patients with peptic ulcer disease: http://www.asge.org/uploadedFiles/Publications_and_Products/Practice_Guidelines/The%20role%20of%20endoscopy%20in%20the%20management%20of%20patientswith%20peptic%20ulcer%20disease.pdf HAS 2009 : Médicaments inhibiteurs de la pompe à protons chez l'adulte : réévaluation : http://www.has-sante.fr/portail/upload/docs/application/pdf/2009-04/argumentaire_ipp_2009-04-27_14-15-18_458.pdf HAS 2009 : Les inhibiteurs de la pompe à protons chez l'adulte : http://www.has-sante.fr/portail/upload/docs/application/pdf/2009-06/ipp_adulte_juin_2009.pdf Summary of products characteristics
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful % of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 92.3 %
55 OP	**Rational**	Treatment with no valid indication. Potential risk of pneumopathy, infection with *Clostridium difficile*, osteoporosis and rebound effect upon stopping PPIs
	Recommendation	Only a small number of indications** justify long-term PPI prescription and should be subjected to a specialist opinion. Gradual stopping of PPIs may be suggested in order to avoid rebound acidity in case of abrupt stop, if the treatment has been extended.
	Remark	*List of risk factors: age > 65 years, concomitant use of NSAIDs, concomitant use of corticoids and/or anticoagulants, cardiovascular disease, long-term NSAIDs use, history of digestive ulcer. **Non-exhaustive list of justified indications: -Ulcer associated with a factor slowing scarring (e.g.: tobacco use, large ulcer size: ≥ 10 mm, gastrotoxic drug use: primarily NSAIDs), -Long-term NSAIDs use in patients with risk of digestive bleeding: > 65 years, history of gastroduodenal ulcer, combination with a antiplatelet drug: particularly low-dose aspirin or clopidogrel and/or corticoids and/or an anticoagulant (these combinations must be avoided as much as possible), -Zollinger Ellison syndrome, -Gastrooesophageal reflux with frequent or early relapse upon stopping PPI, -Severe oesophagitis, peptic stenosis, symptomatic Barrett's oesophagus or Barrett's oesophagus associated with oesophagitis. In the other indications, gradually stopping the PPI may be suggested in order to avoid rebound acidity in case of abrupt stop. ***Calculation of the HAS-BLED score: HBP (sBP > 160 mmHg) (1pt), Abnormal renal function (serum creatinine ≥ 200 µmol/L) or/and Abnormal liver function (Cirrhosis, bilirubin > 2x UNL with AST/ALT/AP > 3x UNL) (1 or 2 pts), Stroke history (1pt), Bleeding (Bleeding history or predisposition (anemia)) (1pt), Labile INR (Therapeutic time in range < 60%) (1pt), Elderly (Greater than 65 years old) (1pt), Drugs or alcohol (Drugs - other antiplatelet agents or NSAIDs, Alcohol - more than 8 drinks per week) (1 or 2 pts).
	References	HAS 2009 : Les inhibiteurs de la pompe à protons chez l'adulte : http://www.has-sante.fr/portail/upload/docs/application/pdf/2009-06/ipp_adulte_juin_2009.pdf ACCF/ACG/AHA 2008: Expert Consensus Document on Reducing the Gastrointestinal Risks of Antiplatelet Therapy and NSAID Use: http://circ.ahajournals.org/content/118/18/1894.full.pdf Lanza FL, et al. Practice Parameters Committee of the American College of Gastroenterology. Guidelines for prevention of NSAID-related ulcer complications. Am J Gastroenterol.2009: http://www.guideline.gov/content.aspx?id=38322
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful % of experts agree or strongly agree: 89.7 % % of experts rating items useful or very useful: 89.7 %
56 OP	**Rational**	Risk of digestive haemorrhage.
	Recommendation	If NSAIDs use is necessary, it must be combined with a PPI.
	Remark	*Non-exhaustive list of drugs with bleeding risk (alone or in combination): NSAIDs, including low-dose aspirin (except COX2-inhibitor), anticoagulants, antiplatelet drugs,

		corticosteroids, antidepressants: SSRIs.	
	References	Abraham N, et al. Risk of Lower and Upper Gastrointestinal Bleeding, Transfusions, and Hospitalizations With Complex Antithrombotic Therapy in Elderly Patients. Circulation 2013: http://circ.ahajournals.org/content/early/2013/09/11/CIRCULATIONAHA.113.004747.full.pdf Laine L, et al. Management of Patients With Ulcer Bleeding. Am J Gastroenterol 2012: http://s3.gi.org/physicians/guidelines/UlcerBleeding.pdf Labos C, et al. Risk of bleeding associated with combined use of selective serotonin reuptake inhibitors and antiplatelet therapy following acute myocardial infarction. CMAJ 2011: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3216455/pdf/1831835.pdf Rostom A, et al. Prevention of NSAID-induced gastroduodenal ulcers (reviews). Cochrane Database Syst Rev 2002 [abstract]: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002296/abstract;jsessionid=0A42A6B840ACAF01DE2C6BAC3B59613C.f01t01	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 92.3 % % of experts rating items useful or very useful: 79.5 %
HEPATIC IMPAIRMENT and CIRRHOSIS			
57 OP	**Rational**	Avoid over-added hepatic toxicities. Avoid toxicities induced by a change in the pharmacokinetics of drugs eliminated by the liver*.	
	Recommendation	See a hepatologist, pharmacist or pharmacologist, or follow the adaptation proposed in the Summary of products characteristics and the data from the literature.	
	Remarks	*Non-exhaustive list of drugs to be adapted in patients with hepatic insufficiency: NSAIDs, Tricyclic antidepressants, VKA, antiretrovirals, barbiturates, BZD (favour oxazepam or lorazepam), carbamates, clindamycin, flecainide, ACEI, isoniazid, lincomycin, metronidazole, morphinics, pefloxacin, pyrazinamide, rifampicin, sulfamides, tetracyclines. Avoid prescribing NSAIDs: drugs with a high risk of digestive bleeding and hepatorenal syndrome. Exercise caution when prescribing psychotropics, hypnotics, antalgics and opiates to patients with cirrhosis (in particular decompensated): high risk of recurrence/worsening of hepatic encephalopathy. Favour glucuro-conjugated psychotropic drugs, start psychotropic drugs and opiates at the minimum effective dose. Suggested dosing regimen for paracetamol/acetaminophen: 2 g/day (4 g/day may cause silent transaminase elevations).	
	Useful link	Livertox: http://livertox.nih.gov/ Hepatoweb : http://hepatoweb.com/ MELD score: http://www.mayoclinic.org/medical-professionals/model-end-stage-liver-disease/meld-model	
	References	Lewis JH, et al. Review articles: prescribing medications in patients with cirrhosis – a practical guide. Aliment Pharmacol Ther 2013 [abstract]: http://www.ncbi.nlm.nih.gov/pubmed/?term=23638982 Chandok N, et al. Pain Management in the Cirrhotic Patient: The Clinical Challenge. Mayo Clin Proc. 2010: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2861975/pdf/mayoclinproc_85_5_008.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 94.9 %
58 UP	**Rational**	Allow to reduce the absorption of nitrates released by the metabolism of the proteins.	
	Remarks	Dosing regimens allowing to obtain 2 to 4 soft stools/day: lactulose: 20 to 30 g orally 2 to 4 times/day, lactitol: 10 g orally 4 times/day. If oral administration is not possible, administration in enema form is one alternative (6 to 20 packets diluted in water, depending on the type of probe used).	
	References	Sharma P, et al. Disaccharides in the treatment of hepatic encephalopathy. Metab Brain Dis 2013 [abstract]: http://link.springer.com/article/10.1007%2Fs11011-013-9392-4 Als-Nielsen B, et al. Nonabsorbable disaccharides for hepatic encephalopathy. BMJ 2004: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC403844/pdf/bmj32801046.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 97.2 %
DIARRHOEA			
59 OP	**Rational**	Risk of faecal and infectious stasis (toxins, spores) that may be harmful.	
	Recommendation	*Transit retarders (ex: loperamide) should be reserved for short-term symptomatic treatment	

		(2 days) of acute non-infectious diarrhoea in addition to rehydration.	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 92.3 % % of experts rating items useful or very useful: 84.2 %
60 Other	**Rational**	Requires quick diagnosis and monitoring of any *Clostridium difficile* infection for individual benefit and to prevent nosocomial transmission.	
	Recommendation	In case of positive diagnosis, if possible, stop the responsible antibiotic and treat the *Clostridium difficile* infection.	
	Reference	ESCMID 2009: Data review and recommendations for diagnosing Clostridium difficile-infection: https://www.escmid.org/fileadmin/src/media/PDFs/4ESCMID_Library/2Medical_Guidelines/ESCMID_Guidelines/fulltext_Data_review_and_recommendations_for_diagnosing_Clostridium_difficile-infection.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 84.6 %
61 UP	**Rational**	Metronidazole efficacy comparable to vancomycin in this indication and lower cost.	
	Recommendations	Metronidazole: suggested dosing regimen for a mild to moderate episode: 500 mg TIW orally, for 10–14 days. IV administration is possible if oral administration is not available. Vancomycin: suggested dosing regimen for a 1st severe episode: 125 mg administered orally, 4 times/day, for 10–14 days. 500 mg orally, 4 times/day in case of severe episode with complications +/- metronidazole. The use of fidaxomicin 200 mg BID orally, can also be considered, in particular in case of recurrence.	
	References	SHEA-IDSA 2010: Clinical Practice Guidelines for Clostridium difficile Infection in Adults: http://www.idsociety.org/uploadedFiles/IDSA/Guidelines-Patient_Care/PDF_Library/cdiff2010a.pdf ESCMID 2009: treatment guidance document for Clostridium difficile infection: https://www.escmid.org/fileadmin/src/media/PDFs/4ESCMID_Library/2Medical_Guidelines/ESCMID_Guidelines/fulltext_treatment_guidance_Clostridium_difficile_infection.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 87.2 % % of experts rating items useful or very useful: 84.6 %
		CONSTIPATION	
62 OP	**Rational**	Risk of exacerbation or induction of constipation.	
	Remark	*Non-exhaustive list of drugs that may cause iatrogenic constipation: drugs with anticholinergic properties** (tricyclic antidepressants, antihistamines, antimuscarinics, some anti-Parkinson medications, antipsychotics, antispasmodics, muscle relaxers), some antihypertensives (beta blockers, calcium inhibitors, central-acting antihypertensives), local-acting antacids, calcium carbonate, cholestyramin, iron, neuroleptics, opiates (strong and weak and derivatives: codeine/tramadol), transit retarders.	
	Useful link	**Evaluation scales for the anticholinergic effect of drugs: http://gerontoprevention.free.fr/articles/Anticholinergiques.pdf	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 92.3 % % of experts rating items useful or very useful: 71.8 %
		RHEUMATOLOGY	
		GOUT	
63 UP	**Rational**	Molecules effective to ease the symptoms of acute gout.	
	Recommendations	Suggested dosing regimens: Colchicine: do not exceed 2 mg/d in 3 administrations (risk of side effects at high doses). NSAIDs: full dose unless there are contraindications. Prednisone or prednisolone: initial dose 0.5 mg/kg/d for 5 to 10 days, administered orally.	
	Remarks	Full-dose NSAIDs act quickly; they should be avoided in patients with high risk of serious side effects. Colchicine acts more slowly; it should only be offered as 1st line treatment if the outbreak has started within the last 48 hours. The occurrence of gastrointestinal problems (in particular diarrhoea) should be monitored, and the treatment should be adapted in case of combination with a cytochrome P450 or P-glycoprotein inhibitor and in case of altered renal function. Oral or intra-articular glucosteroids (gout affecting 1 or 2 major joints) are one possible alternative, in particular if NSAIDs are contraindicated or in case of renal failure.	
	References	ACR 2012: Management of Gout Part II: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3662546/pdf/nihms416577.pdf	

		EULAR 2011: recommendations for calcium pyrophosphate deposition. Part II: Management: http://ard.bmj.com/content/70/4/571.full.pdf+html EULAR 2006: evidence based recommendations for gout. Part II: Management: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1798308/pdf/1312.pdf	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 92.3 % % of experts rating items useful or very useful: 92.3 %
64 UP	**Rational**	Symptomatic hyperuricaemia and gout attacks are associated with certain renal, cardiovascular and metabolic pathologies, responsible for increased long-term morbidity and a deteriorated quality of life.	
	Recommendations	Suggested dosing regimens: initial dosing regimen ≤ 100 mg QD, optionally gradually increased in order to obtain a uric acid level ≤ 6 mg/dl or 360 µmol/l (low initial doses decreased the risk of hypersensitivity). Recommended doses: 100–200 mg optionally increased to 300–600 mg in moderate cases, or even 700 to 900 mg/day in severe cases. The doses will be adapted in case of renal failure.	
	Remarks	*Asymptomatic hyperuricemia alone is not an indication to be treated. It may be prefered to start background treatment separately from a gout attack (1 to 2 weeks after inflammation has decreased) due to the risk of exacerbation of the attack. If allopurinol is not tolerated, a xanthine oxidase inhibitor (ex: febuxostat) or a uricosuric (ex: probenecid) may be considered. *Conditions under which treatment to reduce the uric acid level is necessary: recurring gout attacks (≥ 2/year) or severe attacks (presence of tophus, arthroplasty, or radiographic changes), renal failure ≥ stage 2, history of urinary lithiasis, lifestyle and dietary measures insufficient (weight loss, diet modifications, reduced alcohol consumption, in particular beer, stopping diuretics, care for comorbidity, quitting tobacco use).	
	References	ACR 2012: Management of Gout Part I: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3683400/pdf/nihms416576.pdf ACR 2012: Management of Gout Part II: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3662546/pdf/nihms416577.pdf Richette P, et al. Gout. Lancet 2010 [abstract]: http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(09)60883-7/abstract EULAR 2006: Evidence based recommendations for gout. Part II: Management: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1798308/pdf/1312.pdf	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 89.7 % % of experts rating items useful or very useful: 84.6 %
65 UP	**Rational**	Modifying the uric acid levels may cause a gout attack.	
	Recommendations	Suggested dosing regimens: Colchicine 0.5 to 1 mg/day during the titration of the background treatment (up to 6 months). Decrease the doses in case of combination with cytochrome P450 or P-glycoprotein inhibitors and in case of renal failure or in patients ≥ 75 years.	
	Remark	Prednisone or low-dose prednisolone may be used as 2nd line treatment if NSAIDs and colchicine are contraindicated, ineffective or poorly tolerated.	
	Reference	EULAR 2006: Evidence based recommendations for gout. Part II: Management: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1798308/pdf/1312.pdf	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 92.3 % % of experts rating items useful or very useful: 89.7 %
66 OP	**Rational**	Risk of gout attack.	
	Remark	*Non-exhaustive list of drugs that may increase uric acid levels: chemotherapy, cyclosporine, diuretics (loop and thiazide in particular, by inhibiting the renal excretion of urates), ethambutol, interferon, levodopa, pyrazinamide, ribavirin, salicylates (low dose), tacrolimus, teriparatide. In the treatment of high blood pressure, avoid the use of diuretics if possible.	
	References	Roddy E, et al. Epidemiology of gout. Arthritis Research & Therapy 2010: http://arthritis-research.com/content/pdf/ar3199.pdf Richette P, et al. Gout (review). Lancet 2010 [abstract] : http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(09)60883-7/fulltext	
	Strength of	Experts median agreement: agree	% of experts agree or strongly agree: 97.4 %

	recommendation	Median usefulness rating: useful	% of experts rating items useful or very useful: 79.5 %
		RHEUMATOID ARTHRITIS	
67 Other	**Rational**	Increased risk of transaminase elevation, hepatotoxicity, nephrotoxicity and leukopaenia.	
	Recommendations	Monitoring every 2 to 4 weeks for 3 months, then every 8 to 12 weeks for the following 3 months, then every 12 weeks. More often if combined with another hepatotoxic or haematotoxic drug*.	
	Remarks	*Non-exhaustive list of molecules often combined and that may be hepatotoxic or haematotoxic: azathioprine, cyclosporine, leflunomide, retinoids, sulfasalazine, trimethoprim-sulfamethoxazole. Non-exhaustive list of nephrotoxic drugs: NSAIDs, allopurinol, amphotericin B, some antibiotics: aminoglycosides, cephalosporins, penicillins, quinolones, sulfamides, vancomycin, some antivirals: aciclovir, ganciclovir, foscarnet, antialdosterones, anticalcineurins, diuretics, direct renin inhibitors, lithium, methotrexate.	
	References	ACR 2012: Use of Disease-Modifying Antirheumatic Drugs and Biologic Agents in the Treatment of Rheumatoid Arthritis: http://onlinelibrary.wiley.com/doi/10.1002/acr.21641/pdf ACR 2008: Use of Nonbiologic and Biologic Disease-Modifying Antirheumatic Drugs in Rheumatoid Arthritis: http://onlinelibrary.wiley.com/doi/10.1002/art.23721/pdf Ho J, et al. Considerations when prescribing trimethoprim–sulfamethoxazole. CMAJ 2011: http://www.cmaj.ca/content/183/16/1851.full.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 92.3 %
68 UP	**Rational**	Reduced MTX gastrointestinal side effects and hepatotoxicity, prevention of haematotoxicity related to folate deficiency.	
	Recommendations	Suggested dosing regimens: 1 mg QD or 5 mg/week. Folic acid may be given weekly, 24 to 48 hours after taking MTX, or daily except 24 hours before and after taking MTX. Regardless of the administration regimen, folic acid should not be taken on the day of weekly methotrexate administration.	
	Reference	Shea B, et al. Folic acid and folinic acid for reducing side effects in patients receiving methotrexate for rheumatoid arthritis (Review). Cochrane 2013 [abstract]: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD000951.pub2/pdf/abstract	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 92.3 %
69 OP	**Rational**	Corticosteroids are effective in the treatment of RA, but the risk/benefit ratio is questionable in long-term treatment.	
	Reference	EULAR 2013: management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: http://ard.bmj.com/content/early/2013/10/23/annrheumdis-2013-204573.full.pdf+html	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 89.7 %
		CORTICOSTEROIDS and OSTEOPOROSIS	
70 Other	**Rational**	Avoid complications related to long-term administration of corticosteroids	
	Recommendations	*Lifestyle and dietary counseling: diet low in sodium, in sugars with a high glycaemic index, hypocaloric, rich in calcium (minimum: 1200 mg/day), vitamin D (minimum: 800 IU/day), protein and potassium, physical exercise. If the calcium and vitamin D intake are sufficient, provide supplements.	
	Reference	EULAR 2013: management of medium to high-dose glucocorticoid therapy in rheumatic diseases: http://ard.bmj.com/content/early/2013/07/18/annrheumdis-2013-203249.full.pdf+html	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 84.6 %
71 UP	**Rational**	Possible exacerbation of osteoporosis (including by inhalation). Prevention of bone loss.	
	Recommendations	Minimum recommended intake: 1200 mg/day of calcium and 800 IU/day of vitamin D (cholecalciferol). If intake is insufficient, supplement with calcium and vitamin D.	
	References	Benhamou CL, et al. La vitamine D chez l'adulte : recommendations du GRIO. Press Med 2011:	

		http://www.grio.org/documents/rcd-10-1361186132.pdf ACR 2010: Recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis: http://www.guideline.gov/content.aspx?id=32422 NHLBI/NIH 2007: Guidelines for the Diagnosis and Management of Asthma: http://www.nhlbi.nih.gov/guidelines/asthma/asthsumm.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 97.4 %
72 UP	**Rational**	Prevention and treatment of corticosteroids-induced osteoporosis (including by inhalation). *In patients with an increased fracture risk, taking corticosteroids increases the risk of fracture (anticipated duration ≥ 3 months and/or dose ≥ 7.5 mg of prednisone/d). **In patients with a high risk of osteoporosis, taking corticosteroids, including by inhalation, on a long-term basis and at medium or high doses, increases the risk of osteoporosis.	
	Recommendations	*A bone density measurement and use of the FRAX score** make it possible to evaluate fracture risk. *Patients with increased risk of fracture: menopausal women, men over the age of 50, non-menopausal women and men under the age of 50 with a history of fractures and receiving CS treatment for an anticipated duration ≥ 3 months and/or ≥ 7.5 mg of prednisone/d. Other risk factors: low body mass index, family history of hip fracture, alcohol consumption ≥ 3 glasses/d, tobacco use, high doses of CS, high cumulative doses of CS, significant decrease in bone density.	
	Useful link	**FRAX: Fracture Risk Evaluation Tool: https://www.shef.ac.uk/FRAX/tool.jsp?lang=en	
	References	ACR 2010: recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis: http://www.guideline.gov/content.aspx?id=32422 NHLBI/NIH 2007: Guidelines for the Diagnosis and Management of Asthma: http://www.nhlbi.nih.gov/guidelines/asthma/asthsumm.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 92.3 % % of experts rating items useful or very useful: 87.2 %
73 UP	**Rational**	Prevention of bisphosphonates' side effects: hypocalcaemia and may cause osteonecrosis of the jaw (in particular in case of a parenteral treatment). Risk of oesophageal erosion and ulcers. Decreased absorption of bisphosphonates in the presence of cations.	
	Recommendations	*A dental exam and appropriate preventive dental care should be considered before beginning treatment with bisphosphonates in patients with related risk factors (for example: cancer, chemotherapy, radiotherapy, corticotherapy, poor oral hygiene) due to the risk of osteonecrosis of the jaw. Monitoring kidney function is also useful. **30 minutes before breakfast, with tap water. ***Example of drugs that should not be taken with bisphosphonates: calcium supplements.	
	Reference	Summary of products characteristics	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 94.9 %
	NEUROLOGY		
	EPILEPSY and ANTI-EPILEPTICS		
74 OP	**Rational**	Risk of unbalancing treatment and of epileptic attacks, in particular in case of uncontrolled or recent epilepsy.	
	Recommendation	Favour a therapeutic alternative or monitor signs of destabilisation of the treatment.	
	Remark	*Non-exhaustive list of molecules lowering the epileptogenic threshold: alcohol, amphetamines, general and local anaesthetics (lidocaine, enflurane, ketamine), some antalgics (tramadol), antihistamines (theophylline, methylxanthines), anticholinergics, antidepressants (tricyclic antidepressants, SSRIs, bupropion), antihistamines, anti-infectives (injectable penicillins, cephalosporins, fluoroquinolones, isoniazid poisoning, metronidazole, pyrimethamine, foscarnet, mefloquine), some antineoplastics (busulfan, carmustine (bcnu), chlorambucil, cytosine arabinoside, methotrexate, vincristine), antipsychotics (phenothiazines, haloperidol), domperidone, flumazenil, immunosuppressants: (cyclosporine, tacrolimus), lithium, methylphenidate, sympathomimetics (ephedrine, phenylpropanolamine, terbutaline), some vaccines.	

	References	Public Health England 2013: Guidelines for malaria prevention in travellers from the UK: http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1203496943523 Desfossés C, et al. Les médicaments qui abaissent le seuil de convulsions. Le Médecin du Québec 2002 : http://www.fmoq.org/Lists/FMOQDocumentLibrary/fr/Le%20M%C3%A9decin%20du%20Qu%C3%A9bec/Archives/2000%20-%202009/105-109DESFOSSES1202.pdf Hantson P. Convulsions d'origine toxique. Réanimation 2004 (Mise au point) : http://www.srlf.org/rc/org/srlf/htm/Article/2011/20110808-095540-315/src/htm_fullText/fr/0407-Reanimation-Vol13-N5-p343_348.pdf The Treatment of Epilepsy: Principles and Practice 4th ed, Gupta A, Lachhwani DK: Eisenschenk S, Gilmore RL. Seizures associated with nonneurologic medical conditions. (Eds), Lippincott Williams & Wilkins, Philadelphia 2006
	Strength of recommendation	Experts median agreement: strongly agree — % of experts agree or strongly agree: 97.4 % Median usefulness rating: useful — % of experts rating items useful or very useful: 94.9 %
75 DDI	Rational	Anti-epileptics (except gabapentin, pregabalin, vigabatrin and levetiracetam), at least partially, undergo hepatic metabolism. Some anti-epileptics are enzyme inducers or inhibitors. Risk of toxicity, imbalance or ineffectiveness of various treatments.
	Recommendation	Favour a therapeutic alternative or propose a therapeutic drug concentration monitoring of the anti-epileptics and/or associated treatments.
	Remarks	Enzyme-inducing anti-epileptics: carbamazepine, lacosamide, lamotrigine, oxcarbazepine, phenytoin, primidone, topiramate, zonisamide. Enzyme-inhibiting anti-epileptics: valproic acid, topiramate, felbamate.
	Useful link	*HUG 2014: Drug interactions, cytochromes P450 and P-glycoprotein (Pgp): http://www.hug-ge.ch/sites/interhug/files/structures/pharmacologie_et_toxicologie_cliniques/documents/interactions_medicamenteuses_et_cyp450.pdf
	References	ILAE 2008: Antiepileptic drugs—best practice guidelines for therapeutic drug monitoring: http://rc.kfshrc.edu.sa/rcf/E_Library/Epilepsy/Epilepsia%201-38%202008.pdf Patsalos P, et al. The importance of drug interactions in epilepsy therapy. Epilepsia 2002: http://onlinelibrary.wiley.com/doi/10.1046/j.1528-1157.2002.13001.x/pdf
	Strength of recommendation	Experts median agreement: strongly agree — % of experts agree or strongly agree: 97.4 % Median usefulness rating: very useful — % of experts rating items useful or very useful: 94.9 %
76 UP	**Rational**	Risk of enzyme induction and of failure of contraception when combining oral or intra-vaginal contraceptives, patches or pure progestogen pills are used and risk of foetal malformation.
	Recommendation	Other suggested contraceptive: *e.g. intra-uterine devices with copper or delivering levonorgesterel, condoms.
	Remark	**Non-exhaustive list of anti-epileptics interacting with oral or intra-vaginal contraceptives: carbamazepine, oxcarbazepine, phenytoin, primidone, topiramate.
	Reference	WHO 2009 : Medical eligibility criteria for contraceptive use – 4th ed : http://www.spdc.pt/files/publicacoes/5_11292_2.pdf
	Strength of recommendation	Experts median agreement: strongly agree — % of experts agree or strongly agree: 97.4 % Median usefulness rating: useful — % of experts rating items useful or very useful: 84.6 %
	PARKINSON'S DISEASE and PARKINSON'S MEDICATIONS	
77 UP	**Rational**	In case of abrupt stop or unplanned modification of the treatment, risk of imbalance of Parkinson's disease, complications (falls, fractures, inhalation pneumopathy) and malignant hyperthermia.
	Recommendations	Continue treatment at the usual doses, times and dosing forms. In case of difficulty swallowing or fasting for several days, adapt the dosing form and dose in agreement with a neurologist. See a neurologist, pharmacist or pharmacologist if needed.
	Remark	Substitution and equivalence rules for doses are available at this link: Emergency management of patients with Parkinson's: http://www.parkinsons.org.uk/sites/default/files/publications/download/english/pk0135_emergencymanagement.pdf
	Useful link	Get It On Time campaign 2010: Going into Hospital: http://www.parkinsons.org.uk/sites/default/files/publications/download/english/fs61_goingintohospital.doc

	References	Emergency management of patients with Parkinson's: http://www.parkinsons.org.uk/sites/default/files/publications/download/english/pk0135_emergencymanagement.pdf Brennan KA, et al. Managing Parkinson's disease during surgery. BMJ 2010 [abstract]: http://www.bmj.com/content/341/bmj.c5718 Get It On Time campaign 2010: http://www.parkinsons.org.uk/content/get-it-time-medicine-management-patients-parkinsons-dvd Jones SL, et al. Parkinson's disease in the acute hospital. Clinical Medicine 2011: http://rcpjournal.org/content/11/1/84.full.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 100 % % of experts rating items useful or very useful: 92.3 %
78 OP	**Rational**	Risk of worsening of Parkinson's disease. Domperidone is a peripheral dopamine D_2-receptor antagonist with anti-emetic properties dopamine-antagonist that does not cross the HEB, and therefore does not have those side effects.	
	Recommendations	In case of nausea and vomiting or gastroparesis associated with Parkinson's disease, favour treatment using domperidone*. Risk of dyskinesis with anti-emetics derived from neuroleptics crossing the HEB (metoclopramide, prochlorperazine, promethazine).	
	Remark	*Domperidone use may be associated with an increased risk of serious ventricular arrhythmia and elongation of the QT interval, in particular at high doses (> 30 mg/day). It should be used with caution in patients with a pre-existing elongation of the QT interval, cardiac conduction disorders, significant electrolytic disorders, underlying heart diseases such as congestive heart failure, or who are receiving several drugs with a risk of elongation of the QT interval (see item 148). It should be used at the minimum effective dose.	
	References	NICE: Parkinson's disease national clinical guideline: http://www.nice.org.uk/nicemedia/live/10984/30087/30087.pdf Aminoff MJ, et al. Management of the hospitalized patient with Parkinson's disease: Current state of the field and need for guidelines. Parkinsonism Relat Disord. 2011: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3070297/pdf/nihms277974.pdf	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 92.3 %
	PSYCHIATRY		
	PSYCHOTROPIC ILLNESS and DRUGS		
79 OP	**Rational**	Risk of accumulation of side effects.	
	Recommendation	Avoid prescribing 2 benzodiazepines, 2 antidepressants or 2 neuroleptics from the same therapeutic class, including with different dosing forms and release kinetics, without a specialist opinion.	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 89.7 %
	DEPRESSION and ANTIDEPRESSANTS		
80 UP	**Rational**	The doses must be optimized before therapeutic failure is determined.	
	Recommendations	Target a satisfactory clinical response by the patient and not a partial response. See a psychiatrist if necessary.	
	Reference	NICE 2009: Depression in adults: The treatment and management of depression in adults: http://publications.nice.org.uk/depression-in-adults-cg90	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 92.3 % % of experts rating items useful or very useful: 74,4 %
81 UP	**Rational**	Risk/benefit ratio in favour of the use of an SSRI.	
	Recommendations	*Antidepressants recommended as first-line treatment: SSRIs, SNRIs, mirtazapine or bupropion. See a psychiatrist if necessary.	
	References	APA 2010: Treatment of Patients With Major Depressive Disorder: http://psychiatryonline.org/pdfaccess.ashx?ResourceID=243261&PDFSource=6 NICE 2009: Depression in adults: The treatment and management of depression in adults: http://publications.nice.org.uk/depression-in-adults-cg90	

	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 76.9 %
INSOMNIA, SEDATIVES and HYPNOTICS			
82 OP	**Rational**	Avoid the long-term use of hypnotics. Risk of rebound effect, withdrawal syndrome, secondary complications if treatment is stopped abruptly.	
	Recommendations	Stop these treatments gradually, based on the length of the treatment. In some cases, weaning over several months may be necessary.	
	Reference	Schutte-Rodin S, et al. Clinical Guideline for the Evaluation and Management of Chronic Insomnia in Adults. Journal of Clinical Sleep Medicine 2008: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2576317/pdf/jcsm.4.5.487.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 97.4 %
83 OP	**Rational**	Significant side effects.	
	Recommendation	As 1st line treatment: favour a BZD with a short to medium half-life or a BZD related drug.	
	Reference	NIH 2005: Manifestations and Management of Chronic Insomnia in Adults: http://consensus.nih.gov/2005/insomniastatement.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 87.2 % % of experts rating items useful or very useful: 87.2 %
SCHIZOPHRENIA and NEUROLEPTICS			
84 DDI	**Rational**	Risk of torsade de pointes.	
	Recommendations	Monitor the electrocardiogram if use is necessary, correct any hypokalaemia or hypomagnesaemia and avoid the concomitant use of bradycardiac molecules. If a long QTc syndrome appears, related to taking the drugs, look for interaction, for overdose, for the presence of several at-risk drugs and adapt the patient's treatment.	
	Remarks	*Non-exhaustive list of drugs that may cause an elongation of the QT interval: some antiarrhythmics (amiodarone, disopyramide, dofetilide, dronedarone, flecainide, ibutilide, procainamide, quinidine, sotalol), some antibiotics (azithromycin, bedaquiline, ciprofloxacin, clarithromycin, erythromycin, levofloxacin, moxifloxacin, norfloxacin, ofloxacin, pentamidine, roxithromycin, spitamycin IV, telithromycin, trimethoprim-sulfamethoxazole), some antineoplastics (arsenic, dabrafenib, eribulin, lapatinib, nilotinib, sunitinib, tamoxifen, vorinostat), some antidepressants (amitriptyline, amoxapine, citalopram, clomipramine, desipramine, doxepin, escitalopram, fluoxetine, imipramine, mirtazapine, nortriptyline, paroxetine, protriptyline, sertraline, trazodone, trimipramine, venlafaxine), some antifungals (fluconazole, itraconazole, ketoconazole, posaconazole, voriconazole), some antimalarials (chloroquine, halofantrine, quinine sulphate), some antivirals (amantadine, atazanavir, foscarnet, nelfinavir, rilpivirine, ritonavir, saquinavir, telaprevir), methadone, neuroleptics (amisulpride, aripiprazole, chlorpromazine, clozapine, cyamemazine, domperidone, droperidol, fluphenazine, haloperidol, levomepromazine, olanzapine, pimozide, pipamperone, promethazine, quetiapine, risperidone, sertindole, sulpiride, sultopride, tiapride, zuclopenthixol). Risk factors for elongation of the QTc interval: age > 65 years, female, cardiopathies: heart failure, ischaemia, myocardial hypertrophy, bradycardia, 2nd or 3rd degree atrial-ventricular block, electrolytic disorders (in particular hypokalaemia and hypomagnesaemia), congenital long QT syndrome.	
	Useful link	Crediblemeds: All QTDrugs: http://www.crediblemeds.org/everyone/composite-list-all-qtdrugs/?rf=All	
	Reference	WFSBP 2012: Guidelines for Biological Treatment of Schizophrenia, Part 2: http://www.wfsbp.org/fileadmin/user_upload/Treatment_Guidelines/WFBSP_SZ_Guidelines_Part1_2012.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 94.9 %
PAIN and ANALGESIA			
NEUROPATHIC PAIN			
85 UP	**Rational**	First-line treatments in this indication.	
	Remarks	*Examples of recommended anticonvulsants: gabapentin or pregabalin. ** Examples of recommended antidepressants: tricyclic (amitriptyline, clomipramine,	

		desipramine, imipramine, nortiptyline) or selective serotonin-norepinephrine reuptake inhibitor (SNRI): duloxetine, venlafaxine. Tramadol (in particular combined with paracetamol/acetaminophen) is indicated as 1st line treatment in acute pain exacerbation. Topical lidocaine is also indicated as 1st line treatment for elderly patients	
	References	AAN/ AANEM/ AAPMR 2011: Treatment of painful diabetic neuropathy: http://www.neurology.org/content/76/20/1758.full.pdf+html EFNS 2010: Pharmacological treatment of neuropathic pain. European Journal of Neurology 2010: http://www.efns.org/fileadmin/user_upload/guidline_papers/EFNS_guideline_2010_pharma._treatment_of_neuropathic_pain.pdf O'Connor A, et al. Treatment of Neuropathic Pain: An Overview of Recent Guidelines. The Am J Med 2009: http://www.mypharmajobs.com/uploads/M37_W27_Study_OConnor_neuropathic-pain-treatment-guidelines.pdf Moulin DE, et al. Pharmacological management of chronic neuropathic pain. Consensus statement and guidelines from the Canadian Pain Society. Pain Res Manage 2007: http://www.canadianpainsociety.ca/pdf/PharmacologicalManagementChronicPain_CPS-GUIDELINES.pdf	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 89.7 %
86 UP	**Rational**	Higher efficacy of the combination of two drugs (monitor side effects).	
	Remarks	Monitor side effects. Examples of recommended opiate antalgics: morphine, oxycodone, tramadol +/- combined with paracetamol/acetaminophen. *First-line treatments: antidepressant (tricyclic: amitriptyline, clomipramine, desipramine, imipramine, nortriptyline or SNRI: duloxetine, venlafaxine) or an anticonvulsant (gabapentin or pregabalin).	
	References	NICE 2013: Neuropathic pain – pharmacological management: The pharmacological management of neuropathic pain in adults in non-specialist settings: http://www.nice.org.uk/guidance/cg173 Chaparro LE, et al. Combination pharmacotherapy for the treatment of neuropathic pain in adults. Cochrane Database Syst Rev. 2012 [abstract]: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008943.pub2/abstract O'Connor A, et al. Treatment of Neuropathic Pain: An Overview of Recent Guidelines. The Am J Med 2009: http://www.mypharmajobs.com/uploads/M37_W27_Study_OConnor_neuropathic-pain-treatment-guidelines.pdf	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 89.7 % % of experts rating items useful or very useful: 82.1 %
		ACUTE PAIN and OPIATES	
87 UP	**Rational**	Effective relief for acute moderate to severe pain. Favoured administration and dosing route.	
	Recommendations	Mild opioids (level 2): for VAS: 4-6/7 or strong (level 3): VAS: 6/7-10 or pain not controlled by a level 2 antalgic combined with a level 1 at maximum doses, depending on the intensity of the pain and the local recommendations. Perform titration with an immediate-release form, then favour an extended release form if the foreseeable duration of the treatment and the situation justify it.	
	Remarks	List of non-exhaustive mild opioids: codeine, dihydrocodeine, tramadol. Non-exhaustive list of strong opioids: fentanyl, hydromorphone, morphine (core hydrates, sulphate), oxycodone, pethidine.	
	References	WHO 1996 : Cancer pain relief, second edition: http://apps.who.int/iris/bitstream/10665/37896/1/9241544821.pdf Collège national des enseignants universitaires de la douleur, Collège national des médecins de la douleur, Société française d'accompagnement et de soins palliatifs, Douleurs aiguës, douleurs chroniques, soins palliatifs, Numéro 6 de Modules Med-Line, Modules transdisciplinaires, Med-Line éd., 2001	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 92.3 % % of experts rating items useful or very useful: 89.7 %
88 Other	**Rational**	Need to ease pain.	
	Recommendation	It is suggested, during opiate rotation, to perform a moderate reduction in the equianalgesic dose calculated for the new opiate introduced (25 to 50% of the calculated dose).	
	Remark	*Opiate rotation consists of changing one opioid for another in order to decrease the patient's pain and/or the side effects caused by the treatment.	
	References	Roulet L, et al. Rotation des opioïdes : de la théorie à la pratique. Recommendations interdisciplinaires du réseau douleur des HUG. Rev Med Suisse 2011 : http://soinspalliatifs.hug-ge.ch/_library/pdf/RMS_rotation_opioides_RD_2011.pdf	

		Chou R, et al. Opioid Treatment Guidelines: Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain. J Pain 2009: http://nyheadache.com/wp-content/uploads/2012/11/Opioid-guidelines.pdf Fine P et al. Best practice for opioid rotation: conclusion of an expert panel. J Pain and sympt manag 2009 [abstract]: http://www.jpsmjournal.com/article/S0885-3924(09)00629-0/abstract Quigley C. Opioid switching to improve pain relief and drug tolerability. Cochrane Database Syst Rev 2004 [abstract]: http://www.ncbi.nlm.nih.gov/pubmed/15266542 Pereira J, et al. Equianalgesic Dose Ratios for Opioids: A Critical Review and Proposals for Long-Term Dosing. J Pain Symptom Manage 2001: http://mytopcare.org/wp-content/uploads/2013/08/Pereira.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 89.7 %
89 DDI	**Rational**	Increased side effects.	
	Recommendations	Rotate opiates or combine non-opiate antalgic and adjuvant treatments and titrate the treatment.	
	Remarks	Non-exhaustive list of opioids existing in immediate-release form: transmucosal, sublingual, gingival, nasal fentanyl, morphine sulphate or chlorhydrate IR, oxycodone, pethidine. Non-exhaustive list of opioids existing in an extended release form: percutaneous fentanyl, hydromorphone LP, methadone, morphine sulphate SR, oxycodone SR. Non-exhaustive list of partial agonist and/or agonist-antagonist opioids: buprenorphine (partial agonist μ receptors, ƙ antagonist), nalbuphine, nalorphine (μ antagonists, ƙ agonist).	
	References	WHO 1996 : Cancer pain relief, second edition: http://apps.who.int/iris/bitstream/10665/37896/1/9241544821.pdf Réseau Douleur Sarthe. Guide d'utilisation des opioïdes forts en pratique courante : http://www.intercludvendee.fr/reseau-sarthe/Guidedes-opioides.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 100 % % of experts rating items useful or very useful: 94.9 %
90 UP	**Rational**	One of the most frequent side effects of opiates, with a negative impact on the quality of life.	
	Remark	*Prophylactic measures to be taken gradually: fibre-rich diet combined with a lubricating laxative or osmotic agent and, if necessary, stimulant laxative.	
	References	Canadian Pain Society, 2002: Use of opioid analgesics for the treatment of chronic noncancer pain: http://www.canadianpainsociety.ca/pdf/opioid.pdf ASIPP 2012. Opioid Prescribing in Chronic Non-Cancer Pain: Part 2 – Guidance: http://www.painphysicianjournal.com/2012/july/2012;%2015;S67-S116.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 100 % % of experts rating items useful or very useful: 100 %
		MIGRAINES	
91 UP	**Rational**	Effective migraine treatment.	
	Remarks	1st line treatment for moderate migraines: NSAIDs +/- paracetamol/acetaminophen +/- caffeine. 1st line treatment for severe migraines: triptans (specific migraine agent). *Examples of molecules combined with NSAIDs: paracetamol/acetaminophen, caffeine, anti-emetics.	
	References	Société suisse pour l'étude des céphalées 2014 : Céphalées et algies faciales Recommendations thérapeutiques : http://ehf-org.org/wp-content/uploads/2013/11/IMSKWMTE14-Franz%C3%B6sisch-07-Web.pdf Antonaci F, et al. A review of current European treatment guidelines for migraine. J Headache Pain 2010: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3452183/pdf/10194_2009_Article_179.pdf British Association for the study of headache 2010: Diagnosis and Management of Migraine, Tension-Type Headache, Cluster Headache, Medication-Overuse Headache: http://www.migraineclinic.org.uk/wp-content/uploads/2010/11/2010_BASH_Guidelines1.pdf AAN 2000: Practice parameter: Evidence-based guidelines for migraine headache (an evidence-based review): Report of the Quality Standards Subcommittee of the American Academy of Neurology: http://www.neurology.org/content/55/6/754.full.pdf+html	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 87.2 %
92 UP	**Rational**	Reduce the frequency, duration and severity of migraines, improve the response to treatment during attacks, and avoid headaches due to drug misuse.	
	Remarks	As 1st line treatment: some beta-blockers (metorpolol, propranolol, timolol), anti-epileptic medications (sodium di/valproate, topiramate) or antidepressants (amitriptyline). *Frequent use of migraine treatments: more than 10 to 15 days/month, for more than 3 months.	

	References	IHS 2013: The International Classification of Headache Disorders, 3rd edition. Cephalalgia 2013: http://www.ihs-classification.org/_downloads/mixed/International-Headache-Classification-III-ICHD-III-2013-Beta.pdf AAN/AHS 2012: Evidence based guideline update: pharmacologic treatment for episodic migraine prevention in adults: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3335452/pdf/znl1337.pdf Hollande S, et al. Evidence-based guideline update: NSAIDs and other complementary treatments for episodic migraine prevention in adults. Neurology 2012: http://www.neurology.org/content/78/17/1346.full.pdf+html Antonaci F, et al. A review of current European treatment guidelines for migraine. J Headache Pain 2010: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3452183/pdf/10194_2009_Article_179.pdf AAN/ AHS 2000. Evidence-based guideline update: pharmacologic treatment for episodic migraine prevention in adults: http://www.guideline.gov/content.aspx?id=36898	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 92.3 %
		INFECTIOLOGY	
		URINARY INFECTIONS	
93 Other	**Rational**	Avoid recurrences.	
	Recommendation	*Probabilistic treatment, then adapted to the antibiotic resistance test done on fresh urine after removing or changing the catheter.	
	References	IDSA 2010: Diagnosis, Prevention, and Treatment of Catheter-Associated Urinary Tract Infection in Adults: http://www.idsociety.org/uploadedFiles/IDSA/Guidelines-Patient_Care/PDF_Library/Comp%20UTI.pdf IDSA/ ESMID 2010: International Clinical Practice Guidelines for the Treatment of Acute Uncomplicated Cystitis and Pyelonephritis in Women: http://cid.oxfordjournals.org/content/52/5/e103.full.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 100 % % of experts rating items useful or very useful: 87.2 %
		PULMONARY- and TUBERCULOSIS-RELATED INFECTIONS	
94 UP	**Rational**	Frequent infections that may lead to hospitalisation with a high morbidity-mortality.	
	Recommendation	*The therapeutic suggestions must be modulated based on the epidemiological context, the presence of comorbidity factors, the gravity of the pneumonia and local recommendations.	
	Remarks	In case of nosocomial pulmonary infection, see local recommendations. For macrolide use, see item 114 for patients with a high cardiovascular risk.	
	References	INESSS 2010 : Pneumonie acquise en communauté chez l'adulte : http://www.inesss.qc.ca/fileadmin/doc/CDM/UsageOptimal/Guides-serieI/CdM-Antibio1-Pneumonie-Adulte-fr.pdf BSAC 2008: Guidelines for the management of hospital-acquired pneumonia in the UK: http://jac.oxfordjournals.org/content/62/1/5.full.pdf SPILF 2006 : Prise en charge des infections des voies respiratoires basses de l'adulte immunocompétent : http://www.infectiologie.com/site/medias/_documents/consensus/Inf_respir_court-2006.pdf IDSA/ ATSC 2007: Management of Community-Acquired Pneumonia in Adults: http://www.thoracic.org/statements../resources/mtpi/idsaats-cap.pdf Rotstein C, et al. Clinical practice guidelines for hospital-acquired pneumonia and ventilator-associated pneumonia in adults. Can J Infect Dis Med Microbiol 2008: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2610276/pdf/jidmm19019.pdf	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 87.2 % % of experts rating items useful or very useful: 82.1 %
95 UP	**Rational**	Risk of relapse or resistance if treatment is too short lasting. Do not stop treatment without the opinion of an infectiology specialist.	
	Remark	The duration may be discussed with an infectiology specialist.	
	References	Zumla A, et al. Tuberculosis. NEJM 2013 [abstract]: http://www.nejm.org/doi/full/10.1056/NEJMra1200894 WHO 2010: Treatment of tuberculosis Guidelines Fourth edition: http://whqlibdoc.who.int/publications/2010/9789241547833_eng.pdf ATS/ CDC/ IDSA 2003: Treatment of Tuberculosis: http://www.thoracic.org/statements/resources/tb-opi/rr5211.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 84.6 %
96 OP	**Rational**	The toxicity of tuberculosis drugs may be added to that of other molecules.	
	Recommendation	The hepatic tests must be evaluated before beginning any treatment, then regularly throughout the entire treatment (for example, possible monitoring at 15 days, 1, 2, 4 and 6 months after starting treatment)	
	Useful link	*Livertox: http://livertox.nih.gov/	
	References	Doin, ed. *Du bon usage des antibiotiques 2012*. Doin ed. 2012, Wolters Kluwer France: Rueil-Malmaison. 339	

		WHO 2010: Treatment of tuberculosis Guidelines Fourth edition: http://whqlibdoc.who.int/publications/2010/9789241547833_eng.pdf ATS 2006: Hepatotoxicity of Antituberculosis Therapy: http://www.thoracic.org/statements/resources/tb-opi/hepatotoxicity-of-antituberculosis-therapy.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 100 % % of experts rating items useful or very useful: 82.1 %
97 DDI	**Rational**	Powerful enzyme inducer (in particular CYP2C8, 2C9, 2C19, 3A4 and Pgp).	
	Recommendation	*Favour molecules eliminated by the kidneys, or adapt the doses, or in some cases replace the rifampicin with rifabutin.	
	Useful link	HUG 2014: Drug interactions, cytochromes P450 and P-glycoprotein (Pgp): http://www.hug-ge.ch/sites/interhug/files/structures/pharmacologie_et_toxicologie_cliniques/documents/interactions_medicamenteuses_et_cyp450.pdf	
	References	WHO 2010: Treatment of tuberculosis Guidelines Fourth edition: http://whqlibdoc.who.int/publications/2010/9789241547833_eng.pdf CDC 2013: Managing Drug Interactions in the Treatment of HIV-Related Tuberculosis: http://www.cdc.gov/tb/publications/guidelines/tb_hiv_drugs/recommendations02.htm	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 100 % % of experts rating items useful or very useful: 94.9 %
	ABDOMINAL INFECTIONS		
98 UP	**Rational**	Infections frequently associated with anaerobic germs.	
	Remarks	Follow local recommendations for the choice of antibiotics. *Examples of antibiotics covering anaerobic germs: amoxicillin-clavulanate acid, cefoxitin, doripenem, ertapenem, imipenem-cilastatin, meropenem, metronidazole, moxifloxacin, piperacillin-tazobactam, ticarcillin-clavulanic acid.	
	Reference	SIS/ IDSA 2010: Diagnosis and Management of Complicated Intra-abdominal Infection in Adults and Children: http://cid.oxfordjournals.org/content/50/2/133.full.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 89.7 %
	ENDOCARDITIS		
99 OP	**Recommendation**	Ensure good oral hygiene and regular dental exams in order to avoid bacterial endocarditis in the general population.	
	Remarks	*Most at-risk patients: those with a valvular prosthesis, history of infectious endocarditis, congenital heart pathology or heart transplant patients developing a valvulopathy. ** Examples of high-risk procedures requiring preventive treatment in very high-risk patients: dental procedures in the gums or apical region of the teeth or perforating the oral mucus, invasive pulmonary procedures, gastrointestinal or genitourinary surgery in case of known infection, cutaneous procedures on infected skin or musculoskeletal cutaneous procedures, heart or vascular surgery with implantation of material. **Examples of low-risk procedures for which is not necessary to begin treatment: dental procedures other than those involving handling the gums, the periapical region of the teeth or perforation of the oral mucus, pulmonary procedures other than those which are invasive or seek to treat active infections, certain digestive procedures (gastroscopy, colonoscopy, transoesophageal ultrasound), certain genitourinary procedures (cytoscopy), procedures involving the skin and soft tissue.	
	Reference	ESC 2009: Infective Endocarditis (Guidelines on Prevention, Diagnosis and Treatment of): http://eurheartj.oxfordjournals.org/content/30/19/2369.full.pdf	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 92.3 %
	OSTEOARTICULAR INFECTIONS		
100 UP	**Rational**	Obtain sufficient concentrations in the bone to eradicate microorganisms.	
	Recommendation	See a referring physician in infectiology. The treatment is not urgent; it should be started after identifying the germ and determining its sensitivity. It is generally a long-term treatment.	
	Remark	*Non-exhaustive list of antibiotics diffusing in the bone: fusidic acid, 2nd and 3rd generation cephalosporins, daptomycin, fluoroquinolones, linezolid, rifampicin, vancomycin.	

	Reference	IDSA 2013: Diagnosis and Management of Prosthetic Joint Infection: http://cid.oxfordjournals.org/content/56/1/1.full.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 87.2 %
HUMAN IMMUNODEFICIENCY VIRUS INFECTION			
101 DDI	**Rational**	Risks of inefficacy or toxicity of the introduced drug or of the ARVs (some ARVs are enzyme inhibitors and/or inducers and themselves substrates for CYP and Pgp).	
	Recommendations	Choose a therapeutic alternative with no interaction or adapt dosing regimens. See an infectiologist, pharmacist or pharmacologist if needed.	
	Useful links/ References	AIDSinfo 07.12.2015: Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents. See Drug-Drug Interactions section [pages L1-L49]: https://aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl.pdf HIV-druginteractions.org: http://www.hiv-druginteractions.org/Interactions.aspx HIV/HCV Medication guide: http://www.hivmedicationguide.com/ HUG 2014: Drug interactions, cytochromes P450 and P-glycoprotein (Pgp): http://www.hug-ge.ch/sites/interhug/files/structures/pharmacologie_et_toxicologie_cliniques/documents/interactions_medicamenteuses_et_cyp450.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 100 % % of experts rating items useful or very useful: 97.4 %
102 UP	**Rational**	Patient considered being at high cardiovascular risk.	
	Recommendations	Combine lifestyle and dietary measures. Favour statins not interacting with ARV treatment: fluvastatin, pitastatin, pravastatin (except with boosted darunavir), atorvastatin or rosuvastatin with precaution.	
	Remark	Calculation of the cardiovascular risk based on the Framingham score adapted to HIV^{+} patients*	
	Useful links/	*Modified Framingham score: http://www.hivpv.org/Home/Tools/tabid/91/ctl/ExamView/mid/500/eid/0/lid/0/Default.aspx	
	References	AIDSinfo 07.12.2015: Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents. See Drug-Drug Interactions section [pages L1-L49]: https://aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl.pdf EASC 2013: European AIDS Cinical Society guidelines 7.0] [page 17, 36 modalité de mise en route d'un traitement] : http://www.eacsociety.org/Portals/0/Guidelines_Online_131014.pdf Morlat P, et al Antiretroviral treatment French guidelines 2013: http://www.sante.gouv.fr/IMG/pdf/Rapport_Morlat_2013_Mise_en_ligne.pdf ESC/EAS 2011: Guidelines for the management of dyslipidaemias: http://www.escardio.org/guidelines-surveys/esc-guidelines/guidelinesdocuments/guidelines-dyslipidemias-ft.pdf	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 92.3 % % of experts rating items useful or very useful: 82.1 %
HEPATITIS C VIRUS INFECTION			
103 DDI	**Rational**	The new anti-HCV antivirals have many drug interactions. Anti-proteases are inhibitors for CYP and Pgp and substrates for those enzymes.	
	Recommendations	Choose a therapeutic alternative with no interaction or adapt the dosing regimens. See an infectiologist, pharmacist or pharmacologist if needed.	
	Remark	*Non-exhaustive list of drugs interacting with new anti-HCV antivirals: antihypertensives (amlodipine, carvedilol, irbesartan, losartan, nebivolol), antipsychotics (aripiprazole, iloperidone, quetiapine), anxiolytics (benzodiazepines: flurazepam, quazepam, triazolam, alprazolam, zolpidem, trazodone), ARV, oral contraceptives, immunosuppressants (cyclosporine, tacrolimus), SSRIs (escitalopram), methadone, some statins, etc.	
	Useful links	HUG 2014: Drug interactions, cytochromes P450 and P-glycoprotein (Pgp): http://www.hug-ge.ch/sites/interhug/files/structures/pharmacologie_et_toxicologie_cliniques/documents/interactions_medicamenteuses_et_cyp450.pdf HIV/HCV Medication guide: http://www.hivmedicationguide.com/	
	Reference	Kiser J, et al. Review and Management of Drug Interactions With Boceprevir and Telaprevir. Hepatology 2012: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3345276/pdf/nihms365411.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 89.7 %

HEPATITIS B VIRUS INFECTION			
104 UP	**Rational**	Once started, the anti-HBV treatment must be continued for at least 6 months after Hbe seroconversion and HBV DNA undetectable in the serum. Upon stopping, close monitoring for relapses is necessary.	
	Remark	Molecules often used: adefovir, entecavir, lamivudine, tenofovir +/- emtricitabine.	
	References	EASL 2012: Clinical Practice Guidelines: Management of chronic hepatitis B virus infection: http://www.easl.eu/assets/application/files/ef520780b91cf4f_file.pdf EASL 2009: Clinical Practice Guidelines: Management of chronic hepatitis B: http://www.easl.eu/assets/application/files/b73c0da3c52fa1d_file.pdf AASLD 2009: Chronic Hepatitis B: http://www.aasld.org/practiceguidelines/documents/bookmarked%20practice%20guidelines/chronic_hep_b_update_2009%208_24_2009.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 82.1 %
PREVENTION/PROPHYLAXIS			
105 UP	**Rational**	High risk of infection by *Pneumocystis jirovecii* and *Toxoplasma gondii*.	
	Recommendations	As 1st line treatment: trimethoprim-sulfamethoxazole once QD or TIW. In case of hypersensitivity or intolerance to trimethoprim-sulfamethoxazole, the following alternatives are possible (but less effective): atovaquone, dapsone, pentamidine in aerosol form.	
	Reference	ASBMT 2009: Guidelines for Preventing Infectious Complications among Hematopoietic Cell Transplantation Recipients: http://www.idsociety.org/uploadedFiles/IDSA/Guidelines-Patient_Care/PDF_Library/OI.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 100 % % of experts rating items useful or very useful: 79.5 %
106 UP	**Rational**	High risk of infection by *Pneumocystis jirovecii* and *Toxoplasma gondii*.	
	Recommendations	As 1st line treatment: trimethoprim-sulfamethoxazole once QD or TIW. In case of hypersensitivity or intolerance to trimethoprim-sulfamethoxazole, the following alternatives are possible (but less effective): atovaquone, dapsone, pentamidine in aerosol form.	
	Reference	Green H, et al. Prophylaxis for Pneumocystis pneumonia (PCP) in non-HIV immunocompromised patients (Review). Cochrane Database Syst Rev 2009 [abstract]: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD005590.pub2/abstract;jsessionid=258A7B9B3F791B769F738289DCA2FE20.f04t04	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 84.6 %
107 UP	**Rational**	High risk of infection by *Pneumocystis jirovecii* and *Toxoplasma gondii*.	
	Recommendations	As 1st line treatment: trimethoprim-sulfamethoxazole once QD (400/80 mg or 800/160 mg) or TIW (800/160 mg). In case of hypersensitivity or intolerance to trimethoprim-sulfamethoxazole, the following alternatives are possible (but less effective): atovaquone, dapsone, dapsone + pyrimethamine + folinic acid, pentamidine in aerosol form. The treatment must be continued as long as the CD4 count is < 200/mm3 and 6 months after the CD4 counts have returned to > 200/mm3.	
	Reference	CDC/ NIH/ HIVIAA 20.01.2014: Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents: http://aidsinfo.nih.gov/contentfiles/adult_oi.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 100 % % of experts rating items useful or very useful: 92.3 %
108 UP	**Rational**	High risk of infection by *Pneumocystis jirovecii* and *Toxoplasma gondii*.	
	Recommendations	As 1st line treatment: trimethoprim-sulfamethoxazole once QD or TIW. See a specialist if needed. In case of hypersensitivity or intolerance to trimethoprim-sulfamethoxazole, the following alternatives are possible: atovaquone, dapsone, pentamidine in aerosol form.	
	Remarks	*Non-exhaustive list of highly immunosuppressive treatments: alemtuzumab, analogue of the purine bases (fludarabine) and CD4 count < 200/mm3, anti-TNF alpha combined with another immunosuppressant, high doses of corticosteroids for a duration > 1 month (ex: prednisone > 20 mg) in immunosuppressed patients (pathology or associated	

		immunosuppressive treatment), cyclophosphamide, alemtuzumab, analogue of the purine bases (fludarabine), anti-TNF alpha combined with another immunosuppressant, cyclophosphamide, temozolomide combined with radiotherapy. *Non-exhaustive list of pathologies associated with immune suppression: cancers, rheumatological pathologies (in particular Wegener's disease), malignant haemopathies treated by chemotherapy with a high occurrence of aplasia.	
	References	NCCN 2012: Prevention and Treatment of Cancer-Related Infections: http://www.jnccn.org/content/10/11/1412.full.pdf Green H, et al. Prophylaxis for Pneumocystis pneumonia (PCP) in non-HIV immunocompromised patients (Review). Cochrane Database Syst Rev 2009: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD005590.pub2/abstract;jsessionid=258A7B9B3F791B769F738289DCA2FE20.f04t04 EULAR 2008: recommendations for the management of primary small and medium vessel vasculitis: http://ard.bmj.com/content/68/3/310.full.pdf Yale SH, et al. Pneumocystis carinii pneumonia in patients without acquired immunodeficiency syndrome: associated illness and prior corticosteroid therapy. Mayo Clin Proc 1996 [abstract]: http://www.mayoclinicproceedings.org/article/S0025-6196(11)64914-8/abstract?refuid=S0025-6196(11)63174-1&refissn=0025-6196	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 87.2 %
109 UP	**Rational**	Risk of neuropsychiatric and dermatological disorders.	
	Recommendation	pyridoxine: 25–50 mg/d.	
	Remarks	*Patients with a risk of vitamin B6 deficiency or peripheral neuropathy: high doses of isoniazid, pre-existing causes for peripheral nerve disease (diabetes, alcohol dependency, renal failure, haemodialysis, tobacco use, HIV infection, taking neurotoxic drugs, malnutrition, pregnancy, nursing, chronic hepatopathy, elderly patients, use of oral contraceptives. A vitamin B6 overdose may itself cause neuropathy.	
	Reference	ATS/ CDC/ IDSA 2003: Treatment of Tuberculosis: http://www.atsjournals.org/doi/pdf/10.1164/rccm.167.4.603	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 89.7 %
	PROPER USE OF ANTIBIOTICS		
110 Other	**Rational**	Make it possible to adapt the selection pressure and to avoid resistance.	
	Recommendation	Adaptation of the drug to the sensitivity of the bacterial strain, de-escalation of therapy.	
	References	Manuel O, et al. Impact of standardised review of intravenous antibiotic therapy 72 hours after prescription in two internal medicine wards. J Hosp Infect 2010 [abstract]: http://www.journalofhospitalinfection.com/article/S0195-6701(09)00318-1/abstract HAS 2008: Antibiotic therapy and prevention of bacterial resistance in healthcare organisations: http://www.has-sante.fr/portail/upload/docs/application/pdf/2010-03/antibiotic_therapy_and_prevention_of_bacterial_resistance_-_guidelines.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 100 %
111 Other	**Rational**	Decreased complications (infectious, thrombophlebitis, pain), ease of administration, improvement of patient comfort, lower cost, comparable efficacy and decreased hospital stay.	
	Recommendation	Adaptation of the treatment to the sensitivity of the bacterial strain, using an antibiotic having good oral bioavailability*.	
	Remarks	IV-per os switch criteria: patient showing clinical improvement, stable haemodynamics, with no sign of malabsorption (functional gastrointestinal tract) and leukopaenia. Antibiotic having good bioavailability and good oral tolerance, respecting the rules of bioequivalence with the antibiotic taken by IV and for which the dosing regimen is identical or simplified. *Non-exhaustive list of antibiotics with good oral bioavailability: β-lactamines, fluoroquinolones, linezolid, macrolides, clindamycin, metronidazole, trimethoprim-sulfamethoxazole, rifampicin.	
	References	Owens R, et al. Antimicrobial stewardship: concepts and strategies in the 21st century. Diagnostic Microbiology and Infectious Disease 2008 [abstract]: http://www.dmidjournal.com/article/S0732-8893(08)00148-X/abstract Pablos A, et al. Evaluation of an antibiotic intravenous to oral sequential therapy program. Pharmacoepidemiol Drug Saf 2005 [abstract]: http://onlinelibrary.wiley.com/doi/10.1002/pds.1042/abstract	
	Strength of	Experts median agreement: strongly agree	% of experts agree or strongly agree: 100 %

	recommendation	Median usefulness rating: very useful	% of experts rating items useful or very useful: 94.9 %
112 OP	**Rational**	Decreased needless exposure to antibiotics.	
	Remark	*Non-exhaustive list of infections for which an antibiotic therapy duration exceeding 10 days is recommended: prostatitis, osteoarticular infections, endocarditis, tuberculosis, pyelonephritis, some pneumopathies, late ventilator-associated pneumonia with *Pseudomonas aeruginosa* or Acinetobacter, pulmonary abscess, empyema, deep cutaneous infections, some bacterial meningitis (*Streptococcus agalactiae*, Gram-negative bacillus, *Listeria monocytogenes*), bacteraemia related to intravascular catheters with *Staphylococcus aureus* or *Staphylococcus lugdunensis*, etc.	
	References	Hayashi Y, et al. Strategies for Reduction in Duration of Antibiotic Use in Hospitalized Patients. Clinical Infectious Diseases 2011: http://cid.oxfordjournals.org/content/52/10/1232.full.pdf Pugh R, et al. Short-course versus prolonged-course antibiotic therapy for hospital-acquired pneumonia in critically ill adults (Review). The Cochrane Library 2011. [Abstract]: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD007577.pub2/abstract	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 97.4 %
113 Other	**Rational**	Allow to avoid side effects and therapeutic escapes.	
	Remarks	*Non-exhaustive list of antibiotics having a risk of dose-dependent toxicity: aminoglycosides (treatment > 3 days or high cumulative doses), vancomycin. **Non-exhaustive list of situations creating a risk of modification of drug plasma concentrations: renal failure, pregnancy, severe sepsis, obesity/cachexia.	
	References	Hites M, et al. Case-Control Study of Drug Monitoring of Beta-Lactams in Obese Critically Ill Patients. Antimicrob. Agents Chemother 2013: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3553684/pdf/zac708.pdf IDSA/ ASHSP/ SIDP 2009: Vancomycin Therapeutic Guidelines: A Summary of Consensus Recommendations: http://cid.oxfordjournals.org/content/49/3/325.full.pdf Eyler R, et al. Antibiotic Pharmacokinetic and Pharmacodynamic Considerations in Patients With Kidney Disease. Advances in Chronic Kidney Disease 2010 [abstract]: http://www.ackdjournal.org/article/S1548-5595(10)00084-4/abstract	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 92.3 %
114 DDI	**Rational**	Drugs with pro-arrhythmogenic effects (elongation of the QT interval, ventricular arrhythmia) and with a risk of cardiovascular death.	
	Remark	*Non-exhaustive list of patients with special risk: known elongation of the QT interval, congenital long QT syndrome, taking drugs known to elongate the QT interval**, history of torsade de pointes, non-compensated heart failure, uncorrected hypokalaemia or hypomagnesaemia, clinically significant bradycardia, taking class Ia or class III antiarrhythmics.	
	Useful link	**Crediblemeds.org: List - All QTDrugs: http://www.crediblemeds.org/everyone/composite-list-all-qtdrugs/?rf=All	
	References	Ray WA, et al. Azithromycin and the Risk of Cardiovascular Death. N Engl J Med 2012: http://www.nejm.org/doi/pdf/10.1056/NEJMoa1003833 FDA Drug Safety Communication 2013: Azithromycin (Zithromax or Zmax) and the risk of potentially fatal heart rhythms: http://www.fda.gov/downloads/Drugs/DrugSafety/UCM343347.pdf	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 89.7 % % of experts rating items useful or very useful: 87.2 %
115 Other	**Rational**	Rapid bactericidal activity, concentration-dependent, prolonged post-antibiotic effect. Increased toxicity for treatment durations longer than 5-7 days (primarily renal, auditory and vestibular). Narrow therapeutic window.	
	Recommendations	Monitor the aminoglycoside residual concentration for treatments longer than 5 days (dosing to be done after 48 hours of treatment) or in case of renal insufficiency. Monitoring to be repeated 2 times per week, associated with monitoring of renal function. Adapt administration regimen based on the results of the monitoring.	
	Remarks	In case of pre-existing renal failure, aminoglycosides will only be used if they are absolutely necessary. If use is necessary, a therapeutic drug concentration monitoring (peak and residual) will be done to adjust the dosing modes and intervals between each injection. Short-term treatments will be favoured (as a general rule: 1 or 2 injections) and regular	

		monitoring of renal and auditory function will be done. *Special situation under which administration multiple times a day is traditionally used: endocarditis (except endocarditis with streptococcus and enterococcus for which a single daily administration is recommended or possible, respectively).	
	Reference	AFSSAPS/SPILF/GPIP 2011 : Mise au point sur le bon usage des aminosides administrés par voie injectable : http://www.infectiologie.com/site/medias/_documents/consensus/2011-afssaps_SPILF-MAP_Aminosides_Argumentaire.pdf	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 89.7 % % of experts rating items useful or very useful: 89.7 %
ENDOCRINOLOGY			
DIABETES MELLITUS (DM)			
116 UP	**Rational**	Prevention of microvascular complications and cardiovascular disease.	
	Recommendations	Combination individualized on a case-by-case basis. Metformin as 1st line treatment in T2DM. *Recommended HbA1c targets: HbA1c ≤ 6.5%: in newly diagnosed patients, whose life expectancy is > 15 years and with no cardiovascular history (with no history of major hypoglycaemia), in diabetic patients who are pregnant or plan to become pregnant. HbA1c ≤ 7%: in most adult diabetic patients, patients with moderate chronic renal failure (stage 3: CrCl between 30 and 59 ml/min/1.73 m^2), in elderly patients whose life expectancy is deemed satisfactory. HbA1C ≤ 8%: in patients with proven serious comorbidity and/or a limited life expectancy (< 5 years), or with evolved macrovascular complications, or having a long evolution duration of diabetes (> 10 years) and for whom the 7% target is difficult to achieve because drug intensification causes severe hypoglycaemia, in patients with severe or terminal chronic renal failure (stages 4–5: CrCl < 30 mL/min/1.73 m2), and fragile elderly patients (intermediate health condition and at risk for switching patient categories). HbA1c < 9: in dependent elderly patients, in poor health due to evolved chronic poly-pathology creating handicaps and social isolation.	
	References	HAS 2014 : Stratégie médicamenteuse du contrôle glycémique du diabète de type 2 : http://www.has-sante.fr/portail/upload/docs/application/pdf/2013-02/10irp04_synth_diabete_type_2_objectif_glycemique_messages_cles.pdf ADA 2013: Standards of Medical Care in Diabetes: http://care.diabetesjournals.org/content/36/Supplement_1/S11.full.pdf ESC/ EASD 2013: Diabetes, Pre-Diabetes and Cardiovascular Diseases developed with the EASD: http://eurheartj.oxfordjournals.org/content/34/39/3035.full.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 92.3 %
117 OP	**Rational**	Prevention of hypo and hyperglycaemia.	
	Recommendation	*Customized glycaemic monitoring according to diabetologist opinion.	
	Remarks	**Non-exhaustive list of hyperglycaemic drugs: anticalcineurines (cyclosporine, tacrolimus), some antihypertensives (thiazidic diuretics, diazoxide, non-cardioselective beta-blockers), antipsychotics, some ARVs, β2-agonists, corticosteroids, alpha interferon, oestroprogestatives, pentamidine. Non-exhaustive list of hypoglycaemic drugs: NSAIDs, class 1a antiarrythmics, beta blockers, fluoxetine, fluoroquinolones, ACEI, sulfamethoxazole-trimethoprim.	
	References	Sattar N, et al. Statins and risk of incident diabetes: a collaborative meta-analysis of randomised statin trials. Lancet 2010 [abstract]: http://www.ncbi.nlm.nih.gov/pubmed/20167359 Hassan Murad M, et al. Drug-Induced Hypoglycemia: A Systematic Review. J Clin Endocrinol Metab 2009: http://press.endocrine.org/doi/pdf/10.1210/jc.2008-1416 F. Bosquet, et al. Effets endocriniens et métaboliques iatrogènes des médicaments. EMC - AKOS (Traité de Médecine) 2008 [abstract]: http://www.em-consulte.com/en/article/178169	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 84.6% % of experts rating items useful or very useful: 74.4 %
118 Other	**Rational**	Possible induction of hyperglycaemia and glucose intolerance, which would destabilize treatment.	
	Remark	Reducing doses of corticosteroids or stopping treatment generally allow normalizing	

		glycaemia.	
	Reference	Moghadam-Kia S, et al. Prevention and treatment of systemic glucocorticoid side effects. International Journal of Dermatology 2010: http://onlinelibrary.wiley.com/doi/10.1111/j.1365-4632.2009.04322.x/pdf	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 92.3 %
119 Other	**Rational**	Nephroprotective effect of ACEI and ARB. Many clinical trials conducted for this indication.	
	Recommendation	Blood pressure objective < 140/90 or 85 mmHg.	
	Remark	*microalbuminuria: urinary albumin = 30 to 300 mg/ 24 hours.	
	References	ESH/ESC 2013: Arterial Hypertension (Management of): http://eurheartj.oxfordjournals.org/content/34/28/2159.full.pdf ADA 2013: Standards of Medical Care in Diabetes: http://care.diabetesjournals.org/content/36/Supplement_1/S11.full.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 94.9 %
120 UP	**Rational**	Prevention of cardiovascular diseases.	
	Recommendations	Therapeutic goals: *T1DM or T2DM patient with very high cardiovascular risk** (e.g.: diabet mellitus combined with a cardiovascular disease, severe CKD or one or more cardiovascular risk factors and/or organ impairment): LDL-c level < 1.8 mmol/l (< 70 mg/dL) or a reduction greater than or equal to 50% of the initial LDL-c level. T2DM patient with high cardiovascular risk**: LDLc level < 2.5 mmol/L (< 100 mg/dL). T1DM patient with a high cardiovascular risk**: possible prescription of statins regardless of basal LDL-c level.	
	Remark	**Calculation of cardiovascular risk: see item no. 5.	
	References	ESC/ EASD 2013: Diabetes, Pre-Diabetes and Cardiovascular Diseases developed with the EASD: http://eurheartj.oxfordjournals.org/content/34/39/3035.full.pdf ADA 2013: Standards of Medical Care in Diabetes: http://care.diabetesjournals.org/content/36/Supplement_1/S11.full.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 100 % % of experts rating items useful or very useful: 97.4 %
121 UP	**Rational**	Primary prevention of possible cardiovascular diseases. Secondary prevention of cardiovascular diseases necessary in this population.	
	Recommendations	*Aspirin: 75 to 160 mg QD +/- combined, for one year, with a P2Y12 receptor antagonist (clopidogrel, prasugrel, ticagrelor) in case of acute coronary syndrome. Alternative in case of aspirin intolerance: clopidogrel. Take contraindications for antiplatelet drugs into account.	
	Remark	**Calculation of cardiovascular risk: see item no. 5.	
	References	ESC/ EASD 2013: Diabetes, Pre-Diabetes and Cardiovascular Diseases developed with the EASD: http://eurheartj.oxfordjournals.org/content/34/39/3035.full.pdf ADA 2013: Standards of Medical Care in Diabetes: http://care.diabetesjournals.org/content/36/Supplement_1/S11.full.pdf ESC/EAS 2011: Dyslipidaemias (Management of): http://eurheartj.oxfordjournals.org/content/32/14/1769.full.pdf	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 84.6 % % of experts rating items useful or very useful: 89.7 %
122 UP	**Rational**	Allow to avoid side effects of T2DM. Recommended as 1st line treatment, in particular in case of excess weight or obesity, if there is no contraindication.	
	References	ESC/ EASD 2013: Diabetes, Pre-Diabetes and Cardiovascular Diseases developed with the EASD: http://eurheartj.oxfordjournals.org/content/34/39/3035.full.pdf ADA 2013: Standards of Medical Care in Diabetes: http://care.diabetesjournals.org/content/36/Supplement_1/S11.full.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: indisensable	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 100 %
123 OP	**Rational**	Risk of lactic acidosis.	
	Recommendations	Favour insulin treatment during instability. Stopping possible and recommended 48 hours before an at-risk procedure. Resume	

		administration 48 hours after the procedure.	
	Remark	It is not necessary to suspend the administration of metformin in all patients. In some cases, close monitoring of renal function after the procedure is sufficient. Metformin should be suspended if renal function deteriorates and until it returns to its initial level.	
	References	ESC/ EASD 2013: Diabetes, Pre-Diabetes and Cardiovascular Diseases developed with the EASD: http://eurheartj.oxfordjournals.org/content/34/39/3035.full.pdf ADA 2013: Standards of Medical Care in Diabetes: http://care.diabetesjournals.org/content/36/Supplement_1/S11.full.pdf	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 89.7 % % of experts rating items useful or very useful: 89.7 %
124 Other	**Rational**	Most at risk antidiabetics for hypoglycaemia.	
	Remarks	*Non-exhaustive list of sulfonylurea molecules: chlorpropamide, glibenclamide/glyburide, gliclazide, glimepiride, glipizide, gliquidone, tolbutamide, tolazamide. Taking beta-blockers concomitantly may hide the signs of hypoglycaemia.	
	Reference	ADA 2013: Standards of Medical Care in Diabetes: http://care.diabetesjournals.org/content/36/Supplement_1/S11.full.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 92.3 % % of experts rating items useful or very useful: 84.6 %
125 Other	**Rational**	Risks of side effects and complications increased in these patients.	
	Remark	*Non-exhaustive list of molecules and classes to be adapted or changed: gliptin, long-acting insulin, metformin, sulfonylurea.	
	References	ADA/ endocrine Society 2013: Hypoglycemia and Diabetes: http://care.diabetesjournals.org/content/36/5/1384.full.pdf ADA/ EASD 2012: Management of Hyperglycemia in Type 2 Diabetes: A Patient-Centered Approach: http://care.diabetesjournals.org/content/35/6/1364.full.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 100 % % of experts rating items useful or very useful: 94.8 %
	THYROID DISORDERS		
126 Other	**Rational**	The TSH concentration is balanced after approximately 6 weeks of treatment. In some specific cases, an earlier assay of the TSH may be useful (very high or very low TSH, myxoedematous coma, etc.). Subtle differences may persist in bioavailability between the formulations of levothyroxine.	
	Recommendations	The dose is adapted to the weight and to the TSH target. When possible, keep the same formulation.	
	Reference	ATA/ endocrine society/ AACE 2004: Joint Statement on the U.S. Food and Drug Administration's Decision Regarding Bioequivalence of Levothyroxine Sodium: https://www.endocrine.org/~/media/endosociety/Files/Advocacy%20and%20Outreach/Position%20Statements/Other%20Statements/Joint_Statement_LevothyroxineThyroxine.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 100 % % of experts rating items useful or very useful: 94.6 %
127 Other	**Rational**	Taking on an empty stomach ensures more stable T4 and TSH serous concentrations.	
	Recommendation	When possible, keep the same formulation and same administration methods as usual.	
	Remarks	*On an empty stomach in the morning = at least 30 minutes before breakfast, or optionally in the evening before going to bed = at least 2 hours after the evening meal. **Non-exhaustive list of substances that may decrease the absorption of levothyroxine: antacids containing aluminium hydroxide, caffeine/theine, biliary acid chelators, phosphorus chelators, PPIs, food, sucralfate, calcium salts, iron sulphate.	
	References	Bach-Huynh TG, et al. Timing of Levothyroxine Administration Affects Serum Thyrotropin Concentration. JCEM 2009: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2758731/?report=printable Liwanpo L, et al. Conditions and drugs interfering with thyroxine absorption. Best Practice & Research Clinical Endocrinology & Metabolism 2009 [abstract]: http://www.bprcem.com/article/S1521-690X(09)00076-1/abstract	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 92.3 % % of experts rating items useful or very useful: 84.6 %
128 OP	**Rational**	Long half-life of levothyroxine (approximately 7 days) and oral absorption = approximately 80% of the dose.	

	Recommendation	If the duration exceeds 7 days, administer approximately 80% of the dose normally taken orally, parenterally.	
	Reference	Fish LH, et al. Replacement Dose, Metabolism, and Bioavailability of Levothyroxine in the Treatment of Hypothyroidism. NEJM 1987 [abstract]: http://www.nejm.org/doi/full/10.1056/NEJM198703263161302	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 87.2 % % of experts rating items useful or very useful: 89.7 %
129 OP	**Rational**	Look for induced thyroid disorders. The TSH concentration is balanced after approximately 6 weeks of treatment.	
	Remark	*Non-exhaustive list of drugs that may induce thyroid disorders: aminoglutethimide, amiodarone, certain antineoplastics: tyrosine kinase inhibitors (imatinib, motesanib, sunitinib, sorafenib), bexarotene, thalidomide, thioamides, interferon alpha, interleukin-2, lithium, perchlorate, products containing iodine (iodine, radioactive iodine, iodized contrast products, potassium iodide solutions, iodized povidone), lithium salts.	
	References	ATA/AACE 2012: Clinical practice guidelines for hypothyroidism in adults: http://aace.metapress.com/content/611883025v735392/fulltext.pdf ATA/AACE 2011: Hyperthyroidism and other causes of thyrotoxicosis: management guidelines: https://www.aace.com/files/hyper-guidelines-2011.pdf	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 84.6 %
130 UP	**Rational**	Allow to decrease symptoms caused by the increase beta-adrenergic tonus (palpitations, tachycardia, shaking, anxiety, heat intolerance). Propranolol inhibits the conversion of the T4 into T3.	
	Recommendation	In general, long-acting molecules are favoured: atenolol, metoprolol, nadolol, propranolol, etc.	
	Reference	ATA/AACE 2011: Hyperthyroidism and other causes of thyrotoxicosis: management guidelines: https://www.aace.com/files/hyper-guidelines-2011.pdf	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 92.3 %
	CONTRACEPTION		
131 DDI	**Rational**	Risk of inefficacy of the contraceptive hormonal treatment or of the combination.	
	Recommendation	Another method of contraception may optionally be offered.	
	Remark	*Non-exhaustive list of drugs interacting with hormonal contraceptives: some antibiotics (rifampicin, rifabutin), some anti-epileptics (barbiturates, carbamazepine, lamotrigine, oxcarbamaepine, phenytoin, primidone, topiramate), some antiretrovirals.	
	Reference	CDC 2013: U.S. Selected Practice Recommendations for Contraceptive Use. Adapted from the WHO Selected Practice Recommendations for Contraceptive Use, 2nd Edition: http://www.cdc.gov/mmwr/pdf/rr/rr6205.pdf	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 92.3 % % of experts rating items useful or very useful: 84.6 %
	OPHTHALMOLOGY		
	GLAUCOMA		
132 UP	**Rational**	Avoid forgetting prescriptions and avoid increasing the intraocular pressure during hospitalisation.	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 92.3 %
133 OP	**Rational**	Risk of acute attack in patients with irido-closed angles.	
	Recommendation	Perform a laser iridotomy. After this treatment, these drugs may be administered again.	
	Remark	*Non-exhaustive list of drugs that may induce acute closed angle glaucoma: alpha-adrenergic drugs (apraclonidine, dipivefrin, ephedrine, epinephrine, phenylephrine), drugs with anaesthetic properties (ketamine, succinylcholine), anticholinergics (atropine), anticoagulants (by massive retinal haemorrhage or unsticking of the choroid: rare), antidepressants (citalopram, escitalopram, fluoxetine, fluvoxamine, monoamine oxidase inhibitors, mianserin, paroxetine, tricyclics), certain antihistamines (cimetidine, ranitidine, promethazine), certain Parkinson's medications (orphenadrine, trihexyphenidyl), certain antipsychotics (fluphenazine, perphenazine, trifluoperazine), colchicine combined with opium and tiemonium methysulate, disopyramide, parasympathomimetics (acetylcholine,	

		carbachol, pilocarpine), parasympatholytics (ipratropium bromide, scopolamine, anticholinergics spasmolytics thrombolytics and botulinum toxin.	
	Reference	Razeghinejad MR, et al. Iatrogenic Glaucoma Secondary to Medications. The American Journal of Medicine 2011 (review): http://www.dottnet.it/public/content/Documento/Glaucoma_iatrogeno_causato_da_farmaci.pdf	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 100 % % of experts rating items useful or very useful: 82.1 %
DEPENDENCIES			
ADDICTIONS and HOSPITALIZATION			
134 Other	**Rational**	Allow to improve patients monitoring during hospitalisation and to offer an appropriate care before leaving the hospital.	
	Recommendation	Depending on patient needs: simple information or referral to a specialised consultation.	
	Remark	Possible use of a rapid addiction detection tool such as the WHO-ASSIST *.	
	Useful link	*http://www.who.int/substance_abuse/activities/assist_v3_english.pdf?ua=1	
	Reference	WHO 2008: The Effectiveness of a Brief Intervention for Illicit Drugs Linked to the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) in Primary Health Care Settings: http://www.who.int/substance_abuse/activities/assist_technicalreport_phase3_final.pdf?ua=1	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 89.7 % % of experts rating items useful or very useful: 79.5 %
ALCOHOL DEPENDENCE			
135 Other	**Rational**	Allow to prevent complicated withdrawal during hospitalisation.	
	Recommendation	Use a rapid test such as the Audit, Audit-C, Fast or Cage/Deta tests*.	
	Remark	*Cage/Deta (A total score of 2 or greater is considered clinically significant and is a good predictive criterion for an alcohol consumption problem): Have you ever felt you should cut down on your drinking? Have people annoyed you by criticizing your drinking? Have you ever felt bad or guilty about your drinking? Have you ever had a drink first thing in the morning to steady your nerves or to get rid of a hangover (eye opener)?	
	Useful link	**Cage questionnaire: http://pubs.niaaa.nih.gov/publications/inscage.htm	
	Reference	Anderson P, et al. Alcohol and Primary Health Care: Clinical Guidelines on Identification and Brief Interventions. Department of Health of the Government of Catalonia: Barcelona 2005: http://www.gencat.cat/salut/phepa/units/phepa/pdf/cg_1.pdf	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 87.2 % % of experts rating items useful or very useful: 69.2 %
136 UP	**Rational**	Allow to prevent complicated withdrawal during hospitalisation	
	Recommendations	Use a predictive evolution scale such as the CIWA-Ar* (Clinical Index Withdrawal Assessment-Revised) or the Cushman withdrawal score.	
	Remark	*Non-exhaustive list of benzodiazepines that may be used in case of risk of alcohol withdrawal: chlordiazepoxide (50–100 mg), diazepam (10–20 mg), lorazepam (2–4 mg), oxazepam (15–30 mg), 4 to 6 doses/d. The prescription duration should not exceed 7 days, except in case of complications, and the dose should be gradually reduced (20% per day).	
	Useful link	*Clinical Institute Withdrawal Assessment of Alcohol Scale, Revised (CIWA-Ar): http://wiki.hl7.org/images/2/25/Alcohol-Withdrawal-Assessment-Scale.pdf	
	References	HUG 2010 : alcohol consumption problem: http://www.hug-ge.ch/sites/interhug/files/structures/medecine_de_premier_recours/documents/infos_soignants/probleme_d_alcool_2010df.pdf R. Saitz et al. Unhealthy alcohol use, clinical practice, NEJM, 2005: http://www.nejm.org/doi/pdf/10.1056/NEJM200505193522021 ANAES 1999 : Conférence de consensus Objectifs, indications et modalités du sevrage du patient alcoolodépendant : http://www.has-sante.fr/portail/upload/docs/application/pdf/alcool.court.pdf	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 89.7 %

137 UP	**Rational**	Risk of vitamin B1 deficiency in alcoholic patients due to decreased digestive absorption in case of alcohol abuse and malnutrition.	
	Recommendations	Administer 100 to 300 mg/d of vitamin B1 for 3 weeks (in case of withdrawal). If there are signs of deficiency, favour the parenteral route, 1 to 2 times per day, the 1st week (decreased digestive absorption of vitamin B1 in case of alcohol abuse or malnutrition). Vitamin B6 and vitamin PP (nicotinamide) can be combined over a short period.	
	References	HUG 2010 : alcohol consumption problem: http://www.hug-ge.ch/sites/interhug/files/structures/medecine_de_premier_recours/documents/infos_soignants/probleme_d_alcool_2010df.pdf SFA 2006 : Sevrage simple en alcool : http://www.sfalcoologie.asso.fr/download/Svg_simple.pdf Yersin B, et al. Syndrome de sevrage alcoolique : Prise en charge ambulatoire par le médecin praticien. Rev Méd Suisse romande 1998 : http://cms.addiction-valais.ch/Upload/medrotox/5_3_Syndrome_sevrage_alcoolique.pdf Gian Pietro S, et al. Wernicke's encephalopathy: new clinical settings and recent advances in diagnosis and management. Lancet Neurol 2007 [abstract] : http://www.thelancet.com/journals/laneur/article/PIIS1474-4422(07)70104-7/abstract ANAES/ SFA 1999 : Conférence de sconsensus. Objectifs, indications et modalités du sevrage du patient alcoo-dépendant : http://www.sfmu.org/documents/consensus/cc_sevoh_long.pdf	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 84.6 % % of experts rating items useful or very useful: 89.7 %
	TOBACCO USE and TOBACCO WITHDRAWAL		
138 UP	**Rational**	Allow to prevent withdrawal during hospitalisation	
	Recommendation	Patients in intensive care should not systematically receive nicotine substitutes; only those for whom the expected benefits exceed the toxicity risks should receive them.	
	Reference	Wilby K, et al. Nicotine replacement therapy in the intensive care unit: a systematic review. J Intensive Care Med. 2014 [abstract]: http://jic.sagepub.com/content/29/1/22.abstract	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 89.7 %
139 UP	**Rational**	Quitting tobacco has a large capacity to prevent cardiovascular events and to influence the natural history of chronic respiratory diseases.	
	Recommendation	Treatments using nicotine substitutes, extended-release bupropion or vareniciline may be offered to favour long-term tobacco cessation.	
	References	EMA 2010: Overview of comments received on draft guideline on the development of medicinal products for the treatment of smoking: http://www.ema.europa.eu/docs/en_GB/document_library/Other/2009/11/WC500011384.pdf GOLD 2014: http://www.goldcopd.org/uploads/users/files/GOLD_Report_2014.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 100 % % of experts rating items useful or very useful: 94.9 %
	BENZODIAZEPINE DEPENDENCE		
140 UP	**Rational**	Allow to prevent withdrawal during hospitalisation.	
	Recommendation	Do not stop BZD treatment abruptly.	
	Reference	HUG 2010 : PharmaKit, Formation post-graduée en addictologie: http://www.hug-ge.ch/sites/interhug/files/structures/addictologie/documents/Formation/Postgrade/Starterkit/pharmakit.pdf	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 89.7 % % of experts rating items useful or very useful: 92.3 %
	OPIOID DEPENDENCE		
141 UP	**Rational**	Allow to prevent withdrawal during hospitalization.	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 89.7 %
142 DDI	**Rational**	Risk of lower efficacy of the antalgic treatment by occupation of the opiate receptors by the buprenorphine.	
	Remark	The treatment for the pain and the substitution treatment may be re-evaluated and adapted with the help of a pain specialist	
	Reference	Suboxone summary of product characteritics (2015) : http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000697/WC500058505.pdf	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 89.7 % % of experts rating items useful or very useful: 92.3 %

OBESITY			
PROPER USE OF DRUGS IN CASE OF OBESITY			
143 Other	**Rational**	Obesity is a risk factor for venous thromboembolism.	
	Recommendation	Daily suggested dosing regimen: Use the total body weight to determine the doses to be administered. Prophylactic treatment: increase the dosing regimens by 30% if body mass index (BMI) ≥ 40 kg/m2. Curative treatment: subcutaneous administration (adapt the needle size) of enoxaparin BID and unfractionated heparins TID. Monitor anti-Xa activity for patients with BMI ≥ 40 kg/m2. Fondaparinux recommended dose, in patients over 100 kg with venous thromboembolism: 10 mg QD, administered subcutaneously.	
	References	Nutescu E, et al. Low-Molecular-Weight Heparins in Renal Impairment and Obesity: Available Evidence and Clinical Practice Recommendations Across Medical and Surgical Settings. Ann Pharmacother 2009: http://excellence.acforum.org/sites/default/files/nutescu_dosing%20LMWH%20special%20populations.pdf ACCP 2012: Antithrombotic Therapy and Prevention of Thrombosis (9th Edition): http://journal.publications.chestnet.org/article.aspx?articleID=1159453 ACCP 2008: Prevention of Venous Thromboembolism (8th Edition): http://journal.publications.chestnet.org/data/Journals/CHEST/22073/381S.pdf	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 92.3 % % of experts rating items useful or very useful: 94.9 %
144 Other	**Rational**	Intramuscular (IM), subcutaneous (SC) and cutaneous absorption in obese patients is variable. IM: Frequent intra-lipomatous injection. SC: crossing of the lipophilic layer unpredictable. Cutaneous route: unsuitable transdermal systems.	
	Recommendation	If the IM or SC route must be used, adapt the needle size accordingly.	
	Reference	Cockshott P, et al. Intramuscular or intralipomatous injections. NEJM 1982 [abstract]: http://www.nejm.org/doi/full/10.1056/NEJM198208053070607	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 82.1 % % of experts rating items useful or very useful: 79.5 %
145 Other	**Rational**	Hydrophilic molecules whose kinetic is modified in case of obesity.	
	Recommendations	Monitor plasma concentrations. *Formula to calculate the adjusted weight = ideal weight** + 0.43 x (Total Body Weight - Ideal Weight**). **Ideal weights = (Lorentz formula expressed in kg, used in adults over the age of 18 years measuring between 140 and 220 cm) Women = Waist (cm) – 100 – [(Waist (cm)-150/2.5] Men = Waist (cm) – 100 - [(Waist (cm)-150)/4] Also consider adjusting the dose based on the patient's renal function.	
	Reference	AFSSAPS/ SPILF/ GPIP 2011 : mise au point sur le bon usage des aminosides administrés par voie injectable : gentamicine, tobramycine, nétilmicine, amikacine : http://ansm.sante.fr/var/ansm_site/storage/original/application/3e0d2264e2921c8465d9ad6464e12660.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 92.3 %
146 Other	**Rational**	Molecules whose kinetic is modified in case of obesity.	
	Recommendation	Monitor plasma concentrations.	
	References	ASHSP/ IDSA/ SIDP 2010: Therapeutic Monitoring of Vancomycin in Adult Patients: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2826264/pdf/cbr_31_1_21.pdf Rybak M, et al. Therapeutic monitoring of vancomycin in adult patients: A consensus review of the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, and the Society of Infectious Diseases Pharmacists. Am J Health-Syst Pharm. 2009: http://www.ajhp.org/content/66/1/82.full.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 89.7 %
PHARMACOLOGY AND TOXICOLOGY			
CLINICAL PHARMACOLOGY			
147 OP	**Rational**	Potential allergic reaction.	
	Recommendation	Outline the allergy check in the patient's file and choose a therapeutic alternative in case of	

		allergy.	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 89.7 %
148 OP	**Rational**	Risk of torsade de pointes.	
	Recommendations	Monitor the electrocardiogram in case of necessary use. If long QT syndrome appears in relation to taking the drugs, to an interaction, to an overdose, to the presence of several at-risk drugs, the patient's treatment should be adapted.	
	Remarks	*Non-exhaustive list of drugs that may cause an elongation of the QT interval: some antiarrhythmics (amiodarone, disopyramide, dofetilide, dronedarone, flecainide, ibutilide, procainamide, quinidine, sotalol), some antibiotics (azithromycin, bedaquiline, ciprofloxacin, clarithromycin, erythromycin, levofloxacin, moxifloxacin, norfloxacin, ofloxacin, pentamidine, roxithromycin, spitamycin IV, telithromycin, trimethoprim-sulfamethoxazole), some antineoplastics (arsenic, dabrafenib, eribulin, lapatinib, nilotinib, sunitinib, tamoxifen, vorinostat), some antidepressants (amitriptyline, amoxapine, citalopram, clomipramine, desipramine, doxepin, escitalopram, fluoxetine, imipramine, mirtazapine, nortriptyline, paroxetine, protriptyline, sertraline, trazodone, trimipramine, venlafaxine), some antifungals (fluconazole, itraconazole, ketoconazole, posaconazole, voriconazole), some antimalarials (chloroquine, halofantrine, quinine sulphate), some antivirals (amantadine, atazanavir, foscarnet, nelfinavir, rilpivirine, ritonavir, saquinavir, telaprevir), methadone, neuroleptics (amisulpride, aripiprazole, chlorpromazine, clozapine, cyamemazine, droperidol, fluphenazine, haloperidol, levomepromazine, olanzapine, pimozide, pipamperone, promethazine, quetiapine, risperidone, sertindole, sulpiride, sultopride, tiapride, zuclopenthixol). **Risk factors for elongation of the QTc interval: age > 65 years, female, cardiopathies: heart failure, ischaemia, myocardial hypertrophy, bradycardia, 2nd or 3rd degree intra-ventricular blockage, electrolytic disorders (in particular hypokalaemia and hypomagnesaemia), congenital long QT syndrome.	
	Useful link	Crediblemeds: All QTDrugs: http://www.crediblemeds.org/everyone/composite-list-all-qtdrugs/?rf=All	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 100 % % of experts rating items useful or very useful: 97.4 %
149 DDI	Rational	Risk of serotonin syndrome.	
	Recommendation	Adapt treatments or monitor patients closely.	
	Remark	*Non-exhaustive list of drugs that may increase serotonin concentrations at the SNC: tricyclic antidepressants, some anti-Parkinson medications, antipsychotics, buspirone, codeine, fentanyl, dextromethorphan, SSRIs, SNRIs, monoamine oxidase inhibitors, hypericum, setrons, tramadol, triptans.	
	Reference	Boyer E, et al.The Serotonin Syndrome. NEJM 2005: http://www.nejm.org.gate2.inist.fr/doi/pdf/10.1056/NEJMra041867	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 87.2 %
150 OP	**Rational**	Risk of exacerbation of the extrapyramidal syndrome.	
	Recommendation	Stop the treatments or decrease the dosing regimens if possible (stopping treatments allows a differential diagnosis and a decrease or elimination of symptomatology).	
	Remark	*Non-exhaustive list of drugs that may induce an extrapyramidal syndrome: amphotericin B, some antiarrhythmics (amiodarone, procaine), some antidepressants (selective serotonin reuptake inhibitors: fluoxetine, sertraline, monoamine oxidase inhibitors: moclobemide, phenelzine), some anti-emetics: alizapride, metoclopramide, prochlorperazine, promethazine, certain anti-epileptics (levetiracetam phenytoin, valproate), standard antipsychotics (amisulpride, flupentixol, fluphenazine, haloperidol, levomepromazine, pimozide, prochlorperazine, promazine, sulpiride, thioridazine, thioxantenes, zuclopenthixol), non-standard antipsychotics (aripiprazole, clozapine, olanzapine, quetiapine, risperidone, ziprasidone), some antivirals (aciclovir, antiretrovirals, vidarabine), alpha-methyldopa, cinnarizine, flunarizine, certain hormones (epinephrine (adrenaline), levothyroxine sodium, medroxyprogesterone, some immunosuppressants (cyclosporine, tacrolimus), calcium	

		inhibitors (diltiazem, verapamil), devastatingly, lithium, reserpine, tetrabenazine.	
	Reference	Lopez-Sendon J, et al. Drug-induced parkinsonism. Expert Opin. Drug Saf. 2013 [abstract]: http://informahealthcare.com/doi/abs/10.1517/14740338.2013.787065	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 100 % % of experts rating items useful or very useful: 89.7 %
151 OP	**Rational**	Risk of acute haemolysis.	
	Recommendations	Substances may be contraindicated, not advised (except under particular situations) due to observed cases of acute haemolysis, not advised (except in specific situations) because they belong to an at-risk pharmacological class, or potential risk of haemolysis, or not advised at a high dosing regimen, verification on a list* is advised. Favour a therapeutic alternative if one is available.	
	Useful link	*ANSM Médicaments et déficit en Glucose-6-Phosphate Déshydrogénase (G6PD) Classement des médicaments par substance active: http://ansm.sante.fr/S-informer/Points-d-information-Points-d-information/Medicament-et-deficit-en-G6PD-l-ANSM-actualise-le-referentiel-Point-d-Information	
	Reference	ANSM 2014 : Médicaments et déficit en Glucose-6-Phosphate Déshydrogénase (G6PD). Classement des médicaments par substance active : http://www.vigifavisme.com/wp-content/uploads/2014/06/liste_substances2014.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 100 % % of experts rating items useful or very useful: 89.7 %
152 UP	**Rational**	Allow to treat induced hematotoxicities.	
	Recommendation	Adapt the dosing regimen of the folinic acid based on the indication and the antagonist in question.	
	Remark	*Non-exhaustive list of folic acid antagonistic treatment: methotrexate, pyrimethamine, trimethoprim, trimetrexate, salazopyrin.	
	Reference	Résumé des caractéristiques de l'acide folinique (monographie) : http://agence-prd.ansm.sante.fr/php/ecodex/rcp/R0226090.htm	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 92.3 %
	DRUG-DRUG INTERACTIONS		
153 DDI	**Rational**	Potential DDI.	
	Useful link	HUG 2014: Drug interactions, cytochromes P450 and P-glycoprotein (Pgp): http://www.hug-ge.ch/sites/interhug/files/structures/pharmacologie_et_toxicologie_cliniques/documents/interactions_medicamenteuses_et_cyp450.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 94.9 % % of experts rating items useful or very useful: 92.3 %
154 DDI	**Rational**	Upon stopping an inducer treatment, enzymatic activity gradually returns to normal (in approximately 2 weeks). Gradual lifting of interaction.	
	Recommendation	Adapt the dosing regimens.	
	Useful link	**HUG 2014: Drug interactions, cytochromes P450 and P-glycoprotein (Pgp): http://www.hug-ge.ch/sites/interhug/files/structures/pharmacologie_et_toxicologie_cliniques/documents/interactions_medicamenteuses_et_cyp450.pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: useful	% of experts agree or strongly agree: 89.7 % % of experts rating items useful or very useful: 92.3 %
	TRANSPLANTS		
155 UP	**Rational**	Risk of destabilisation of the immunosuppression, of rejection or of toxicity. Prevention of side effects related to immunosuppressant overdose or rejection and deterioration of the grft's functions in case of underdosing.	
	Recommendations	**Monitoring of plasma or blood concentrations proposed: For cyclosporine: C0 and/or C2h after the dose. For tacrolimus and mTOR inhibitors (everolimus, sirolimus): C0. For mycophenolate mofetil: Area under the curve.	
	Remarks	* Typical immunosuppressive therapy: In cardiac and pulmonary grafts: immunosuppressive tri-therapy, often with higher	

		immunosuppression levels in the pulmonary graft. In renal grafts: bi- or tri-therapy. In hepatic grafts: bi- or tri-therapy, sometimes reduced by a specialist to monotherapy in chronic phase. Typical immunosuppressive therapy most often comprises an anti-calcineurin, an anti-metabolite +/- corticosteroids.
	References	ACCP 2011: Pulmonary Complications of Lung Transplantation: http://journal.publications.chestnet.org/data/Journals/CHEST/22093/101048.pdf ISHLT 2010: Guidelines for the care of heart transplant recipients: http://download.journals.elsevierhealth.com/pdfs/journals/1053-2498/PIIS105324981000358X.pdf AST/ ASTS 2009: Long-term Management of the Liver Transplant Patient: Recommendations for the Primary Care Doctor: http://onlinelibrary.wiley.com/doi/10.1111/j.1600-6143.2009.02733.x/pdf KDIGO 2009: Clinical practice guideline for the care of kidney transplant recipients. American Journal of Transplantation: http://www.kdigo.org/pdf/KDIGO%20Txp%20GL%20publ%20version.pdf
	Strength of recommendation	Experts median agreement: strongly agree — % of experts agree or strongly agree: 100 % Median usefulness rating: very useful — % of experts rating items useful or very useful: 94.9 %
156 DDI	**Rational**	Prevention of side effects related to immunosuppressive overdose or rejection and deterioration of the grft's functions in case of underdosing.
	Recommendations	* Monitoring of plasma or blood concentrations proposed: For cyclosporine: C0 and/or C2h after the dose. For tacrolimus and mTOR inhibitors (everolimus, sirolimus): C0. For mycophenolate mofetil: area under the curve.
	Useful link	HUG 2014: Drug interactions, cytochromes P450 and P-glycoprotein (Pgp): http://www.hug-ge.ch/sites/interhug/files/structures/pharmacologie_et_toxicologie_cliniques/documents/interactions_medicamenteuses_et_cyp450.pdf
	References	ISHLT 2010: Guidelines for the care of heart transplant recipients: http://download.journals.elsevierhealth.com/pdfs/journals/1053-2498/PIIS105324981000358X.pdf KDIGO 2009: Clinical practice guideline for the care of kidney transplant recipients. American Journal of Transplantation: http://www.kdigo.org/pdf/KDIGO%20Txp%20GL%20publ%20version.pdf
	Strength of recommendation	Experts median agreement: strongly agree — % of experts agree or strongly agree: 100 % Median usefulness rating: very useful — % of experts rating items useful or very useful: 94.9 %
	VACCINATIONS	
157 UP	**Rational**	Increased risk of complications in case of infection, superinfections or decompensations of the underlying disease.
	Recommendation	Offer an annual flu vaccine (preferably between October and December).
	Remarks	*Non-exhaustive list of patients with a high risk of complications: patients with chronic respiratory disease (asthma, COPD, mucoviscidosis, etc.), a chronic cardiac pathology, CKD, diabetes, hepatic failure, patients receiving treatment with DMARD, biologic treatments, immunosuppressive treatment, age > 65 years, frequent travellers. In immunocompromised patients, use only inactive vaccines.
	References	Vaccine recommendations are constantly changing; they should therefore be consulted regularly. Infovac Suisse : http://www.infovac.ch/index.php?Itemid=95 Calendrier vaccinal et recommendations vaccinales 2013 France : http://www.sante.gouv.fr/IMG/pdf/Calendrier_vaccinal_detaille_2013_ministere_Affaires_sociales_et_Sante-_pdf.pdf Vacc.info Belgique : http://www.vaccination-info.be/ Protocole d'immunisation du Québec : http://publications.msss.gouv.qc.ca/acrobat/f/documentation/piq/piq_complet.pdf KDIGO 2012: Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease: http://www.kdigo.org/clinical_practice_guidelines/pdf/CKD/KDIGO_2012_CKD_GL.pdf ACCR 2012: Use of Disease-Modifying Antirheumatic Drugs and Biologic Agents in the Treatment of Rheumatoid Arthritis: http://onlinelibrary.wiley.com/doi/10.1002/acr.21641/pdf Jacobs J, et al. Biometric fingerprinting for visa application: device and procedure are risk factors for infection transmission. J Travel Med 2008: http://onlinelibrary.wiley.com/doi/10.1111/j.1708-8305.2008.00232.x/pdf
	Strength of recommendation	Experts median agreement: strongly agree — % of experts agree or strongly agree: 100 % Median usefulness rating: very useful — % of experts rating items useful or very useful: 92.3 %
158 UP	**Rational**	Vulnerability to pneumococcal infection, risk of invasive infection.
	Recommendation	Vaccine regimen according to the national vaccine plan, optionally offer new vaccine every 5 years in immunocompromised patients.

	Remark	*Non exhaustive list of patients at high risk for invasive pneumococcal infection: Patients with chronic respiratory disease (asthma, COPD, mucoviscidosis, etc.), chronic cardiac pathology, CKD, diabetes, hepatic failure, patients receiving treatment with DMARD, biologic treatment, immunosuppressive treatment (ex: azathioprine, 6-mercaptopurine, methotrexate), splenectomised patients or patients with functional asplenia.	
	References	Vaccine recommendations are constantly changing; they should therefore be consulted regularly. Infovac Suisse : http://www.infovac.ch/index.php?Itemid=95 Calendrier vaccinal et recommendations vaccinales 2013 France : http://www.sante.gouv.fr/IMG/pdf/Calendrier_vaccinal_detaille_2013_ministere_Affaires_sociales_et_Sante-_pdf.pdf Vacc.info Belgique : http://www.vaccination-info.be/ Protocole d'immunisation du Québec : http://publications.msss.gouv.qc.ca/acrobat/f/documentation/piq/piq_complet.pdf CDC/ ACIP 2012: Use of 13-Valent Pneumococcal Conjugate Vaccine and 23-Valent Pneumococcal Polysaccharide Vaccine for Adults with Immunocompromising Conditions: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6140a4.htm KDIGO 2012: Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease: http://www.kdigo.org/clinical_practice_guidelines/pdf/CKD/KDIGO_2012_CKD_GL.pdf ACCR 2012: Use of Disease-Modifying Antirheumatic Drugs and Biologic Agents in the Treatment of Rheumatoid Arthritis: http://onlinelibrary.wiley.com/doi/10.1002/acr.21641/pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 94.9 %
159 OP	**Rational**	Safety and efficacy of these vaccines are not established. Unfavourable risk/benefit ratio.	
	Remarks	*Non-exhaustive list of affected patients: graft patients, receiving immunosuppressants (eg: azathioprine, 6-mercatopurine, methotrexate), DMARD, bi-therapy, patients with a CD4 T cell count < 200/mm3. *Non-exhaustive list of live attenuated vaccines: combined measles-mumps-rubella vaccine, rotavirus vaccine, chickenpox vaccine, yellow fever vaccine, oral poliomyelitis vaccine, tuberculosis vaccine.	
	References	IDSA 2013: Clinical Practice Guideline for Vaccination of the Immunocompromised Host: http://cid.oxfordjournals.org/content/early/2013/11/26/cid.cit684.full.pdf Danzinger-Isakov L, et al. Guidelines for Vaccination of Solid Organ Transplant Candidates and Recipients. Am J Transplant 2009: http://onlinelibrary.wiley.com/doi/10.1111/j.1600-6143.2009.02917.x/pdf	
	Strength of recommendation	Experts median agreement: strongly agree Median usefulness rating: very useful	% of experts agree or strongly agree: 97.4 % % of experts rating items useful or very useful: 100 %
160 UP	**Rational**	Individual protection against infections and collective benefit.	
	Recommendations	*An adult patient should be vaccinated against diphtheria, tetanus, whooping cough, Haemophilus Influenzae type B, poliomyelitis, measles, mumps, and rubella. Depending on the infantile, family infection status, profession and travel, other vaccines may be recommended: hepatitis A and B, yellow fever, typhoid vaccines, etc.	
	References	Vaccine recommendations are constantly changing; they should therefore be consulted regularly. Infovac Suisse : http://www.infovac.ch/index.php?Itemid=95 Calendrier vaccinal et recommendations vaccinales 2013 France : http://www.sante.gouv.fr/IMG/pdf/Calendrier_vaccinal_detaille_2013_ministere_Affaires_sociales_et_Sante-_pdf.pdf Vacc.info Belgique : http://www.vaccination-info.be/ Protocole d'immunisation du Québec : http://publications.msss.gouv.qc.ca/acrobat/f/documentation/piq/piq_complet.pdf CDC/ ACIP 2012: Use of 13-Valent Pneumococcal Conjugate Vaccine and 23-Valent Pneumococcal Polysaccharide Vaccine for Adults with Immunocompromising Conditions: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6140a4.htm	
	Strength of recommendation	Experts median agreement: agree Median usefulness rating: useful	% of experts agree or strongly agree: 89.7 % % of experts rating items useful or very useful: 82.1 %

Colour code of PIM: green stands for under-prescriptions, red for over-prescriptions, amber for interactions and grey for other kind of PIM

Abbreviations: ACEI: Angiotensin conversion enzyme inhibitors, ACTH: Adrenocorticotropic hormone, AF: atrial fibrillation, ARB: angiotensin II receptor antagonists, ARV: antiretroviral therapy, BMI: body mass index, BP: blood pressure, BPH: benign prostatic hyperplasia, BZD: benzodiazepine, C0: trough plasma concentration (before the next dose is administered), C2h: plasma concentration 2h after drug administration, CIWA-Ar: Clinical Index Withdrawal Assessment-Revised, CNS: central nervous system, COPD: chronic obstructive pulmonary disorder, COX2-inhibitor: cyclooxygenase 2 inhibitor, CrCl: creatinine clearance, CKD: chronic kidney disease, CS: corticosteroids, ICS: inhaled corticosteroids, CYP: cytochrome P450, dBP: diastolic blood pressure, DDI: drug-drug interaction, DMARD: Disease-Modifying Antirheumatic Drug, DOAC: direct-acting

oral anticoagulant, DM: diabete mellitus, T1DM: type 1 diabete mellitus, T2DM: type 2 diabete mellitus, DVT: deep vein thrombosis, ER: extended-release, FEV1: forced expiratory volume in one second, G6PD: glucose-6-phosphate dehydrogenase, Hb: haemoglobin, HBA1c: glycated haemoglobin, HBP: high blood pressure, HBV: hepatitis B virus, HCV: hepatitis C virus, HDL-c: high-density lipoprotein cholesterol, HEB: haematoencephalic barrier, HF: heart failure, HIV: human immunodeficiency virus, IM: Intramuscular, INR: International Normalized Ratio, IR: immediate-release, IV: intravenous, LA: long acting, LDL-c: low-density lipoprotein cholesterol, LVEF: left ventricular ejection fraction, MAOI: Monoamine oxidase inhibitor, mTOR: mammalian target of rapamycin, MTX: methotrexate, NSAIDs: nonsteroidal anti-inflammatory drugs, OP: over-prescription, OR: oral route, PE: pulmonry embolism, Pgp: P-glycoprotein, PPIs: proton pump inhibitors, RA: rheumatoid arthritis, sBP: systolic blood pressure, SC: subcutaneous route, SNRI: serotonin-norepinephrine reuptake inhibitor, SR: sustained-release, SSRI: selective serotonin reuptake inhibitors, STEMI: ST-segment elevation myocardial infarction, T3: triiodothyronine, T4: thyroxine, TIA: transient ischaemic attack, TNF: Tumor Necrosis Factor, TSH: Thydroïd Stimulating Hormone, UP: under-prescription, VAS: visual analogue scale, Vitamin B1: thiamine, Vitamin B6: pyridoxine, Vitamin PP: nicotinamide, VKA: vitamin K antagonist, VTE: venus thromboembolism, WHO: World Health Organization.