

# The EURO-FORTA (Fit fOR The Aged) List Version 2: Consensus Validation of a Clinical Tool for Improved Pharmacotherapy in Older Adults

Drugs & Aging

Farhad Pazan<sup>1</sup>, Christel Weiss<sup>2</sup>, Martin Wehling<sup>1</sup> \*FORTA

## Affiliations:

- 1 Clinical Pharmacology Mannheim, Medical Faculty Mannheim, Heidelberg University, Theodor-Kutzer-Ufer 1-3, 68167 Mannheim, Germany
- 2 Department of Medical Statistics, Biomathematics and Information Processing, Medical Faculty Mannheim, Heidelberg University, 68167 Mannheim, Germany

## Corresponding author:

Dr. Farhad Pazan

e-mail: [farhad.pazan@medma.uni-heidelberg.de](mailto:farhad.pazan@medma.uni-heidelberg.de)

Phone: +49 621 383 9629

**The F O R T A List**  
**“Fit for The Aged“**  
**Expert Consensus Validation**  
**France**

<b>F O R T A</b>			
A	B	C	D

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Farhad Pazan<sup>1</sup>, Christel Weiß<sup>2</sup>, Martin Wehling<sup>1</sup>

<sup>1</sup>Institute of Clinical Pharmacology, Center for Geriatric Pharmacology, Medical Faculty of the University of Heidelberg in Mannheim

<sup>2</sup>Department of Medical Statistics, Biomathematics and Information Processing, Medical Faculty of the University of Heidelberg in Mannheim

## **Disclaimer**

While building on an international foundation of medical evidence and experience for the medications listed, including already existing “negative lists” and classification systems, this FORTA List primarily reflects prescribing tendencies in France. The FORTA labels themselves, being evidence-based, may possibly be subject to change during the course of further consensus evaluation procedures, depending on the state of evidence and clinical experience for a given substance<sup>5</sup>. Meanwhile, the FORTA principle has been validated in a randomized clinical trial (VALFORTA) showing a large improvement of medication quality and amelioration of clinical parameters<sup>6</sup>.

With the goal of creating a user-friendly clinical tool, a summary of relevant comments is given directly in the FORTA List, drawing on the Delphi experts’ extensive clinical experience. This is however by no means comprehensive and does not necessarily refer to specific evidence or sources. Therefore, the authors’ selection of suggestions, comments and warnings may be subjective<sup>5</sup>. ‘No comment’ reflects the absence of noteworthy or relevant words of information or caution within the context of the expert evaluation. All information herein is believed to be true and accurate. Neither the authors nor the University of Heidelberg or affiliated institutions, as the publishers of this list, can accept legal responsibility for any errors or omissions made in the contents of this list<sup>5</sup>.

We welcome all comments and criticism which may contribute to the quality, safety and usability of the FORTA List in daily clinical practice.

## **The FORTA Concept: expert panel for the FORTA classification system**

### **FORTA Expert Review Panel**

The following 3 colleagues, representing **France**, provided their expertise for purposes of evaluating the proposed FORTA List. They received no honoraria in connection with this project. All panel members contributed actively to the development of the content of the FORTA List.

### **Expert Panel Members and their affiliations**

**Cedric Annweiler:** Department of Neuroscience and Memory Clinic, Division of Geriatric Medicine, Angers University Hospital, 49933 Angers cedex 9

**Dominique Somme:** Chef de pôle Anesthésie, SAMU, Urgences, Réanimations, Médecine Interne et Gériatrie, Chef de service de Gériatrie, UFR Médecine, Université de Rennes 1, UMR 6051 ARENES, Hôpital Pontchaillou, 2 rue Henri Le Guilloux, 35033 Rennes cedex 9

**Mounir Rhalimi:** Service Pharmacie, Centre Hospitalier Bertinot Juel, 34 bis rue Pierre Budin, 60240 Chaumont en Vexin

## F O R T A – Physician’s guide<sup>1,2,5,7</sup>

1. FORTA is evidence-based + real-life-oriented (factors such as compliance issues, age-dependent tolerance and frequency of relative contraindications are considered).
2. Classifications are indication (or diagnosis)-dependent: a medication can receive different FORTA classifications based on differing indications.
3. Contraindications always take precedence over the FORTA-classification (for example, even Class A medications may not be given if allergies are present).
4. FORTA is designed to be a quick and user-friendly clinical tool to aid in the pharmacotherapy of older patients\*. The system is not intended to take the place of individual therapeutic considerations or decisions. As with any simplified model, it does allow for exceptions.

## F O R T A – Classification System A-D<sup>1,2,3,4,7</sup>

<p><b>Class A</b></p> <p>= Indispensable drug, clear-cut benefit in terms of efficacy/safety ratio proven in elderly patients for a given indication</p>	<p><b>Class B</b></p> <p>= Drugs with proven or obvious efficacy in the elderly, but limited extent of effect and/or safety concerns</p>	<p><b>Class C</b></p> <p>= Drugs with questionable efficacy/safety profiles in the elderly which should be avoided or omitted in the presence of too many drugs, absence of benefits or emerging side effects; explore alternatives</p>	<p><b>Class D</b></p> <p>= Avoid if at all possible in the elderly, omit first and use alternative substances</p>
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\* FORTA aims at older patients, has been validated primarily for patients 65 years of age or older with significant comorbidities (3 or more diagnoses and drugs) and should be used in all patients 80 years of age or older will. These target groups are mostly defined as geriatric patients.

# The F O R T A List<sup>3,4,5</sup>

## Delphi Expert Consensus Validation

F	O	R	T	A
A	B	C	D	

**Classification of the most frequently used long-term medications†  
for the pharmacotherapy of older patients**

**by indication/diagnosis, ranked according to FORTA classification**

**Newly proposed drugs are mentioned under the respective diagnosis and marked by \*; they are listed in greater detail in the second part.**

**(† long-term defined as > 4 weeks. Please note that the distinction between acute/chronic may not always be clear-cut; exceptions are noted)**

<b>ARTERIAL HYPERTENSION</b>	<b>FORTA Class</b> (original FORTA class in parentheses if different from consensus results)	<b>Nr. of raters</b>	<b>Consensus coefficient, Round 1 (cutoff 0.800)</b>	<b>Expert ratings on a numerical scale: A=1, B=2, C=3, D=4</b>  <b>Mean; Mode</b>	<b>Selection of pertinent comments given by participating experts during the consensus procedure</b>
<b>Substance/Group</b>					
<b>Renin-Angiotensin system inhibitors</b>		3	1.000	1.0; 1	
<b>ACE inhibitors</b>	<b>A</b>				
<b>Angiotensin receptor antagonists</b>	<b>B</b>	3	0.833	1.7; 2	<b>Note:</b> Theoretically less side-effects
<b>Long-acting calcium antagonists, dihydropyridine type, for example amlodipine</b>	<b>A</b>	3	1.000	1.0; 1	
<b>Betablockers außer atenolol</b>	<b>(C)</b> <b>B</b>	3	0.667	2.3; 2	
<b>Atenolol</b>	<b>(D)</b> <b>C</b>	3	0.667	3.3; 4	
<b>Diuretics except indapamid</b>	<b>B</b>	3	1.000	2.0; 2	
<b>Indapamid</b>	<b>(A)</b> <b>B</b>	3	0.667	1.7; 2	
<b>Alpha blockers</b>	<b>C</b>	3	0.833	3.3; 3	<b>Note:</b> Not well studied in very old patients in term of benefit as well as risks
<b>Spirolactone</b>	<b>C</b>	3	1.000	3.0; 3	
<b>Moxonidine</b>	<b>C</b>	2	1.000	3.0; 3	
<b>Aliskiren</b>	<b>(C)</b> <b>D</b>	2	0.750	3.5; -	

Urapidil	C	3	1.000	3.0; 3	
Clonidine	D	3	0.833	3.7; 4	
Minoxidil	D	1	1.000	4.0; 4	
Calcium antagonists, verapamil type	D	3	1.000	4.0; 4	
Methyropa	D	3	1.000	4.0; 4	
Rilmenidine	C	3	1.000	3.0; 3	
<b>CARDIAC INSUFFICIENCY</b>	<b>FORTA Class</b> (original FORTA class in parentheses if different from consensus results)	<b>Nr. of raters</b>	<b>Consensus coefficient, Round 1 (cutoff 0.800)</b>	<b>Expert ratings on a numerical scale: A=1, B=2, C=3, D=4</b>  <b>Mean; Mode</b>	<b>Selection of pertinent comments given by participating experts during the consensus procedure</b>
<b>Substance/Group</b>					
<b>Renin-angiotensin system inhibitors</b>		3	1.000	1.0; 1	
<b>ACE inhibitors</b>	<b>A</b>				
<b>Angiotensin receptor antagonists</b>	<b>A</b>	3	1.000	1.0; 1	
<b>Betablockers (metoprolol, carvedilol, bisoprolol)</b>	<b>A</b>	3	1.00000	1.0; 1	
<b>Diuretics</b>	<b>A</b>	3	1.000	1.0; 1	
<b>Gliflozins (SGLT2 inhibitors) only those substances which have been approved for this indication (dapgliflozine)</b>	<b>B</b>	2	0.500	2.0; -	
<b>Spironolactone</b>	<b>B</b>	3	1.000	2.0; 2	

<b>Digitalis preparations</b>	<b>C</b>	3	1.000	3.0; 3	
<b>Ivabradine</b>	<b>C</b>	3	0.833	3.3; 3	
<b>Nitroglycerin (Trinitrine)</b>	<b>C</b>	3	0.833	3.3; 3	<b>Note:</b> Too many orthostatic hypotension and falls
<b>Iron substitution in patients with iron deficiency</b>	<b>A</b>	3	0.833	1.3; 1	

<b>ACUTE CORONARY SYNDROME</b>	<b>FORTA Class</b> (original FORTA class in parentheses if different from consensus results)	<b>Nr. of raters</b>	<b>Consensus coefficient, Round 1 (cutoff 0.800)</b>	<b>Expert ratings on a numerical scale: A=1, B=2, C=3, D=4</b>  <b>Mean; Mode</b>	<b>Selection of pertinent comments given by participating experts during the consensus procedure</b>
<b>Substance/Group</b>					
<b>Renin-Angiotensin-System-Blocker: ACE-Hemmer</b>	<b>A</b>	3	1.000	1.0; 1	
<b>Acetylsalicylic acid</b>	<b>A</b>	3	1.000	1.0; 1	
<b>Unfractionated heparin and low molecular weight heparin</b>	<b>A</b>	3	1.000	1.0; 1	
<b>Frequency-lowering betablockers, e.g. metoprolol or bisoprolol</b>	<b>A</b>	3	1.000	1.0; 1	
<b>Atorvastatin</b>	<b>A</b>	3	1.000	1.0; 1	
<b>Nitroglycerin spray, single use, acute as on-demand medication</b>	<b>A</b>	3	0.833	1.3; 1	<b>Note:</b> Only for symptomatic reason and if the pain persists on treatment
<b>Clopidogrel, prasugrel</b>	<b>B</b> <b>B for stent (A)</b>	2 2	1.000 0.750	2.0; 2 1.5; -	
<b>Thrombolytics, especially rTPA (recombinant tissue-type plasminogen activator)</b>	<b>B</b>	3	1.000	2.0; 2	

Nitrates, long-term	C	3	0.833	2.7; 3	
Gp IIb/IIIa antagonists (glycoprotein 2b/3a inhibitors)	C	3	1.000	3.0; 3	
Antalgic	A	3	1.000	1.0; 1	
Other statins	A	3	0.833	1.3; 1	
Diltiazem, Nifedipine, Verapamil	B	3	0.833	2.3; 2	
<b>CHRONIC THERAPY FOLLOWING MYOCARDIAL INFARCTION</b>	<b>FORTA Class</b> (original FORTA class in parentheses if different from consensus results)	<b>Nr. of raters</b>	<b>Consensus coefficient, Round 1 (cutoff 0.800)</b>	<b>Expert ratings on a numerical scale: A=1, B=2, C=3, D=4</b>  <b>Mean; Mode</b>	<b>Selection of pertinent comments given by participating experts during the consensus procedure</b>
<b>Substance/group</b>					
Renin angiotensin system blockers ACE Inhibitors	A	3	1.000	1.0; 1	
Acetylsalicylic acid (100 mg/d)	A	3	1.000	1.0; 1	
Frequency-lowering beta blockers up to 3 years	A	3	1.000	1.0; 1	
Frequency-lowering beta blockers longer than 3 years	C	3	1.000	3.0; 3	
Nitroglycerin spray, single use as on-demand medication	B (A)	3	0.667	2.0; 1	<b>Note:</b> Too many falls
Influenza vaccination	See				

(inactivated subunit vaccines)/pneumococcal immunizations	vaccinations				
Statins	A	3	1.000	1.0; 1	
	B for very old (>85 years) patients	1	1.000	2.0; 2	
Clopidogrel (12 months after acute coronary syndrome)	A with aspirin intolerance	2	1.000	1.0; 1	
Nitrates, long-term	D (C)	2	0.750	3.5; -	
Fibrates	C	3	1.000	3.0; 3	
Ezetimibe	D (C)	2	0.750	3.5; -	<b>Note:</b> Badly studied in very old patients
Amiodarone	C	3	1.000	3.0; 3	
All other class-I-III antiarrhythmic agents	D	3	1.000	4.0; 4	
Dihydropyridine antagonists (if no hypertension)	D	3	1.000	4.0; 4	

STROKE	FORTA Class (original FORTA class in parentheses if different from consensus results)	Nr. of raters	Consensus coefficient, Round 1 (cutoff 0.800)	Expert ratings on a numerical scale: A=1, B=2, C=3, D=4  Mean; Mode	Selection of pertinent comments given by participating experts during the consensus procedure
Substance/Group					
Acetylsalicylic acid	A	3	1.000	1.0; 1	
Atorvastatin	A	3	1.000	1.0; 1	

rTPA (recombinant tissue-type plasminogen activator); only for emergency use	A	2	1.000	1.0; 1	
Simvastatin	A	3	0.833	1.3; 1	<b>Note:</b> We prefer hepatic elimination- statins as Atorvastatin
Anticoagulants including new oral anticoagulants	A	3	1.000	1.0; 1	
Clopidogrel	B	3	1.000	2.0; 2	
Dipyridamole plus acetylsalicylic acid	C	3	1.000	3.0; 3	
Renin angiotensin system blockers, ACE Inhibitors	A	3	1.000	1.0; 1	

ATRIAL FIBRILLATION	FORTA Class (original FORTA class in parentheses if different from consensus results)	Nr. of raters	Consensus coefficient, Round 1 (cutoff 0.800)	Expert ratings on a numerical scale: A=1, B=2, C=3, D=4  Mean; Mode	Selection of pertinent comments given by participating experts during the consensus procedure
Substance/group					
Frequency-lowering betablockers	A	3	1.000	1.0; 1	
Digoxin, digitoxin	C	3	1.000	3.0; 3	
New Oral Anticoagulants (NOACs)	A (B)	3	0.500	1.0; 1	

Except dabigatran	C	3	1.000	3.0; 3	
Oral anticoagulation by vitamin-K-antagonists (e.g. phenprocoumon, warfarin)	B	3	0.833	1.7; 2	
Alternative: low molecular weight heparin	D	2	0.750	3.5; -	<b>Note:</b> When oral tract is unavailable
Diltiazem, verapamil	C	3	1.000	3.0; 3	
Class III antiarrhythmic agent amiodarone	C	3	1.000	3.0; 3	
All other class I or III antiarrhythmic agents	D	3	1.000	4.0; 4	
Acetylsalicylic acid (100 mg/d)	D (C)	3	0.667	3.7; 4	
Class III antiarrhythmic agent dronedarone	D	3	1.000	4.0; 4	

<b>CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)</b>	<b>FORTA Class</b> (original FORTA class in parentheses if different from consensus results)	<b>Nr. of raters</b>	<b>Consensus coefficient, Round 1 (cutoff 0.800)</b>	<b>Expert ratings on a numerical scale: A=1, B=2, C=3, D=4</b>  <b>Mean; Mode</b>	<b>Selection of pertinent comments given by participating experts during the consensus procedure</b>
<b>Substance/group</b>					
<b>Inhalative long-acting parasympatholytic agents</b>	<b>A</b>	3	0.833	1.3; 3	<b>Note:</b> Not very well studied in geriatric patients highly anticholinergic
<b>Systemic glucocorticoids, acute, short-term use in cases of exacerbation</b>	<b>A</b>	3	1.000	1.0; 1	
<b>Antibiotics (acute) in cases of exacerbation, after calculated selection and, if necessary, according to antibiogram</b>	<b>B (A)</b>	2	0.750	1.5; -	
<b>Long-term administration of oxygen</b>	<b>A</b>	3	0.833	1.3; 1	
<b>Annual influenza immunizations</b>	<b>See vaccinations</b>				
<b>Pneumococcal immunizations for persons ≥ 65 years</b>	<b>See vaccinations</b>				
<b>Inhalative beta 2 mimetic agents</b>	<b>B</b>	3	1.000	2.0; 2	
<b>Inhalative glucocorticoids</b>	<b>C</b>	3	0.833	2.7; 3	
<b>Theophylline</b>	<b>D</b>	3	1.000	4.0; 4	

Mucolytic agents, e.g, acetyl cysteine, bromhexine	D	3	1.000	4.0; 4	
Roflumilast	D	1	1.000	4.0; 4	Note: Never used
Systemic glucocorticoids, chronic use	D	3	1.000	4.0; 4	
Antitussives: opioid A., e.g. codein; non-opioid A., e.g. butamirate	D	3	1.000	4.0; 4	
<b>OSTEOPOROSIS</b>	<b>FORTA Class</b> (original FORTA class in parentheses if different from consensus results)	<b>Nr. of raters</b>	<b>Consensus coefficient, Round 1 (cutoff 0.800)</b>	<b>Expert ratings on a numerical scale: A=1, B=2, C=3, D=4</b>  <b>Mean; Mode</b>	<b>Selection of pertinent comments given by participating experts during the consensus procedure</b>
Substance/Group					
Calcium and vitamin D supplements (as prophylaxis for persons ≥ 65 years)	(A) B	1	0.500	2.0; 2	
Parenteral bisphosphonates (e.g. ibandronate, IV every 3 months)	B	2	0.750	1.5; -	
Raloxifene for women	B	3	0.833	2.3; 2	
Denosumab	B	3	1.000	2.0; 2	
Bisphosphonates, oral	B	2	1.000	2.0; 2	
Teriparatide	C	3	0.833	2.7; 3	
Alfacalcidol	C	3	1.000	3.0; 3	

Parathormone	C	3	1.000	3.0; 3	
Strontium ranelate	D	3	1.000	4.0; 4	
Nandrolone decanoate	D	3	1.000	4.0; 4	
Fluoride	D	3	1.000	4.0; 4	
Hormone replacement therapy (HRT): estrogen, except for perimenopausal)	D	3	1.000	4.0; 4	
<b>TYPE II DIABETES MELLITUS</b>	<b>FORTA Class</b> (original FORTA class in parentheses if different from consensus results)	<b>Nr. of raters</b>	<b>Consensus coefficient, Round 1 (cutoff 0.800)</b>	<b>Expert ratings on a numerical scale: A=1, B=2, C=3, D=4</b>  <b>Mean; Mode</b>	<b>Selection of pertinent comments given by participating experts during the consensus procedure</b>
<b>Substance/group</b>					
DPP4 (Dipeptidylpeptidase) Inhibitors	B	3	1.000	2.0; 2	
Insulin and insulin analogs (if absolutely necessary)	A	3	1.000	1.0; 1	
Metformin	A	3	1.000	1.0; 1	
GLP1 (Glucagon-Like Peptide-1) analogs	B	3	1.000	2.0; 2	
Acarbose	C	3	1.000	3.0; 3	
3rd generation sulfonylureas (for example, glimepiride)	C	3	1.000	3.0; 3	
Glinides (for example, nateglinide)	C	3	1.000	3.0; 3	
PPAR-γ Ligands (Peroxisomal Proliferator-Activated Receptor gamma)		3	1.000	4.0; 4	
Pioglitazone	D				

Rosiglitazone	D	3	1.000	4.0; 4	
SGLT-2 inhibitors/gliflozins	D	3	1.000	4.0; 4	
1st generation sulfonylureas (for example, glibenclamide)	D	3	0.833	3.7; 4	
<b>DEMENTIA</b>	<b>FORTA Class</b> (original FORTA class in parentheses if different from consensus results)	<b>Nr. of raters</b>	<b>Consensus coefficient, Round 1 (cutoff 0.800)</b>	<b>Expert ratings on a numerical scale: A=1, B=2, C=3, D=4</b>  <b>Mean; Mode</b>	<b>Selection of pertinent comments given by participating experts during the consensus procedure</b>
<b>Substance/group</b>					
Acetylcholinesterase inhibitors e.g. donepezil, galantamine, rivastigmine (Only if indicated for the present stage of the disease)	(B) C	3	0.500	3.0; -	
Memantine	B	3	0.500	2.3; -	
Ginkgo biloba	D	3	1.000	4.0; 4	
Statins	D	3	1.000	4.0; 4	
Selegiline	D	3	1.000	4.0; 4	
Nimodipine	D	3	1.000	4.0; 4	
Ergoline derivatives	D	3	1.000	4.0; 4	
Piracetam	D	3	1.000	4.0; 4	
Pyritinol	D	3	1.000	4.0; 4	
Antioxidants: Vitamin E, selenium, vitamin C	D	3	1.000	4.0; 4	

Phytherapeutic agents, e.g. ginseng	D	3	1.000	4.0; 4	
Hormone preparations, e.g. DHEA (Dehydroepiandrosterone), testosterone	D	3	1.000	4.0; 4	
Antiphlogistics, e.g. indomethacin	D	3	1.000	4.0; 4	
Desferrioxamine	D	2	1.000	4.0; 4	
Risperidone	C	3	0.667	3.0; -	
<b>BEHAVIORAL AND PSYCHOLOGICAL SYMPTOMS OF DEMENTIA (BPSD)</b>	<b>FORTA Class (original FORTA class in parentheses if different from consensus results)</b>	<b>Nr. of raters</b>	<b>Consensus coefficient, Round 1 (cutoff 0.800)</b>	<b>Expert ratings on a numerical scale: A=1, B=2, C=3, D=4</b>	<b>Selection of pertinent comments given by participating experts during the consensus procedure</b>
				<b>Mean; Mode</b>	
<b>DEPRESSION</b>					
<b>Substance/group</b>					
<b>SSRI (Selective Serotonin Reuptake Inhibitors)</b> Citalopram/escitalopram, sertraline, fluoxetine in the usual dosages	<b>B</b>	3	0.833	1.7; 2	
<b>Mirtazapine (15-45mg/d)</b>	<b>C</b>	3	0.833	2.7; 3	
<b>SNRI (Serotonin-Noradrenalin-Reuptake-Inhibitors)</b> Venlafaxine, duloxetine	<b>C</b>	3	0.833	2.7; 3	
<b>Tricyclics</b>	<b>D</b>	3	1.000	4.0; 4	

BPSD: PARANOIA, HALLUCINATION	FORTA Class (original FORTA class in parentheses if different from consensus results)	Nr. of raters	Consensus coefficient, Round 1 (cutoff 0.800)	Expert ratings on a numerical scale: A=1, B=2, C=3, D=4  Mean; Mode	Selection of pertinent comments given by participating experts during the consensus procedure
<b>Substance/group</b>					
Risperidone (initially 0,5-1 mg/d)	C	3	0.833	2.7; 3	
Melperone (25-150mg/d)	D	2	1.000	4.0; 4	
Quetiapine (25-200 mg/d)	C	3	0.833	3.3; 3	
Aripiprazole (2-15 mg/d)	D	3	0.833	3.7; 4	
Clozapine (10-50 mg/d)	(D) C	3	0.667	3.0; 4	
Haloperidol (initially 0.5 mg/d, max. 3 mg/d)	C	3	0.833	3.3; 3	<b>Note:</b> Not well studied and very frequent side effect
Loxapine	C	3	1.000	3.0; 3	
BPSD: RESTLESSNESS, AGITATION, (AGGRESSIVENESS)	FORTA Class (original FORTA class in parentheses if different from consensus results)	Nr. of raters	Consensus coefficient, Round 1 (cutoff 0.800)	Expert ratings on a numerical scale: A=1, B=2, C=3, D=4  Mean; Mode	Selection of pertinent comments given by participating experts during the consensus procedure
<b>Substance/group</b>					
Trazodone (50-200 mg/d)	C	1	1.000	3.0; 3	<b>Note:</b> Never used (not really used in France)
Risperidone (initially 0,5-1	C	3	0.833	2.7; 3	

mg/d, Maximum 3 mg/d)					
Quetiapine (25-200 mg/d)	C	3	1.000	3.0; 3	
Pipamperone (20-120 mg/d)	D	2	1.000	4.0; 4	
Citalopram (10-30mg)	C	3	1.000	3.0; 3	
Clomethiazole (5-15 mg/d)	D	2	1.000	4.0; 4	
Mirtazapine, Mianserine	B	3	0.833	2.3; 2	
<b>BPSD: SLEEP DISORDERS</b>	<b>FORTA Class (original FORTA class in parentheses if different from consensus results)</b>	<b>Nr. of raters</b>	<b>Consensus coefficient, Round 1 (cutoff 0.800)</b>	<b>Expert ratings on a numerical scale: A=1, B=2, C=3, D=4</b>	<b>Selection of pertinent comments given by participating experts during the consensus procedure</b>
<b>Substance/group</b>				<b>Mean; Mode</b>	
Slow-release melatonin (2-4 mg)	(C) B	3	0.667	2.3; 3	
Tetracyclic antidepressant Mirtazapine (15-30mg)	C	3	1.000	3.0; 3	
Tricyclic antidepressant Doxepine (25-50 mg)	D	3	1.000	4.0; 4	
Zopiclone (3,75-7,5 mg)	C	3	1.000	3.0; 3	
Mianserine	C	3	0.833	3.3; 3	<b>Note:</b> Very few evidence in Geriatrics, possible alterations of cognitive status
Zolpidem	(C) D	3	0.667	3.7; 4	

DEPRESSION Prophylaxis and therapy for patients with moderate to major depression	FORTA Class (original FORTA class in parentheses if different from consensus results)	Nr. of raters	Consensus coefficient, Round 1 (cutoff 0.800)	Expert ratings on a numerical scale: A=1, B=2, C=3, D=4  Mean; Mode	Selection of pertinent comments given by participating experts during the consensus procedure
<b>Substance/group</b>					
<b>SSRIs (Selective Serotonin Reuptake Inhibitor)</b>		3	1.000	2.0; 2	
Sertraline	<b>B</b>				
Escitalopram	<b>B</b>	3	1.000	2.0; 2	
Citalopram	<b>B</b>	3	1.000	2.0; 2	
<b>Tricyclic antidepressant Nortriptyline</b>	<b>D</b>	3	1.000	4.0; 4	
<b>Tetracyclic antidepressant Mirtazapine</b>	<b>C</b>	3	1.000	3.0; 3	
<b>SNRIs (Serotonin- Noradrenalin Reuptake Inhibitors)</b>		3	0.833	2.7; 3	
Venlafaxine	<b>C</b>				
Duloxetine	<b>C</b>	3	1.000	3.0; 3	
<b>Monoamine oxidase A (MAO) inhibitor Moclobemide</b>	<b>D</b>	3	1.000	4.0; 4	
<b>Dopamine and norepinephrine reuptake inhibitor Bupropion</b>	<b>(C) D</b>	1	0.500	4.0; 4	<b>Note:</b> Never used (not frequently used in France)
<b>Quetiapine</b>	<b>(C)</b>	3	0.667	3.7; 4	

	D				
Trazodone	(C) D	2	0.750	3.5; -	
Olanzapine	(C) D	3	0.667	3.7; 4	
Benzodiazepines: General	(D) C	3	0.667	3.3; 4	
Long-acting,	D	3	1.000	4.0; 4	
Short-acting	(D) C	3	0.667	3.3; 4	
Agomelatine	D	3	1.000	4.0; 4	
Selective noradrenaline re-uptake inhibitor Reboxetine	D	2	1.000	4.0; 4	
<b>BIPOLAR DISORDER</b>	<b>FORTA Class (original FORTA class in parentheses if different from consensus results)</b>	<b>Nr. of raters</b>	<b>Consensus coefficient, Round 1 (cutoff 0.800)</b>	<b>Expert ratings on a numerical scale: A=1, B=2, C=3, D=4</b>  <b>Mean; Mode</b>	<b>Selection of pertinent comments given by participating experts during the consensus procedure</b>
<b>Substance/group</b>					
Lithium	C	3	1.000	3.0; 3	
Quetiapine	B	3	1.000	2.0; 2	
Valproic acid	C	3	1.000	3.0; 3	
Lamotrigine	C	3	1.000	3.0; 3	
Carbamazepine	(D) C	3	0.667	3.3; 3	<b>Note:</b> Difficult to use because of interaction but not excluded

INSOMNIA / SLEEP DISORDERS	FORTA Class (original FORTA class in parentheses if different from consensus results)	Nr. of raters	Consensus coefficient, Round 1 (cutoff 0.800)	Expert ratings on a numerical scale: A=1, B=2, C=3, D=4  Mean; Mode	Selection of pertinent comments given by participating experts during the consensus procedure
Substance/group					
ω1-Benzodiazepine agonists Zolpidem	(C) D	3	0.667	3.7; 4	<b>Note:</b> Fall-Risk-Increasing-Drug (FRID) and increased-risk of hip fracture
Non-benzodiazepine hypnotic Zopiclone	C	3	1.000	3.0; 3	
Butyrophenone derivative Pipamperone	D	2	1.000	4.0; 4	
Tetracyclic antidepressant Mirtazapine	C	3	1.000	3.0; 3	
Tricyclic antidepressant Doxepine	D	3	1.000	4.0; 4	
Benzodiazepines, e.g. Oxazepam (medium half- life)	(C) B	3	0.667	2.3; 3	
Triazolam (very short half-life)	D	2	1.000	4.0; 4	
Sigma receptor agonist Opipramole	D	1	1.000	4.0; 4	
Antihistamine Diphenhydramine	D	3	1.000	4.0; 4	
Mianserine	(C) D	3	0.667	3.7; 4	

<b>CHRONIC PAIN</b>	<b>FORTA Class (original FORTA class in parentheses if different from consensus results)</b>	<b>Nr. of raters</b>	<b>Consensus coefficient, Round 1 (cutoff 0.800)</b>	<b>Expert ratings on a numerical scale: A=1, B=2, C=3, D=4  Mean; Mode</b>	<b>Selection of pertinent comments given by participating experts during the consensus procedure</b>
<b>Substance/group</b>					
<b>Paracetamol (acetaminophen)</b>	<b>(A) B</b>	3	0.667	1.7; 1	<b>Note:</b> Very few evidence of efficacy
<b>Opioids, e.g. Buprenorphine, oxycodone, hydromorphone</b>	<b>B</b>	3	1.000	2.0; 2	
<b>Primary use of a combination of an agonist and an antagonist, e.g. Oxycodone/naloxone</b>	<b>C</b>	2	0.750	2.5; -	
<b>Morphine</b>	<b>C</b>	3	0.833	2.7; 3	
<b>SSRI (Selective Serotonin Reuptake Inhibitors) / SNRI (Serotonin- Norepinephrine-Reuptake Inhibitor), e.g. venlafaxine (only if absolutely necessary)</b>	<b>C</b>	3	0.833	2.7; 3	
<b>Antiepileptic agents (only for neuropathic pain) Pregabalin/gabapentin</b>	<b>B</b>	3	0.833	2.3; 2	

Carbamazepine	(D) C	2	0.500	2.5; -	
Tricyclic antidepressant amitriptyline	D	3	0.833	3.7; 4	
NSAIDs (nonsteroidal anti- inflammatory drugs, for long-term use), e.g. naproxen	D	3	1.000	4.0; 4	
Cox-2 inhibitors, e.g. celecoxib	D	3	1.000	4.0; 4	
Codein	C	3	0.833	3.3; 3	
Tramadol	C	3	0.500	3.3; 4	<b>Note:</b> No clear evidence and too many delirium
<b>EPILEPSY</b>	<b>FORTA Class (original FORTA class in parentheses if different from consensus results)</b>	<b>Nr. of raters</b>	<b>Consensus coefficient, Round 1 (cutoff 0.800)</b>	<b>Expert ratings on a numerical scale: A=1, B=2, C=3, D=4</b>  <b>Mean; Mode</b>	<b>Selection of pertinent comments given by participating experts during the consensus procedure</b>
<b>Substance/group</b>					
Levetiracetam	B	3	0.833	1.7; 2	
Lamotrigine	B	3	0.833	1.7; 2	
Gabapentin	B	3	0.833	2.3; 2	
Topiramate	(B) C	3	0.667	2.7; 3	<b>Note:</b> Very few evidence in Geriatrics patients
Lorazepam (emergency use)	C	3	1.000	3.0; 3	
Lorazepam (long-term use)	D	2	1.000	4.0; 4	

Pregabalin	C	3	0.833	2.7; 3	
Oxcarbazepine	C	3	0.833	3.3; 3	
Valproic acid	C	3	1.000	3.0; 3	
Carbamazepine	C	3	1.000	3.0; 3	
Diazepam (emrgency use)	C	2	1.000	3.0; 3	
Diazepam (long-term use)	D	3	1.000	4.0; 4	
Midazolam (emergency use)	C	3	0.833	2.7; 3	
Phenytoin	D	3	1.000	4.0; 4	
Phenobarbital	D	3	1.000	4.0; 4	
Ethosuximide	D	2	1.000	4.0; 4	

PARKINSON'S DISEASE	FORTA Class (original FORTA class in parentheses if different from consensus results)	Nr. of raters	Consensus coefficient, Round 1 (cutoff 0.800)	Expert ratings on a numerical scale: A=1, B=2, C=3, D=4  Mean; Mode	Selection of pertinent comments given by participating experts during the consensus procedure
Substance/group					
L-DOPA	A	3	1.000	1.0; 1	
COMT (Catechol-O- Methyltransferase)	B	3	1.000	2.0; 2	

<b>Inhibitor</b> Entacapone, opicapone					
<b>Dopamine agonists, e.g.</b> Ropinirole	<b>B</b>	3	1.000	2.0; 2	
Pramipexole	<b>B</b>	3	1.000	2.0; 2	
Piribedil, quinagolide, rotigotine	<b>(B)</b> <b>C</b>	2	0.750	2.5; -	<b>Note:</b> Not as a first line treatment because of side effects
<b>MAO-B inhibitors</b>	<b>C</b>	3	1.000	3.0; 3	
Rasagiline					
Selegiline	<b>C</b>	3	0.833	3.3; 3	<b>Note:</b> Toxicité hépatique
Bromocriptine, cabergoline	<b>D</b>	3	1.000	4.0; 4	
<b>Glutamate antagonists</b> Amantadine	<b>D</b>	3	1.000	4.0; 4	
<b>Anticholinergics</b> Biperidene	<b>D</b>	3	1.000	4.0; 4	
<b>INCONTINENCE</b> Drug therapy for urge incontinence	<b>FORTA Class</b> (original FORTA class in parentheses if different from consensus results)	<b>Nr. of raters</b>	<b>Consensus coefficient, Round 1 (cutoff 0.800)</b>	<b>Expert ratings on a numerical scale: A=1, B=2, C=3, D=4</b>  <b>Mean; Mode</b>	<b>Selection of pertinent comments given by participating experts during the consensus procedure</b>
<b>Substance/group</b>					
Fesoterodine	<b>D</b>	3	1.000	4.0; 4	

Tolterodine	D	3	1.000	4.0; 4	
Trospium chloride	C	3	0.833	3.3; 3	
Extended-release Oxybutynin	C	3	0.833	3.3; 3	
Immediate-release Oxybutynin	D	3	1.000	4.0; 4	
Finasteride	C	3	1.000	3.0; 3	
Tamsulosine	C	3	1.000	3.0; 3	
Alfuzosine	D	3	1.000	4.0; 4	

GASTROINTESTINAL ILLNESSES/ CONCOMITANT THERAPY WITH NSAIDs	FORTA Class (original FORTA class in parentheses if different from consensus results)	Nr. Of raters	Consensus coefficient, Round 1 (cutoff 0.800)	Expert ratings on a numerical scale: A=1, B=2, C=3, D=4	Selection of pertinent comments given by participating experts during the consensus procedure
				Mean; Mode	
Substance/group					
Proton pump inhibitors (PPI), only if absolutely necessary	B	3	0.833	1.7; 2	
H <sub>2</sub> receptor antagonists	C	3	1.000	3.0; 3	

Anemia	FORTA Class (original FORTA class in parentheses if different from consensus results)	Nr. of raters	Consensus coefficient, Round 1 (cutoff 0.800)	Expert ratings on a numerical scale: A=1, B=2, C=3, D=4	Selection of pertinent comments given by participating experts during the consensus procedure

				Mean; Mode	
<b>Substance/group</b>					
<b>Substitution (iron, vitamin B12, folic acid in cases of deficiency)</b>	A	3	1.000	1.0; 1	
<b>Erythropoetin-stimulating agents (ESA) in patients with renal insufficiency</b>	(A) B	3	0.667	1.7; 1	
<b>Iron substitution in patients with cardiac insufficiency</b>  <b>With Proof of iron deficiency</b>	See cardiac insufficiency				

	FORTA Class (original FORTA class in parentheses if different from consensus results)	Nr. of raters	Consensus coefficient, Round 1 (cutoff 0.800)	Expert ratings on a numerical scale: A=1, B=2, C=3, D=4  Mean; Mode	Selection of pertinent comments given by participating experts during the consensus procedure
<b>Vaccinations</b>					
<b>Substance/group</b>					
<b>Annual influenza immunizations</b>	A	3	1.000	1.0; 1	
<b>Pneumococcal immunizations for persons ≥ 65 years</b>	A	3	1.000	1.0; 1	

<b>Shingles (Herpes Zoster) Vaccination</b>	<b>(A) B</b>	2	0.500	2.0; -	<b>Note:</b> It depends, in very old patients not really proven. My opinion varies based on age of the patient
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<b>ONCOLOGICAL DISEASES: SOLID TUMORS</b>	<b>FORTA Class (original FORTA class in parentheses if different from consensus results)</b>	<b>Nr. of raters</b>	<b>Consensus coefficient, Round 1 (cutoff 0.800)</b>	<b>Expert ratings on a numerical scale: A=1, B=2, C=3, D=4  Mean; Mode</b>	<b>Selection of pertinent comments given by participating experts during the consensus procedure</b>
<b>INDICATION Substance/group</b>					
<b>BREAST CANCER Adjuvant therapy</b>					
<b>Hormone therapy, e.g.  Tamoxifen</b>	<b>B</b>	2	1.000	2.0; 2	
<b>Aromatase inhibitors</b>	<b>B</b>	2	1.000	2.0; 2	
<b>Immunotherapy / "Targeted" therapy Trastuzumab</b>	<b>B</b>	1	1.000	2.0; 2	
<b>Chemotherapy, e.g.  CMF (Combination Cyclophosphamide,</b>	<b>C</b>	1	1.000	3.0; 3	

<b>Methotrexate, 5-Fluorouracil</b>					
<b>AC/EC Regimen(Anthracycline/ Epirubicin, Cyclophosphamide)</b>	<b>C</b>	1	1.000	3.0; 3	
<b>BREAST CANCER Advanced Stage</b>					
<b>Hormone therapy, e.g. tamoxifen, aromatase inhibitors</b>	<b>B</b>	2	1.000	2.0; 2	
<b>Immunotherapy/Targeted Therapy Trastuzumab/ lapatinib</b>	<b>B</b>	2	1.000	2.0; 2	
<b>Chemotherapy, e.g. anthracyclins, taxanes</b>	<b>C</b>	2	1.000	3.0; 3	
<b>VEGF (Vascular Endothelial Growth Factor) Inhibition Bevacizumab</b>	<b>D</b>	2	0.750	3.5; -	
<b>COLORECTAL CARCINOMA Adjuvant Therapy</b>					
<b>FOLFOX Regimen (Folinic acid, Fluorouracil, Oxaliplatin)</b>	<b>C</b>	2	1.000	3.0; 3	
<b>5-Fluorouracil based infusion regimen</b>	<b>C</b>	2	0.750	2.5; -	
<b>Capecitabine</b>	<b>C</b>	2	0.750	2.5; -	
<b>COLORECTAL CARCINOMA Advanced stage</b>					
<b>Chemotherapy FOLFOX (Folinic acid,</b>	<b>C</b>	2	1.000	3.0; 3	

Fluorouracil, Oxaliplatin)					
VEGF (Vascular Endothelial Growth Factor) Inhibition Bevacizumab	C	2	1.000	3.0; 3	
EGFR (Epidermal-Growth-Factor-Receptor) Inhibition Cetuximab	C	2	1.000	3.0; 3	
Panitumumab	C	2	1.000	3.0; 3	
BRONCHIAL CARCINOMA Adjuvant therapy					
Adjuvant chemotherapy (Cisplatin-based)	C	2	1.000	3.0; 3	
BRONCHIAL CARCINOMA Advanced Stage					
Docetaxel	B	2	1.000	2.0; 2	
Vinorelbin	B	2	1.000	2.0; 2	
Primary combination therapy Cisplatin/gemcitabin, or cisplatin/vinorelbin	C	2	1.000	3.0; 3	
GASTRIC CANCER					
ECF Regime (Epirubicin, Cisplatin, 5-Fluorouracil)	B	1	1.000	2.0; 2	
ONCOLOGICAL DISEASES HEMATOLOGICAL NEOPLASIAS	FORTA Class (original FORTA class in parentheses if different from consensus results)	Nr. of raters	Consensus coefficient, Round 1 (cutoff 0.800)	Expert ratings on a numerical scale: A=1, B=2, C=3, D=4  Mean; Mode	Selection of pertinent comments given by participating experts during the consensus procedure
INDICATION Substance/group					

<b>MDS (Myelodysplastic syndrome)</b> <b>Azacytidine</b>	<b>(B)</b> <b>C</b>	1	0.500	3.0; 3	
<b>AML (Acute myeloid leukemia)</b> <b>Anthracyclines + cytosine arabinoside (cytarabine)</b>	<b>B</b>	1	1.000	2.0; 2	
<b>CLL (Chronic lymphatic leukemia)</b> <b>Chlorambucil, Fludarabin, Bendamustin</b>	<b>B</b>	1	1.000	2.0; 2	
<b>CLL</b> <b>Obinutuzumab</b>	<b>B</b>	1	1.000	2.0; 2	
<b>CLL</b> <b>Rituximab</b>	<b>B</b>	1	1.000	2.0; 2	
<b>Multiple myeloma</b>  <b>Primary therapy with</b>  <b>Prednisolone</b>	<b>B</b>	1	1.000	2.0; 2	
<b>Thalidomide</b>	<b>B</b>	1	1.000	2.0; 2	
<b>Melphalan</b>	<b>B</b>	1	1.000	2.0; 2	
<b>CLL</b> <b>Ibrutinib</b>	<b>C</b>	1	1.000	3.0; 3	
<b>CLL</b> <b>Idelalisib</b>	<b>C</b>	1	1.000	3.0; 3	

ONCOLOGICAL SUPPORTIVE THERAPY	FORTA Class (original FORTA class in parentheses if different from consensus results)	Nr. of raters	Consensus coefficient, Round 1 (cutoff 0.800)	Expert ratings on a numerical scale: A=1, B=2, C=3, D=4  Mean; Mode	Selection of pertinent comments given by participating experts during the consensus procedure
Substance/group					
G-CSF (Granulocyte Colony Stimulation Factor)	A	3	1.000	1.0; 1	
Antiemetic agents (e.g. 5-HT receptor inhibitors)	A	3	1.000	1.0; 1	
Erythropoiesis Stimulating Agents, ESA	B	3	1.000	2.0; 2	

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## SUMMARY OF STATISTICAL METHODS

(The following descriptions of the statistical methods and calculations are based on the first version of the FORTA List<sup>5</sup>. Former definitions and explanations are adopted unchanged.)

### Consensus Coefficient<sup>5</sup>

Consensus parameters were generated by calculating the percentage of experts' FORTA ratings (minus abstentions) agreeing with the original FORTA values, both overall and for each item separately (n = 268; two of the 268 proposed items were removed: see below). The coefficients were then corrected (cons\_corr) to weight the degree of deviation between the experts' individual FORTA ratings, expressed in terms of range class, from 0-3 as defined:

- Range = 0: unanimity among all experts (no deviation);
- Range = 1: greatest range only from A to B or B to C, or C to D (neighboring classes), ½ weight;
- Range = 2: greatest distance from A to C or B to D, weight=0;
- Range = 3: greatest distance from A to D, weight=0.

### Frequency of substances in defined range groups according to degree of consensus

Range	Frequency (n total=266)	%
0	183	68.80
1	67	25.20
2	12	4.50
3	4	1.50

Cons\_corr coefficients ranged from 0.500 to 1.000 (mean 0.916, median 1.000). 40 substances fell short of our established cons\_corr cutoff of 0.800. Due to the low number of participating experts (N=3) no second round was performed.

## Confirmation/determination of FORTA labels<sup>5</sup>

In order to compare the rater-based FORTA labels with the original author-based labels, the labels A, B, C and D were transformed as follows<sup>5</sup>:

A → 1  
B → 2  
C → 3  
D → 4

These numerical “grades” were used for the calculation of arithmetic mean. The mode (=grade appearing most frequently for rated item) is also shown. The rater-based FORTA labels are derived from the arithmetic mean from Round 1. The range for each grade was set at:

If  $1 \leq m < 1.5$  → FORTA Class **A**  
If  $1.5 \leq m < 2.5$  → FORTA Class **B**  
If  $2.5 \leq m < 3.5$  → FORTA Class **C**  
If  $m \geq 3.5$  → FORTA Class **D**

m= arithmetic mean based on the grades 1-4

The results of The Delphi Consensus Validation Procedure confirmed the suggested FORTA labels for 85.1% of all substances (n=268; final number of items was 266). All consensus-based FORTA ratings are listed in bold print: **A B C D**, and the original author-based FORTA ratings are supplied in parentheses: (A) (B) (C) (D).

We removed a total of 2 substances (bortezomib & lenalidomide for hematological neoplasias) from the suggested FORTA list which were either not available in France and/or evaluated by  $\leq 1$  experts.