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[1], Christel Weiss[2], Martin Wehling[1] *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
Phone: +49 621 383 9629

The F O R T A List

"Fit for The Aged"

Expert Consensus Validation

Poland

Farhad Pazan[1], Christel Weiß[2], Martin Wehling[1]
[1]Institute of Clinical Pharmacology, Center for Geriatric Pharmacology, Medical Faculty of the University of Heidelberg in Mannheim
[2] Department of Medical Statistics, Biomathematics and Information Processing, Medical Faculty of the University of Heidelberg in Mannheim

Disclaimer

Please keep in mind that the FORTA Concept was conceived and developed in Germany. 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 Poland. 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[5]. 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[6].

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[5]. '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[5].

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 7 colleagues, representing Poland, 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

Katarzyna Wieczorowska-Tobis, MD, PhD: Laboratory for Geriatric Medicine, Department of Palliative Medicine, Karol Marcinkowski University of Medical Sciences, Poznan

Tomasz Kostka, MD: Department of Geriatrics, Healthy Ageing Research Centre, Medical University of Lodz, Lodz

Alicja Klich-Rączka, MD: Department of Internal Medicine and Gerontology, Jagiellonian University Medical College, Krakow

Barbara Bień, MD: Department of Geriatrics, Medical University of Bialystok, Bialystok

Marlena Broncel, PhD: Department of Internal Diseases and Clinical Pharmacology, Medical University of Łódź, Lodz

Pawel Mierzejewski, MD: Department of Pharmacology, Institute of Psychiatry and Neurology, Warsaw

Agnieszka Neumann-Podczaska Department of Palliative Medicine, Poznan University of Medical Sciences, 61-245 Poznan

F O R T A – Physician's guide[1,2,5,7]

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[1,2,3,4,7]

Class A	Class B	Class C	Class D
= Indispensable drug, clear-cut benefit in terms of efficacy/safety ratio proven in elderly patients for a given indication	= Drugs with proven or obvious efficacy in the elderly, but limited extent of effect and/or safety concerns	= 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	= Avoid if at all possible in the elderly, omit first and use alternative substances

*** 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[3,4,5]
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)

ARTERIAL HYPERTENSION	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					
Renin-Angiotensin system inhibitors **ACE inhibitors**	**A**	7	1.000	1.0; 1	
Angiotensin receptor antagonists	**A**	7	1.000	1.0; 1	
Long-acting calcium antagonists, dihydropyridine type, for example amlodipine	**A**	7	1.000	1.0; 1	
Betablockers except atenolol	**C**	5	0.857	2.7; 3	
Atenolol	**D**	7	1.000	4.0; 4	
Diuretics except indapamid	**B**	6	1.000	2.0; 2	
Indapamid	**A**	6	1.000	1.0; 1	
Alpha blockers	**C**	6	0.833	3.3; 3	
Spironolactone	**C**	7	1.000	3.0; 3	
Moxonidine	**C**	6	0.917	3.2; 3	
Aliskiren	**C**	5	0.900	3.2; 3	
Urapidil	**C**	6	1.000	3.0; 3	
Clonidine	**D**	7	1.000	4.0; 4	

Minoxidil	**D**	6	1.000	4.0; 4	
Calcium antagonists, verapamil type	**C**	7	0.857	3.0; 3	
Eplerenone	**C**	6	1.000	3.0; 3	
Nitroglycerin i.v.	**C**	7	0.857	3.0; 3	
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**
Substance/Group					
Renin-angiotensin system inhibitors **ACE inhibitors**	**A**	7	1.000	1.0; 1	
Angiotensin receptor antagonists	**A**	7	1.000	1.0; 1	
Betablockers (metoprolol, carvedilol, bisoprolol)	**A**	7	1.000	1.0; 1	
Diuretics	**A**	7	1.000	1.0; 1	
Gliflozins (SGLT2 inhibitors) only those substances which have been approved for this indication (dapgliflozine)	**B**	7	0.917	1.8; 2	
Spironolactone	**B**	7	1.000	2.0; 2	
Digitalis preparations	**C**	7	1.000	3.0; 3	
Ivabradine	**C**	7	1.000	3.0; 3	
Indapamide	**A**	6	1.000	1.0; 1	
Nebivolol	**A**	7	1.000	1.0; 1	
Thiazides or thiazide-like	**B**	5	1.000	2.0; 2	

Eplerenone	**B**	7	1.000	2.0; 2	
Iron substitution in patients with iron deficiency	**A**	7	0.928	1.1; 1	

ACUTE CORONARY SYNDROME	**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					
Renin-Angiotensin-System-Blocker: ACE-Hemmer	**A**	7	1.000	1.0; 1	
Acetylsalicylic acid	**A**	7	1.000	1.0; 1	
Unfractionated heparin and low molecular weight heparin	**A**	7	1.000	1.0; 1	
Frequency-lowering betablockers, e.g. metoprolol or bisoprolol	**A**	7	1.000	1.0; 1	
Atorvastatin	**A**	7	1.000	1.0; 1	
Nitroglycerin spray, single use, acute as on-demand medication	**A**	7	0.928	1.1; 1	
Clopidogrel, prasugrel	**B** **A** for stent	6 7	1.000 0.857	2.0; 2 1.3; 1	
Thrombolytics, especially rTPA (recombinant tissue-type plasminogen activator)	**B**	7	1.000	2.0; 2	
Nitrates, long-term	**C**	6	0.917	3.2; 3	

Gp IIb/IIIa antagonists (glycoprotein 2b/3a inhibitors)	**C**	6	0.917	2.8; 3	
Ivabradine	**C**	7	1.000	3.0; 3	
Rosuvastatin	**A**	7	1.000	1.0; 1	
Simvastatin	**B**	7	0.929	1.9; 2	
CHRONIC THERAPY FOLLOWING MYOCARDIAL INFARCTION	**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					
Renin angiotensin system blockers **ACE Inhibitors**	**A**	7	1.000	1.0; 1	
Acetylsalicylic acid (100 mg/d)	**A**	7	1.000	1.0; 1	
Frequency-lowering beta blockers up to 3 years	**A**	7	1.000	1.0; 1	
Frequency-lowering beta blockers longer than 3 years	**(C)** **B**	7 (R1) 5 (R2)	0.786(R1) 0.700 (R2)	2.6; 3(R1) 2.4; 2 (R2)	**Note:** The drug is needed as it lowers oxygen demand
Nitroglycerin spray, single use as on-demand medication	**A**	7	0.929	1.1; 1	
Influenza vaccination (inactivated subunit vaccines)/pneumococcal	**See vaccinations**				

immunizations					
Statins	**A** **B** for very old (>85 years) patients	6 4	0.917 0.875	1.2; 1 2.3; 2	
Clopidogrel (12 months after acute coronary syndrome)	**A** with aspirin intolerance	6	1.000	1.0; 1	
Nitrates, long-term	**C**	7	0.857	3.3; 3	
Fibrates	**C**	7	0.929	3.1; 3	
Ezetimibe	**C**	7	0.929	2.9; 3	
Amiodarone	**C**	7	1.000	3.0; 3	
All other class-I-III antiarrhythmic agents	**D**	7	1.000	4.0; 4	
Dihydropyridine antagonists (if no hypertension)	**D**	7	1.000	4.0; 4	
Niacin	**D**	6	1.000	4.0; 4	
Rosuvastatin	**A**	7	0.929	1.1; 1	
Trimetazidine	**C**	7	0.929	3.1; 3	

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**	7	1.000	1.0; 1	
Atorvastatin	**A**	7	1.000	1.0; 1	

rTPA (recombinant tissue-type plasminogen activator), only for emergency use	**A**	7	1.000	1.0; 1	
Simvastatin	**(A)** **B**	7 (R1) 5 (R2)	0.714 (R1) 0.500 (R2)	1.6; 2 (R1) 2;2 (R2)	**Note:** Atorvastatin is preferred statin in the treatment of stroke. The SPARCL trial has shown that high dose atorvastatin is an effective medication for secondary prevention of stroke cardiovascular events in patients with no known history of cardiac disease.; Often used incorrectly (to low dose etc.)
Anticoagulants including new oral anticoagulants	**A**	7	1.000	1.0; 1	
Clopidogrel	**A**	7	1.000	1.0; 1	
Dipyridamole plus acetylsalicylic acid	**B**	5	1.000	2.0; 2	
Rosuvastatin	**B**	7	0.857	1.7; 2	

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**	7	1.000	1.0; 1	
Digoxin	**B**	7(R1) 5 (R2)	0.714(R1) 0.800(R2)	2.6; 2(R1) 2.4; 2(R2)	**Note:** According to Beers Criteria should be avoided as first line-therapy for atrial fibrillation, avoid dosage >0,125 mg/d when

					used for atrial fibrillation; Only for AF (with fast ventricular rate) with coexisting heart failure with reduced ejection fraction.
New Oral Anticoagulants (NOACs)	**(B)** **A**	7(R1) 5(R2)	0.714(R1) 0.700(R2)	1.4; 1(R1) 1.4; 1(R2)	**Note:** NOACs are preferred in the AF. In elderly we should reduce only the dose of dabigatran, but this drug is not contraindicated in elderly exception patients with GFR <30ml/min
Except dabigatran	**C**	5	0.900	2.8; 3	
Oral anticoagulation by vitamin-K-antagonists (e.g. phenprocoumon, warfarin)	**B**	7	0.929	1.9; 2	
Alternative: low molecular weight heparin	**C**	7	1.000	3.0; 3	
Digitoxin	**C**	5(R1) 1(R2)	0.700(R1) 0.833(R2)	3.2; -(R1) 3.3;3(R2)	**Note:** a lot of side effects in old age
Diltiazem, verapamil	**C**	7	0.929	3.1; 3	
Class III antiarrhythmic agent amiodarone	**C**	7	0.857	2.7; 3	
All other class I-III antiarrhythmic agents	**D**	7	1.000	4.0; 4	
Acetylsalicylic acid (100 mg/d)	**C**	6	0.917	2.8; 3	
Class III antiarrhythmic agent dronedarone	**D**	7	1.000	4.0; 4	
Clopidogrel	**B**	6	1.000	2.0; 2	
Propafenone	**B**	7	1.000	2.0; 2	
Vernakalant	**C**	5	1.000	3.0; 3	

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)	**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					
Inhalative long-acting parasympatholytic agents	**A**	6	1.000	1.0; 1	
Systemic glucocorticoids, acute, short-term use in cases of exacerbation	**A**	6	0.833	1.3; 1	
Antibiotics (acute) in cases of exacerbation, after calculated selection and, if necessary, according to antibiogram	**A**	6	0.917	1.2; 1	
Long-term administration of oxygen	**A**	6	1.000	1.0; 1	
Annual influenza immunizations	**See vaccinations**				
Pneumococcal immunizations for persons ≥ 65 years	**See vaccinations**				
Inhalative beta 2 mimetic agents	**B**	6	0.917	1.8; 2	
Inhalative glucocorticoids	**B**	6	0.917	2.2; 2	
Theophylline	**D**	6	0.833	3.7; 4	
Mucolytic agents, e,g, acetyl cysteine,	**C**	6	0.917	2.8; 3	

bromhexine					
Roflumilast	**C**	5	1.000	3.0; 3	
Systemic glucocorticoids, chronic use	**D**	5	0.900	3.8; 4	
Antitussives: opioid A., e.g. codein; non-opioid A., e.g. butamirate	**D**	5	1.000	4.0; 4	
LABA-Long-acting β adrenoceptor agonists	**A**	6	1.000	1.0; 1	
OSTEOPOROSIS	**FORTA Class** (original FORTA class in parenteses 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					
Calcium and vitamin D supplements (as prophylaxis for persons ≥ 65 years)	**A**	7	1.000	1.0; 1	
Parenteral bisphosphonates (e.g. ibandronate, IV every 3 months)	**B**	7	1.000	2.0; 2	
Raloxifene for women	**B**	5	1.000	2.0; 2	
Denosumab	**B**	6	1.000	2.0; 2	
Bisphosphonates, oral	**B**	7	1.000	2.0; 2	
Teriparatide	**C**	4	1.000	3.0; 3	
Alfacalcidol	**C**	6	0.833	2.7; 3	
Parathormone	**C**	6	1.000	3.0; 3	
Strontium ranelate	**D**	6	1.000	4.0; 4	
Nandrolone decanoate	**D**	6	1.000	4.0; 4	
Fluoride	**D**	6	1.000	4.0; 4	
Hormone replacement	**D**	6	1.000	4.0; 4	

therapy (HRT): estrogen, except for perimenopausal)					
TYPE II DIABETES MELLITUS	**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					
DPP4 (Dipeptidylpeptidase) Inhibitors	**B**	6	1.000	2.0; 2	
Insulin and insulin analogs (if absolutely necessary)	**B**	7	0.857	1.7; 2	
Metformin	**A**	7	0.929	1.1; 1	
GLP1 (Glucagon-Like Peptide-1) analogs	**B**	6	1.00000	2.0; 2	
Acarbose	**B**	7	0.857	2.3; 2	
3rd generation sulfonylureas (for example, glimepiride)	**B**	7	0.929	2.1; 2	
Glinides (for example, nateglinide)	**C**	5	1.000	3.0; 3	
PPAR-ɣ Ligands (Peroxisomal Proliferator-Activated Receptor gamma) **Pioglitazone**	**C**	5	1.000	3.0; 3	
Rosiglitazone	**D**	5	1.000	4.0; 4	
SGLT-2 inhibitors/Gliflozins	**(D)** **B**	5(R1) 5(R2)	0.600 (R1) 0.100 (R2)	3.0; 4(R1) 2.0; 2 (R2)	**Note:** Reduction of cardiovascular risk !!!!, heart failure.

1st generation sulfonylureas (for example, glibenclamide)	**D**	6	1.000	4.0; 4	
DEMENTIA	**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					
Acetylcholinesterase inhibitors e.g. donepezil, galantamine, rivastigmine (Only if indicated for the present stage of the disease)	**B**	7	0.857	1.7; 2	
Memantine	**B**	7	0.929	1.9; 2	
Ginkgo biloba	**D**	7	1.000	4.0; 4	
Statins	**D**	7	0.929	3.9; 4	
Selegiline	**D**	7	1.000	4.0; 4	
Nimodipine	**D**	7	1.000	4.0; 4	
Ergoline derivatives	**D**	7	1.000	4.0; 4	
Piracetam	**D**	7	1.000	4.0; 4	
Pyritinol	**D**	7	1.000	4.0; 4	
Antioxidants: Vitamin E, selenium, vitamin C	**D**	7	1.000	4.0; 4	

Phytotherapeutic agents, e.g. ginseng	**D**	7	1.000	4.0; 4	
Hormone preparations, e.g. DHEA (Dehydroepiandrosterone), testosterone	**D**	7	1.000	4.0; 4	
Antiphlogistics, e.g. indomethacin	**D**	7	1.000	4.0; 4	
Desferrioxamine	**D**	6	1.000	4.0; 4	
Citalopram/Escitalopram	**B**	7	0.929	2.1; 2	
BEHAVIORAL AND PSYCHOLOGICAL SYMPTOMS OF DEMENTIA (BPSD)	**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**
DEPRESSION					
Substance/group					
SSRI (Selective Serotonin Reuptake Inhibitors) Citalopram/escitalopram, sertraline, fluoxetine in the usual dosages	**B**	6	0.917	2.2; 2	
Mirtazapine (15-45mg/d)	**C**	7	1.000	3.0; 3	
SNRI (Serotonin-Noradrenalin-Reuptake-Inhibitors) Venlafaxine, duloxetine	**C**	7	0.929	2.9; 3	
Quetiapine	**B**	7	1.000	2.0; 2	
Trazodone	**B**	7	1.000	2.0; 2	

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
Substance/group					
Risperidone (initially 0,5-1 mg/d)	**C**	6	1.000	3.0; 3	
Melperone (25-150mg/d)	**C**	5	1.000	3.0; 3	
Quetiapine (25-200 mg/d)	**B**	7	1.000	2.0; 2	
Aripiprazole (2-15 mg/d)	**D**	7	1.000	4.0; 4	
Clozapine (10-50 mg/d)	**D**	7	1.000	4.0; 4	
Haloperidol (initially 0.5 mg/d, max. 3 mg/d)	**C**	7(R1) 5(R2)	0.786(R1) 0.700(R2)	3.1; 3(R1) 3.2; -(R2)	**Note: Sa**fer than quetiapine; only in delirium for a few days; B in case of short time usage it is as safe as quetiapine and may start to work faster
Olanzapine	**B**	7	1.000	2.0; 2	
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**
Substance/group					
Trazodone (50-200 mg/d)	**C**	7	0.929	2.9; 3	
Risperidone (initiallly 0,5-1 mg/d, Maximum 3 mg/d)	**C**	7	1.000	3.0; 3	

Quetiapine (25-200 mg/d)	**B**	7	1.000	2.0; 2	
Melperone (25-150 mg/d)	**C**	6	1.000	3.0; 3	
Pipamperone (20-120 mg/d)	**D**	6	0.917	3.8; 4	
Citalopram (10-30mg)	**C**	6	1.000	3.0; 3	
Clomethiazole (5-15 mg/d)	**D**	6	1.000	4.0; 4	
Valproic acid	**C**	7	0.929	3.1; 3	
Benzodiazepines: Short-acting	**C**	7	0.929	3.1; 3	
Benzodiazepines: Long-acting	**D**	7	1.000	4.0; 4	
BPSD: 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					
Slow-release melatonin (2-4 mg)	**C**	7	0.857	2.7; 3	
Tetracyclic antidepressant Mirtazapine (15-30mg)	**C**	7	1.000	3.0; 3	
Tricyclic antidepressant Doxepine (25-50 mg)	**D**	7	0.929	3.9; 4	
Zopiclone (3,75-7,5 mg)	**C**	7	0.857	3.0; 3	
Quetiapine 12,5mg/night	**C**	7 (R1) 5 (R2)	0.786 (R1) 0.800(R2)	2.6; 3 (R1) 2.6; 3(R2)	**Note:** For short time usage when pharmacotherapy is needed
Zolpidem 5mg/night	**C**	7(R1) 5(R2)	0.786(R1) 0.900(R2)	3.1; 3(R1) 3.2; 3(R2)	**Note:** BEERS CRITERIA – AVOID IN ELDERLY, THE RISK OF ADE IS SIMILAR TO BZD; high risk of side effects and addiction;

					For short time usage when pharmacotherapy is needed
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**
Substance/group					
SSRIs (Selective Serotonin Reuptake Inhibitor) **Sertraline**	**B**	7	0.857	2.0; 2	
Escitalopram	**B**	7	0.929	1.9; 2	
Citalopram	**B**	7	0.929	1.9; 2	
Tricyclic antidepressant Nortriptyline	**D**	7	1.000	4.0; 4	
Tetracyclic antidepressant Mirtazapine	**C**	7	1.000	3.0; 3	
SNRIs (Serotonin-Noradrenalin Reuptake Inhibitors) **Venlafaxine**	**C**	7	0.857	2.7; 3	
Duloxetine	**C**	7	0.857	2.7; 3	
Monoamine oxidase A (MAO) inhibitor Moclobemide	**D**	7	1.000	4.0; 4	
Dopamine and norepinephrine reuptake	**C**	7	0.929	2.9; 3	

inhibitor Bupropion					
Vortioxetine	**C**	6	0.917	2.8; 3	
Quetiapine	**C**	7	1.000	3.0; 3	
Trazodone	**C**	7	0.857	2.7; 3	
Olanzapine	**C**	6	1.000	3.0; 3	
Benzodiazepines: General	**D**	7	1.000	4.0; 4	
Long-acting,	**D**	7	1.000	4.0; 4	
Short-acting	**D**	7	1.000	3.9; 4	
St. John's Wort	**D**	5	1.000	4.0; 4	
Agomelatine	**D**	7	1.000	4.0; 4	
Selective noradrenaline re-uptake inhibitor Reboxetine	**D**	7	0.857	3.7; 4	
BIPOLAR DISORDER	**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					
Lithium	**C**	7	1.000	3.0; 3	
Quetiapine	**B**	7	0.929	2.1; 2	
Valproic acid	**C**	7	1.000	3.0; 3	
Lamotrigine	**C**	7	1.000	3.0; 3	
Carbamazepine	**C**	7	1.000	3.0; 3	

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					
Melatonin (slow-release)	**B**	7	1.000	2.0; 2	
ω1-Benzodiazepine agonists **Zolpidem**	**C**	7 (R1) 5(R2)	0.786(R1) 0.800(R2)	2.9; 3(R1) 3.0; 3(R2)	**Note:** high risk of side effects and addiction; Recommended for the treatment of insomnia with relatively fewer ADR
Zaleplone	**C**	7	0.857	3.0; 3	
Non-benzodiazepine hypnotic Zopiclone	**C**	7	0.857	3.0; 3	
Butyrophenone derivative Pipamperone	**C**	6	1.000	3.0; 3	
Melperone	**C**	6	1.000	3.0; 3	
Tetracyclic antidepressant Mirtazapine	**C**	7	1.000	3.0; 3	
Tricyclic antidepressant Doxepine	**D**	7	0.929	3.9; 4	
Benzodiazepines, e.g. Oxazepam (medium half-life)	**D**	6	1.000	4.0; 4	
Triazolam (very short half-life)	**D**	6	1.000	4.0; 4	
Sigma receptor agonist Opipramole	**D**	6	1.000	4.0; 4	
Antihistamine Diphenhydramine	**D**	6	0.917	3.8; 4	

CHRONIC PAIN	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					
Paracetamol (acetaminophen)	**A**	7	0.929	1.1; 1	
Metamizole	**B**	7(R1) 5 (R2)	0.786(R1) 0.800(R2)	2.4; 2(R1) 2.4; 2(R2)	**Note:** FORTA D (chronic use); for chronic use it is not recommended due to severe ARD FORTA B – in case of acute pain
Opioids, e.g. Buprenorphine, oxycodone, hydromorphone	**B**	7(R1) 5(R2)	0.786(R1) 0.900(R2)	2.1; 2(R1) 2.2; 2(R2)	**Note:** tolerance; high risk of side effects and addiction; hydroxymorphone is not available in Poland oxycdone and buprenorphine are safe
Primary use of a combination of an agonist and an antagonist, e.g. **Tilidine/naloxone**	**C**	4	1.000	3.0; 3	
Oxycodone/naloxone	**C**	6	1.000	3.0; 3	
Morphine	**C**	6	0.917	2.8; 3	
SSRI (Selective Serotonin Reuptake Inhibitors) / SNRI (Serotonin-Norepinephrine-Reuptake	**C**	6	1.000	3.0; 3	

Inhibitor), e.g. venlafaxine (only if absolutely necessary)					
Antiepileptic agents (only for neuropathic pain) **Pregabalin/gabapentin**	**C**	6	1.000	3.0; 3	
Carbamazepine	**D**	6	1.000	4.0; 4	
Tricyclic antidepressant amitriptyline (does not apply to doses up to 10mg per day)	**D**	6	1.000	4.0; 4	
NSAIDs (nonsteroidal anti-inflammatory drugs, for long-term use), e.g. naproxen	**D**	6	1.000	4.0; 4	
Cox-2 inhibitors, e.g. celecoxib	**D**	6	1.000	4.0; 4	
Tramadol	**B**	7	0.929	2.1; 2	
Duloxetine	**B**	6	1.000	2.0; 2	
EPILEPSY	**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					
Levetiracetam	**B**	7	1.000	2.0; 2	
Lamotrigine	**B**	7	1.000	2.0; 2	

Gabapentin	**B**	7	1.000	2.0; 2	
Topiramate	**B**	7	0.857	2.3; 2	
Lorazepam (emergency use)	**B**	7	0.929	2.1; 2	
Lorazepam (long-term use)	**D**	5	1.000	4.0; 4	
Pregabalin	**C**	7	1.000	3.0; 3	
Oxcarbazepine	**C**	7	1.000	3.0; 3	
Valproic acid	**C**	7	1.000	3.0; 3	
Eslicarbazepine	**C**	4	1.000	3.0; 3	
Lacosamide	**C**	5	1.000	3.0; 3	
Zonisamide	**C**	5	1.000	3.0; 3	
Carbamazepine	**C**	7	1.000	3.0; 3	
Diazepam (emrgency use)	**C**	6	1.000	3.0; 3	
Diazepam (long-term use)	**D**	5	1.000	4.0; 4	
Midazolam (emrgency use)	**C**	7	1.000	3.0; 3	
Midazolam (long-term use)	**D**	5	1.000	4.0; 4	
Phenytoin	**D**	7	1.000	4.0; 4	
Phenobarbital	**D**	7	1.000	4.0; 4	
Ethosuximide	**D**	7	1.000	4.0; 4	
Clonazepam	**B**	6	0.917	2.2; 2	

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**	7	1.000	1.0; 1	
COMT (Catechol-O-Methyltransferase) Inhibitor Entacapone, opicapon	**B**	7	1.000	2.0; 2	
Dopamine agonists, e.g.					
Ropinirole	**B**	7	1.000	2.0; 2	
Pramipexole	**C**	7	0.929	2.9; 3	
Piribedil, quinagolide, rotigotine	**B**	7	0.929	2.1; 2	
MAO-B inhibitors					
Rasagiline	**C**	7	1.000	3.0; 3	
Selegiline	**D**	7	1.000	4.0; 4	
Bromocriptine, cabergoline	**D**	7	1.000	4.0; 4	

Glutamate antagonists **Amantadine**	**D**	7	0.929	3.9; 4	
Anticholinergics **Biperidene**	**D**	6	1.000	4.0; 4	
INCONTINENCE **Drug therapy for urge incontinence**	**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					
Fesoterodine	**B**	5	1.000	2.0; 2	
Tolterodine	**C**	7	1.000	3.0; 3	
Trospium chloride	**C**	7	1.000	3.0; 3	
Extended-release Oxybutynin	**C**	7	1.000	3.0; 3	
Immediate-release Oxybutynin	**D**	7	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** **Mean; Mode**	**Selection of pertinent comments given by participating experts during the consensus procedure**
Substance/group					
Proton pump inhibitors (PPI), only if absolutely	**B**	7	1.000	2.0; 2	

necessary					
H_2 receptor antagonists	**C**	7	0.929	3.1; 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** **Mean; Mode**	**Selection of pertinent comments given by participating experts during the consensus procedure**
Substance/group					
Substitution (iron, vitamin B12, folic acid in cases of deficiency)	**A**	7	0.929	1.1; 1	
Erythropoetin-stimulating agents (ESA) in patients with renal insufficiency	**A**	6	1.000	1.0; 1	
Iron substitution in patients with cardiac insufficiency **With proof of iron deficiency**	**See cardiac insufficiency**				

Vaccinations	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					
Annual influenza immunizations	**A**	7	0.857	1.3; 1	
Pneumococcal immunizations for persons ≥ 65 years	**A**	7	0.929	1.1; 1	
Shingles (Herpes Zoster) Vaccination	**(A)** **B**	6 (R1) 4(R2)	0.750 (R1) 0.750(R2)	1.5; 1 (R1) 1.5; 1(R2)	**Note:** Less than 20% efficacy

ONCOLOGICAL DISEASES: SOLID TUMORS	**FORTA Class (original FORTA class in parentheses if different from consensus results)**	**Nr. of**	**Consensus coefficient, Round 1 (cutoff**	**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**

		raters	**0.800)**		
INDICATION **Substance/group**					
BREAST CANCER **Adjuvant therapy**					
Hormone therapy, e.g. **Tamoxifen**	**B**	5	1.000	2.0; 2	
Aromatase inhibitors	**B**	5	1.000	2.0; 2	
Immunotherapy / **"Targeted" therapy** **Trastuzumab**	**B**	5	1.000	2.0; 2	
Chemotherapy, e.g. **CMF (Combination Cyclophosphamide, Methotrexate, 5-Fluorouracil)**	**C**	5	1.000	3.0; 3	
AC/EC Regimen(Anthracycline/ Epirubicin, Cyclophosphamide)	**C**	5	1.000	3.0; 3	
BREAST CANCER **Advanced Stage**					
Hormone therapy, e.g. tamoxifen, aromatase inhibitors	**B**	4	1.000	2.0; 2	
Immunotherapy/Targeted		4	1.000	2.0; 2	

Therapy **Trastuzumab / lapatinib**	**B**				
Chemotherapy, e.g. anthracyclins, taxanes	**C**	4	1.000	3.0; 3	
VEGF (Vascular Endothelial Growth Factor) Inhibition Bevacizumab	**D**	4	1.000	4.0; 4	
COLORECTAL CARCINOMA Adjuvant Therapy					
FOLFOX Regimen (Folinic acid, Fluorouracil, Oxaliplatin)	**C**	4	1.000	3.0; 3	
5-Fluorouracil based infusion regimen	**C**	4	1.000	3.0; 3	
Capecitabine	**C**	4	1.000	3.0; 3	
COLORECTAL CARCINOMA Advanced stage					
Chemotherapy FOLFOX (Folinic acid, Fluorouracil, Oxaliplatin)	**C**	4	1.000	3.0; 3	
VEGF (Vascular Endothelial Growth Factor) Inhibition Bevacizumab	**C**	4	1.000	3.0; 3	
EGFR (Epidermal-Growth-Factor-Receptor) Inhibition Cetuximab	**C**	4	1.000	3.0; 3	
Panitumumab	**C**	4	1.000	3.0; 3	
BRONCHIAL CARCINOMA Adjuvant therapy					
Adjuvant chemotherapy (Cisplatin-based)	**C**	4	1.000	3.0; 3	
BRONCHIAL CARCINOMA					

Advanced Stage					
Docetaxel	**B**	4	1.000	2.0; 2	
Vinorelbin	**B**	4	1.000	2.0; 2	
Primary combination therapy Cisplatin/gemcitabin, or cisplatin/vinorelbin	**C**	4	1.000	3.0; 3	
GASTRIC CANCER					
ECF Regime (Epirubicin, Cisplatin, 5-Fluorouracil)	**B**	4	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					
MDS (Myelodysplastic syndrome)		4	1.000	2.0; 2	
Azacytidine	**B**				
AML (Acute myeloid leukemia)		4	1.000	2.0; 2	
Anthracyclines + cytosine arabinoside (cytarabine)	**B**				
CLL (Chronic lymphatic leukemia)		4	1.000	2.0; 2	
Chlorambucil, Fludarabin, Bendamustin	**B**				

CLL Obinutuzumab	**B**	4	1.000	2.0; 2	
CLL Rituximab	**B**	4	1.000	2.0; 2	
Multiple myeloma Primary therapy with Prednisolone	**B**	4	1.000	2.0; 2	
Thalidomide	**B**	4	1.000	2.0; 2	
Melphalan	**B**	4	1.000	2.0; 2	
Bortezomib	**B**	4	1.000	2.0; 2	
Lenalidomide	**B**	4	1.000	2.0; 2	
CLL Ibrutinib	**C**	4	1.000	3.0; 3	
CLL Idelalisib	**C**	4	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**	5	1.000	1.0; 1	
Antiemetic agents (e.g. 5-HT receptor inhibitors)	**A**	5	1.000	1.0; 1	
Erythropoesis Stimulating	**B**	5	1.000	2.0; 2	

Agents, ESA					

*This substance or indication was suggested by the participating experts during the course of Round 1 and evaluated by the experts during Round 2, see second table below.

R1= Round 1

R2= Round 2

Delphi Expert Consensus Validation[5]

F	O	R	T	A
A	B	C	D	

NEW SUBSTANCES/INDICATIONS SUGGESTED BY EXPERTS
Results to be corroborated in future consensus/research projects

Classification of long-term medications†
for the pharmacotherapy of older patients
by indication/diagnosis, ranked according to FORTA classification

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

EXISTING INDICATION **Vaccinations**	**Rater-based FORTA Class (bold if: κ > 0.500, rater number ≥ 4 and label distance < 2)**	**Nr. of raters**	**κ-Index**	**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					
Covid-19 vaccination	**A**	4	1.000	1.0; 1	

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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[5]. Former definitions and explanations are adopted unchanged.)

Consensus Coefficient[5]

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 = 292). 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, full weight**;**
- Range = 3: greatest distance from A to D, full weight.

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

Range	Frequency (n total=292)	%
0	199	68.15
1	73	25.00
2	19	6.51
3	1	0.34

Cons_corr coefficients ranged from 0.600 to 1.000 (mean 0.962, median 1.000). Substances falling short of our established cons_corr cutoff of 0.800 underwent re-evaluation in a second round: n=13

Confirmation/determination of FORTA labels[5]

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[5]:

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. For the 12 re-evaluated items, grading was performed twice. The rater-based FORTA labels are derived from the arithmetic mean from Round 1, or if re-evaluated, from Round 2. 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 original FORTA labels for 98.3% of all substances (n=92); for 5/292 substances (1.7%), the FORTA labels changed over the course of two rounds. 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).

Asterisks in the first table mark substances or indications suggested by the panel members during the course of Round 1 and assessed by the experts during Round 2.

Selection process for new substances and indications[5]

- One substance was accepted for potential addition to the revised FORTA List. Due to the large number of substances suggested, a selection procedure was adopted: 1) acceptance of all substances suggested by ≥ 2 experts during Round 1, and all suggested indication areas; 2) acceptance of all substances/indication areas affirmed by >50% of experts during Round 2 that the substance/indication should be included in the FORTA List; 3) acceptance of all substances assigned a FORTA label by ≥ 2 raters (excluding abstentions) during Round 2. The one substance

    - belonged to a pre-existing FORTA indication

- A kappa index was generated for each of those added substances to analyze the distribution of the raters' FORTA labels given. The kappa index is defined as the (proportion of "matching" labels – 0.25) / 0.75. This gives due consideration to the fact that a figure of 25% can theoretically be attained by chance alone with this particular constellation (the choice of 4 distinct labels, as with multiple choice).

Mean and mode were calculated according to the numerical scale used for the original FORTA substances

A → 1
B → 2
C → 3
D → 4

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 new substance had a kappa index higher than 0.500. Suggesting a high level of inter-rater agreement for this substance.