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

Drugs & Aging

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The F O R T A List

"Fit for The Aged"

Expert Consensus Validation

The Netherlands

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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 the Netherlands. 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 4 colleagues, representing The Netherlands, 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

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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**	4	1.000	1.0; 1	
Angiotensin receptor antagonists	**A**	4	1.000	1.0; 1	
Long-acting calcium antagonists, dihydropyridine type, for example amlodipine	**A**	4	1.000	1.0; 1	
Betablockers except atenolol	**C**	4	0.875	2.8; 3	
Atenolol	**D**	4 (R1) 3 (R2)	0.750 (R1) 0.833(R2)	3.5; - (R1) 3.7; 4(R2)	
Diuretics except indapamid	**B**	4	1.000	2.0; 2	
Indapamid	**(A)** **B**	4(R1) 3(R2)	0.750(R1) 0.667(R2)	1.5; -(R1) 1.7; 2(R2)	
Alpha blockers	**C**	4	0.875	3.3; 3	
Spironolactone	**C**	4	0.875	3.3; 3	
Moxonidine	**C**	4(R1) 3(R2)	0.750(R1) 1.000(R2)	3.5; -(R1) 3.0; 3(R2)	
Aliskiren	**C**	4	1.000	3.0; 3	
Urapidil	**C**	3	0.833	3.3; 3	

Clonidine	**D**	4	1.000	4.0; 4	
Minoxidil	**D**	4	1.000	4.0; 4	
Calcium antagonists, verapamil type	**D**	4	1.000	4.0; 4	
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**	4	1.000	1.0; 1	
Angiotensin receptor antagonists	**A**	4	1.000	1.0; 1	
Betablockers (metoprolol, carvedilol, bisoprolol)	**A**	4	1.000	1.0; 1	
Diuretics	**(B)** **A**	4(R1) 3 (R2)	0.625(R1) 0.667 (R2)	1.3; 1(R1) 1.3; 1 (R2)	**Note:** Loop diuretics are important in cardiac insufficiency
Gliflozins (SGLT2 inhibitors) only those substances which have been approved for this indication (dapgliflozine)	**B**	4	1.000	2.0; 2	
Spironolactone	**B**	4	1.000	2.0; 2	
Digitalis preparations	**C**	4	1.000	3.0; 3	
Ivabradine	**C**	4	1.000	3.0; 3	
Iron substitution in patients with iron deficiency	**A**	3	1.000	1.0; 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**	4	1.000	1.0; 1	
Acetylsalicylic acid	**A**	4	1.000	1.0; 1	
Unfractionated heparin and low molecular weight heparin	**A**	4 (R1) 3 (R2)	0.750(R1) 1.000(R2)	1.5; 1(R1) 1.0; 1(R2)	
Frequency-lowering betablockers, e.g. metoprolol or bisoprolol	**A**	4	1.000	1.0; 1	
Atorvastatin	**A**	4	1.000	1.0; 1	
Nitroglycerin spray, single use, acute as on-demand medication	**A**	4	1.000	1.0; 1	
Clopidogrel, prasugrel	**B** **A** for stent	4 4	0.875 1.000	1.8; 2 1.0; 1	
Thrombolytics, especially rTPA (recombinant tissue-type plasminogen activator)	**C**	3	1.000	3.0; 3	
Nitrates, long-term	**B**	4	1.000	2.0; 2	
Gp IIb/IIIa antagonists (glycoprotein 2b/3a inhibitors)	**B**	4	0.875	1.8; 2	
Ivabradine	**B**	4(R1)	0.750(R1)	2.0; 2(R1)	**Note:** Not first or second choice; perhaps B if cardiac failure is also present

		3(R2)	0.833(R2)	2.3; 2(R2)	
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**	4	1.000	1.0; 1	
Acetylsalicylic acid (100 mg/d)	**A**	4	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	0.833	2.7; 3	
Nitroglycerin spray, single use as on-demand medication	**A**	3	1.000	1.0; 1	
Influenza vaccination (inactivated subunit vaccines)/pneumococcal immunizations	**See vaccinations**	-	-	-	
Statins	**A** **B** for very old (>85 years) patients	4 4	1.000 0.875	1.0; 1 1.8; 2	
Clopidogrel (12 months	**A** with aspirin	4	1.000	1.0; 1	

after acute coronary syndrome)	intolerance				
Nitrates, long-term	**C**	4	1.000	3.0; 3	
Fibrates	**C**	4	0.875	3.3; 3	
Ezetimibe	**C**	4	0.875	2.8; 3	
Amiodarone	**D**	4	1.000	4.0; 4	
All other class-I-III antiarrhythmic agents	**D**	4	1.000	4.0; 4	
Dihydropyridine antagonists (if no hypertension)	**D**	4	0.875	3.8; 4	
Niacin	**D**	4	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	**B**	4 (R1) 3 (R2)	0.750(R1) 1.000(R2)	2.0; 2(R1) 2.0; 2(R2)	
Atorvastatin	**A**	4	0.875	1.3; 1	
rTPA (recombinant tissue-type plasminogen activator) ; only for emergency use	**A**	3	1.000	1.0; 1	
Simvastatin	**A**	4	0.875	1.3; 1	
Anticoagulants including new oral anticoagulants	**B**	4	0.875	1.8; 2	
Clopidogrel	**(B)**	4(R1)	0.625(R1)	1.3; 1(R1)	**Note:** Belongs to primary management (with aspirin as second

	A	3(R2)	0.500(R2)	1.0; 1(R2)	choice)
Dipyridamole plus acetylsalicylic acid	**B**	4	1.000	2.0; 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**	4	0.875	1.3; 1	
Digoxin	**B**	4 (R1) 3 (R2)	0.750(R1) 0.833(R2)	2.5; -(R1) 2.3; 2(R2)	**Note:** Narrow therapeutic window
New Oral Anticoagulants (NOACs)	**(B)** **A**	4(R1) 3(R2)	0.750(R1) 0.667(R2)	1.5; -(R1) 1.3; 1(R2)	**Note:** FORTA A for all DOACs; evidence is growing for safe use in elderly with positive risk/benefit balance (except towards end of life)
Except dabigatran	**C**	3(R1) 3(R2)	0.667(R1) 1.000(R2)	2.3; 3(R1) 3.0; 3(R2)	
Oral anticoagulation by vitamin-K-antagonists (e.g. phenprocoumon, warfarin)	**B**	4	0.875	1.8; 2	
Alternative: low molecular weight heparin	**C**	4	0.875	3.3; 3	
Digitoxin	**C**	3	0.833	3.3; 3	

Diltiazem, verapamil	**C**	4	1.000	3.0; 3	
Class III antiarrhythmic agent amiodarone	**C**	4	1.000	3.0; 3	
All other class I-III antiarrhythmic agents	**D**	4	0.875	3.8; 4	
Acetylsalicylic acid (100 mg/d)	**D**	4	1.000	4.0; 4	
Class III antiarrhythmic agent dronedarone	**D**	3	0.833	3.7; 4	

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**	4	1.000	1.0; 1	
Systemic glucocorticoids, acute, short-term use in cases of exacerbation	**A**	4	1.000	1.0; 1	
Antibiotics (acute) in cases of exacerbation, after calculated selection and, if necessary, according to antibiogram	**A**	4	1.000	1.0; 1	
Long-term administration of oxygen	**A**	4	1.000	1.0; 1	
Annual influenza immunizations	**See vaccinations**				
Pneumococcal immunizations for persons ≥ 65 years	**See vaccinations**				
Inhalative beta 2 mimetic agents	**B**	4 (R1) 3 (R2)	0.750(R1) 0.833(R2)	1.5; -(R1) 1.7; 2(R2)	Note: Same level (classification) as parasympatholytics
Inhalative glucocorticoids	**C**	4	0.875	2.8; 3	
Theophylline	**D**	4	1.000	4.0; 4	
Mucolytic agents, e,g,		4	1.000	4.0; 4	

acetyl cysteine, bromhexine	**D**				
Roflumilast	**C**	4(R1) 3(R2)	0.750(R1) 1.000(R2)	3.5; -(R1) 3.0; 3(R2)	
Systemic glucocorticoids, chronic use	**D**	4	1.00	4.00; 4	
Antitussives: opioid A., e.g. codein; non-opioid A., e.g. butamirate	**D**	4	1.00	4.00; 4	
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)	**B**	4 (R1) 2	0.750(R1) 1.000	1.5; -(R1) 2.0; 2	**Note:** Safe and efficacious if blood concentrations of calcium and vitamin D are low
Parenteral bisphosphonates (e.g. ibandronate, IV every 3 months)	**A**	4	1.000	1.0; 1	
Raloxifene for women	**B**	4	0.875	1.8; 2	
Denosumab	**B**	4	0.875	1.8; 2	
Bisphosphonates, oral	**B**	4(R1) 3	0.750(R1) 0.833	1.5; -(R1) 1.7; 2	**Note:** No difference with parenteral; parenteral has its disadvantages as well in the elderly
Teriparatide	**C**	4(R1) 3	0.750(R1) 1.000	2.5; 3(R1) 3.0; 3	

Alfacalcidol	**C**	4	1.000	3.0; 3	
Parathormone	**C**	4	0.875	2.8; 3	
Strontium ranelate	**D**	4	0.875	3.8; 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**	4	0.875	3.8; 4	
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**	4	1.000	2.0; 2	
Insulin and insulin analogs (if absolutely necessary)	**B**	4	0.875	1.8; 2	
Metformin	**(B)** **A**	4 (R1) 3 (R2)	0.750(R1) 0.500(R2)	1.5; -(R1) 1.0; 1(R2)	**Note:** First choice in normal to high risk (stratification in Dutch GP guideline); second choice in very high risk
GLP1 (Glucagon-Like Peptide-1) analogs	**C**	4	0.875	2.8; 3	
Acarbose	**C**	4	0.875	3.3; 3	
3rd generation sulfonylureas (for example, glimepiride)	**B**	4	1.000	2.0; 2	
Glinides (for example, nateglinide)	**C**	4	1.000	3.0; 3	
PPAR-ɣ Ligands (Peroxisomal Proliferator-		4	0.875	3.3; 3	

Activated Receptor gamma) **Pioglitazone** **Rosiglitazone**	**C** **D**	 4	 1.000	 4.0; 4	
SGLT-2 inhibitors/Gliflozins	**(D)** **B**	3(R1) 3 (R2)	0.333(R1) 0.333 (R2)	2.7; 2(R1) 2.0; 2 (R2)	**Note:** In my opinion, proven efficacy in older adults but with some safety concerns, justifying B.; Depending on risk; first choice in very high risk (stratification in Dutch GP guideline)
1st generation sulfonylureas (for example, glibenclamide)	**C**	4	0.875	3.3; 3	
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)**	**C**	4 (R1) 3 (R2)	0.750 (R1) 0.833 (R2)	3.0; 3 (R1) 3.3; 3 (R2)	**Note:** no effect
Memantine	**C**	4	0.875	3.3; 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	
Phytotherapeutic 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**	3	1.000	4.0; 4	
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)** **C**	4 (R1) 3 (R2)	0.750(R1) 0.333(R2)	2.5; 2(R1) 3.3; 4(R2)	**Note:** In BPSD, the evidence for applying pharmacotherapeutical interventions (if any) is scarce. In combination with the potential safety issues in vulnerable patients, these medications should be avoided in my opinion
Mirtazapine (15-45mg/d)	**(B)** **C**	4(R1) 3(R2)	0.750(R1) 0.333(R2)	2.5; 2(R1) 3.3; 4(R2)	**Note:** In BPSD, the evidence for applying pharmacotherapeutical interventions (if any) is scarce. In

					combination with the potential safety issues in vulnerable patients, these medications should be avoided in my opinion
SNRI (Serotonin-Noradrenalin-Reuptake-Inhibitors) Venlafaxine, duloxetine	**(C) D**	4(R1) 3(R2)	0.750(R1) 0.667(R2)	3.0; 3(R1) 3.7; 4(R2)	**Note:** In BPSD, the evidence for applying pharmacotherapeutical interventions (if any) is scarce. In combination with the potential safety issues in vulnerable patients, these medications should be avoided in my opinion
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) B**	4 (R1) 3 (R2)	0.750(R1) 0.667(R2)	2.5; -(R1) 2.3; 2(R2)	**Note:** Proven efficacy, but of limited extent. To be prescribed only short-term
Melperone (25-150mg/d)	**C**	3	1.000	3.0; 3	
Quetiapine (25-200 mg/d)	**C**	4	0.875	3.3; 3	
Aripiprazole (2-15 mg/d)	**C**	4	0.875	3.3; 3	
Clozapine (10-50 mg/d)	**C**	4(R1) 3(R2)	0.625(R1) 1.000(R2)	2.3; 3(R1) 3.0; 3(R2)	**Note:** Proven efficacy, but of limited extent. To be prescribed only short-term
Haloperidol (initially 0.5 mg/d, max. 3 mg/d)	**C**	4(R1) 3(R2)	0.750(R1) 1.000(R2)	3.0; 3(R1) 3.0; 3(R2)	**Note:** Should be avoided unless symptoms are severe and non-pharmacological treatments have failed

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**	4	0.875	3.3; 3	
Risperidone (initiallly 0,5-1 mg/d, Maximum 3 mg/d)	**C**	4	0.875	2.8; 3	
Quetiapine (25-200 mg/d)	**C**	4	0.875	3.3; 3	
Melperone (25-150 mg/d)	**C**	2	1.000	3.0; 3	
Pipamperone (20-120 mg/d)	**C**	4	0.875	3.3; 3	
Citalopram (10-30mg)	**D**	4	0.875	3.8; 4	
Clomethiazole (5-15 mg/d)	**D**	2	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)	**D**	4	1.000	4.0; 4	
Tetracyclic antidepressant Mirtazapine (15-30mg)	**(C) D**	4 (R1) 3(R2)	0.750 (R1) 0.667(R2)	3.5; - (R1) 3.7; 4(R2)	
Tricyclic antidepressant		4	1.000	4.0; 4	

Doxepine (25-50 mg)	**D**				
Zopiclone (3,75-7,5 mg)	**C**	4	0.875	3.3; 3	
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**	**C**	4 (R1) 3 (R2)	0.750(R1) 0.667(R2)	2.5; -(R1) 3.0; -(R2)	
Escitalopram	**C**	4(R1) 3(R2)	0.625(R1) 0.667(R2)	2.8; 2(R1) 3.0; -(R2)	
Citalopram	**(C)** **B**	4(R1) 3(R2)	0.750(R1) 0.667(R2)	2.5; -(R1) 2.3; 2(R2)	
Tricyclic antidepressant **Nortriptyline**	**(C)** **B**	4(R1) 3(R2)	0.750(R1) 0.667(R2)	2.5; -(R1) 2.3; 2(R2)	**Note:** Moderate/major depression is serious condition hampering QoL, also in the elderly. In case medication needs to be given, nortriptyline is best choice after SSRIs
Tetracyclic antidepressant **Mirtazapine**	**C**	4	0.875	2.8; 3	
SNRIs (Serotonin-Noradrenalin Reuptake Inhibitors) **Venlafaxine**	**C**	4	0.875	2.8; 3	

Duloxetine	**C**	4	0.875	2.8; 3	
Monoamine oxidase A (MAO) inhibitor Moclobemide	**D**	4	1.000	4.0; 4	
Dopamine and norepinephrine reuptake inhibitor Bupropion	**C**	4	0.875	3.3; 3	
Vortioxetine	**C**	4(R1) 3(R2)	0.750(R1) 1.000(R2)	3.5; -(R1) 3.0; 3(R2)	
Quetiapine	**C**	4	0.875	3.3; 3	
Trazodone	**C**	4	0.875	3.3; 3	
Olanzapine	**(C)** **D**	4(R1) 3(R2)	0.750(R1) 0.667(R2)	3.5; -(R1) 3.7; 4(R2)	
Benzodiazepines: General	**D**	4	1.000	4.0; 4	
Long-acting,	**D**	4	1.000	4.0; 4	
Short-acting	**D**	4	1.000	4.0; 4	
St. John's Wort	**D**	4	1.000	4.0; 4	
Agomelatine	**D**	4	1.000	4.0; 4	
Selective noradrenaline re-uptake inhibitor Reboxetine	**D**	3	1.000	4.0; 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**	**Selection of pertinent comments given by participating experts during the consensus procedure**

				Mean; Mode	
Substance/group					
Lithium	**B**	4 (R1) 3(R2)	0.750 (R1) 0.833(R2)	1.5; - (R1) 1.7; 2(R2)	**Note:** Needs treatment; with good monitoring no issue in the elderly
Quetiapine	**B**	4	1.000	2.0; 2	
Valproic acid	**B**	4	0.875	1.8; 2	
Lamotrigine	**C**	4	1.000	3.0; 3	
Carbamazepine	**D**	4	1.000	4.0; 4	

	FORTA Class (original FORTA class in			**Expert ratings on a numerical scale: A=1, B=2, C=3, D=4**	

INSOMNIA / SLEEP DISORDERS	parentheses if different from consensus results)	Nr. of raters	Consensus coefficient, Round 1 (cutoff 0.800)	Mean; Mode	Selection of pertinent comments given by participating experts during the consensus procedure
Substance/group					
Melatonin (slow-release)	**C**	4	0.875	3.3; 3	
ω1-Benzodiazepine agonists					
Zolpidem	**D**	4	0.875	3.8; 4	
Zaleplone	**C**	3	0.833	3.3; 3	
Non-benzodiazepine hypnotic Zopiclone	**D**	4	0.875	3.8; 4	
Butyrophenone derivative Pipamperone	**D**	3	0.833	3.7; 4	
Melperone	**(C) D**	2 (R1) 2(R2)	0.750 (R1) 0.750(R2)	3.5; - (R1) 3.5; (R2)	**Note:** Not on the market in The Netherlands.
Tetracyclic antidepressant Mirtazapine	**D**	3	1.000	4.0; 4	
Tricyclic antidepressant Doxepine	**D**	3	1.000	4.0; 4	
Benzodiazepines, e.g.					
Oxazepam (medium half-life)	**D**	4	1.000	4.0; 4	
Triazolam (very short half-life)	**D**	3	1.000	4.0; 4	
Sigma receptor agonist	**D**	3	1.000	4.0; 4	

Opipramole					
Antihistamine Diphenhydramine	**D**	3	1.000	4.0; 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**	4	0.875	1.3; 1	
Metamizole	**C**	4	1.000	3.0; 3	
Opioids, e.g. Buprenorphine, oxycodone, hydromorphone	**B**	4	1.000	2.0; 2	
Primary use of a combination of an agonist and an antagonist, e.g. tilidine/naloxone	**C**	3	0.833	3.3; 3	
Oxycodone/naloxone	**C**	4	0.875	3.3; 3	
Morphine	**C**	4	0.875	2.8; 3	
SSRI (Selective Serotonin Reuptake Inhibitors) / SNRI (Serotonin-Norepinephrine-Reuptake	**C**	4	1.000	3.0; 3	

Inhibitor), e.g. venlafaxine (only if absolutely necessary)					
Antiepileptic agents (only for neuropathic pain) **Pregabalin/gabapentin**	**C**	4	1.000	3.0; 3	
Carbamazepine	**D**	4	0.875	3.8; 4	
Tricyclic antidepressant Amitriptyline (does not apply to doses up to 10mg per day)	**D**	4	1.000	4.0; 4	
NSAIDs (nonsteroidal anti-inflammatory drugs, for long-term use), e.g. naproxen	**D**	4	0.875	3.8; 4	
Cox-2 inhibitors, e.g. celecoxib	**D**	4	1.000	4.0; 4	
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**	4	1.000	2.0; 2	
Lamotrigine	**B**	4	1.000	2.0; 2	
Gabapentin	**B**	4	1.000	2.0; 2	
Topiramate	**B**	4	1.000	2.0; 2	
Lorazepam	**B**	4	1.000	2.0; 2	

(emergency use)					
Lorazepam (long-term use)	**D**	4	1.000	4.0; 4	
Pregabalin	**B**	4	1.000	2.0; 2	
Oxcarbazepine	**C**	4	1.000	3.0; 3	
Valproic acid	**B**	4	1.000	2.0; 2	
Eslicarbazepine	**C**	2	1.000	3.0; 3	
Lacosamide	**C**	3	1.000	3.0; 3	
Zonisamide	**C**	3	1.000	3.0; 3	
Carbamazepine	**C**	4	1.000	3.0; 3	
Diazepam (emrgency use)	**C**	4(R1) 3(R2)	0.750(R1) 1.000(R2)	2.5; 3(R1) 3.0; 3(R2)	
Diazepam (long-term use)	**D**	3	1.000	4.0; 4	
Midazolam (emrgency use)	**B**	4	0.875	2.3; 2	
Midazolam (long-term use)	**D**	3	1.000	4.0; 4	
Phenytoin	**D**	4	1.000	4.0; 4	
Phenobarbital	**D**	4	1.000	4.0; 4	
Ethosuximide	**D**	3	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**	4	1.000	1.0; 1	
COMT (Catechol-O-Methyltransferase) Inhibitor Entacapone, opicapone	**B**	4	0.875	1.8; 2	
Dopamine agonists, e.g. Ropinirole	**B**	4	1.000	2.0; 2	
Pramipexole	**B**	4	1.000	2.0; 2	
Piribedil, quinagolide, rotigotine	**B**	3	1.000	2.0; 2	
MAO-B inhibitors **Rasagiline**	**C**	4	0.875	2.8; 3	

Selegiline	**C**	4	0.875	2.8; 3	
Bromocriptine, cabergoline	**D**	4	1.000	4.0; 4	
Glutamate antagonists **Amantadine**	**C**	4	0.875	3.3; 3	
Anticholinergics **Biperidene**	**D**	4	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)** **C**	4(R1) 3(R2)	0.750(R1) 0.667(R2)	2.5; -(R1) 2.7; 3(R2)	**Note:** Little effect so risk-benefit negative
Tolterodine	**C**	4	1.000	3.0; 3	
Trospium chloride	**C**	2	1.000	3.0; 3	
Extended-release Oxybutynin	**D**	4	1.000	4.0; 4	
Immediate-release Oxybutynin	**D**	4	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 necessary	**B**	4	0.875	1.8; 2	
H_2 receptor antagonists	**C**	4	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 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**	4	1.000	1.0; 1	
Erythropoetin-stimulating agents (ESA) in patients with renal insufficiency	**A**	4	1.000	1.0; 1	

Iron substitution in patients with cardiac insufficiency **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**	4	1.000	1.0; 1	
Pneumococcal immunizations for persons ≥ 65 years	**A**	4	1.000	1.0; 1	
Shingles (Herpes Zoster) Vaccination	**A**	4	1.000	1.0; 1	

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

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

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

Fludarabin, Bendamustin					
CLL Obinutuzumab	**B**	3	1.000	2.0; 2	
CLL Rituximab	**B**	3	1.000	2.0; 2	
Multiple myeloma **Primary therapy with** **Prednisolone**	**B**	3	1.000	2.0; 2	
Thalidomide	**B**	3	1.000	2.0; 2	
Melphalan	**B**	3	1.000	2.0; 2	
Bortezomib	**B**	3	1.000	2.0; 2	
Lenalidomide	**B**	3	1.000	2.0; 2	
CLL Ibrutinib	**C**	3	1.000	3.0; 3	
CLL Idelalisib	**C**	3	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	
Erythropoesis Stimulating Agents, ESA	**B**	3	1.000	2.0; 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 ≥ 10 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**	2	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 = 264). 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=264)	%
0	164	62.12
1	86	32.58
2	14	5.3
3	0	-

Cons_corr coefficients ranged from 0.333 to 1.000 (mean 0.931, median 1.000). 36 substances fall short of our established cons_corr cutoff of 0.800.

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. 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 original FORTA labels for 93.94% of all substances (n=264); for 16/264 substances (6.06%), the FORTA labels were not confirmed over the two rounds (consensus coefficient≤0.800). 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 was

    - a new substance belonging to a pre-existing FORTA indication (vaccinations)

- 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 these substances