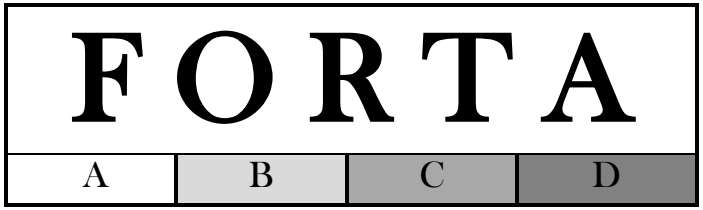
The U.S. F O R T A List

"Fit for The Aged"

Expert Consensus Validation

[1]



Disclaimer

Please keep in mind that the FORTA concept was conceived 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 version of the FORTA List primarily reflects prescribing tendencies in the United States. 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[1]. 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[2].

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 and existing evidence. 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[1]. ‘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. However, the use of the content does not acquit the reader of critical examination in individual cases. 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[1]. We would also like to point out that the FORTA list has been developed for physicians and is not suitable for direct use by patients or any other persons.

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

The U.S.-FORTA expert panel

The following 8 colleagues, representing the United States, 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.

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F O R T A – Physician's guide[1,3,4,7]

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[3,4,5,6,7]

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 addresses older people and is mainly validated for patients aged 65 y or older with significant comorbidities (3 or more diagnoses and drugs); it should be applied to all patients aged 80 y and above. These are people commonly defined as geriatric patients.**

The F O R T A List[1,5,6]
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**	8	1.000	1.0; 1	
Angiotensin receptor antagonists	**A**	8	1.000	1.0; 1	
Long-acting calcium antagonists, dihydropyridine type, for example amlodipine	**A**	8	1.000	1.0; 1	
Diuretics	**(B)** **A**	8 (R1) 8 (R2)	0.750 (R1)	1.7; 2 (R1) 1.3; 1 (R2)	**Note:** 2017 ACC guidelines recommend diuretics as first line. Thiazides are generally safe with low doses in older adults; JNC 8 still advises diuretics as first choice; Thiazides are a first line treatment option in elderly; for thiazides, clear benefit in elderly; many studies demonstrating use is safe; FORTA A for diuretics such as indapamide in light of HYVET trial. Requires lab electrolyte monitoring
Betablockers	**B**	8	0.937	2.1; 2	
Aliskiren	**C**	6	0.833	3.3; 3	**Note:** JNC8 (December 2013) states to avoid for initial treatment; risk of hyperkalemia, especially in setting of renal impairment and and/or diabetes; risk of hypotension, falls/fractures, and increased mortality, especially during initiation of treatment. Older patients may already have other risk factors such as frailty and impaired baroreceptor response;

					acute changes in renal function may occur; potentially serious drug interactions may occur; sensitive to changes in renal function, high risk of hyperkalemia
Alpha blockers	**C**	8	0.875	3.2; 3	**Note:** ALLHAT study showed the harm of alpha-blockers. Orthostatic hypotension and dizziness are common in daily practice. I hardly use them; not first line monotherapy for HTN in any age group due to lack of beneficial outcomes; may be appropriate in men with HTN and BPH, but not as monotherapy for HTN. High risk for orthostasis. Exacerbation of SUI in female patients
Spironolactone	**C**	7	0.928	3.1; 3	**Note:** we have so many other choice. It is associated with hyperkalemia and other side effect; weak antihypertensive. Not a primary antihypertensive agent in the absence of another compelling indication for use
Clonidine	**D**	8	0.937	3.8; 4	**Note:** for HTN urgency or crisis for short term use such as few days, clonidine is effective
Minoxidil	**D**	8	1.000	4.0; 4	
Calcium antagonists, verapamil type	**D**	8	0.812	3.6; 4	**Note:** for resistant HTN, cardizium or verapamil could be tried; in real life it is used for HFPEF/AFIB. Understand the high risk of constipation
Hydralazine*					
HEART FAILURE	**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**	8	1.000	1.0; 1	
	A	8	1.000	1.0; 1	

Angiotensin receptor antagonists					
Betablockers (metoprolol, carvedilol, bisoprolol)	**A**	8	1.000	1.0; 1	
Diuretics	**B**	8	0.937	1.8; 1	**Note:** symptom benefit is greater than mortality benefit
Spironolactone	**B**	8	1.000	2.0; 2	
Digitalis preparations	**C**	8	0.937	3.1; 3	**Note:** not much for good evidence for benefit
Ivabradine	**C**	4	1.000	3.0; 3	
Sacubitril/valsartan⁺					
Isosorbide/hydralazine combo⁺					

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-inhibitors	**A**	8	1.000	1.0; 1	
Acetylsalicylic acid	**A**	8	1.000	1.0; 1	
Unfractionated heparin and low molecular weight heparin	**A**	8	1.000	1.0; 1	
Frequency-lowering betablockers	**A**	8	1.000	1.0; 1	
Atorvastatin	**A**	8	1.000	1.0; 1	

Nitroglycerin spray, single use, acute as on-demand medication	**A**	8	1.000	1.0; 1	
Clopidogrel, prasugrel	**B**	7	0.928	1.8; 2	**Note:** FORTA A for stent = limited duration (at least 1 year) based on guidelines
	A for stent	7	1.000	1.0; 1	
Thrombolytics, especially rTPA (recombinant tissue-type plasminogen activator)	**B**	5	0.900	1.8; 2	**Note:** within 12 hours of symptom onset and unable to receive PCI within 120 minutes; for a high functioning older adult. With appropriate indications thrombolytic have a better outcomes
Nitrates, long-term	**C**	8	1.000	3.0; 3	
Gp IIb/IIIa antagonists (glycoprotein 2b/3a inhibitors)	**C**	7	1.000	3.0; 3	
Ivabradine	**C**	4	0.875	3.2; 3	
Rosuvastatin*					
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**	8	1.000	1.0; 1	
Acetylsalicylic acid (81mg/d, 100 mg/d in Europe)	**A**	8	1.000	1.0; 1	**Note:** in US usual dose is 81mg. It is not marketed as a 100mg tablet.

Frequency-lowering beta blockers up to 3 years **Frequency-lowering beta blockers longer than 3 years**	**A** **C**	8 7	1.000 0.928	1.0; 1 2.8; 3	
Nitroglycerin spray, single use as on-demand medication	**A**	8	1.000	1.0; 1	
Influenza vaccination (inactivated subunit vaccines)	**A**	8	1.000	1.0; 1	
Clopidogrel (12 months after acute coronary syndrome)	**A** with aspirin intolerance	8	1.000	1.0; 1	
Statins	**A** **B** for very old (>85 years) patients	8 7 (R1) 8 (R2)	1.000 0.750 (R1)	1.0; 1 2.0; 2(R1) 2.2; 2(R2)	**Note:** treatment needs to be individualized; very few evidence for oldest old i.e. 85 and above; guidelines recommend if tolerated, but very little data to support benefit after age 85
Nitrates, long-term	**C**	8	1.000	3.0; 3	
Fibrates	**C**	8	0.937	3.1; 3	
Ezetimibe	**C**	8	1.000	3.0; 3	
Amiodarone **All other class-I/III antiarrhythmic agents**	**C** **D**	8 8	1.000 1.000	3.0; 3 4.0; 4	
Dihydropyridine antagonists (if no hypertension)	**D**	8	1.000	4.0; 4	
Niacin	**D**	7	0.928	3.8; 4	
NTG, SL (acute, on demand)*					

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**	8	1.000	1.0; 1	
Atorvastatin	**A**	8	1.000	1.0; 1	
rTPA (recombinant tissue-type plasminogen activator)	**A**	8	1.000	1.0; 1	
Simvastatin	**A**	8	1.000	1.0; 1	
Anticoagulants including new oral anticoagulants	**A**	8	1.000	1.0; 1	**Note:** only if atrial fibrillation
Clopidogrel	**A**	8	1.000	1.0; 1	
Dipyridamole plus acetylsalicylic acid	**B**	8	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**	8	1.000	1.0; 1	
New Oral Anticoagulants (NOACs)	**B**	8	0.937	1.8; 2	
Except apixaban	**A**	8	1.000	1.0; 1	
Digoxin	**B**	8	1.000	2.0; 2	
Oral anticoagulants (e.g. warfarin)	**B**	8	0.937	1.8; 2	
Alternative: low molecular weight heparin	**C**	8	0.937	2.8; 3	**Note:** LMWH is still preferred in cancer patients per guidelines
Diltiazem, verapamil	**C**	8	0.875	2.7; 3	**Note:** reasonable alternative to BB, preferred over digoxin (safer)
Class III antiarrhythmic agent amiodarone	**C**	8	1.000	3.0; 3	
All other class I/III antiarrhythmic agents	**D**	8	0.937	3.8; 4	

Class III antiarrhythmic agent dronedarone	**D**	8	1.000	4.0; 4	
Acetylsalicylic acid (100 mg/d)	**(D)** **C**	7 (R1) 8 (R2)	0.785 (R1)	3.5; 4 (R1) 3.3; 4 (R2)	**Note:** although not as effective in preventing strokes may provide some protection in those unable to take anticoagulants; while some protection is provided for those not able to take anticoagulants, my classification would still be a D. It is just not that effective, in my opinion; FORTA C for patients unable to take anticoagulants or with known ASCVD + Afib; In U.S. dose is 81 or 325mg/day. This can be used if patient is low risk (CHADS-VASC = 0), but unclear efficacy. Clopidogrel + ASA recommended if intermediate or high risk and not a candidate for anticoagulation, but lower efficacy

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**	8	1.000	1.0; 1	
Systemic glucocorticoids, acute, short-term use in cases of exacerbation	**A**	8	1.000	1.0; 1	
Antibiotics (acute) in cases of exacerbation, after calculated selection and, if necessary, according to antibiogram	**A**	8	1.000	1.0; 1	

Long-term administration of oxygen (only in cases of respiratory failure and pulmonary heart disease)	**A**	8	1.000	1.0; 1	
Annual influenza immunizations	**A**	8	1.000	1.0; 1	
Pneumococcal immunizations for persons ≥ 65 years	**A**	8	1.000	1.0; 1	
Inhalative glucocorticoids	**(C)** **B**	8 (R1) 8 (R2)	0.562 (R1)	2.1; 2 (R1) 2.1; 2 (R2)	**Note:** per GOLD 2017 guidelines, effective when combined with LABA/LAMA; triple therapy with LABA and LAMA showed improved lung function, symptoms, and health status; Long-term use at recommended doses associated w/ good safety profile and adverse side effects are dose related; best evidence; per updated GOLD guidelines; ICS are recommended in addition to LABA or LA anticholinergic for Group C/D patients (high risk).
Inhalative beta 2 mimetic agents	**B**	8	0.875	1.7; 2	**Note:** clear evidence on beneficial role of beta-2 agonists; GOLD 2018 guidelines indicate these can be considered first line and even in combination with LAMA
Theophylline	**C**	8	0.937	3.1; 3	**Note:** not much evidence for benefit. Side effects are common
Mucolytic agents, e,g, acetyl cysteine, bromhexine	**C**	6	1.000	3.0; 3	
Roflumilast	**C**	6	1.000	3.0; 3	
Systemic glucocorticoids, chronic use	**D**	8	1.000	4.0; 4	
Antitussives: opioid A., e.g. codein; non-opioid A., e.g. butamirate	**D**	7	1.000	4.0; 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					
Parenteral bisphosphonates (e.g. ibandronate, IV every 3 months)	**A**	8	0.937	1.1; 1	**Note:** zolendronic acid has best data; ibandronate data not good for nonvertebral; would change this to zolendronic acid; no evidence for everyone
Denosumab	**A**	8	0.937	1.1; 1	**Note:** no evidence for everyone
Bisphosphonates, orally administered	**B**	8	0.937	1.8; 2	**Note:** in general, elderly can take oral bisphosphonates safely. Individual patient concerns (e.g. swallowing, immobility, cognitive impairment) may impact safety
Raloxifene (for women)	**B**	8	1.000	2.0; 2	
Calcium and vitamin D supplements (as prophylaxis for persons ≥ 65 years)	**(A)** **B**	8 (R1) 8 (R2)	0.687 (R1)	1.6; 2 (R1) 2.2; 3 (R2)	**Note:** evidence suggests that supplementation with Calcium and Vitamin D is not necessary, if oral food intake is adequate; no evidence for everyone; no proven benefit for prevention in patients who have adequate dietary calcium intake and normal vitamin D levels; FORTA C based on new 2018 US preventative task force recommendations; calcium increases BMD, but fracture prevention is minimal. Dietary intake preferred. No clear role when dietary intake is adequate and vitamin D level s are normal; inconsistent evidence to support benefit in fracture prevention
Teriparatide	**C**	8	0.875	2.7; 3	
Parathormone	**C**	5	1.000	3.0; 3	
Nandrolone decanoate	**D**	4	1.000	4.0; 4	
Fluoride	**D**	6	1.000	4.0; 4	
Hormone replacement therapy (HRT): estrogen, except for perimenopausal)	**D**	8	1.000	4.0; 4	
Calcitonin, nasal*					

Calcium + vitamin D* Osteoporosis (treatment) and as adjunct to drug therapy to ensure adequate Ca and vitamin D intake necessary.					
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					
Insulin and insulin analogs (if absolutely necessary)	**B**	8	0.937	1.8; 2	**Note:** can be used safely if monitor; avoid in frail, cognitively impaired; insulin is indispensable (when absolutely necessary)
Metformin	**(B)** **A**	8 (R1) 8 (R2)	0.750 (R1)	1.5; - (R1) 1.3; 1(R2)	**Note:** decades of experience, well-established safety and efficacy profile; first line agent, accumulating mortality benefits across conditions; lower risk for hypoglycemia when given as monotherapy; safety and efficacy well-established in literature with decades of evidence; proven efficacy, but some safety concerns
Acarbose	**B**	8	0.812	2.3; 2	**Note:** adverse events preclude its use – bloating, flatulence, etc.; GI upset, no specific studies in older adults
DPP4 (Dipeptidylpeptidase) Inhibitors	**B**	8	1.000	2.0; 2	
GLP1 (Glucagon-Like Peptide-1) analogs	**B**	8	1.000	2.0; 2	

3rd generation sulfonylureas (for example, glimepiride)	**C**	8	0.812	2.6; 3	**Note:** proven efficacy, with some safety concerns. Shorter acting agents preferred over longer acting agents. Key to management is to have less rigid HgA1C goals
Glinides (for example, nateglinide)	**C**	8	0.937	2.8; 3	**Note:** less hypoglycemia compared to sulfonylureas. Key to management is to have less rigid HgA1C goals
PPAR-ɣ Ligands (Peroxisomal Proliferator-Activated Receptor gamma)					
Pioglitazone	**C**	8	0.937	2.8; 3	**Note:** pioglitazone well tolerated in patients with renal insufficiency as long as there is no heart failure
Rosiglitazone	**D**	8	0.937	3.8; 4	
1st generation sulfonylureas (for example, glyburide)	**D**	8	1.000	4.0; 4	
SGLT-2 inhibitors	**D**	6	0.916	3.8; 4	**Note:** potential cardiovascular benefits but must monitor for GFR, volume status, urination frequency/infections
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 (in phases when clearly indicated)	**B**	8	0.875	2.2; 2	**Note:** the outcomes are not easy to monitor in daily practice. The effect is not that much (less clinically significant); questionable efficacy
Memantine	**C**	8	0.875	2.7; 3	**Note:** efficacy questionable for dementias other than AD and no proven benefit in mild AD. Similar efficacy and better tolerated for patients with moderate AD

Statins	**D**	8	1.000	4.0; 4	**Note:** FORTA D as a specific treatment of dementia; but management of vascular risk factors is critical in vascular dementia and if patient has known cerebrovascular disease, statins should be part of dementia management as well as aspirin
Selegiline	**D**	6	1.000	4.0; 4	
Nimodipine	**D**	6	1.000	4.0; 4	
Ginkgo biloba	**D**	8	1.000	4.0; 4	
Ergoline derivatives	**D**	7	1.000	4.0; 4	
Pyritinol	**D**	5	1.000	4.0; 4	
Antioxidants: Vitamin E, selenium, vitamin C	**D**	7	0.928	3.8; 4	
Phytotherapeutic agents, e.g. ginseng	**D**	8	1.000	4.0; 4	
Hormone preparations, e.g. DHEA (Dehydroepiandrosterone), testosterone	**D**	8	1.000	4.0; 4	
Antiphlogistics, e.g. indomethacin	**D**	8	1.000	4.0; 4	
Desferrioxamine	**D**	6	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)	**C**	7	1.000	3.0; 3	

Citalopram/escitalopram, sertraline, fluoxetine in the usual dosages					
Mirtazapine (15-45mg/d)	**C**	8	1.000	3.0; 3	
SNRI (Serotonin-Noradrenalin-Reuptake-Inhibitors) venlafaxine, duloxetine	**C**	8	1.000	3.0; 3	
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**	8	1.000	3.0; 3	
Haloperidol (initially 0.5 mg/d, max. 3 mg/d)	**C**	8	0.937	3.1; 3	**Note:** should be avoided if possible due to increased risk of EPS in elderly population
Quetiapine (25-200 mg/d)	**C**	8	1.000	3.0; 3	
Aripiprazole	**D**	8	0.937	3.8; 4	**Note:** unclear why this would be different than others, except clozapine and first-generation agents. It has fewer SEs compared to risperidone, quetiapine, olanzapine
Clozapine (10-50 mg/d)	**D**	8	1.000	4.0; 4	
Olanzapine*					

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**	8	1.000	3.0; 3	
Risperidone (initiallly 0.5-1 mg/d, Maximum 3 mg/d)	**C**	8	1.000	3.0; 3	
Quetiapine (25-200 mg/d)	**C**	7	1.000	3.0; 3	
Citalopram	**C**	8	0.937	2.8; 3	
Valproic acid*					
Other SGAs (e.g. aripiprazole, olanzapine)*					
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**	8	0.812	2.6; 3	**Note:** much lower side effects/adverse events compared to hypnotic agents. Very commonly used in the US
Tetracyclic antidepressant Mirtazapine (15-30mg)	**C**	8	0.875	2.7; 3	**Note:** very commonly used as an adjunct agent for improved sleep (at 7.5-15 mg nightly) and as an appetite stimulant. Side effect profile minimal compared to benefits

Tricyclic antidepressant Doxepine	**(C)** **D**	8 (R1) 8 (R2)	0.750 (R1)	3.5; 4 (R1) 3.6; 4 (R2)	**Note:** risk for falls/fractures too high, in addition to cognitive impairment; avoid; can worsen cognitive status; not aware of studies examining efficacy for this indication; not recommended for use due to exacerbation of dementia/cognitive impairment; increased risk of falls/fractures; not recommended for use as hypnotic in elderly due to poor tolerability; should be avoided. Risk outweighs benefit
Zolpidem	**(C)** **D**	8 (R1) 8 (R2)	0.625 (R1)	3.7; 4 (R1) 3.6; 4 (R2)	**Note:** risks outweigh benefits in older adults; avoid if possible due to risk of psychomotor impairment, delirium, falls, fractures, MVAs. Adverse effects similar to benzodiazepines. Minimal efficacy; not recommended for use due to exacerbation of dementia/cognitive impairment; increased risk of falls/fractures; avoid; can worsen cognitive status; not aware of studies examining efficacy for this indication; risk for falls and delirium; although non-dependence forming, same risks as BZDs. Risks clearly outweigh benefits.
Trazodone*					
Zaleplon*					
Eszopiclone*					
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)					**Note:** very commonly used - very effective, especially when dose is optimized to patient response and tolerability

Sertraline **Escitalopram** **Citalopram**	**B**	8	0.875	1.7; 2	
	B	8	0.875	1.7; 2	**Note:** very commonly used - very effective, especially when dose is optimized to patient response and tolerability
	B	8	1.000	2.0; 2	
Tricyclic antidepressant **Nortriptyline**	**(C)** **D**	8 (R1) 8 (R2)	0.750 (R1)	3.5; - (R1) 3.5; - (R2)	**Note:** risks outweigh benefits, especially when newer, safer agents have been available for some time now; due to increased risk of anticholinergic effects, sedation, delirium, orthostasis and overall poor tolerability at antidepressant doses. Should be avoided if at all possible; avoid because of ADEs; safer alternatives; risks clearly outweigh benefits. While better tolerated than amitriptyline, still highly anticholinergic and may cause confusion, falls; much safer alternatives available
Tetracyclic antidepressant **Mirtazapine**	**C**	8 (R1) 8 (R2)	0.687 (R1)	2.3; 3 (R1) 2.5; - (R2)	**Note:** limited data suggests it is as effective as other AD classes. May be beneficial in patients with anorexia, weight loss, or insomnia; good adjunct agent, with SSRI or SNRI. Curvilinear dose response is ideal for patients with sleep disturbances; data supports efficacy and may be beneficial in some patients for weight loss or insomnia; but some mild anticholinergic activity may limit use in some patients.
SNRIs (Serotonin-Noradrenalin Reuptake Inhibitors) **Venlafaxine**	**C**	8 (R1) 8 (R2)	0.687 (R1)	2.3; 3 (R1) 2.6; 3 (R2)	**Note:** studies support that SNRIs are both efficacious and well-tolerated in elderly population; may be useful when there is concurrent neuropathic pain; safety and efficacy is well documented; some variance between agents; must be appropriately prescribed and dosed; data support efficacy and tolerability; somewhat higher drop-out rates than SSRIs and risk of HTN (though impact is small)
Duloxetine	**C**	8 (R1) 8 (R2)	0.687 (R1)	2.3, 3 (R1) 2.5; - (R2)	**Note:** studies support that SNRIs are both efficacious and well-tolerated in elderly population; may be useful when there is concurrent neuropathic pain; safety and efficacy is well documented; some variance between agents; must be appropriately prescribed and dosed; should be same as venlafaxine

Dopamine and norepinephrine reuptake inhibitor Bupropion	**C**	8	0.937	2.8; 3	
Trazodone	**C**	8	0.875	3.0; 3	**Note:** used as an adjunct, effective when dosed responsibly
Olanzapine	**C**	6	0.833	3.3; 3	**Note:** not much good evidence; as augmenting agent
Vortioxetine	**C**	5	0.900	3.2; 3	**Note:** not much good evidence
Quetiapine	**C**	7	0.857	3.2; 3	**Note:** not much good evidence; as augmenting agent
Benzodiazepines: General	**D**	8	1.000	4.0; 4	**Note:** not much good evidence and high risk for delirium; not even short-acting for depression, highly addictive
Long-acting,	**D**	7	1.000	4.0; 4	**Note:** not much good evidence and high risk for delirium
Short-acting	**(C)** **D**	7 (R1) 8 (R2)	0.571 (R1)	3.8; 4 (R1) 3.7; 4 (R2)	**Note:** should not be used to treat depression; may exacerbate; depression is an inappropriate indication for benzodiazepines; not much good evidence and high risk for delirium
St. John's Wort	**D**	8	1.000	4.0; 4	
Aripiprazole*					
Vilazodone*					
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					
Quetiapine	**B**	7	1.000	2.0; 2	
Lamotrigine	**C**	8	0.937	2.8; 3	
Valproic acid	**C**	7	1.000	3.0; 3	
Lithium	**C**	7	1.000	3.0; 3	
Carbamazepine	**D**	7	1.000	4.0; 4	

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**	8	0.812	2.1; 2	
Tetracyclic antidepressant Mirtazapine	**C**	8	0.875	2.7; 3	**Note:** very commonly used as an adjunct agent for improved sleep (at 7.5-15 mg nightly) and as an appetite stimulant. Side effect profile minimal compared to benefits
ω1-Benzodiazepine agonists **Zolpidem**	**(C)** **D**	8 (R1) 8 (R2)	0.750 (R1)	3.5; 3 (R1) 3.6; 4 (R2)	**Note:** avoid if possible due to risk of psychomotor impairment, delirium, falls, fractures, MVAs. Adverse effects similar to benzodiazepines. Minimal efficacy; risks outweigh benefits, increased risk of sedation, fall/fractures; avoid because of ADEs; adverse effects far outweigh any minimal benefits. Cannot be used long term due to buildup of tolerance; although non-dependence forming, same risks as BZDs. Risks clearly outweigh benefits
Zaleplone	**(C)** **D**	7 (R1) 8 (R2)	0.785 (R1)	3.4; 3 (R1) 3.6; 4 (R2)	**Note:** avoid if possible due to risk of psychomotor impairment, delirium, falls, fractures, MVAs. Adverse effects similar to benzodiazepines. Minimal efficacy; risks outweigh benefits, increased risk of sedation, fall/fractures; adverse effects far outweigh any minimal benefits. Cannot be used long term due to buildup of tolerance; although non-dependence forming, same risks as BZDs. Risks clearly outweigh benefits
Benzodiazepines, e.g. Oxazepam (medium half-life)	**D**	8	1.000	4.0; 4	
	D	8	1.000	4.0; 4	

Triazolam (very short half-life)					
Tricyclic antidepressant Doxepine	**D**	8	0.812	3.6; 4	**Note:** low dose as safer alternative; data exists to support that ADEs associated with 6mg/d or less are similar to placebo
Antihistamine Diphenhydramine	**D**	8	1.000	4.0; 4	
Eszopiclone*					
Ramelteon*					
Surovexant*					
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**	8	0.875	1.3; 1	
Opioids, e.g. Buprenorphine, oxycodone, hydromorphone	**B**	8	0.875	2.2; 2	**Note:** opioids only if absolutely necessary (cancer pain okay—A)
Morphine	**C**	8	0.937	2.8; 3	
Tramadol	**C**	8	0.937	2.8; 3	**Note:** same as opiates. Safety concern with other serotonergic agents. Less sedation vs. opiates
SSRI (Selective Serotonin Reuptake Inhibitors) / SNRI (Serotonin-Norepinephrine-Reuptake Inhibitor), e.g. venlafaxine	**C**	8	0.812	2.6; 3	**Note:** evidence exists with respect to ascending pathway pain modulation, especially when used concurrently with other agents.

(only if absolutely necessary)					
Antiepileptic agents (only for neuropathic pain) **Pregabalin/gabapentin**	**C**	8	0.812	2.6; 3	**Note:** has place in therapy for patients with neuropathic pain – diabetics, neurodegenerative diseases, etc. Renal dosing is needed, and careful assessment for possible potentiating effects with other agents that may be sedating or centrally depressing.
Carbamazepine	**D**	8	0.937	3.8; 4	
Tricyclic antidepressant amitriptyline	**D**	8	1.000	4.0; 4	
NSAIDs (nonsteroidal anti-inflammatory drugs, for long-term use), e.g. naproxen	**D**	8	1.000	4.0; 4	
Cox-2 inhibitors, e.g. celecoxib	**D**	8	0.875	3.7; 4	
Lidocaine (topical)*					
Capsaicin (topical)*					
Skeletal muscle relaxants (e.g. cyclobenzaprine, metaxolone, methocarbamol, chlorzoxazone)*					
Meperidine*					

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	0.928	2.1; 2	**Note:** probably not as effective as others; not much good evidence
Topiramate	**B**	7	0.857	2.2; 2	**Note:** cognitive ADEs (worse than others); don't know of studies specifically in older adults; not much good evidence
Lorazepam (emergency use)	**B**	7	1.000	2.0; 2	
Lorazepam (long-term use)	**D**	7	1.000	4.0; 4	
Eslicarbazepine	**C**	2	1.000	3.0; 3	
Lacosamide	**C**	5	1.000	3.0; 3	
Zonisamide	**C**	5	1.000	3.0; 3	
Valproic acid	**C**	7	1.000	3.0; 3	
Pregabalin	**C**	7	0.928	2.8; 3	
Carbamazepine	**C**	7	1.000	3.0; 3	
Oxcarbazepine	**C**	7	1.000	3.0; 3	

Midazolam (emergency use)	**C**	7	1.000	3.0; 3	
Midazolam (long-term use)	**D**	7	1.000	4.0; 4	
Diazepam (emergency use)	**C**	7	1.000	3.0; 3	
Diazepam (long-term use)	**D**	7	1.000	4.0; 4	
Phenytoin	**D**	6	1.000	4.0; 4	
Ethosuximide	**D**	5	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**	8	1.000	1.0; 1	
COMT (Catechol-O-Methyltransferase) Inhibitor entacapone	**B**	8	1.000	2.0; 2	
Dopamine agonists, e.g. ropinirole	**B**	8	0.875	2.2; 2	**Note:** potential to exacerbate Impulse Control Disorders (ICDs) and Dopamine Agonist Withdrawal Syndrome (DAWS); rate of drug intolerance in elderly population is very high. Commonly causes psychiatric side effects (e.g. psychosis)

pramipexole	**B**	8	0.937	2.1; 2	**Note:** potential to exacerbate Impulse Control Disorders (ICDs) and Dopamine Agonist Withdrawal Syndrome (DAWS)
Piribedil, quinagolide, (rotigotine)	**B**	7	1.000	2.0; 2	**Note:** rotigotine was proposed to be re-rated separately and re-labeled under new entries at the end
MAO-B inhibitors					
selegiline	**C**	8	1.000	3.0; 3	
rasagiline	**C**	8	1.000	3.0; 3	
Bromocriptine, cabergoline	**D**	8	1.000	4.0; 4	
Glutamate antagonists Amantadine	**D**	8	0.937	3.8; 4	
Dopamine agonist Rotigotine*					
Anticholinergics benztropine, trihexyphenidyl*					
lower urinary tract symptoms (LUTS), includes benign prostate hyperplasia and 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					
Antimuscarinics	**C**	8	1.000	3.0; 3	

except: **Fesoterodine** **immediate-release oxybutynin**	**B** **D**	7 8	0.928 1.000	2.1; 2 4.0; 4	
5α-reductase inhibitors	**B**	8	0.937	1.8; 2	**Note:** metaanalysis has shown effectiveness in LUT symptoms, maximum flow rate, episodes of urinary retention, need for surgical intervention
Mirabegron	**C**	8	0.937	2.8; 3	
α1-blockers **except: silodosin and tamsulosin**	**D** **C**	7 8 (R1) 8 (R2)	0.928 0.750 (R1)	3.8; 4 2.5; 3 (R1) 2.5; 2 (R2)	**Note:** reasonable therapy for BPH; FORTA D/C if not effective **Note:** studies support efficacy and safety; better tolerated that non-selective alpha-blockers; metaanalysis have found to be effective in bph symptoms; better safety profile compared to non-selective alpha blockers; data support efficacy, better tolerated than non-selective agents; some concern with drug interactions

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**	8	0.937	2.1; 2	**Note:** not much good evidence; if older patient must be treated with NSAID, then concurrent PPI should be standard of care. Potential benefit clearly outweighs risk
H_2 receptor antagonists	**C**	8	0.937	2.8; 3	**Note:** H2 receptor antagonists may exacerbate underlying cognitive impairment in patients with mild cognitive impairment or Alzheimer's and other related dementias; hypersecretion of acid and tachyphylaxis can occur with continued use; seems reasonable to use if can avoid using PPIs
Metoclopramide*					
Sucralfate*					
GI antispasmodics (e.g. atropine, dicyclomine, hyoscamine, propantheline, scopolamine)*					

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**	8	1.000	1.0; 1	
Erythropoetin-stimulating agents (ESA) in patients with renal insufficiency	**A**	8	0.937	1.1; 1	**Note:** not much good evidence
Iron substitution in patients with cardiac insufficiency **Proof of iron deficiency**	**A**	8	1.000	1.0; 1	

No proof of iron deficiency					
	B	7	0.928	2.1; 2	**Note:** if not iron deficient, consider FORTA C or D. Iron can cause constipation and likely ineffective if no iron deficiency

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**	4	1.000	2.0; 2	
Aromatase inhibitors	**B**	4	1.000	2.0; 2	
Immunotherapy / "Targeted" therapy Trastuzumab	**B**	3	1.000	2.0; 2	
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 inhibitors	**B**	3	1.000	2.0; 2	
Immunotherapy/Targeted Therapy **Trastuzumab / lapatinib**	**B**	3	1.000	2.0; 2	
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**	2	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	**B**	3	0.833	2.3; 2	**Note:** not much good evidence
Vinorelbin	**B**	3	0.833	2.3; 2	**Note:** not much good evidence
Primary combination therapy **Cisplatin/gemcitabin, or cisplatin/vinorelbin**	**C**	3	1.000	3.0; 3	
GASTRIC CANCER					
ECF Regime (Epirubicin, Cisplatin, 5-Fluorouracil)	**B**	3	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) **Azacytidine**	**B**	2	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, Fludarabin, Bendamustin**	**B**	2	1.000	2.0; 2	
CLL **Obinutuzumab**	**B**	3	1.000	2.0; 2	
CLL **Rituximab**	**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	
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	
Multiple myeloma **Bortezomib**	**B**	3	1.000	2.0; 2	
Multiple myeloma **Lenalidomide**	**B**	3	1.000	2.0; 2	

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	

*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[1]

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 ARTERIAL HYPERTENSION	**Rater-based FORTA Class (bold if: κ > 0.500 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					
Hydralazine	**C**	7	1.000	3.0; 3	
	Rater-based FORTA Class (bold if:			**Expert ratings on a numerical scale: A=1, B=2, C=3, D=4**	

EXISTING INDICATION HEART FAILURE	κ > 0.500 and label distance < 2)	Nr. of raters	κ-Index	Mean; Mode	Selection of pertinent comments given by participating experts during the consensus procedure
Substance/group					
Isosorbide/hydralazine combo	**B**	7	0.787	2.1; 2	**Note:** for patients unable to take ACE inhibitors/ ARBs or in African Americans
Sacubitril/valsartan	**C**	4	1.000	3.0; 3	**Note:** for now because drug is relatively new
EXISTING INDICATION ACUTE CORONARY SYNDROME	**Rater-based FORTA Class (bold if: κ > 0.500 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					
Rosuvastatin	**A**	7	1.000	1.0; 1	
EXISTING INDICATION CHRONIC THERAPY FOLLOWING MYOCARDIAL INFARCTION	**Rater-based FORTA Class (bold if: κ > 0.500 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					
Nitroglycerine, sublingual (acute, on demand)	**A**	7	1.000	1.0; 1	

EXISTING INDICATION OSTEOPOROSIS	Rater-based FORTA Class (bold if: κ > 0.500 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					
Calcium + vitamin D **Osteoporosis (treatment) and as adjunct to drug therapy to ensure adequate Ca and vitamin D intake necessary.**	**A**	7	0.580	1.3; 1	**Note:** recommended for osteoporosis treatment as adjunct to drug therapy; efficacy data unclear, but good safety profile (with vitamin D)
Calcitonin, nasal	**C**	7	0.788	3.1; 3	

EXISTING INDICATION INSOMNIA / SLEEP DISORDERS:	Rater-based FORTA Class (bold if: κ > 0.500 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					
Ramelteon	**B**	7	0.645	2.2; 2	
Surovexant	**C**	6	0.553	2.5; 3	
Eszopiclone	**D**	8	0.817	3.8; 4	

EXISTING INDICATION BPSD: RESTLESSNESS, AGITATION, (AGGRESSIVENESS)	**Rater-based FORTA Class (bold if: κ > 0.500 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					
Valproic acid	**C**	6	0.606	3.3; 3	**Note:** no evidence in dementia patients unless patient has underlying mood disorder
Other second-generation antipsychotics (e.g. aripiprazole, olanzapine)	**C**	7	0.788	3.1; 3	
EXISTING INDICATION BPSD: SLEEP DISORDERS	**Rater-based FORTA Class (bold if: κ > 0.500 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					
Trazodone	**C**	7	0.787	2.8; 3	**Note:** most evidence is lacking for sleep
Zaleplon	**D**	7	1.000	4.0; 4	
Eszopiclone	**D**	7	1.000	4.0; 4	
	Rater-based FORTA Class (bold if: κ > 0.500 and label distance < 2)			**Expert ratings on a numerical scale: A=1, B=2, C=3, D=4**	

EXISTING INDICATION BPSD: PARANOIA, HALLUCINATION		**Nr. of raters**	**κ-Index**	**Mean; Mode**	**Selection of pertinent comments given by participating experts during the consensus procedure**
Substance/group					
Olanzapine	**C**	7	0.788	3.1; 3	**Note:** must do NPI questionnaire and if positive then use is appropriate
EXISTING INDICATION DEPRESSION Prophylaxis and therapy for patients with moderate to major depression	**Rater-based FORTA Class (bold if: κ > 0.500 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					
Aripiprazole	**C**	6	1.000	3.0; 3	**Note:** must do NPI questionnaire and if positive then use is appropriate
Vilazodone	**C**	5	1.000	3.0; 3	**Note:** must do NPI questionnaire and if positive then use is appropriate
	Rater-based FORTA Class (bold if: κ > 0.500 and label distance < 2)			**Expert ratings on a numerical scale: A=1, B=2, C=3, D=4**	

EXISTING INDICATION PAIN		Nr. of raters	κ-Index	Mean; Mode	Selection of pertinent comments given by participating experts during the consensus procedure
Substance/group					
Lidocaine (topical)	**B**	8	0.813	2.1; 2	**Note:** low quality evidence for efficacy
Capsaicin (topical)	**B**	7	0.787	2.1; 2	**Note:** usually has lot of skin irritation in elderly
Skeletal muscle relaxants (e.g. cyclobenzaprine, metaxolone, methocarbamol, chlorzoxazone)	**D**	8	1.000	4.0; 4	**Note:** no evidence for use in elderly
Meperidine	**D**	8	1.000	4.0; 4	**Note:** high risk of seizures with repeated dosing. Poor efficacy with oral administration; increases delirium
EXISTING INDICATION PARKINSON'S DISEASE	**Rater-based FORTA Class (bold if: κ > 0.500 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					
Rotigotine**	**C**	5	1.000	3.0; 3	**Note:** same as ropinirole, pramipexole; higher risk of psychiatric ADEs in elderly
Anticholinergics benztropine, trihexyphenidyl	**D**	7	1.000	4.0; 4	**Note:** lot of adverse effects in elderly
	Rater-based FORTA Class (bold if:			**Expert ratings on a numerical scale: A=1, B=2, C=3, D=4**	

EXISTING INDICATION GASTROINTESTINAL ILLNESSES/ CONCOMITANT THERAPY WITH NSAIDs	κ > 0.500 and label distance < 2)	Nr. of raters	κ-Index	Mean; Mode	Selection of pertinent comments given by participating experts during the consensus procedure
Substance/group					
Sucralfate	**C**	6	0.606	3.3; 3	**Note:** may impair absorption of other drugs and doses must be separated. Unclear benefit compared to PPIs, H2 blockers
Metoclopramide	**D**	6	0.609	3.6; 4	**Note:** should be avoided for treatment of GERD or N/V (unless due to gastroparesis)
Gastrointestinal antispasmodics (e.g. atropine, dicyclomine, hyoscyamine, propantheline, scopolamine)	**D**	7	0.791	3.8; 4	**Note:** questionable benefit; highly anticholinergic. Risks clearly outweigh benefits.
NEW INDICATION Allergic conjunctivitis/rhinitis	**Rater-based FORTA Class (bold if: κ > 0.500 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					
Corticosteroids (inhaled, nasal)	**A**	8	0.817	1.1; 1	
Second generation antihistamines (e.g.) Loratadine, fexofenadine, cetirizine	**B**	8	1.000	2.0; 2	
First generation antihistamines (e.g. diphenhydramine, hydroxyzine, doxylamine)	**D**	7	0.651	3.7; 4	**Note:** avoid except for acute allergic reactions

**: Rotigotine was proposed to be re-rated separately (see on p. 30)

SUMMARY OF STATISTICAL METHODS
(The following descriptions of the statistical methods and calculations are based on the first version of the FORTA List[1]. Former definitions and explanations are adopted unchanged.)

Consensus Coefficient[1]

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 = 243). 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, 2/3 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=243)	%
0	152	62.55
1	74	30.45
2	15	6.17
3	2	0.82

Cons_corr coefficients ranged from 0.563 to 1.000 (mean 0.950, median 1.000). Substances falling short of our established cons_corr cutoff of 0.800 underwent re-evaluation in a second round: n=16

Confirmation/determination of FORTA labels[1]

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[1]:

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 16 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 96.3% of all substances (n=243); for 9/243 substances (3.7%), 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[1]

- A total of 31 substances were accepted for potential addition to the revised FORTA List. Selection criteria: 1) acceptance of all substances suggested by ≥ 1 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 ≥ 4 raters (excluding abstentions) during Round 2. The 30 substances included:

    - 27 new substances belonging to pre-existing FORTA indications and
    - 3 new substances belonging to a new 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

- All new substances had a kappa index higher than 0.500. Suggesting a high level of inter-rater agreement for these substances

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