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

Italy

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Disclaimer

Please keep in mind that the FORTA Concept was conceived and developed in Germany. While building on an international foundation of medical evidence and experience for the medications listed, including already existing "negative lists" and classification systems, this FORTA List primarily reflects prescribing tendencies in Italy. 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 5 colleagues, representing Italy, 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**	5	1.000	1.0 ; 1	
Angiotensin receptor antagonists	**A**	5	1.000	1.0; 1	
Long-acting calcium antagonists, dihydropyridine type, for example amlodipine	**A**	5	0.900	1.2; 1	
Betablockers except atenolol	**C**	5	0.900	3.2; 3	
Atenolol	**D**	5	0.900	3.8; 4	
Diuretics except indapamid	**B**	5 (R1) 5 (R2)	0.800 (R1) 0.900 (R2)	2.0; 2 (R1) 1.8; 2 (R2)	**Note:** I guess that diuretics are class B not for limited efficacy but for safety concerns, then also indapamide has adverse effects that should be monitored; May increase the risk of dehydration, acute kidney injury and electrolyte imbalance among frail patients.
Indapamid	**A**	5	0.900	1.2; 1	
Alpha blockers	**C**	5	0.900	3.2; 3	**Note:** Alpha blockers are strongly related to adverse events and, in addition, may increase the risk of syncope and falls. The extended-release tablets should be avoided among pre-frail or frail patients
Spironolactone	**C**	4	1.000	3.0; 3	

Moxonidine	**C**	4	0.875	3.3; 3	
Aliskiren	**C**	4	1.000	3.0; 3	
Urapidil	**C**	4	1.000	3.0; 3	
Clonidine	**D**	5	1.000	4.0; 4	**Note:** I suggest to use it only in case of acute stress and under strict medical monitoring (for instance, as a "rescue" drugs before surgery among people with very high blood pressure not previously recognized as affected by hypertension
Minoxidil	**D**	4	1.000	4.0; 4	
Calcium antagonists, verapamil type	**D**	5	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**	5	1.000	1.0; 1	
Angiotensin receptor antagonists	**A**	5	1.000	1.0; 1	
Betablockers (metoprolol, carvedilol, bisoprolol)	**A**	5	1.000	1.0; 1	
Diuretics	**A**	4	1.000	1.0; 1	
Gliflozins (SGLT2 inhibitors) only those substances which have been approved for this indication (dapgliflozine)	**B**	5	0.900	2.2; 2	
Spironolactone	**B**	5 (R1)	0.800 (R1)	2.0; 2 (R1)	**Note:** Strong evidence of its positive effect

		5 (R2)	0.900 (R2)	1.8; 2 (R2)	
Digitalis preparations	**C**	5	0.900	3.2; 3	
Ivabradine	**C**	4	1.000	2.8; 3	
Nebivolol	**A**	4	1.000	1.0; 1	
Iron substitution in patients with iron deficiency	**A**	4	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**	5	1.000	1.0; 1	
Acetylsalicylic acid	**A**	5	1.000	1.0; 1	
Unfractionated heparin and low molecular weight heparin	**A**	5	1.000	1.0; 1	
Frequency-lowering betablockers, e.g. metoprolol or bisoprolol	**A**	5	1.000	1.0; 1	
Atorvastatin	**A**	5	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	5 4	1.000 1.000	2.0; 2 1.0; 1	
Thrombolytics, especially rTPA (recombinant tissue-type plasminogen activator)	**B**	3	0.833	2.3; 2	
Nitrates, long-term	**C**	5	1.000	3.0; 3	

Gp IIb/IIIa antagonists (glycoprotein 2b/3a inhibitors)	**C**	5	1.000	3.0; 3	
Ivabradine	**C**	4	1.000	3.0; 3	
Other statins	A	5	1.000	1.0; 1	
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**	5	1.000	1.0; 1	
Acetylsalicylic acid (100 mg/d)	**A**	5	1.000	1.0; 1	
Frequency-lowering beta blockers up to 3 years	**A**	5	1.000	1.0; 1	
Frequency-lowering beta blockers longer than 3 years	**C**	4	1.000	3.0; 3	
Nitroglycerin spray, single use as on-demand medication	**A**	5	1.000	1.0; 1	
Influenza vaccination (inactivated subunit vaccines)/pneumococcal immunizations	**See vaccinations**				
Statins	**A**	5	1.000	1.0; 1	**Note:** In secondary prevention statins are useful also in the very

	B for very old (>85 years) patients	5 (R1) 5 (R2)	0.800 (R1) 0.900 (R2)	2.0; 2 (R1) 1.8; 2 (R2)	old. It might be worthy to specify the clinical status, e.g. end of life patients or extremely frail, better than age; Uncertain risk/benefit ratio, likely unfavorable
Clopidogrel (12 months after acute coronary syndrome)	**A** with aspirin intolerance	5	1.000	1.0; 1	
Nitrates, long-term	**C**	4	0.875	3.3; 3	
Fibrates	**C**	4	0.875	3.3; 3	
Ezetimibe	**C**	5	1.000	3.0; 3	
Amiodarone	**C**	4	0.875	3.3; 3	
All other class-I-III antiarrhythmic agents	**D**	4	1.000	4.0; 4	
Dihydropyridine antagonists (if no hypertension)	**D**	5	1.000	4.0; 4	
Niacin	**D**	5	1.000	4.0; 4	
Ranolazine	**B**	5	1.000	2.0; 2	
Calcium antagonists, verapamil type	**C**	5	1.000	3.0; 3	

STROKE	**FORTA Class** (original FORTA class in parentheses if different from consensus results)	**Nr. of raters**	**Consensus coefficient, Round 1 (cutoff 0.800)**	**Expert ratings on a numerical scale: A=1, B=2, C=3, D=4** **Mean; Mode**	**Selection of pertinent comments given by participating experts during the consensus procedure**
Substance/Group					
Acetylsalicylic acid	**A**	5	1.000	1.0; 1	
Atorvastatin	**A**	5	1.000	1.0; 1	

rTPA (recombinant tissue-type plasminogen activator) ; only for emergency use	**A**	5	1.000	1.0; 1	
Simvastatin	**A**	5	1.000	1.0; 1	
Anticoagulants including new oral anticoagulants	**A**	5	1.000	1.0; 1	
Clopidogrel	**A**	5	1.000	1.0; 1	
Dipyridamole plus acetylsalicylic acid	**B**	5	1.000	2.0; 2	
Ramipril	**A**	5	0.900	1.2; 1	
Perindopril/indapamide	**A**	5	1.000	1.0; 1	

ATRIAL FIBRILLATION	**FORTA Class** (original FORTA class in parentheses if different from consensus results)	**Nr. of raters**	**Consensus coefficient, Round 1 (cutoff 0.800)**	**Expert ratings on a numerical scale: A=1, B=2, C=3, D=4** **Mean; Mode**	**Selection of pertinent comments given by participating experts during the consensus procedure**
Substance/group					
Frequency-lowering betablockers	**A**	5	0.900	1.2; 1	
Digoxin	**B**	5 (R1) 5 (R2)	0.800 (R1) 0.800 (R2)	2.4; 2 (R1) 2.4; 2 (R2)	**Note:** The limited benefit and several side effects are more compatible with a C classification; Would specify low dose; Only in case of high rate not well controlled by betablockers
New Oral Anticoagulants (NOACs)	**(B)** **A**	5 (R1) 5 (R2)	0.700 (R1) 0.600 (R2)	1.4; 1 (R1) 1.2; 1 (R2)	**Note:** There are now data supporting efficacy and safety of NOACS in older people; There is no significant age-interaction for edoxaban and rivaroxaban. Apixaban is approved at reduced dose (2.5 mg bid) if ≥2 of: age ≥80 years, body weight ≤60 kg, serum Cr ≥1.5 mg/dL, or if CrCl <15-29 mL/min as single criterion.; There is enough evidence to support the use of apixaban and edoxaban, in the elderly

Except dabigatran	**C**	5	0.900	2.8; 3	
Oral anticoagulation by vitamin-K-antagonists (e.g. phenprocoumon, warfarin)	**B**	5	0.900	1.8; 2	
Alternative: low molecular weight heparin	**C**	2	1.000	3.0; 3	
Digitoxin	**C**	4	0.875	3.3; 3	
Diltiazem, verapamil	**C**	5	1.000	3.0; 3	
Class III antiarrhythmic agent amiodarone	**C**	5 (R1) 5 (R2)	0.800 (R1) 0.900 (R2)	3.4; 3 (R1) 3.2; 3 (R2)	
All other class I-III antiarrhythmic agents	**D**	5	1.000	4.0; 4	
Acetylsalicylic acid (100 mg/d)	**(C)** **D**	5 (R1) 4 (R2)	0.800 (R1) 0.625 (R2)	3.4; 3 (R1) 3.8; 4 (R2)	**Note:** The use of this drug is not recommended by guidelines
Class III antiarrhythmic agent dronedarone	**D**	4	1.000	4.0; 4	
Acetylsalicylic acid plus clopidogrel	**(C)** **D**	5 (R1) 5 (R2)	0.700 (R1) 0.600 (R2)	3.6; 4 (R1) 3.8; 4 (R2)	
Clopidogrel	**D**	5	1.000	4.0; 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**	5	1.000	1.0; 1	
Systemic glucocorticoids, acute, short-term use in cases of exacerbation	**A**	5	1.000	1.0; 1	
Antibiotics (acute) in cases of exacerbation, after calculated selection and, if necessary, according to antibiogram	**A**	5	1.000	1.0; 1	
Long-term administration of oxygen	**A**	5	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	1.000	2.0; 2	
Inhalative glucocorticoids	**C**	5 (R1) 3 (R2)	0.800 (R1) 0.833 (R2)	2.6; 3 (R1) 2.7; 3 (R2)	**Note:** There is evidence of efficacy although with side effects; Depends on GOLD group; Even if associated with risk of pneumonia, mycosis …, they are very effective in asthma-like or frequently exacerbated COPD at any age
Theophyllin	**D**	4	0.875	3.8; 4	

Mucolytic agents, e,g, acetyl cysteine, bromhexine	**C**	5	0.900	2.8; 3	
Roflumilast	**C**	2	1.000	3.0; 3	
Systemic glucocorticoids, chronic use	**D**	5	1.000	4.0; 4	
Antitussives: opioid A., e.g. codein; non-opioid A., e.g. butamirate	**D**	5	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					
Calcium and vitamin D supplements (as prophylaxis for persons ≥ 65 years)	**A**	4	1.000	1.0; 1	
Parenteral bisphosphonates (e.g. ibandronate, IV every 3 months)	**B**	3 (R1) 2 (R2)	0.667 (R1) 0.500 (R2)	2.0; - (R1) 2.0; - (R2)	**Note:** I believe that zoledronic acid should be given a rate A, other, such as clodronate a rate C; Zoledrocin acid may be classified as A among high risk people
Raloxifene for women	**(B)** **C**	5 (R1) 4 (R2)	0.800 (R1) 0.750 (R2)	2.4; 2 (R1) 2.5; 2 (R2)	**Note:** There is no biological plausibility among women aged 75 and more. Be careful because of the high risk of TVP among frail people
Denosumab	**B**	5 (R1) 4 (R2)	0.800 (R1) 0.750 (R2)	1.1; 2 (R1) 2.0; - (R2)	**Note:** It is also highly effective; High safety profile, high efficacy and high adherence
Bisphosphonates, oral	**B**	5	0.900	1.8; 2	
Teriparatide	**B**	4	1.000	2.0; 2	

Alfacalcidol	**C**	5	0.900	3.2; 3	
Parathormone	**C**	4	1.000	3.0; 3	
Strontium ranelate	**D**	4	1.000	4.0; 4	
Nandrolone decanoate	**D**	5	1.000	4.0; 4	
Fluoride	**D**	5	1.000	4.0; 4	
Hormone replacement therapy (HRT): estrogen, except for perimenopausal)	**D**	5	1.000	4.0; 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	**A**	5	1.000	1.0; 1	
Insulin and insulin analogs (if absolutely necessary)	**B**	5 (R1) 5 (R2)	0.800(R1) 0.700(R2)	2.0; 2(R1) 2.2; 2(R2)	**Note:** when they are needed they are highly effective
Metformin	**A**	5	1.000	1.0; 1	
GLP1 (Glucagon-Like Peptide-1) analogs	**B**	4	1.000	2.0; 2	
Acarbose	**B**	5	0.900	2.2; 2	
3rd generation sulfonylureas (for example, glimepiride)	**C**	5	0.900	3.2; 3	
Glinides (for example, nateglinide)	**C**	5	0.900	2.8; 3	

PPAR-ɣ Ligands (Peroxisomal Proliferator-Activated Receptor gamma) **Pioglitazone**	**C**	5	0.900	3.2; 3	
Rosiglitazone	**D**	5	1.000	4.0; 4	
SGLT-2 inhibitors/Gliflozins	**(D)** **B**	4(R1) 5(R2)	0.500(R1) 0.200(R2)	2.8; 4(R1) 1.8; 1(R2)	Note: Good evidence supporting their efficacy; Well selected, elderly diabetic patients can benefit form SGLT-2 inhibitors
1st generation sulfonylureas (for example, glibenclamide)	**D**	5	1.000	4.0; 4	
DEMENTIA	**FORTA Class** (original FORTA class in parentheses if different from consensus results)	**Nr. of raters**	**Consensus coefficient, Round 1 (cutoff 0.800)**	**Expert ratings on a numerical scale: A=1, B=2, C=3, D=4** **Mean; Mode**	**Selection of pertinent comments given by participating experts during the consensus procedure**
Substance/group					
Acetylcholinesterase inhibitors **e.g. donepezil, galantamine, rivastigmine (Only if indicated for the present stage of the disease)**	**B**	5	0.900	1.8; 2	
Memantine	**C**	5 (R1) 5 (R2)	0.800 (R1) 0.800 (R2)	2.6; 3 (R1) 2.6; 3 (R2)	
Ginkgo biloba	**D**	5	1.000	4.0; 4	
Statins	**D**	5	1.000	4.0; 4	

Selegiline	**D**	5	1.000	4.0; 4	
Nimodipine	**D**	5	1.000	4.0; 4	
Ergoline derivatives	**D**	5	1.000	4.0; 4	
Piracetam	**D**	5	1.000	4.0; 4	
Pyritinol	**D**	5	1.000	4.0; 4	
Antioxidants: Vitamin E, selenium, vitamin C	**D**	5	1.000	4.0; 4	
Phytotherapeutic agents, e.g. ginseng	**D**	5	1.000	4.0; 4	
Hormone preparations, e.g. DHEA (Dehydroepiandrosterone), testosterone	**D**	5	1.000	4.0; 4	
Antiphlogistics, e.g. indomethacin	**D**	5	1.000	4.0; 4	
Desferrioxamine	**D**	5	1.000	4.0; 4	
Cytidinediphosphocholine (CDP-choline)	**C**	5	1.000	3.0; 3	
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	**C**	5	1.000	3.3; 3	

usual dosages					
Mirtazapine (15-45mg/d)	**C**	5	1.000	3.3; 3	
SNRI (Serotonin-Noradrenalin-Reuptake-Inhibitors) Venlafaxine, duloxetine	**C**	5	1.000	3.3; 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**	5	1.000	3.0; 3	
Melperone (25-150mg/d)	**C**	3	1.000	3.0; 3	
Quetiapine (25-200 mg/d)	**C**	5	1.000	3.0; 3	
Aripiprazole (2-15 mg/d)	**C**	5	1.000	3.0; 3	
Clozapine (10-50 mg/d)	**D**	5	0.900	3.8; 4	
Haloperidol (initially 0.5 mg/d, max. 3 mg/d)	**C**	5	1.000	3.0; 3	
Olanzapine	**C**	5	1.000	3.0; 3	
Citalopram	**C**	5	0.900	3.2; 3	
Promazine/Chlorpromazine	**D**	5	0.900	3.8; 4	

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**	5	1.000	3.0; 3	
Risperidone (initiallly 0,5-1 mg/d, Maximum 3 mg/d)	**C**	5	1.000	3.0; 3	
Quetiapine (25-200 mg/d)	**C**	5	0.900	2.8; 3	
Melperone (25-150 mg/d)	**C**	3	1.000	3.0; 3	
Pipamperone (20-120 mg/d)	**D**	3	1.000	4.0; 4	
Citalopram (10-30mg)	**C**	5	0.900	3.2; 3	
Clomethiazole (5-15 mg/d)	**D**	4	1.000	4.0; 4	
Acetylcholinesterase inhibitors	**C**	4	1.000	3.0; 3	
Memantine	**C**	4	1.000	3.0; 3	
Pregabalin, Gabapentin	**C**	5	0.900	3.2; 3	
Benzodiazepines	**D**	5	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	**C**	5	1.000	3.0; 3	

(2-4 mg)					
Tetracyclic antidepressant Mirtazapine (15-30mg)	**C**	5	1.000	2.8; 3	
Tricyclic antidepressant Doxepine (25-50 mg)	**C**	4	1.000	3.0; 3	
Zopiclone (3,75-7,5 mg)	**C**	5	1.000	3.0; 3	
Trazodone	**C**	5	0.900	2.8; 3	
Gabapentin	**C**	5	1.000	3.0; 3	
ω1-Benzodiazepine agonists Zolpidem	**D**	5	1.000	4.0; 4	
Benzodiazepines	**D**	3	1.000	4.0; 4	
DEPRESSION Prophylaxis and therapy for patients with moderate to major depression	**FORTA Class (original FORTA class in parentheses if different from consensus results)**	**Nr. of raters**	**Consensus coefficient, Round 1 (cutoff 0.800)**	**Expert ratings on a numerical scale: A=1, B=2, C=3, D=4** **Mean; Mode**	**Selection of pertinent comments given by participating experts during the consensus procedure**
Substance/group					
SSRIs (Selective Serotonin Reuptake Inhibitor)		5	0.900	2.2; 2	
Sertraline	**B**				
Escitalopram	**B**	5	0.900	2.2; 2	
Citalopram	**B**	5	0.900	2.2; 2	
Tricyclic antidepressant Nortriptyline	**D**	5	0.900	3.8; 4	
Tetracyclic antidepressant Mirtazapine	**C**	5	0.900	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**	3	1.000	4.0; 4	
Dopamine and norepinephrine reuptake inhibitor Bupropion	**C**	3	1.000	3.0; 3	
Vortioxetine	**C**	5 (R1) 4 (R2)	0.800 (R1) 0.750 (R2)	3.0; 3 (R1) 2.5; 3 (R2)	**Note:** Many adverse effects among frail people
Quetiapine	**C**	5	1.000	3.0; 3	
Trazodone	**C**	5	0.900	3.2; 3	
Olanzapine	**C**	5	1.000	3.0; 3	
Benzodiazepines: General	**D**	5	1.000	4.0; 4	
Long-acting,	**D**	5	1.000	4.0; 4	
Short-acting	**D**	5	1.000	4.0; 4	
St. John's Wort	**D**	5	1.000	4.0; 4	
Agomelatine	**D**	5	1.000	4.0; 4	
Selective noradrenaline re-uptake inhibitor Reboxetine	**D**	5	1.000	4.0; 4	
SSRIs (Selective Serotonin Reuptake Inhibitor) Paroxetine	**B**	5	0.900	2.2; 2	
Aripiprazole	**C**	4	1.000	3.0; 3	
S-Adenosyl methionine (Ademetionina)	**C**	5	0.900	2.8; 3	

BIPOLAR DISORDER	FORTA Class (original FORTA class in parentheses if different from consensus results)	Nr. of raters	Consensus coefficient, Round 1 (cutoff 0.800)	Expert ratings on a numerical scale: A=1, B=2, C=3, D=4 Mean; Mode	Selection of pertinent comments given by participating experts during the consensus procedure
Substance/group					
Lithium	**C**	5 (R1) 4(R2)	0.800 (R1) 0.750(R2)	3.0; 3 (R1) 2.5; - (R2)	
Quetiapine	**B**	5	1.000	2.0; 2	
Valproic acid	**C**	5	0.900	2.8; 3	
Lamotrigine	**C**	5	1.000	3.0; 3	
Carbamazepine	**D**	5	1.000	4.0; 4	
Olanzapine	**C**	5	1.000	3.0; 3	
Aripiprazole	**C**	5	1.000	3.0; 3	
Risperidone	**C**	5	1.000	3.0; 3	
Levetiracetam	**C**	5	1.000	3.0; 3	
Haloperidol	**C**	5	1.000	3.0; 3	

INSOMNIA / SLEEP DISORDERS	FORTA Class (original FORTA class in parentheses if different from consensus results)	Nr. of raters	Consensus coefficient, Round 1 (cutoff 0.800)	Expert ratings on a numerical scale: A=1, B=2, C=3, D=4 Mean; Mode	Selection of pertinent comments given by participating experts during the consensus procedure
Substance/group					
Melatonin (slow-release)	**B**	5	1.000	2.0; 2	
ω1-Benzodiazepine agonists **Zolpidem**	**C**	5	1.000	3.0; 3	
Zaleplone	**C**	4	1.000	3.0; 3	
Non-benzodiazepine hypnotic Zopiclone	**C**	5	1.000	3.0; 3	
Butyrophenone derivative Pipamperone	**C**	3	1.000	3.0; 3	
Melperone	C	3	1.000	3.0; 3	
Tetracyclic antidepressant Mirtazapine	**C**	5	1.000	3.0; 3	
Tricyclic antidepressant Doxepine	**D**	4	1.000	4.0; 4	
Benzodiazepines, e.g. Oxazepam (medium half-life)	**D**	5	0.900	3.8; 4	
Triazolam (very short half-life)	**D**	5	1.000	4.0; 4	
Sigma receptor agonist	**D**	3	1.000	4.0; 4	

Opipramole					
Antihistamine Diphenhydramine	**D**	4	1.000	4.0; 4	
Trazodone	**B**	5	1.000	2.0; 2	
Pramipexole	**C**	4	1.000	3.0; 3	
Pregabalin/gabapentin	**C**	5	1.000	3.0; 3	
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**	5	1.000	1.0; 1	
Metamizole	**C**	4	0.875	3.3; 3	
Opioids, e.g. Buprenorphine, oxycodone, hydromorphone	**B**	5	1.000	2.0; 2	
Primary use of a combination of an agonist and an antagonist, e.g. Tilidine/naloxone	**C**	4	0.875	2.8; 3	
Oxycodone/naloxone	**B**	5	1.000	2.0; 2	
Morphine	**C**	5	1.000	3.0; 3	
SSRI (Selective Serotonin Reuptake Inhibitors) /	**C**	5	1.000	3.0; 3	

SNRI (Serotonin-Norepinephrine-Reuptake Inhibitor), e.g. venlafaxine (only if absolutely necessary)					
Antiepileptic agents (only for neuropathic pain) **Pregabalin/gabapentin**	**C**	5	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**	5	1.000	4.0; 4	
NSAIDs (nonsteroidal anti-inflammatory **drugs, for long-term use), e.g. naproxen**	**(D)** **C**	5 (R1) 5(R2)	0.800(R1) 0.700(R2)	3.6; 4(R1) 3.4; 3 (R2)	**Note:** If needed in selected cases NSAIDs can be used. Ketorolac can be FORTA D; NSAIDs can be associated to PPI to reduce the GI bleeding risk
Cox-2 inhibitors, e.g. celecoxib	**(D)** **C**	5(R1) 5(R2)	0.800(R1) 0.700(R2)	3.6; 4(R1) 3.4; 3(R2)	**Note:** In low-risk elderly patients, coxib. may in fact avoid the bleeding risk
Fentanyl	**B**	5	1.000	2.0; 2	
Codeine (also in association with Paracetamol)	**C**	5	1.000	3.0; 3	
Tramadole	**C**	5	1.000	3.0; 3	
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 (emergency use)	**B**	4	1.000	2.0; 2	
Lorazepam (long-term use)	**D**	3	1.000	4.0; 4	
Pregabalin	**B**	4	1.000	2.0; 2	
Oxcarbazepine	**C**	4	1.000	3.0; 3	
Valproic acid	**C**	4	1.000	3.0; 3	
Eslicarbazepine	**C**	2	1.000	3.0; 3	
Lacosamide	**C**	3	1.000	3.0; 3	
Zonisamide	**C**	2	1.000	3.0; 3	
Carbamazepine	**C**	4	1.000	3.0; 3	
Diazepam (emrgency use)	**C**	4	1.000	3.0; 3	
Diazepam (long-term use)	**D**	4	1.000	4.0; 4	
Midazolam (emrgency use)	**C**	4	1.000	3.0; 3	
Midazolam (long-term use)	**D**	4	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**	5	1.000	1.0; 1	
COMT (Catechol-O-Methyltransferase) Inhibitor Entacapone, opicapon	**B**	4	1.000	2.0; 2	
Dopamine agonists, e.g. Ropinirole	**C**	5	1.000	3.0; 3	
Pramipexole	**C**	5	1.000	3.0; 3	
Piribedil, quinagolide, rotigotine	**B**	4	1.000	2.0; 2	
MAO-B inhibitors **Rasagiline**	**C**	5	1.000	3.0; 3	
Selegiline	**C**	5	1.000	3.0; 3	

Bromocriptine, cabergoline	**D**	5	1.000	4.0; 4	
Glutamate antagonists **Amantadine**	**D**	5	1.000	4.0; 4	
Anticholinergics **Biperidene**	**D**	5	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**	4	0.875	2.3; 2	
Tolterodine	**C**	4	1.000	3.0; 3	
Trospium chloride	**C**	4	1.000	3.0; 3	
Extended-release Oxybutynin	**C**	5	1.000	3.0; 3	
Immediate-release Oxybutynin	**D**	5	1.000	4.0; 4	
Mirabegron	**C**	4	1.000	3.0; 3	
OnabotulinumtoxinA	**C**	2	1.000	3.0; 3	

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

				Mean; Mode	
Substance/group					
Proton pump inhibitors (PPI), only if absolutely necessary	**B**	5 (R1) 5 (R2)	0.800 (R1) 0.800(R2)	1.6; 2 (R1) 1.6; 2(R2)	**Note:** I feel is good practice to co-prescribe PPI with NSAIDs; Recent trails have shown the efficacy in preventing upper GI bleeding in patients on NSAIDs
H_2 receptor antagonists	**C**	5 (R1) 5(R2)	0.800(R1) 1.000(R2)	2.6; 3(R1) 3.0; 3(R2)	**Note:** Alternative to PPIs

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**	5	1.000	1.0; 1	
Erythropoetin-stimulating agents (ESA) in patients with renal insufficiency	**A**	5	1.000	1.0; 1	

Iron substitution in patients with cardiac insufficiency **With proof of iron deficiency**	**See cardiac insufficiency**				

Vaccinations	**FORTA Class (original FORTA class in parentheses if different from consensus results)**	**Nr. of raters**	**Consensus coefficient, Round 1 (cutoff 0.800)**	**Expert ratings on a numerical scale: A=1, B=2, C=3, D=4** **Mean; Mode**	**Selection of pertinent comments given by participating experts during the consensus procedure**
Substance/group					
Annual influenza immunizations	**A**	5	1.000	1.0; 1	
Pneumococcal immunizations for persons ≥ 65 years	**A**	5	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**	4	1.000	2.0; 2	
Aromatase inhibitors	**B**	4	1.000	2.0; 2	
Immunotherapy / "Targeted" therapy **Trastuzumab**	**B**	2	1.000	2.0; 2	
Chemotherapy, e.g. **CMF (Combination Cyclophosphamide, Methotrexate, 5-Fluorouracil)**	**C**	2	1.000	3.0; 3	
AC/EC Regimen(Anthracycline/ Epirubicin, Cyclophosphamide)	**C**	2	1.000	3.0; 3	
BREAST CANCER **Advanced Stage**					
Hormone therapy, e.g. tamoxifen, aromatase		3	1.000	2.0; 2	

inhibitors	**B**				
Immunotherapy/Targeted Therapy **Trastuzumab / lapatinib**	**B**	2	1.000	2.0; 2	
Chemotherapy, e.g. anthracyclins, taxanes	**C**	2	1.000	3.0; 3	
VEGF (Vascular Endothelial Growth Factor) Inhibition Bevacizumab	**D**	2	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**	2	1.000	3.0; 3	
Capecitabine	**C**	2	1.000	3.0; 3	
COLORECTAL CARCINOMA Advanced stage					
Chemotherapy FOLFOX (Folinic acid, Fluorouracil, Oxaliplatin)	**C**	2	1.000	3.0; 3	
VEGF (Vascular Endothelial Growth Factor) Inhibition Bevacizumab	**C**	2	1.000	3.0; 3	
EGFR (Epidermal-Growth-Factor-Receptor) Inhibition Cetuximab	**C**	2	1.000	3.0; 3	
Panitumumab	**C**	2	1.000	3.0; 3	
BRONCHIAL CARCINOMA Adjuvant therapy					
Adjuvant chemotherapy	**C**	2	1.000	3.0; 3	

(Cisplatin-based)					
BRONCHIAL CARCINOMA Advanced Stage					
Docetaxel	**B**	2	1.000	2.0; 2	
Vinorelbin	**B**	2	1.000	2.0; 2	
Primary combination therapy Cisplatin/gemcitabin, or cisplatin/vinorelbin	**C**	1	1.000	3.0; 3	
GASTRIC CANCER					
ECF Regime (Epirubicin, Cisplatin, 5-Fluorouracil)	**B**	5	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**	2	1.000	2.0; 2	
CLL (Chronic lymphatic leukemia) Chlorambucil, Fludarabin,	**B**	2	1.000	2.0; 2	

Bendamustin					
CLL **Obinutuzumab**	**B**	2	1.000	2.0; 2	
CLL **Rituximab**	**B**	2	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**	2	1.000	2.0; 2	
CLL **Ibrutinib**	**C**	2	1.000	3.0; 3	
CLL **Idelalisib**	**C**	2	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**	4	1.000	1.0; 1	
Antiemetic agents (e.g. 5-	**A**	4	1.000	1.0; 1	

HT receptor inhibitors)					
Erythropoesis Stimulating Agents, ESA	**B**	4	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[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**	3	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 = 300). The coefficients were then corrected (cons_corr) to weight the degree of deviation between the experts' individual FORTA ratings, expressed in terms of range class, from 0-3 as defined:

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

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

Range	Frequency (n total=300)	%
0	229	76.33
1	62	20.67
2	8	2.67
3	1	0.33

Cons_corr coefficients ranged from 0.500 to 1.000 (mean 0.966, median 1.000). Substances falling short of our established cons_corr cutoff of 0.800 underwent re-evaluation in a second round: n=21

Confirmation/determination of FORTA labels[5]

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

A→ 1
B → 2
C → 3
D → 4

These numerical "grades" were used for the calculation of arithmetic mean. The mode (=grade appearing most frequently for rated item) is also shown. For the 21 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 97.6% of all substances (n=293); for 7/300 substances (2.3%), the FORTA labels changed over the course of two rounds. All consensus-based FORTA ratings are listed in bold print**:** **A B C D**, and the original author-based FORTA ratings are supplied in parentheses: (A) (B) (C) (D).

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

Selection process for new substances and indications[5]

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