

The F O R T A List
“Fit for The Aged”
Expert Consensus Validation 2021

F O R T A ¹			
A	B	C	D

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Disclaimer

Please keep in mind that the FORTA Concept was conceived in Germany and has been further developed in that region. While building on an international foundation of medical evidence and experience for the medications listed, including already existing “negative lists” and classification systems, this new version of the FORTA List primarily reflects prescribing tendencies in Germany, Austria and Switzerland. 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 substance¹. Meanwhile, the FORTA principle has been validated in a randomized clinical trial (VALFORTA) showing a large improvement of medication quality and amelioration of clinical parameters².

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. ‘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 list¹. 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 FORTA Concept: initiators and expert panel for the FORTA classification system 2021

FORTA Expert Review Panel 2021

The following 20 colleagues, representing Germany, Austria and Switzerland 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 = Indispensable drug, clear-cut benefit in terms of efficacy/safety ratio proven in elderly patients for a given indication	Class B = Drugs with proven or obvious efficacy in the elderly, but limited extent of effect and/or safety concerns	Class C = 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	Class D = Avoid if at all possible in the elderly, omit first and use alternative substances
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* FORTA aims at older patients, has been validated primarily for patients 65 years of age or older with significant comorbidities (3 or more diagnoses and drugs) and should be used in all patients 80 years of age or older will. These target groups are mostly defined as geriatric patients.

The F O R T A List^{1,5,6}

Delphi Expert Consensus Validation 2021

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		19	1.000	1; 1	
ACE inhibitors	A				
Angiotensin receptor antagonists	A	19	1.000	1; 1	
Long-acting calcium antagonists, dihydropyridine type, for example amlodipine	A	19	1.000	1; 1	
Betablockers	C	19	0.895	2.8; 3	
Except Atenolol	D	16	1.000	4.0; 4	
Diuretics	B	18	0.972	2.1; 2	
except Indapamide	A	12	0.833	1.3; 1	
Alpha blockers	C	19	0.974	3.1; 3	
Spironolactone	C	18	0.972	3.1; 3	Note: Except for primary hyperaldosteronism (Conn syndrome), then FORTA A

Moxonidine	C	18	1.000	3.0; 3	
Urapidil	C	18	1.000	3.0; 3	
Aliskiren	C	17	0.971	3.1; 3	
Clonidine	D	18	0.972	3.9; 4	
Minoxidil	D	18	1.000	4.0; 4	
Calcium antagonists, verapamil type	D	18	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	19	1.000	1.0; 1	
Angiotensin receptor antagonists	A	19	1.000	1.1; 1	
Sacubitril/Valsartan	A	18	0.944	1.1; 1	
Betablockers (metoprolol, carvedilol, bisoprolol)	A	19	0.974	1.1; 1	
Diuretics	B	19	0.921	1.8; 2	
SGLT2 inhibitor (gliflozins) with approval (dapagliflozin)	B	17	0.971	1.9; 2	Note: Empagliflozin also new
Spironolactone	C	19	0.947	2.9; 3	
Digitalis preparations	C	19	0.947	3.1; 3	
Ivabradine	C	18	0.972	2.9; 3	

Iron substitution in patients with proof of iron deficiency (even without anemia)	A	19	0.895	1.2; 2	

	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
ACUTE CORONARY SYNDROME					
Substance/Group					
Renin-Angiotensin-System-Blocker: ACE-inhibitors	A	19	1.000	1.0; 1	
Acetylsalicylic acid	A	19	1.000	1.0; 1	
Unfractionated heparin and low molecular weight heparin	A	19	1.000	1.0; 1	
Frequency-lowering betablockers, e.g. metoprolol, bisoprolol	A	19	1.000	1.0; 1	
Atorvastatin	A	19	1.000	1.0; 1	Note: More like all statins
Nitroglycerin spray, single use, acute as on-demand medication	A	19	0.947	1.1; 1	
Clopidogrel, Prasugrel	A	19	1.000	1.0; 1	
Thrombolytics, especially rTPA (recombinant tissue-type plasminogen activator)	B	17	1.000	2.0; 2	
Nitrates, long-term	C	19	0.947	3.1; 3	

Gp IIb/IIIa antagonists (glycoprotein 2b/3a inhibitors)	C	16	1.000	3.0; 3	
Ivabradine	C	17	1.000	3.0; 3	
Molsidomine	D	18	0.972	3.9; 4	
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/Angiotensin-Receptor-Blockers	A	19	1.000	1.0; 1	
Acetylsalicylic acid (100 mg/d)	A	19	1.000	1.0; 1	
Clopidogrel 6-12 months 12 months after acute coronary syndrome	A	19	1.000	1.0; 1	
	A in case of ASA intolerance	18	1.000	1.0; 1	
Frequency-lowering beta blockers up to 3 years	A	19	1.000	1.0; 1	
Frequency-lowering beta blockers longer than 3 years	C	18	0.917	2.8; 3	
Nitroglycerin spray, single use as on-demand medication	A	19	0.921	1.2; 1	

Influenza vaccination/ Pneumococcus vaccination	See new section below (vaccination)				
Statins	A	18	1.000	1.0; 1	
Statins for very old (>85 years) patients	B	19	0.895	1.9; 2	
Ezetimibe	B	16	1.000	2.0; 2	
Nitrates, long-term	C	19	0.947	3.1; 3	
Ranolazine	C	18	1.000	3.0; 3	
Fibrates	C	19	0.921	3.2; 3	
Amiodarone	C	18	0.972	2.9; 3	
All other class-I/III antiarrhythmic agents	D	17	1.000	4.0; 4	
Dihydropyridine antagonists (if no hypertension)	D	18	1.000	4.0; 4	
Niacin	D	18	1.000	4.0; 4	

STROKE	FORTA Class (original FORTA class in parentheses if different from consensus results)	Nr. of raters	Consensus coefficient, Round 1 (cutoff 0.800)	Expert ratings on a numerical scale: A=1, B=2, C=3, D=4 Mean; Mode	Selection of pertinent comments given by participating experts during the consensus procedure
Substance/Group					
Acetylsalicylic acid (100mg/d)	A	19	1.000	1.0; 1	
Statins	A	18	1.000	1.0; 1	
rt-PA (only acute)	A	19	1.000	1.0; 1	
Clopidogrel in case of ASA	A	19	1.000	1.0; 1	

intolerance					
Dipyridamole plus acetylsalicylic acid	C	19	0.947	2.9; 3	

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	19	1.000	1.0; 1	
Direct Oral Anticoagulants (DOACs)	B	19	0.895	1.8; 2	
Except Apixaban	A	19	1.000	1.0; 1	
Oral anticoagulation by vitamin-K-antagonists (warfarin) except	B	18	0.972	2.1; 2	Note: No drugs containing warfarin are approved in Switzerland
Phenprocoumon	C	19	0.921	2.8; 3	
Alternative in exceptional cases: low molecular weight heparin	C	19	1.000	3.0; 3	

Digoxin, digitoxin	C	18	0.944	3.0; 3	
Class III antiarrhythmic agent amiodarone	C	19	0.947	3.0; 3	
All other class I or III antiarrhythmic agents including dronedarone	D	19	1.000	4.0; 4	
Diltiazem, verapamil	D	19	1.000	4.0; 4	
Acetylsalicylic acid (100 mg/d)	D	19	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	18	1.000	1.0; 1	
Systemic glucocorticoids, acute, short-term use (5-7 days) in cases of exacerbation	A	18	0.972	1.1; 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 with strict indications	A	18	1.000	1.0; 1	
Annual influenza immunizations	See bacterial infections and vaccinations				
Pneumococcal immunizations for persons ≥ 65 years	See bacterial infections and vaccinations				
Inhalative, especially long-acting beta 2 mimetic agents	B	17	0.912	1.8; 2	
Inhalative glucocorticoids	C	18	0.917	2.9; 3	

Theophylline	D	17	1.000	4.0; 4	
Mucolytic agents, e.g., acetyl cysteine, bromhexine	C	18	0.972	3.1; 3	
Roflumilast	C	17	1.000	3.0; 3	
Systemic glucocorticoids, chronic use	D	18	1.000	4.0; 4	
Antitussives: opioid A., e.g. codein; non-opioid A., e.g. butamirate	D	18	1.000	4.0; 4	
OSTEOPOROSIS	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					
Calcium and vitamin D supplements (as prophylaxis for persons ≥ 65 years)	A	19	0.921	1.2; 1	Note: Calcium can be omitted with an appropriate diet
Parenteral bisphosphonates (IV every 3 months)	A	19	1.000	1.0; 1	
Raloxifene for women	A	18	1.000	1.0; 1	
Denosumab	A	18	0.972	1.1; 1	
Bisphosphonates, oral	B	19	0.947	2.0; 2	Note: Tolerance is often significantly worse than for parenteral bisphosphonates
Alfacalcidol	C	18	1.000	3.0; 3	Note: In Switzerland we use calcitriol

In case of renal insufficiency (eGFR <30 ml/min)	B	17	0.971	1.9; 2	
Teriparatide	C	17	0.941	2.9; 3	Note: High efficacy, rapid therapeutic effect
Parathormone	C	18	1.000	3.0; 3	
Strontium ranelate	D	18	1.000	4.0; 4	
Nandrolone decanoate	D	18	1.000	4.0; 4	
Fluoride	D	17	1.000	4.0; 4	
Hormone replacement therapy (HRT): estrogen, except up to 3 years postmenopausal)	D	17	0.911	3.8; 4	
TYPE II DIABETES MELLITUS	FORTA Class (original FORTA class in parentheses if different from consensus results)	Nr. of raters	Consensus coefficient, Round 1 (cutoff 0.800)	Expert ratings on a numerical scale: A=1, B=2, C=3, D=4 Mean; Mode	Selection of pertinent comments given by participating experts during the consensus procedure
Substance/group					
DPP4 (Dipeptidylpeptidase) Inhibitors	A	19	0.921	1.2; 1	
Insulin and insulin analogs (if absolutely necessary)	B	19	0.868	1.7; 2	
Metformin	B	19	0.868	1.7; 2	
GLP1 (Glucagon-Like Peptide-1) analogs	B	19	0.947	1.9; 2	
Acarbose	C	19	0.894	3.2; 3	

3rd generation sulfonylureas (for example, glimepiride)	C	19	0.947	3.1; 3	
Glinides (for example, nateglinide)	C	19	0.974	3.1; 3	
Gliflozins	C	18	0.806	2.6; 3	Note: FORTA B with existing cardiac or renal insufficiency
PPAR-γ Ligands (Peroxisomal Proliferator-Activated Receptor gamma) Pioglitazone	C	18	0.944	3.1; 3	
Rosiglitazone	D	16	1.000	4.0; 4	Note: No longer available
1st generation sulfonylureas (for example, glibenclamide)	D	19	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 (mild or moderate stage of Alzheimer disease)	B	19	0.895	2.0; 2	

Memantine (moderate or advanced stage of Alzheimer disease)	B	19	0.947	2.1; 2	
Ginkgo biloba	C	20	0.875	2.9; 3	Note: The effect is comparable to that of the cholinesterase inhibitors; I cannot confirm an “unfavorable” risk-benefit analysis that would justify a “C”, at most a neutral one. See also new review 2021: Tomino C et al. doi: 10.3390 / ph14040305
Statins	D	20	1.000	4.0; 4	
Piracetam	D	20	1.000	4.0; 4	
Antioxidants: Vitamin E, selenium, vitamin C	D	20	1.000	4.0; 4	
ginseng	D	20	1.000	4.0; 4	
Hormone preparations, e.g. DHEA (Dehydroepiandrosterone), testosterone	D	20	0.975	3.9; 4	
BEHAVIORAL AND PSYCHOLOGICAL SYMPTOMS OF DEMENTIA (BPSD)	FORTA Class (original FORTA class in parentheses if different from consensus results)	Nr. of raters	Consensus coefficient, Round 1 (cutoff 0.800)	Expert ratings on a numerical scale: A=1, B=2, C=3, D=4 Mean; Mode	Selection of pertinent comments given by participating experts during the consensus procedure
DEPRESSION					
Substance/group					
SSRI (Selective Serotonin Reuptake Inhibitors) Citalopram/escitalopram, sertraline, fluoxetine in the usual dosages	C	20	0.900	2.8; 3	
Mirtazapine (15-45mg/d)	C	20	0.925	2.9; 3	
SNRI (Serotonin-		20	0.875	3.8; 4	

Noradrenalin-Reuptake-Inhibitors) Venlafaxine, duloxetine	D				
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	C	20	0.850	2.7; 3	
Melperone	C	18	0.917	3.1; 3	Note: No longer available in Switzerland
Quetiapine	C	19	0.921	2.8; 3	
Olanzapine	C	19	0.842	3.3; 3	Note: Clearly anticholinergic side effect; Not used in Switzerland
Aripiprazole	D	19	0.895	3.8; 4	
Clozapine	D	20	0.950	3.9; 4	
Haloperidol	D	19	0.921	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	C	19	0.895	3.1; 3	

Risperidone	C	20	0.900	2.8; 3	
Quetiapine	C	19	0.921	2.9; 3	
Melperone	C	18	0.972	2.9; 3	
Pipamperone	C	19	0.947	3.0; 3	
Citalopram	C	18	0.861	3.3; 3	
Clomethiazole	D	18	0.944	3.9; 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	18	0.944	3.0; 3	
Tetracyclic antidepressant Mirtazapine	C	20	0.850	2.9; 3	
Trazodone	C	20	0.825	2.9; 3	
Tricyclic antidepressant Doxepine	D	19	1.000	4.0; 4	
Zopiclone	D	18	0.944	3.9; 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) Sertraline Escitalopram Citalopram	B	20	0.975	2.1; 2	
	B	20	0.975	2.1; 2	
	B	20	0.950	2.0; 2	
Tricyclic antidepressant Amitriptyline, Doxepine	C	20	0.850	3.3; 3	Note: Anticholinergic side effects
Tetracyclic antidepressant Mirtazapine	C	18	0.972	2.9; 3	
SNRIs (Serotonin-Noradrenalin Reuptake Inhibitors) Venlafaxine Duloxetine	C	20	0.950	2.9; 3	
	C	20	0.950	2.9; 3	
Monoamine oxidase A (MAO) inhibitor Moclobemide	D	20	0.975	3.9; 4	
Dopamine and norepinephrine reuptake inhibitor Bupropion	C	20	0.950	3.0; 3	
Quetiapine	C	20	0.900	3.2; 3	Note: Not used in Switzerland for this indication
Tianeptine (Serotonin-Reuptake-Enhancer)	C	16	0.937	3.1; 3	Note: Not approved in Switzerland
Benzodiazepines: General Long-acting, Short-acting	D	20	1.000	4.0; 4	
	D	20	1.000	4.0; 4	
	C	20	0.950	3.0; 3	
Trazodone	D	20	0.900	3.8; 4	

St. John's Wort	D	18	0.972	3.9; 4	
Agomelatine	D	20	0.950	3.9; 4	
Selective noradrenaline re-uptake inhibitor Reboxetine	D	20	1.000	4.0; 4	
BIPOLAR DISORDER	FORTA Class (original FORTA class in parentheses if different from consensus results)	Nr. of raters	Consensus coefficient, Round 1 (cutoff 0.800)	Expert ratings on a numerical scale: A=1, B=2, C=3, D=4 Mean; Mode	Selection of pertinent comments given by participating experts during the consensus procedure
Substance/group					
Lithium	B	20	0.925	2.1; 2	Note: Frequent side effects in geriatric patients, FORTA B with close monitoring; poor tolerance (tremor, weight gain; narrow therapeutic window)
Quetiapine	B	20	1.000	2.0; 2	
Valproic acid	C	20	0.925	3.1; 3	
Lamotrigine	C	20	0.975	2.9; 3	
Carbamazepine	D	20	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), only if effective (rarely)	B	19	0.894	2.2; 2	
ω1-Benzodiazepine agonists Zolpidem	C	20	1.000	3.0; 3	
Zaleplone	C	19	1.000	3.0; 3	Note: Not approved in Switzerland
Zopiclone	C	20	0.975	3.1; 3	
Butyrophenone derivative Pipamperone	C	20	0.975	3.1; 3	
Melperone	C	19	0.974	3.1; 3	
Tetracyclic antidepressant Mirtazapine	C	20	0.925	2.9; 3	
Trazodone	C	20	0.900	3.0; 3	
Tricyclic antidepressant Doxepine in low dosage (10- 25mg/d)	C	19	0.947	3.1; 3	
Tricyclic antidepressant Doxepine	D	20	1.000	4.0; 4	
Benzodiazepines, e.g. Oxazepam (medium half-	D	20	0.950	3.9; 4	

life)					
Triazolam (very short half-life)	D	19	0.947	3.9; 4	
Opipramole	D	20	0.975	3.9; 4	
Sedative Antihistamines such as diphenhydramine/doxylamine	D	19	1.000	4.0; 4	
CHRONIC PAIN	FORTA Class (original FORTA class in parentheses if different from consensus results)	Nr. of raters	Consensus coefficient, Round 1 (cutoff 0.800)	Expert ratings on a numerical scale: A=1, B=2, C=3, D=4 Mean; Mode	Selection of pertinent comments given by participating experts during the consensus procedure
Substance/group					
Paracetamol	A	19	0.868	1.3; 1	
Metamizole	B	20 (R1) 19 (R2)	0.800	1.8; 2 (R1) 1.7; 2 (R2)	Note: Overall, side effects are very rare. More effective than paracetamol, so actually the first choice; Paracetamol is often not potent enough and side effects of opiates are undesirable; Indispensable level 1 WHO; Agranulocytosis; Interaction with antihypertensive drugs; FORTA A, if it weren't for the risk of agranulocytosis. This should be pointed out explicitly; Even if it were only because of the power of facts. Number 1 pain reliever in geriatrics by a wide margin. Paracetamol is often no alternative because it is not very effective. Also available as drops. We have many patients on metamizole, very few on paracetamol

Opioids, cautious dose increase e.g. Buprenorphine, oxycodone, hydromorphone, fentanyl	B	20	0.975	1.9; 2	
Primary use of agonist / antagonist combinations, e.g. Tilidine/naloxone Oxycodone/naloxone	C	19	0.974	2.9; 3	
Morphine	C	19	0.974	2.9; 3	
Tramadol	C	20	0.925	3.1; 3	Note: Poor efficacy, serotonin syndrome; high risk for ADRs
Tapentadol	C	18	0.944	2.9; 3	
SSRI (Selective Serotonin Reuptake Inhibitors) / SNRI (Serotonin-Norepinephrine-Reuptake Inhibitor), e.g. venlafaxine (only if absolutely necessary)	C	19	0.974	3.1; 3	
Antiepileptic agents (only for neuropathic pain)	C	19	0.947	3.0; 3	Note: Development of tolerance, habituation, potential for addiction, withdrawal is often difficult
Pregabalin/gabapentin					
Carbamazepine	D	19	0.974	3.9; 4	
Tricyclic antidepressant amitriptyline (does not apply to doses up to 10 mg /	D	18	1.000	4.0; 4	

day)					
NSAIDs (nonsteroidal anti-inflammatory drugs, for long-term use), e.g. naproxen	D	19	1.000	4.0; 4	
Cox-2 inhibitors, e.g. celecoxib	D	19	0.921	3.8; 4	
EPILEPSY	FORTA Class (original FORTA class in parentheses if different from consensus results)	Nr. of raters	Consensus coefficient, Round 1 (cutoff 0.800)	Expert ratings on a numerical scale: A=1, B=2, C=3, D=4 Mean; Mode	Selection of pertinent comments given by participating experts during the consensus procedure
Substance/group					
Levetiracetam	B	19	1.000	2.0; 2	
Lamotrigine	B	19	1.000	2.0; 2	
Gabapentin	B	19	0.911	2.2; 2	
Topiramate	B	19	0.853	2.3; 2	
Lacosamide	B	16	0.969	2.1; 2	
Lorazepam (emergency use)	B	19	0.971	1.9; 2	
Lorazepam (long-term use)	D	19	0.941	3.9; 4	
Pregabalin	C	19	0.941	3.1; 3	
Oxcarbazepine	C	19	1.000	3.0; 3	
Valproic acid	C	19	0.971	3.1; 3	
Eslicarbazepine	C	17	1.000	3.0; 3	

Zonisamide	C	15	1.000	3.0; 3	
Carbamazepine	C	19	0.971	3.1; 3	
Diazepam (emergency use)	C	20	0.971	2.9; 3	
Diazepam (long-term use)	D	19	1.000	4.0; 4	
Midazolam (emergency use)	C	20	0.844	2.7; 3	
Midazolam (long-term use)	D	19	0.941	3.9; 4	
Phenytoin	D	19	1.000	4.0; 4	
Phenobarbital	D	19	1.000	4.0; 4	
Ethosuximide	D	18	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	19	1.000	1.0; 1	
COMT (Catechol-O- Methyltransferase) Inhibitor Entacapone, opicapone	B	19	0.947	2.0; 2	

Dopamine agonists, e.g. Ropinirole, Rotigotin (preferred as patch if possible)	B	19	1.000	2.0; 2	
	C	19	0.973	2.9; 3	
Piribedil, pramipexole	C	17	1.000	3.0; 3	
Safinamide	C	17	1.000	3.0; 3	
MAO-B inhibitors					
Rasagiline	C	19	0.921	3.1; 3	
Selegiline	D	18	1.000	4.0; 4	Note: Not approved in Switzerland
Bromocriptine, Cabergoline	D	19	1.000	4.0; 4	
Glutamate antagonists					
Amantadine	D	19	1.000	4.0; 4	
Anticholinergics					
Biperidene	D	18	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	18	0.889	2.2; 2	Note: Anticholinergic side effects not less with other compounds
Tolterodine	C	17	0.971	2.9; 3	
Trospium chloride	C	17	0.941	2.9; 3	
Extended-release Oxybutynin	C	17	0.971	3.1; 3	
Duloxetine	C	16	0.968	2.9; 3	Note: Not approved in Switzerland with this indication
Immediate-release Oxybutynin	D	17	1.000	4.0; 4	
GASTROINTESTINAL ILLNESSES/ CONCOMITANT THERAPY WITH NSAIDs	FORTA Class (original FORTA class in parentheses if different from consensus results)	Nr. Of raters	Consensus coefficient, Round 1 (cutoff 0.800)	Expert ratings on a numerical scale: A=1, B=2, C=3, D=4 Mean; Mode	Selection of pertinent comments given by participating experts during the consensus procedure
Substance/group					
Proton pump inhibitors (PPI), only if absolutely necessary	B	19	0.921	1.8; 2	
H₂ receptor antagonists	C	19	1.000	3.0; 3	

Anemia	FORTA Class (original FORTA class in parentheses if different from consensus results)	Nr. of raters	Consensus coefficient, Round 1 (cutoff 0.800)	Expert ratings on a numerical scale: A=1, B=2, C=3, D=4 Mean; Mode	Selection of pertinent comments given by participating experts during the consensus procedure
Substance/group					
Substitution (iron, vitamin B12, folic acid in cases of deficiency)	A	18	1.000	1.0; 1	
Erythropoietin-stimulating agents (ESA) in patients with renal insufficiency	A	18	0.972	1.1; 1	
Iron substitution in patients with cardiac insufficiency Proof of iron deficiency (even without anemia)	See cardiac insufficiency				

NAUSEA AND VOMITING (Antiemetic agents)	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					

Metoclopramide: short term use	B	19	0.947	2.1; 2	
Long term use	C	17	1.000	3.0; 3	
Dimenhydrinate	C	19	1.000	3.0; 3	
Domperidone	C	19	1.000	3.0; 3	
OBSTIPATION (Laxatives)	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					
Macrogol	A	19	1.000	1.0; 1	
Lactulose	B	19	1.000	2.0; 2	
Sodium picosulfate, short term use	B	17	1.000	2.0; 2	

long term use	C	17	0.971	2.9; 3	
Prucalopride, Linaclotide	C	15	0.967	2.9; 3	
HYPOTHYRIOSIS	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-Thyroxin (if TSH range remain between 4-8 mU/l)	A	18	1.000	1.0; 1	
BACTERIAL INFECTIONS AND VACCINATIONS (the following FORTA-classifications only represent general recommendations. Bacterial Infection treatment MUST be assessed on an individual basis and fitted to diagnosis and pathogenic bacteria)	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					
Penicilline e.g. Amoxicillin +/- beta-lactamase inhibitors	A	19	1.000	1.0; 1	
Cephalosporins	B	19	1.000	2.0; 2	

Macrolide, e.g. Clarithromycin, cave: QT prolongation, Interactions	B	19	1.000	2.0; 2	
Fluoroquinolone, e.g. Moxifloxacin, Levofloxacin	C	19	0.974	3.1; 3	
except Ciprofloxacin	D	19	0.974	3.9; 4	
Vaccinations: Annual influenza vaccination Pneumococcal vaccination in patients ≥ 65 y. Herpes zoster vaccine (Shingrix®)	A A A	18 18 18	1,000 1,000 1,000	1,0; 1 1,0; 1 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					
Endocrine therapy (ER+/PR+), e.g. Tamoxifen	B	11	0.954	2.1; 2	Note: Aromatase inhibitors are considered more effective
Aromatase inhibitors	B	11	1.000	2.0; 2	
Antibody therapy (HER2+) CTX+Trastuzumab	B	10	1.000	2.0; 2	
Chemotherapy, e.g. CMF (Combination Cyclophosphamide, Methotrexate, 5- Fluorouracil)	C	10	1.000	3.0; 3	
6*AC/6*EC Regimen(Anthracycline/ Epirubicin, Cyclophosphamide)	C	10	1.000	3.0; 3	
4xA/EC+T	C	10	1.000	3.0; 3	
TC	C	10	1.000	3.0; 3	

BREAST CANCER Advanced Stage					
Endocrine therapy, (ER+/PR+) tamoxifen	B	11	1.000	2.0; 2	
aromatase inhibitors	B	11	1.000	2.0; 2	
CDK4/6-Inhibitors (ER+/HER-) Palbociclib	B	11	1.000	2.0; 2	
Antibody-therapy (HER2+)					
Trastuzumab + CTX (or AI)	B	10	1.000	2.0; 2	
Trastuzumab + Pertuzumab + Taxane	C	10	1.000	3.0; 3	
Chemotherapy					
Capecitabine	C	10	1.000	3.0; 3	
Taxane (mono)	C	10	1.000	3.0; 3	
Epirubicin (mono)	C	10	1.000	3.0; 3	

Epirubin +Cyclophosphamid	C	10	1.000	3.0; 3	
PROSTATE CANCER Adjuvante therapy					
Endocrine Therapie					
Bicalutamide	B	11	1.000	2.0; 2	
GnrH-analogue	B	11	1.000	2.0; 2	
PROSTATE CANCER Local advanced Castration-resistant prostate cancer (CRPC)					
Androgen deprivation therapy (ADT) + Chemotherapie ADT + Enzalutamide	B	9	0.944	2.1; 2	Note: My recommendation for all newer anti-hormonal substances + ADT is FORTA B
PROSTATE CANCER Advanced stage					
Endocrine therapy					
Bicalutamide	B	11	1.000	2.0; 2	
GnrH-analogue	B	11	1.000	2.0; 2	
Abiraterone	B	11	1.000	2.0; 2	

Enzalutamid	C	11	0.954	2.9; 3	Note: The side effect profiles of abiraterone and enzalutamide are different, but there are patients for whom one of the two drugs is better suited, so my recommendation is FORTA B also for enzalutamide
Chemotherapy-Hormone therapy Cabazitaxel + ADT	C	10	1.000	3.0; 3	
PROSTATE CANCER Advanced stage Castration-resistant prostate cancer (CRPC)					
Chemotherapy Docetaxel	C	10	1.000	3.0; 3	
COLORECTAL CARCINOMA Adjuvant Therapy					
5-Fluorouracil based infusion regimen	B	10	1.000	2.0; 2	
Capecitabine	B	10	1.000	2.0; 2	
FOLFOX Regimen (Folinic acid, Fluorouracil, Oxaliplatin)	C	10	1.000	3.0; 3	
COLORECTAL CARCINOMA Advanced stage					
Chemotherapy Capecitabine	C	10	1.000	3.0; 3	
5-Fluorouracil based infusion regimen	C	10	1.000	3.0; 3	
FOLFOX (Folinic acid, Fluorouracil, Oxaliplatin)	C	10	1.000	3.0; 3	

FOLFIRI	C	10	1.000	3.0; 3	
COLORECTAL CARCINOMA Advanced stage + RAS mutated					
Antibodytherapy FOLFIRI + Cetuximab	C	10	1.000	3.0; 3	
BRONCHIAL CARCINOMA Adjuvant therapy					
Adjuvant chemotherapy (Cisplatin-based)	C	10	1.000	3.0; 3	
BRONCHIAL CARCINOMA Advanced Stage ALK- translocated or ROS- translocated					
Tyrosine kinase inhibitor Crizotinib	B	10	0.950	2.1; 2	Note: There are newer and more effective substances
BRONCHIAL CARCINOMA Advanced stage. EGFR- activated mutations					
Tyrosine kinase inhibitors: Afatinib, Erlotinib, Gefitinib	B	9	1.000	2.0; 2	Note: There are newer and more effective substances
BRONCHIAL CARCINOMA Advanced stage: PD-L1 Expression ≥ 50%					
PD-1 Inhibitor: Pembrolizumab	B	10	1.000	2.0; 2	
BRONCHIAL CARCINOMA Advanced stage + fit: PD-L1					

Expression < 50%					
Chemotherapie					
Carboplatin based chemotherapy combination	C	10	1.000	3.0; 3	
BRONCHIAL CARCINOMA advanced stage + vulnerable: PD-L1 Expression < 50%					
Chemotherapy					
Docetaxel	C	10	1.000	3.0; 3	
ONCOLOGICAL DISEASES HEMATOLOGICAL NEOPLASIAS	FORTA Class (original FORTA class in parentheses if different from consensus results)	Nr. of raters	Consensus coefficient, Round 1 (cutoff 0.800)	Expert ratings on a numerical scale: A=1, B=2, C=3, D=4 Mean; Mode	Selection of pertinent comments given by participating experts during the consensus procedure
INDICATION Substance/group					
CLL (Chronic lymphatic leukemia) fit: without del(17p13) or TP53mut Immune chemotherapy: Rituximab-Bendamustin	B	10	1.000	2.0; 2	
CLL fit: with del(17p13) or TP53mut Tyrosine kinase inhibitor: Ibrutinib	B	10	1.000	2.0; 2	

CLL unfit: without del(17p13) or TP53mut Immune chemotherapy: Obinutuzumab- Chlorambucil or Ofatumumab- Chlorambucil	B	10	1.000	2.0; 2	
CLL unfit: ohne del(17p13) oder TP53mut Tyrosine kinase inhibitor: Ibrutinib	B	10	1.000	2.0; 2	
Multiple Myeloma fit: therapy combination MPT (see footnote)	B	10	1.000	2.0; 2	
VMP (see footnote)	B	10	1.000	2.0; 2	
Multiple Myeloma Unfit: Rd (see footnote)	B	10	1.000	2.0; 2	
VRd (see footnote)	B	10	1.000	2.0; 2	

DIFFUSE LARGE B-ZELL-LYMPHOMA	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
> 80+, fit Immune chemotherapy: adapted R-CHOP	B	10	1.000	2.0; 2	
> 80+, compromised Immune chemotherapy: Rituximab-Bendamustine	B	10	0.950	2.1; 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	13	1.000	1.0; 1	
Antiemetic agents (e.g. 5- HT receptor inhibitors)	A	13	1.000	1.0; 1	
Erythropoiesis Stimulating Agents, ESA	B	13	0.962	1.9; 2	Note: Has clear advantages, even in old age

*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

Rd = Lenalidomid plus low-dose Dexamethason;

V=Bortezomib;

MPT = Melphalan-Prednisone-Thalidomid;

VMP = Bortezomib-Melphalan-Prednisone

Delphi Expert Consensus Validation 2021¹

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 Osteoporosis	Rater-based FORTA Class (bold if: $\kappa > 0.500$, 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					
Romosozumab	C	11	0.534	2.5; 3	Note: FORTA C because of unclear cardiovascular risk; FORTA B, since there is little experience, but the spectrum of side effects is not significantly more dangerous than for bisphosphonates currently. If necessary, new evaluation in a few years.; FORTA C important future option
EXISTING INDICATION Dementia	Rater-based FORTA Class (bold if: $\kappa > 0.500$, 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					
Aducanumab	D	8	0.818	3.9; 4	Note: Not approved yet
EXISTING INDICATION BPSD: Sleep disorders	Rater-based FORTA Class (bold if: $\kappa > 0.500$, 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					
Benzodiazepines	D	17	0.720	3.8; 4	Note: Ultimately, the medication maybe required in individual cases
EXISTING INDICATION Bacterial infections and vaccinations	Rater-based FORTA Class (bold if: $\kappa > 0.500$, 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	16	0.909	1.1; 1	Note: FORTA A, but with a warning that in the case of very severe frailty / functional impairment, especially in a palliative situation, the side effects of the vaccination may also lead to a cascade of functional deterioration.

SUMMARY OF STATISTICAL METHODS

(The following descriptions of the statistical methods and calculations are based on the first version of the FORTA List¹. Former definitions and explanations are adopted unchanged.)

Consensus Coefficient¹

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 = 295). 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=295)	%
0	150	50.85
1	110	37.29
2	30	10.17
3	5	1.69

Cons_corr coefficients ranged from 0.800 to 1.000 (mean 0.968, median 1.000). Substances falling short of our established cons_corr cutoff of 0.800 underwent re-evaluation in a second round: n=1

Confirmation/determination of FORTA labels¹

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 follows⁵:

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 1 re-evaluated item, 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 proposed FORTA labels for 99.66% of all substances (n=295) after the first round; for one substance (0.34%), the FORTA label was confirmed 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 indications¹

- 4 substances were 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 ≥ 8 raters (excluding abstentions) during Round 2.
 - The new substances belonged to pre-existing FORTA indications
- 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 $\rightarrow$ 1
B $\rightarrow$ 2
C $\rightarrow$ 3
D $\rightarrow$ 4

If $1 \leq m < 1.5$ $\rightarrow$ FORTA Class **A**

If $1.5 \leq m < 2.5$ $\rightarrow$ FORTA Class **B**

If $2.5 \leq m < 3.5$ $\rightarrow$ FORTA Class **C**

If $m \geq 3.5$ $\rightarrow$ FORTA Class **D**

m= arithmetic mean based on the grades 1-4

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