The F O R T A List
"Fit for The Aged"
Expert Consensus Validation 2018

[1]

F O R T A			
A	B	C	D

Farhad Pazan[*], Christel Weiß[**], Martin Wehling[*]

[*]Clinical Pharmacology, Center for Geriatric Pharmacology, Medical Faculty of the University of Heidelberg in Mannheim

[**] Department of Medical Statistics, Biomathematics and Information Processing, Medical Faculty of the University of Heidelberg in Mannheim

Disclaimer

Please keep in mind that the FORTA Concept was conceived 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 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. '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 FORTA Concept: initiators and expert panel for the FORTA classification system 2018

Initiators of the FORTA List 2018 who prepared the proposal of the updated list

Martin Wehling, MD (Creator of the FORTA Concept); Clinical Pharmacology, Center for Geriatric Pharmacology, Medical Faculty Mannheim, Heidelberg University, Theodor-Kutzer-Ufer 1-3, 68167 Mannheim, Germany

Heinrich Burkhardt, MD; II. Medical Department, Center for Geriatrics, University Hospital Mannheim, Heidelberg University, Theodor-Kutzer-Ufer 1-3, 68167, Mannheim, Germany

Stefan Schwarz, MD; Central Institute of Mental Health, Mannheim, Germany

Ulrich Wedding, MD; Division of Palliative Care, University Hospital Jena, Clinic for Internal Medicine II, Erlanger Allee 101, 07740 Jena, Germany

FORTA Expert Review Panel 2018

The following 22 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.

Expert Panel Members and their affiliations

Jürgen Bauer, MD: Geriatric Centre of the Medical Faculty of the University of Heidelberg, AGAPLESION Bethanien Hospital Heidelberg, Rohrbacher Straße 149, 69126 Heidelberg, Germany

Heiner K. Berthold, MD: Department of Internal Medicine and Geriatrics, Bielefeld Evangelical Hospital (EvKB), Schildescher Strasse 99, 33611 Bielefeld, Germany

Michael Denkinger, MD: AGAPLESION Bethesda Clinic Ulm, University Hospital Ulm, Zollernring 26, 89073 Ulm, Germany

Peter Dovjak, MD: Gmunden Hospital, Department of Acute Geriatric Medicine, Miller-von-Aichholz-Straße 49, A-4810 Gmunden, Austria

Helmut Frohnhofen, MD: Department of Nephrology, Geriatrics and Internal Medicine, Alfried Krupp Hospital Rüttenscheid, Alfried-Krupp-Straße 21, 45276 Essen, Germany

Markus Gosch, MD: Medical Clinic 2, Geriatric Department, University Hospital of the Paracelsus Medical University, Nürnberg Hospital North, Prof.-Ernst-Nathan-Str. 1, 90419 Nürnberg, Germany

Hans Gutzmann, MD: Hedwigshöhe Hospital, Clinic for Psychiatry, Psychotherapy and Psychosomatic Medicine, Höhensteig 1, 12526 Berlin, Germany

Isabella Heuser-Collier, MD: Charité University Hospital Berlin, Department of Psychiatry and Psychotherapy, University Medicine Berlin, Hindenburgdamm 30, 112203 Berlin, Germany

Priv. Doz. Dr. Dr. Friedemann Honecker: General Internal Medicine, Hematology, Senology/Breast medicine, Tumor- und Brustzentrum ZeTuP, Silberturm, Rorschacherstrasse 150, 9006 St. Gallen, Switzerland

Michael Hüll, MD: Clinic for Geriatric psychiatry and psychotherapy, Center for Psychiatry Emmendingen, Neubronnstr. 25, 79312 Emmendingen, Germany

Bernhard Iglseder, MD: Department of Geriatric Medicine, Christian-Doppler-Klinik, Paracelsus Medical University, Ignaz-Harrer-Str. 79, 5020 Salzburg, Austria

Prof. Dr. Ulrich Jaehde: Friedrich-Wilhelms-University Bonn, Pharmaceutical Institute, clinical Pharmacy, An der Immenburg 4, 53121 Bonn, Germany

Siegfried Kasper, MD: Department of Psychiatry and Psychotherapy, Medical University of Vienna, AKH, Währinger Gürtel 18-20, A-1090 Vienna, Austria

Prof. Dr. Dr. Gerald Kolb: Department of Geriatric Medicine, Bonifatius Hospital Lingen gGmbH, Wilhelmstraße 13, 49808 Lingen (Ems), Germany

Prof. Dr. med. Reto W. Kressig : University Basel, Memory Clinic - Academic Geriatric Medicine, Burgfelderstrasse 101, 4055 Basel, Switzerland

Anja Kwetkat, MD: Jena University Hospital, Department of Geriatric Medicine, Bachstraße 18, 07740 Jena, Germany

PD Dr. med. Thomas Münzer, EAMA Board Member, Competence Center Healthy Ageing, Geriatric Clinic St. Gallen AG, Rorschacherstrasse 94, 9000 St. Gallen, Switzerland

Christoph Schindler, MD: Clinical Research Center Hannover, CRC- MHH Core Facility, Feodor-Lynen-Strasse 15, 30625 Hannover, Germany

Matthias Schuler, MD: Diakonissenhospital Mannheim, Geriatric Clinic, Speyerer Straße 91-93, 68163 Mannheim, Germany

Ralf-Joachim Schulz, MD: Geriatric Clinic at the St.-Marien Hospital, Kunibertkloster 11-13 50668 Köln, Germany

Ulrike Sommeregger, MD: Hietzing Hospital and Neurological Center Rosenhügel, Wolkersbergenstraße 1, 1130 Vienna, Department of Acute geriatric medicine, Donauspital, Langobardenstraße 122, 120 Vienna, Austria

Andrej Zeyfang, MD: Clinic for General Internal, Geriatric and Palliative Medicine, KLINIK OSTFILDERN-RUIT, Academic Educational hospital of the University Tübingen, Hedelfinger Str. 166, 73760 Ostfildern, Germany

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 <u>always</u> 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 <u>not</u> intended to take the place of individual therapeutic considerations or decisions. As with any simplified model, it <u>does</u> 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 2018

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)
Substance/Group	
Renin-Angiotensin system inhibitors	
ACE inhibitors	A
Angiotensin receptor antagonists	A
Long-acting calcium antagonists, dihydropyridine type, for example amlodipine	A
Betablockers	B
Except Atenolol	D
Diuretics (preferred as Thiazide Indapamide)	B
Alpha blockers	C
Spironolactone	C
Moxonidine	C
Urapidil	C
Aliskiren	C
Clonidine	D
Minoxidil	D

Calcium antagonists, verapamil type	**D**

CARDIAC INSUFFICIENCY	**FORTA Class** (original FORTA class in parentheses if different from consensus results)
Substance/Group	
Renin-angiotensin system inhibitors **ACE inhibitors**	
	A
Angiotensin receptor antagonists	A
Sacubitril/Valsartan	A
Betablockers (metoprolol, carvedilol, bisoprolol)	A
Diuretics	B
Spironolactone	C
Digitalis preparations	C
Ivabradine	C

ACUTE CORONARY SYNDROME	**FORTA Class** (original FORTA class in parentheses if different from consensus results)
Substance/Group	

Renin-Angiotensin-System- Blocker: ACE-inhibitors	**A**
Acetylsalicylic acid	**A**
Unfractionated heparin and low molecular weight heparin	**A**
Frequency-lowering betablockers	**A**
Atorvastatin	**A**
Nitroglycerin spray, single use, acute as on-demand medication	**A**
Clopidogrel, Prasugrel	**A**
Thrombolytics, especially rTPA (recombinant tissue-type plasminogen activator)	**B**
Nitrates, long-term	**C**
Gp IIb/IIIa antagonists (glycoprotein 2b/3a inhibitors)	**C**
Ivabradine	**C**
Molsidomine	D
CHRONIC THERAPY FOLLOWING MYOCARDIAL INFARCTION	**FORTA Class** (original FORTA class in parentheses if different from consensus results)
Substance/group	
Renin angiotensin system blockers ACE-Inhibitors/Angiotensin-Receptor-Blockers	**A**
Acetylsalicylic acid (100 mg/d)	**A**
Clopidogrel 6-12 months *12 months after acute coronary syndrome*	**A**

	A in case of ASA intolerance
Frequency-lowering beta blockers up to 3 years	A
Frequency-lowering beta blockers longer than 3 years	C
Nitroglycerin spray, single use as on-demand medication	A
Influenza vaccination/ Pneumococcus vaccination	A
Statins	A
Statins for very old (>85 years) patients	B
Ezetimibe	B
Nitrates, long-term	C
Ranolazine	C
Fibrates	C
Amiodarone	C
All other class-I-III antiarrhythmic agents	D
Dihydropyridine antagonists (if no hypertension)	D
Niacin	D

STROKE	FORTA Class (original FORTA class in parentheses if different from consensus results)
Substance/Group	
Acetylsalicylic acid (100mg/d)	A
Statins	A
rt-PA	A
Clopidogrel in case of ASA intolerance	A
Dipyridamole plus acetylsalicylic acid	C

ATRIAL FIBRILLATION	FORTA Class (original FORTA class in parentheses if different from consensus results)
Substance/group	
Frequency lowering Betablockers	A
Direct Oral Anticoagulants (DOACs)	B
Except Apixaban	A

Oral anticoagulation by vitamin-K-antagonists (warfarin) except	B
Phenprocoumon	C
Alternative in exceptional cases: low molecular weight heparin	C
Digoxin	C
Digitoxin	C
Class III antiarrhythmic agent amiodarone	C
All other class I-III antiarrhythmic agents including Dronedarone	D
Diltiazem, verapamil	D
Acetylsalicylic acid (100 mg/d)	D

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)	FORTA Class (original FORTA class in parentheses if different from consensus results)
Substance/group	
Inhalative long-acting parasympatholytic agents	A
Systemic glucocorticoids, acute, short-term use (5-7days) in cases of exacerbation	A
Antibiotics (acute) in cases of exacerbation, after calculated selection and, if necessary, according to antibiogram	A
Long-term administration of oxygen	A
Annual influenza immunizations	A
Pneumococcal immunizations for persons ≥ 65 years	A
Inhalative beta 2 mimetic agents	B
Inhalative glucocorticoids	C
Theophylline	C
Mucolytic agents, e,g, acetyl cysteine, bromhexine	C
Roflumilast	C
Systemic glucocorticoids, chronic use	D
Antitussives: opioid A., e.g. codein; non-opioid A., e.g. butamirate	D

OSTEOPOROSIS	FORTA Class (original FORTA class in parenteses if different from consensus results)
Substance/Group	
Calcium and vitamin D supplements (as prophylaxis for persons ≥ 65 years)	A
Parenteral bisphosphonates (IV every 3 months)	A
Raloxifene for women	A
Denosumab	A
Bisphosphonates, oral	B
Alfacalcidol	C
In case of renal insufficiency(eGFR <30 ml/min)	B
Teriparatide	C
Parathormone	C
Strontium ranelate	D
Nandrolone decanoate	D
Fluoride	D
Hormone replacement therapy (HRT): estrogen, except up to 3 years postmenopausal)	D

TYPE II DIABETES MELLITUS	FORTA Class (original FORTA class in parentheses if different from consensus results)
Substance/group	
DPP4 (Dipeptidylpeptidase) Inhibitors	A
Insulin and insulin analogs (if absolutely necessary)	B
Metformin	B
GLP1 (Glucagon-Like Peptide-1) analogs	B
Acarbose	C
3rd generation sulfonylureas (for example, glimepiride)	C
Glinides (for example, nateglinide)	C
Gliflozins	(D) C
PPAR-ɣ Ligands (Peroxisomal Proliferator-Activated Receptor gamma) **Pioglitazone**	C
Rosiglitazone	D
1st generation sulfonylureas (for example, glibenclamide)	D

DEMENTIA	FORTA Class (original FORTA class in parentheses if different from consensus results)
Substance/group	
Acetylcholinesterase inhibitors **e.g. donepezil, galantamine,** **rivastigmine** **(mild or moderate stage of Alzheimer disease)**	**B**
Memantine **(moderate or advanced stage of Alzheimer disease)**	**B**
Ginkgo biloba	**C**
Statins	**D**
Piracetam	**D**
Antioxidants: Vitamin E, selenium, vitamin C	**D**
ginseng	**D**
Hormone preparations, e.g. DHEA (Dehydroepiandrosterone), testosterone	**D**

BEHAVIORAL AND PSYCHOLOGICAL SYMPTOMS OF DEMENTIA (BPSD)	FORTA Class (original FORTA class in parentheses if different from consensus results)
DEPRESSION	
Substance/group	
SSRI (Selective Serotonin Reuptake Inhibitors) **Citalopram/escitalopram, sertraline, fluoxetine in the usual dosages**	**C**

	FORTA Class
Mirtazapine (15-45mg/d)	**C**
SNRI (Serotonin-Noradrenalin-Reuptake-Inhibitors) **Venlafaxine, duloxetine**	**D**

BPSD: PARANOIA, HALLUCINATION	**FORTA Class** **(original FORTA class in parentheses if different from consensus results)**
Substance/group	
Risperidone	**C**
Melperone	**C**
Quetiapine	**C**
Olanzapine	**C**
Aripiprazole	**D**
Clozapine	**D**
Haloperidol	**D**

BPSD: RESTLESSNESS, AGITATION, (AGGRESSIVENESS)	**FORTA Class** **(original FORTA class in parentheses if different from consensus results)**
Substance/group	
Trazodone	**C**

	FORTA Class
Risperidone	**C**
Quetiapine	**C**
Melperone	**C**
Pipamperone	**C**
Citalopram	**C**
Clomethiazole	**D**

BPSD: SLEEP DISORDERS	**FORTA Class** **(original FORTA class in parentheses if different from consensus results)**
Substance/group	
Slow-release melatonin	**C**
Tetracyclic antidepressant Mirtazapine	**C**
Trazodone	**C**
Tricyclic antidepressant Doxepine	**D**
Zopiclone	**D**

DEPRESSION **Prophylaxis and therapy for patients with moderate to major depression**	**FORTA Class** **(original FORTA class in parentheses if different from consensus results)**
Substance/group	
SSRIs (Selective Serotonin Reuptake Inhibitor) **Sertraline**	**B**

Escitalopram	B
Citalopram	B
Tricyclic antidepressant Amitriptyline, Doxepine	C
Tetracyclic antidepressant Mirtazapine	C
SNRIs (Serotonin-Noradrenalin Reuptake Inhibitors) **Venlafaxine**	C
Duloxetine	C
Monoamine oxidase A (MAO) inhibitor Moclobemide	C
Dopamine and norepinephrine reuptake inhibitor Bupropion	C
Quetiapine	C
Tianeptine (Serotonin-Reuptake-Enhancer)	C
Benzodiazepines: **General**	D
Long-acting,	D
Short-acting	C
Trazodone	D
St. John's Wort	D
Agomelatine	D
Selective noradrenaline re-uptake inhibitor Reboxetine	D

BIPOLAR DISORDER	FORTA Class (original FORTA class in parentheses if different from consensus results)
Substance/group	
Lithium	**B**
Quetiapine	**B**
Valproic acid	**C**
Lamotrigine	**C**
Carbamazepine	**D**

INSOMNIA / SLEEP DISORDERS	FORTA Class (original FORTA class in parentheses if different from consensus results)
Substance/group	
Melatonin (slow-release)	**B**
ω1-Benzodiazepine agonists **Zolpidem**	**C**
Zaleplone	**C**
Zopiclone	**C**
Butyrophenone derivative Pipamperone	**C**
Melperone	**C**

	FORTA Class
Tetracyclic antidepressant Mirtazapine	C
Tricyclic antidepressant Doxepine in low dosage (10-25mg/d)	C
Tricyclic antidepressant Doxepine	D
Benzodiazepines, e.g. Oxazepam (medium half- life)	D
Triazolam (very short half-life)	D
Opipramole	D
Sedative Antihistamine Diphenhydramine/Doxylamin	D

CHRONIC PAIN	FORTA Class (original FORTA class in parentheses if different from consensus results)
Substance/group	
Paracetamol	A
Metamizole	B
Opioids, cautious dose incrrease e.g. Buprenorphine, oxycodone, hydromorphone	B
Tilidine/naloxone Oxycodone/naloxone	C

	FORTA Class (original FORTA class in parentheses if different from consensus results)
Morphine	C
Tramadol	C
Tapentadol	C
SSRI (Selective Serotonin Reuptake Inhibitors) / SNRI (Serotonin- Norepinephrine-Reuptake Inhibitor), e.g. venlafaxine (only if absolutely necessary)	C
Antiepileptic agents (only for neuropathic pain)	
Pregabalin/gabapentin	C
Carbamazepine	D
Tricyclic antidepressant amitriptyline	D
NSAIDs (nonsteroidal anti-inflammatory drugs, for long-term use), e.g. naproxen	D
Cox-2 inhibitors, e.g. celecoxib	D

EPILEPSY	
Substance/group	
Levetiracetam	B
Lamotrigine	B
Gabapentin	B
Topiramate	B
Lacosamide	B
Lorazepam (emergency use)	B
Lorazepam (long-term use)	D
Pregabalin	C
Oxcarbazepine	C
Valproic acid	C
Eslicarbazepine	C
Zonisamide	C
Carbamazepine	C
Diazepam (emergency use)	C
Diazepam (long-term use)	D
Midazolam (emergency use)	C

	FORTA Class
Midazolam (long-term use)	D
Phenytoin	D
Phenobarbital	D
Ethosuximide	D

INCONTINENCE Drug therapy for urge incontinence	FORTA Class (original FORTA class in parentheses if different from consensus results)
Substance/group	
Fesoterodine/Solifenacin	B
Tolterodine	C
Trospium chloride	C
Extended-release Oxybutynin	C
Duloxetin	C
Immediate-release Oxybutynin	D

GASTROINTESTINAL ILLNESSES/ CONCOMITANT THERAPY WITH NSAIDs	FORTA Class (original FORTA class in parentheses if different from consensus results)
Substance/group	
Proton pump inhibitors (PPI), only if absolutely necessary	B
H$_2$ receptor antagonists	C

Anemia	FORTA Class (original FORTA class in parentheses if different from consensus results)
Substance/group	
Substitution (iron, vitamin B12, folic acid in cases of deficiency)	A
Erythropoetin-stimulating agents (ESA) in patients with renal insufficiency	A
Iron substitution in patients with cardiac insufficiency **Proof of iron deficiency**	A
No proof of iron deficiency	B

NAUSEA AND VOMITING (Antiemetic agents)	FORTA Class (original FORTA class in parentheses if different from consensus results)
Substance/group	

	FORTA Class
Metoclopramide: short term use	B
Long term use	C
Dimenhydrinate	C
Domperidone	C

OBSTIPATION **(Laxatives)**	FORTA Class (original FORTA class in parentheses if different from consensus results)
Substance/group	
Macrogol	A
Lactulose	B
Sodium picosulfate, **short term use**	B
long term use	C
Prucalopride, Linaclotide	C

HYPOTHYRIOSIS	FORTA Class (original FORTA class in parentheses if different from consensus results)
Substance/group	
L-Thyroxin **(if TSH range remain between 4-8 mU/l)**	A

BACTERIAL INFECTIONS (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)
Substance/group	
Penicilline e.g. Amoxicillin +/- beta-lactamase inhibitors	A
Cephalosporins	B
Macrolide, e.g. Clarithromycin, cave: QT prolongation, Interactions	B
Fluoroquinolone, z.B. Moxifloxacin, Levofloxacin	C
except Ciprofloxacin	D

ONCOLOGICAL DISEASES: SOLID TUMORS	FORTA Class (original FORTA class in parentheses if different from consensus results)
INDICATION Substance/group	
BREAST CANCER **Adjuvant therapy**	
Endocrine therapy (ER+/PR+), e.g. **Tamoxifen**	B
Aromatase inhibitors	B
Antibody therapy (HER2+) CTX+Trastuzumab	B
Chemotherapy, e.g. **CMF (Combination Cyclophosphamide, Methotrexate, 5-Fluorouracil)**	C
6*AC/6*EC Regimen(Anthracycline/ Epirubicin, Cyclophosphamide)	C

4xA/EC+T	C
TC	C
BREAST CANCER **Advanced Stage**	
Endocrine therapy, (ER+/PR+) tamoxifen	B
aromatase inhibitors	B
CDK4/6-Inhibitors (ER+/HER-) Palbociclib	B
Antibody-therapy (HER2+)	
Trastuzumab + CTX (or AI)	B
Trastuzumab + Pertuzumab + Taxane	C

Chemotherapy **Capecitabine**	**C**
Taxane (mono)	**C**
Epirubicin (mono)	**C**
Epirubin +Cyclophosphamid	**C**
PROSTATE CANCER **Adjuvante therapy**	
Endocrine Therapie **Bicalutamide**	**B**
GnrH-analogue	**B**
PROSTATE CANCER **Local advanced Castration-resistant prostate cancer (CRPC)**	
Androgen deprivation therapy (ADT) + Chemotherapie **ADT + Enzalutamide**	**B**
PROSTATE CANCER **Advanced stage**	
Endocrine therapy **Bicalutamide**	**B**

GnrH-analogue	B
Abiraterone	B
Enzalutamid	C
Chemotherapy-Hormone therapy Carbacitaxel + ADT	C
PROSTATE CANCER **Advanced stage Castration-resistant prostate cancer (CRPC)**	
Chemotherapy Docetaxel	C
COLORECTAL CARCINOMA **Adjuvant Therapy**	
5-Fluorouracil based infusion regimen	B
Capecitabine	B
FOLFOX Regimen (Folinic acid, Fluorouracil, Oxaliplatin)	C
COLORECTAL CARCINOMA **Advanced stage**	
Chemotherapy Capecitabine	C
5-Fluorouracil based infusion regimen	C
FOLFOX (Folinic acid, Fluorouracil, Oxaliplatin)	C

FOLFIRI	**C**
COLORECTAL CARCINOMA **Advanced stage + RAS mutated**	
Antibodytherapy **FOLFIRI + Cetuximab**	**C**
BRONCHIAL CARCINOMA **Adjuvant therapy**	
Adjuvant chemotherapy (Cisplatin-based)	**C**
BRONCHIAL CARCINOMA **Advanced Stage ALK-translocated or ROS-translocated**	
Tyrosine-cinase inhibitor Crizotinib	**B**
BRONCHIAL CARCINOMA **Advanced stage. EGFR-activated mutations**	
Tyrosine-cinase inhibitors: **Afitinib, Erlotinib, Gefitinib**	**B**
BRONCHIAL CARCINOMA **Advanced stage: PD-L1 Expression ≥ 50%**	
PD-1 Inhibitor: **Pembrolizumab**	**B**
BRONCHIAL CARCINOMA **Advanced stage + fit: PD-L1 Expression < 50%**	
Chemotherapie **Carboplatin based chemotherapy combination**	**C**

BRONCHIAL CARCINOMA advanced stage + vulnerable: PD-L1 Expression < 50%	
Chemotherapy **Docetaxel**	**C**

ONCOLOGICAL DISEASES HEMATOLOGICAL NEOPLASIAS	FORTA Class (original FORTA class in parentheses if different from consensus results)
INDICATION **Substance/group**	
CLL (Chronic lymphatic leukemia) **fit: without del(17p13) or TP53mut** **Immune chemotherapy: Rituximab-Bendamustin**	B
CLL **fit: with del(17p13)** **or TP53mut** **Tyrosine-cinase inhibitor: Ibrutinib**	B
CLL **unfit: without del(17p13)** **or TP53mut** **Immune chemotherapy: Obinutuzumab-Chlorambucil** **or** **Ofatumumab-Chlorambucil**	B
CLL **unfit: ohne del(17p13)** **oder TP53mut** **Tyrosine-cinase inhibitor: Ibrutinib**	B

	FORTA Class
Multiple Myeloma fit:	
therapy combination	
MPT (see footnote)	B
VMP (see footnote)	B
Multiple Myeloma Unfit:	
Rd (see footnote)	B
VRd (see footnote)	B

DIFFUSE LARGE B-ZELL-LYMPHOMA	FORTA Class (original FORTA class in parentheses if different from consensus results)
> 80+, fit Immune chemotherapy: adapted R-CHOP	B
> 80+, compromised Immune chemotherapy: Rituximab-Bendamustine	B

ONCOLOGICAL SUPPORTIVE THERAPY	FORTA Class (original FORTA class in parentheses if different from consensus results)
Substance/group	
G-CSF (Granulocyte Colony Stimulation Factor)	A
Antiemetic agents (e.g. 5-HT receptor inhibitors)	A
Erythropoesis Stimulating Agents, ESA	B

*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

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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 INSOMNIA / SLEEP DISORDERS	Rater-based FORTA Class (bold if: $\kappa > 0.500$, rater number ≥ 10 and label distance < 2)
Substance/group	
Trazodone	C

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