The Wise List 2015

The Wise List with recommended essential medicines for common diseases in patients in Stockholm County Council (Healthcare Region), Sweden

Table of Contents:

Foreword to the English edition

The Wise List for recommended essential medicines for common diseases in patients in Stockholm County Council has gained international interest. The Stockholm Drug and Therapeutics Committee has been asked to publish our Wise List for the benefit of interested colleagues and institutions. The Wise List concept was designed and introduced in 2001 as part of the multifaceted approach described as Stockholm Model for Wise Use of Medicines as described (1-3). The aim is to improve the quality of medicine prescribing and use in Stockholm metropolitan region.

The Wise List concept builds on the essential medicine concept introduced by the World Health Organization in the 1970s in which the role of independent medicine experts in the selection and evaluation of medicines (1,4) is pivotal. Trusted medical colleagues and pharmacotherapeutic experts have shared the responsibility in this work, carried out together with clinical pharmacologists, pharmacists, nurses and administrative staff. This joint effort has been a prerequisite in achieving respect for the model of selecting 200 medicines to be prescribed for common diseases and an additional 100 for specialised care in Stockholm. We are convinced that without a clear strategy for communication, continuous medical education and follow-up of adherence to our recommendations, the Wise List would not have been accepted as a benchmark and guide in healthcare across institutions in Stockholm. The concepts of critical medicine evaluation (5), involvement of clinical pharmacology in healthcare), communication and continuous medical education (1,3) and Drug Utilization 90% (DU 90%) method for follow-up of adherence to the recommendations (6) are presented elsewhere (1,3,6). Currently, the adherence rate to recommendations is about 90% among primary healthcare institutions in Stockholm metropolitan region (2 million people).

We hope this English edition will inspire colleagues and other Drug and Therapeutics Committees (DTC) to develop their own formulary to be used as an indispensable part of daily clinical work. Remember that it is important that each DTC make their own selections and recommendations based on an agreed guideline for evaluating efficacy, safety and medical suitability of medicines, considering the importance of a policy to handle conflict of interest (1). This English version is available freely and openly for your use at www.janusinfo.se. We appreciate that you acknowledge the use of Wise List referring to the website and the conceptual description of the content (1). We are not responsible for, and expressly disclaims all liability for, damages of any kind arising out of use, reference to, or reliance on any information contained within this version.

Stockholm September 21, 2015

Eva Andersén Karlsson MD
Associate professor
Chair
Drug and Therapeutics Committee
Stockholm County Council

Lars L Gustafsson MD
Professor
Chair 2000-2009
Drug and Therapeutics Committee
Stockholm County Council
lars-l.gustafsson@ki.se

Kristina Ateva
Pharmacist
Drug and Therapeutics Committee
Stockholm County Council
kristina.ateva@sll.se

Any inaccuracies found in this version may be submitted via email to kristina.ateva@sll.se.

References, see page 93

The 2015 Wise List Foreword

The Wise List includes medicines recommended for the treatment of common diseases. The recommendations are based on scientific evidence regarding efficacy and safety, pharmaceutical suitability, cost-effectiveness and environmental aspects.

The Wise List is the result of extensive work. The 21 expert panels of the Stockholm County Council Drug and Therapeutics Committee (DTC) review and evaluate the scientific literature within their respective therapeutic areas and suggest medicines to be recommended. The recommendations are targeted on the needs of recommendations for primary care and general practioners but are also the essential therapy for patients in outpatient hospital and specialist clinics. The proposals of the expert panels are presented to the DTC, which is an independent, multidisciplinary medical steering committee for medicine use and policy within Stockholm County Council (SCC). The medicine recommendations are decided after careful reviews of the proposals from the expert panels. So called Wise Advice is established in areas where preventive measures and medicine treatment can be improved according to the joint recommendation of the DTC. It is then the task of the DTC to disseminate and gain support for evidence-based recommendations among prescribers in SCC primary care, specialised outpatient care and inpatient care in different hospitals.

The DTC also works towards the wise introduction of new and effective medicines. By providing continuing medical education, monitoring and evaluating the role of medicines in therapy, the population of Stockholm country can be offered the best medical care. Learn more about this on page 85.

Patient safety is an important issue for the patients and for the health care system. Many patients face drug-related problems. All prescribers have a major responsibility to help ensure that the medicine treatment which patients receive is medically appropriate. General prescribing guidelines are found on page 4.

Learn more about the Wise List and about Wise Advice on www.janusinfo.se, which provides manufacturer-independent information and expert IT decision-making services on medicines for the health care system. The joint website for physicians and other healthcare staff in Stockholm www.janusinfo.se is freely available and includes some information in English.

Eva Andersén Karlsson
Chair
Drug and Therapeutics Committee
Stockholm County Council

Johan Bratt
Vice Chair
Drug and Therapeutics Committee
Stockholm County Council

Reading Notes

Recommendations relating only to specialised care are available in yellow boxes with the heading "Specialised Care" (about 100 medicines). The essential recommendations include about 200 medicines.

Mandatory generic substitution by pharmacies: interchangeable prescription medicines

Generic prescribing is not allowed in Sweden but community pharmacists are required to dispense the generic equivalent which is chosen by The Dental and Pharmaceutical Benefits Agency, for that month.

In order for pharmacies to be able to substitute one medicine with another, the medicine must be listed on the list of interchangable medicines of the Medical Product Agency (MPA), see www.mpa.se. Pharmacy interchangeability only applies to medicines within the pharmaceutical benefit scheme, see http://www.tlv.se/In-English/in-english/

As for generic interchangeable medicines, in principle only the actual substance is recommended. The Wise List includes all of the brand names in use (at the time of printing) according to the above-mentioned criteria. This means that some brand names are not provided, because they have not been included in the medicine benefit scheme, and therefore may not be exchanged at the pharmacy.

When the list of proprietary names begins with "Substance name ...", followed by inverted commas ("..."), this denotes that the name of the company has been omitted and that generics are available from one or more different companies.

The adherence of health care providers to the Wise List is monitored at the level of individual substances. Stockholm DTC has widely implemented the DU90% concept introduced by Bergman and co-workers (6) that has gained acceptance internationally. Compliance is not affected by which generic medicine has been prescribed or dispensed.

The Wise List is available in several versions

- The Wise List on www.janusinfo.se also contains the justifications for the recommendations and references. This information is in Swedish only.
- The Wise List recommendations appear in the electronic patient record systems through SIL (Swedish Information Database for Pharmaceuticals). Medicines recommended for specialised care are not marked in the patient record systems.
- "The Wise List for patients" is adapted in terms of language to the target audience and in some areas includes advice and recommendations for self-care. Recommendations relating only to specialised care are not included in this version.
- "The Wise List - Recommended and Procured Medicines with Synonyms" is available as an aid in prescribing and ordering of medicines for medication stocks in various forms of health care.

All printed versions (in Swedish) can be ordered by email: klokalistan@sll.se.

Wise Advice

The owl symbol is used to indicate the Wise Advice of the Stockholm County Council Drug and Therapeutics Committee for improving the use of medicines.

We welcome comments on the Wise List
Comments may be submitted via email to lakemedelskommitten@sll.se

Prescribing Guidelines in Stockholm County Council

- Apply a holistic view of the patient and consider medicine treatment against other methods of treatment and health promotive measures.
- Take full responsibility for the patient's treatment, including for medicines prescribed by other prescribers.
- Elicit and consider the patient's attitude towards the treatment. What treatment s/he would be willing to take and what support is desired or needed.
- Follow the best evidence. Consider the recommendations of the Wise List, the Wise Advice and follow the local, regional and national health care programs.
- Take the patient's individual circumstances into account. Age, renal function, weight, ethnicity, sex and gender, and other medicines may impact on efficacy and side effects. Check if the patient is using alternative therapies.
- Prescribing should be done in accordance with the requirements of the patient and be cost-effective.
- Make sure that the patient understands how the medicine should be taken and why, so that you as the prescriber achieve consensus on the goal of treatment.
- When you start the patient on a medicine intended for prolonged use, prescribe a starter pack if possible.
- Follow up the medicine treatment to monitor compliance, efficacy and side effects.
- Use monitoring protocols for the medicines covered by structured follow-up schedules.
- Use non-commercial decision support aids for medicine selection and for consideration of important drug-drug interactions, effects of medicines during pregnancy, etc.
- Participate in non-commercial continued medical education to optimize medication use. Adopt an investigative approach to information activities arranged by pharmaceutical companies.
- Conduct medicine reviews to evaluate the efficacy, reduce the risk of side effects and undesired interactions and to identify medicine use that is not evidence-based.
- Report suspected adverse reactions to the Medical Products Agency (MPA), especially for medicines that are subject to enhanced monitoring. These are marked with a black triangle in the package leaflet and the summary of product characteristics
- Medicines that are not included in the pharmaceutical benefit scheme will not be substituted at the pharmacy even if they are interchangeable according to the MPA. This means that the medicine preparation written on the prescription will be dispensed even if cheaper alternatives are available. The rights of pharmacies to free pricing of medicines outside the reimbursement scheme also means that the price can vary between pharmacies in Sweden for the same preparations.

Wise Advice

The DTC and its expert panels produce advice on how to improve drug utilization in Stockholm County. Background information to the Wise Advice is available at www.janusinfo.se (in Swedish).

Wise Advice 2015

- Always give the patient an updated medication list.
- Estimate and consider renal function in the selection and dosing of medicines.
- Improve antihypertensive treatment – determine a target blood pressure together with the patient, combine medicines more often and follow up.
- Verify the diagnosis before treating according to the”heart failure treatment ladder” and seek to establish good heart rate control (below 70 beats/min in sinus rhythm).
- In atrial fibrillation, always estimate the stroke risk with CHA_2DS_2-VASc and decide about thromboembolic prophylaxis. Choose anticoagulant therapy before ASA.
- Do not treat uncomplicated acute bronchitis with antibiotics.
- Do not treat asymptomatic bacteriuria in the elderly and only culture from urine if the patient is experiencing urinary tract symptoms.
- Treatment with proton pump inhibitors is not advisable in the case of stomach pains of unknown cause.
- Use preventative treatment in patients who suffer from three or more monthly migraine attacks, which require treatment.
- Treat depression to complete remission.
- Increase the use of medicines to prevent relapse in alcohol dependence and follow up on treatment.
- Avoid giving tramadol and propiomazine to the elderly.

Anaesthesia

Local Anaesthesia

Choice of a local anaethetic compound should be based on the desired duration of effect and the risk of toxicity.

Surface Anaesthesia of Intact Skin or for Leg Ulcers

Substance	Brand name/names
lidocaine *+ prilocaine*	Emla, Tapin *lotion* Emla *patch*

Mucous Membrane Anaesthesia

lidocaine	Xylocain *gel, spray*

Infiltration Anaesthesia and Peripheral Blocks

Adding adrenaline prolongs the duration of effect. Should not be used for blocks of fingers or toes.

lidocaine	Xylocain
lidocaine *+ adrenaline*	Xylocain adrenaline

Specialised Care

Intravenous Regional Anaesthesia

prilocaine	Citanest

Lower cardiotoxicity than the other local anaesthetics.

Post-Operative Nausea and Vomiting

ANTIEMETICS

betamethasone	Betapred *injection*
droperidol	Dridol *injection*
ondansetron	Ondansetron ..., Zofran *injection* Ondansetron ..., Zofran, Zofron *pill*

Post-Operative Nausea and Vomiting; www.janusinfo.se (in Swedish)

Anaphylaxis and Severe Allergic Reactions

Acute Allergic Reactions

ADRENALINE

It is important for the physician or nurse to instruct patients how to use the injection pen. The patient should always have two adrenaline pens available, as the injection may have to be repeated.

Substance	Brand name/names
adrenaline	Emerade *injection pen (auto-injector)*
adrenaline	EpiPen *injection pen (auto-injector)* EpiPen jr *injection pen (auto-injector)*
adrenaline	Adrenaline Mylan *1 mg/ml im*

ANTIHISTAMINE

desloratadine	Desloratadine …, Aerius, Dasselta

STEROID

betamethasone	Betapred *pill* Betapred *injection*

Anaphylaxis, management of, see www.viss.nu (only in Swedish)

Anemia

B12 Deficiency

Substance	Brand name/names
cyanokobalamin	Behepan, Betolvex, Betolvidon

Folic Acid Deficiency

folic acid	Folic acid ..., Folacin, Folvidon

Iron Deficiency

ferrous sulfate	Duroferon
ferrous glycine sulfate	Niferex*
järnsackaros	Venofer *injection*
dextriferron	Ferinject** *injection*

* Not included in the reinbursement scheme in Sweden

** Limited reimbursement, see www.tlv.se (in Swedish)

Renal anemia page 77

Cardiovascular Disease (CVD), except Stroke

These recommendations for medicine treatment of cardiovascular disease apply equally to men and women and regardless of their chronological age. Symptomatic treatment and quality of life should be prioritized ahead of prevention in frail older patients with short life expectancy.

Prevention of CVD

Lifestyle measures

Lifestyle measures are the foundation of cardiovascular prevention.

- Smoking cessation. See **Nicotine Addiction**, page 73.
- Physical activity. Consider Physical Activity on Prescription (FaR), see www.viss.nu or http://www.fyss.se/2011/02/fyss-in-english/.
- A balanced diet.

Blood Pressure Lowering Medicines

See **Hypertension** below

Lipid-Lowering Medicines

Statins are well documented for reducing morbidity and mortality. In patients without serious lipid disorders, the estimated risk and not the cholesterol level should guide treatment. Statins are grossly underutilized in patients with established atherosclerotic disease and many patients stop taking their medicines.

STATINS

Substance	Brand name/names
simvastatin	Simvastatin …, Simidon *(20–) 40 mg/day*
atorvastatin	Atorvastatin …, Atorbir, Atorstad, Atorvastad, Lipitor, Zarator *10–(80) mg/day*

For very high-risk patients and patients with serious lipid disorders, more intense statin treatment is desirable (atorvastatin 40-80 mg/day). Consider interactions and that the risk of side effects is dose-dependent.

Serious lipid disorders – investigation and treatment recommendations, see www.janusinfo.se (in Swedish)

Arterial Thrombosis Prevention

Thrombosis prevention in ischemic heart disease page 11, post MI page 12, in atrial fibrillation page 16, peripheral artery disease page 18, TIA/ischemic stroke page 57.

ASA or other antiplatelet treatment is not recommended as primary prevention treatment for patients without manifest atherosclerotic disease.

Hypertension

Improve antihypertensive treatment – determine a target blood pressure together with the patient, combine medicines more often and follow up.

Good antihypertensive treatment is an important part of CVD prevention for persons of all ages and is well documented up until at least 85 years of age. Currently, hypertension is markedly undertreated and many patients stop treatment. More patients need to reach target blood pressure levels, and this is particularly important for high-risk patients.

In uncomplicated hypertension, the target blood pressure level is <140/90 mm Hg. Combination treatment is often required. In very high CVD risk cases, e.g., prior stroke/TIA, MI, heart failure or peripheral arterial disease, a lower target blood pressure level (130–135/80–85 mmHg) is desirable.

24-hour ambulatory blood pressure monitoring may provide more exact information concerning the diagnosis and prognosis than the office blood pressure. Home blood pressure measurements offer valuable additional information and increases patient participation in treatment. For practical advice, go to **Preventing atherosclerotic cardiovascular disease with medicines – background information,** www.mpa.se (in Swedish).

Multifactorial treatment in diabetes mellitus page 31
Renal protection in medical renal disease page 76
Recommendations for the treatment of hypertension, www.janusinfo.se (in Swedish)

First-Line Treatment

ACE INHIBITORS

Substance	Brand name/names
enalapril	Enalapril …, Renitec
ramipril	Ramipril …, Triatec

ANGIOTENSIN-RECEPTOR BLOCKERS (ARB)

*candesartan**	Candesartan ..., Amias, Candesarstad, Candexetil, Kairasec, Kandrozid
losartan	Losartan …, Losarstad, Losatrix

* Limited reimbursement, see www.tlv.se (in Swedish)

Hypertension in patients with diabetes mellitus with or without nephropathy should be treated with an ACE inhibitor or an ARB.

CALCIUM ANTAGONIST

amlodipine	Amlodipine …, Amloratio, Norvasc

DIURETICS

bendroflumethiazide	Bendroflumethiazide …, Salures
hydrochlorothiazide	Hydrochlorothiazide ..., Esidrex
hydrochlorothiazide + amiloride	Normorix mite, Sparkal mite Amiloferm, Normorix, Sparkal
chlortalidone	Hygropax

Consider the risk of hypokalemia and hyponatremia as well as metabolic side effects. Furosemide is recommended instead of thiazide diuretics in cases with reduced renal function (eGFR <30 ml/min).

COMBINATIONS
An ACE inhibitor or ARB plus amlodipine and/or thiazides are recommended combinations. Combination of an ACE inhibitor and ARB is not recommended due to the increased risk of side effects (renal dysfunction, electrolyte disorders) without any further improvement of the prognosis.

Fixed combinations

Substance	Brand name/names
enalapril *+ hydrochlorothiazide*	Enalapril Comp ..., Enalapril/Hydrochlorothiazide ..., Linatil comp, Renitec comp, Synerpril
candesartan *+ hydrochlorothiazide**	Candesartan/Hydrochlorothiazide ..., Atacand Plus, Candemox Comp, Candesarstad Comp, Candexetil Comp
losartan *+ hydrochlorothiazide*	Losartan/Hydrochlorothiazide …, Losarstad Comp, Losatrix Comp, Marozid

* Limited reimbursement, see www.tlv.se (in Swedish)

Second-Line Treatment

BETA BLOCKER

*metoprolol succinate**	Metoprolol …, Metomylan, Seloken ZOC

* Limited reimbursement, see www.tlv.se

Beta blockers are given as adjunct antihypertensive treatment or in cases with concomitant ischemic heart disease, arrhythmia, heart failure or migraine. The combination of thiazides and betablockers increase the risk of diabetogenic effects.

Adjunct treatment

ALDOSTERONE ANTAGONIST (Mineralocorticoid receptor antagonist)

spironolactone	Spironolakton …, Aldactone

ALPHA BLOCKER

*doxazosin**	Doxazosin …, Alfadil, Cardura

* Limited reimbursement, see www.tlv.se (in Swedish)

Specialised Care

ALPHA AND BETA BLOCKER

*labetalol**	Trandate

* Limited reimbursement, see www.tlv.se (in Swedish)

Ischemic Heart Disease

Prevention

STATINS
Lipid-Lowering Medicines page 9

PLATELET INHIBITORS

acetylsalicylic acid	Trombyl *75 mg/day*

On suspicion of unstable coronary artery disease/MI, a loading dose of 500 mg of preferably buffered ASA is recommended.

clopidogrel	Clopidogrel ..., Cloriocard, Grepid, Plavix

Time-limited combination treatment with ASA in unstable coronary artery disease or PCI with stent implantation or as an alternative in cases of hypersensitivity to ASA. In cases with previous peptic ulcer disease, it is safer to add a PPI to ASA than to switch to clopidogrel.

Recommendations for treating coronary artery disease with ADP receptor inhibitors, see www.janusinfo.se (in Swedish)

Specialised Care

PLATELET INHIBITOR

Substance	**Brand name/names**
ticagrelor	Brilique

OTHER ANTITHROMBOTIC MEDICINES

bivalirudin	Angiox
enoxaparin	Klexane
fondaparinux	Arixtra
heparin	Heparin LEO

Secondary Prevention after Myocardial Infarction (MI)

PLATETET INHIBITORS

See page 11

BETA BLOCKER

metoprolol succinate	Metoprolol …, Metomylan, Seloken ZOC *100–200 mg/day*

STATINS

Lipid-lowering medicines page 9

ACE INHIBITOR

In cases with left ventricular dysfunction, diabetes mellitus or hypertension

ramipril	Ramipril ..., Triatec *target dose 10 mg/day**

* The target dose has been shown to reduce morbidity and should be aimed for if the patient can tolerate it.

ALDOSTERONE ANTAGONISTS
(Mineralocorticoid receptor antagonists)

In cases with heart failure or MI, consider

First-Line Treatment

spironolactone	Spironolakton …, Aldactone *25(–50) mg/day*

Consider the risk of hyperkalemia

Second-Line Treatment – in case of endocrine side effects

eplerenone	Inspra *50 mg/day*

Consider the risk of hyperkalemia.

Angina Pectoris

Rescue medication

NITROGLYCERINE

Substance	Brand name/names
glyceryl trinitrate	Glytrin, Nitrolingual *spray*
glyceryl trinitrate	Nitroglycerin Recip *resoriblett*

Specialised Care	
glyceryl trinitrate	Nitroglycerin Abcur *inf*

Attack prevention

BETA BLOCKERS

bisoprolol	Bisoprolol …, Bisocard, Bisomyl, Bisostad, Emconcor, Emconcor CHF
metoprolol succinate	Metoprolol …, Metomylan, Seloken ZOC

CALCIUM ANTAGONISTS

amlodipine	Amlodipine …, Amloratio, Norvasc
verapamil	Isoptin Retard

LONG-ACTING NITRATE

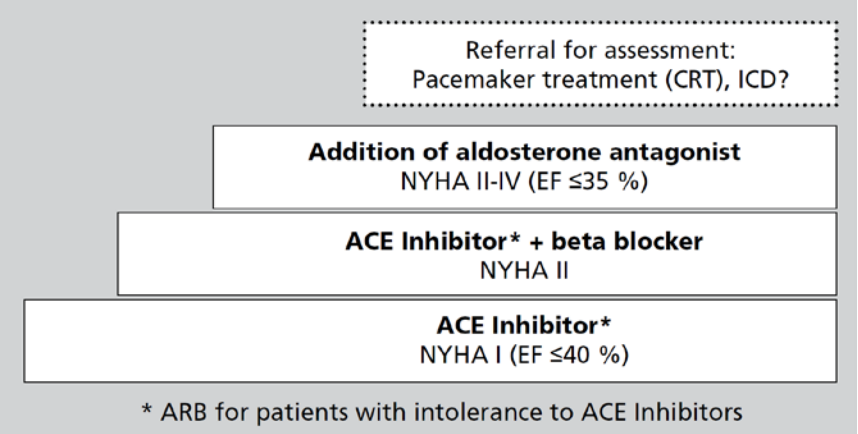
isosorbide mononitrate	Isosorbide mononitrate …, Imdur

Heart Failure with preserved left ventricular systolic function (diastolic heart failure)

Treatment of the underlying condition (e.g., hypertension) may exert a positive influence on the course of the disease. No heart failure treatment has yet been shown to improve prognosis in patients with heart failure and preserved systolic left ventricular function. Symptomatic treatment is given as in heart failure with reduced systolic left ventricular function.

Heart Failure with Reduced left ventricular systolic function (EF ≤40 %)

Verify the diagnosis before treating according to the"heart failure treatment ladder" and seek to establish good heart rate control (below 70 beats/min in sinus rhythm).



The treatments in the "heart failure treatment ladder" improve both symptoms and prognosis. If possible, titrate medicine treatment to target doses. In addition, give diuretics to relieve congestive symptoms and digoxin, particular with concomitant atrial fibrillation, or for symptomatic needs. Lifestyle measures (diet and exercise) are also important in heart failure. Referral to heart failure clinics at hospitals may be used to assist with dose titration and information. After optimizing medicine treatment, functional status and ventricular function should be re-evaluated. If the ejection fraction remains low (EF ≤35 %), the patient should be referred for an evaluation concerning biventricular pacing (CRT) or an implantable defibrillator (ICD). For CRT, wide QRS complexes (≥120 ms) are required.

Asymptomatic Heart Failure; NYHA I

ACE INHIBITORS

Substance	Brand name/names
enalapril	Enalapril …, Renitec *target dose 20–40 mg/day**
ramipril	Ramipril …, Triatec *target dose 10 mg/day**

* The target dose has been shown to reduce morbidity and should be aimed for if the patient can tolerate it.

Heart Failure with Symptoms; NYHA II–IV

ACE inhibitor as above in combination with

BETA BLOCKERS

bisoprolol	Bisoprolol …, Bisocard, Bisomyl, Bisostad, Emconcor, Emconcor CHF *target dose 10 mg/day**
metoprolol succinate	Metoprolol …, Metomylan, Seloken ZOC *target dose 200 mg/day**

* The target dose has been shown to reduce morbidity and should be aimed for if the patient can tolerate it.

Symptomatic Heart Failure (NYHA II-IV) with Moderately to Markedly Reduced Ejection Fraction (EF ≤35%)

Medicines as above in combination with

ALDOSTERONE ANTAGONISTS
(Mineral corticoid receptor antagonists)

First-Line Treatment

Substance	Brand name/names
spironolactone	Spironolakton …, Aldactone *25(–50) mg/day*

Added after adequate basic treatment. Consider the risk of hyperkalemia.

Second-Line Treatment – in cases with endocrine side effects

eplerenone	Inspra *50 mg/day*

Consider the risk of hyperkalemia.

In cases with intolerance to ACE inhibitors

ANGIOTENSIN-RECEPTOR BLOCKERS (ARB)

*candesartan**	Candesartan ..., Amias, Candesarstad, Candexetil, Kairasec, Kandrozid *target dose 32 mg/day***
losartan	Losartan …, Losarstad, Losatrix *target dose 150 mg/day***

* Limited reimbursement, see www.tlv.se (in Swedish)
** The target dose has been shown to reduce morbidity and should be aimed for if the patient can tolerate it.

Symptomatic Heart Failure Treatment

DIURETICS

*bendroflumethiazide****	Bendroflumethiazide …, Salures
furosemide	Furosemide …, Furix, Impugan
furosemide	Lasix Retard
*hydrochlorothiazide****	Hydrochlorothiazide ..., Esidrex

*** Thiazides are less effective in cases with reduced renal function. Should not be used when eGFR is <30 ml/min.

In hypokalemia

First-Line Treatment

spironolactone	Spironolakton …, Aldactone

Second-Line Treatment

amiloride	Amiloride Mylan
kaliumklorid	Kaleorid

In Atrial Fibrillation or as Symptomatic Adjunct Treatment in Severe Heart Failure

Consider

digoxin	Digoxin BioPhausia

Atrial Fibrillation, Atrial Flutter

Decide if anticoagulant treatment should be instituted. The choice between rate control or rhythm control should be made on the basis of the patient´s symptoms and the choice does not affect prognosis. Treat underlying diseases and risk factors such as hypertension.

Rate Control

Good heart rate control is important in atrial fibrillation/atrial flutter. Digoxin is not recommended as monotherapy for rate control.

First-Line Treatment

Substance	Brand name/names
bisoprolol	Bisoprolol …, Bisocard, Bisomyl, Bisostad, Emconcor, Emconcor CHF
metoprolol succinate	Metoprolol …, Metomylan, Seloken ZOC
verapamil	Isoptin Retard *(two-dose technique)*

Second-Line Treatment – if the effect is insufficient, consider adding	
digoxin	Digoxin BioPhausia

Rhythm Control

In symptomatic atrial fibrillation/atrial flutter, cardioversion, anti-arrhythmic medicines or invasive measures should be considered. These treatments are managed by specialists. Anti-arrhythmic medicines may cause serious side effects. Consider any new contraindications ocurring during ongoing treatment (e.g., heart failure, ischemic heart disease, kidney failure, QT prolongation). Anti-arrhythmic medicines should be discontinued when there is a change from paroxysmal to permanent atrial fibrillation/flutter.

Specialised Care
ANTI-ARRHYTHMIC MEDICINES

First-Line Treatment

*dronedarone**	Multaq
*flecainide***	Tambocor
sotalol	Sotalol Mylan

* Limited reimbursement, see www.tlv.se (in Swedish)
** Should normally be combined with beta blockers

Second-Line Treatment – in structural heart disease

amiodarone	Cordarone *pill* Amiodarone Stragen *injection*

Amiodarone and dronedarone interact importantly with anticoagulants.

Thromboembolic Prophylaxis

Use risk scoring with the CHA_2DS_2-VASc scale when deciding on antithrombotic therapy. CHA_2DS_2-VASc ≥2 gives an indication for anticoagulant therapy. At CHA_2DS_2-Vasc = 1, consider anticoagulant therapy, especially with increasing age above 65 years. Address the potential risks of bleeding such as high blood pressure and excessive alcohol consumption. Avoid medicines that increase the risk of bleeding, such as COX inhibitors (NSAIDs) and omega-3 fatty acids. In frail elderly patients at high risk of bleeding, a clinical judgment should be made about the benefits of treatment.

In atrial fibrillation, always estimate the stroke risk with CHA_2DS_2-VASc and decide about thromboembolic prophylaxis. Choose anticoagulant therapy before ASA.

Oral Anticoagulants
Choose the appropriate medicine after an individual evaluation of the risk of adverse effects, opportunities for adequate follow-up and patient preference. Warfarin is an effective medicine that our health care system is very familiar with. In addition treatment is individualized by monitoring. Hence, there is no need to replace well-functioning warfarin therapy. Treatment with a New Oral AntiCoagulant (NOAC) is an alternative for patients who belong to well-documented categories and are expected to be compliant. NOACs are contraindicated for patients who have a mechanical heart valve or when there is significant mitral stenosis.

You must have the same respect for NOACs as for warfarin. All oral anticoagulants place special demands on patient information and systematic follow up including monitoring of compliance, renal function, the risk of interactions with other medicines and the risk of bleeding. The patient should be provided with a medical ID tag for the respective medicine.
For detailed information, see www.janusinfo.se (in Swedish).

First-Line Treatment
ANTIVITAMIN K MEDICINES

Substance	Brand name/names
warfarin	Waran *contains blue dye, indigo carmine*
warfarin	Warfarin Orion

For safety reasons, a special Dosett box (pill organizer) should be used for white warfarin pills, so that they can be distinguished from other pills. It is important that medicine records are updated when changing the warfarin prescription so that dual therapy with Waran and Warfarin Orion is prevented.

Warfarin should be used for patients with mechanical valves or significant mitral stenosis.

Warfarin is recommended as first-line anticoagulant treatment of elderly frail patients, as the treatment effect can be monitored and the dose adjusted individually.

Warfarin is also primarily recommended for patients with concomitant ischemic heart disease because of better documentation.

PT-INR target: between 2.0 and 3.0. For some patients, self-testing and possibly also dose adjustment by the patient may be appropriate.

Information for prescribers about self-testing and self-care in warfarin treatment, see www.janusinfo.se (in Swedish).

DIRECTLY ACTING FACTOR Xa INHIBITOR	
apixaban	Eliquis

Of all currently used NOACs, apixaban is the least dependent on renal function for its elimination but it has not been documented at eGFR <25 mL/min.

Second-Line Treatment

DIRECTLY ACTING THROMBIN INHIBITOR	
dabigatran	Pradaxa

An alternative to apixaban in cases with side effects and/or risks of significant medicine interactions. Be particularly careful with older patients. Dabigatran is less suitable if renal function is moderately to severely impaired and contraindicated with an eGFR <30 mL/min.

In patients with atrial fibrillation and manifest athesclerotic disease, when anticoagulants cannot or should not be used.

acetylsalicylic acid	Trombyl *75 mg/day*

ASA offers considerably less protection against thromboembolic stroke than anticoagulants but still involves a considerable risk of bleeding.

Antithrombotic treatment in atrial fibrillation, see www.janusinfo.se (in Swedish)

Secondary Prevention after TIA/ischemic Stroke in Cases of Cardioembolic Source page 57

Valve Disease and Congential Heart Disease

Endocarditis Prophylaxis page 53
Anticoagulant treatment, see www.viss.nu (in Swedish)
Warfarin is the anticoagulant which should be used by patients with a mechanical heart valve.

Peripheral artery disease

Lifestyle measures
Walking training, see www.fyss.se
Smoke cessation, see **Nicotine Addiction** page 73

Antihypertensive treatment
Target blood pressure 130–135/80–85 mmHg. **Hypertension** page 9

Blood glucose control
Diabetes mellitus page 31

PLATELET INHIBITORS

Substance	Brand name/names
acetylsalicylic acid	Trombyl *75 mg/day*

or

clopidogrel	Clopidogrel ..., Cloriocard, Grepid, Plavix

In cases of previous ulcer disease, it is safer to add an PPI to ASA than to switch to clopidogrel.

STATINS
Lipid-lowering medicines page 9

Venous thromboembolic disease

Prophylaxis in connection with surgery and when the patient is immobilsed

Consider the risk of bleeding, e.g., in cases of impaired renal function.

LOW-MOLECULAR WEIGHT HEPARINS

dalteparin	Fragmin
tinzaparin	Innohep

Specialised Care
DIRECT-ACTING FACTOR Xa INHIBITOR

rivaroxaban	Xarelto

Prophylaxis in elective orthopedic hip and knee replacement.

Treatment of venous thrombosis and pulmonary embolism

In acute venous thrombosis and pulmonary embolism, we recommend a medical follow-up within 3 months to evaluate the anticoagulant treatment and, if needed, determine possible causes of thrombosis.

Note the risk of bleeding, e.g., in renal impairment.

LOW-MOLECULAR WEIGHT HEPARINS

dalteparin	Fragmin
tinzaparin	Innohep

ANTIVITAMIN K MEDICINES

Substance	Brand name/names
warfarin	Waran *contains a blue dye, indigo carmine*
warfarin	Warfarin Orion

For safety reasons, a separate pill organizer should be used for white warfarin pills, so that they can be distinguished from other pills. It is important that medicine records are updated when medicines are changed so that dual therapy with Waran and Warfarin Orion is prevented.

Specialiserd Care

DIRECT-ACTING FACTOR Xa INHIBITOR	
rivaroxaban	Xarelto

For updated information on oral anticoagulants, see www.viss.nu and www.janusinfo.se.

Specialised Care

UNFRACTIONATED HEPARIN	
heparin	Heparin LEO

THROMBOLYTIC/FIBRINOLYTIC ACTING MEDICINE	
alteplase	Actilyse

Hemostatic Acting Medicines

VITAMIN K	
phytomenadione	Konakion Novum *injection*

When using Konakion Novum injection, see www.viss.nu (in Swedish).

ANTIFIBRINOLYTIC MEDICINE	
tranexamic acid	Tranexamsyra ..., Cyklokapron, Cyklonova, Tranon *tablet* Cyklokapron *effervescent tablet*

Specialised Care

RELEASE OF VON WILLEBRAND FACTOR AND FACTOR VIII	
desmopressin	Octostim

ANTIFIBRINOLYTIC MEDICINE	
tranexamic acid	Cyklokapron *injection*

PROTROMBIN COMPLEX CONCENTRATE	
coagulation factors II, VII, IX, X	Confidex

Prothrombin complex concentrate is first-line treatment in cases of serious bleeding during warfarin treatment and should usually be administered together with vitamin K.

Reversing the antihemostatic effect page 69

Prophylaxis against and reversal of bleeding caused by antivitamin K medicines, see www.mpa.se.

Children and Medicines

Few medicine studies have been performed on children, therefore medicine recommendations for children are largely based on extensive clinical experience. Given the lack of documentation, manufacturers are cautious in recommending their products for use in this patient group. Prescribing for other ages than those recommended and for other indications, so called off-label prescribing, is common.

Drug Metabolism
Prescribing should adhere to dosage recommendations based on age, weight or body surface area. Medicines are often metabolized slower in babies and infants up to the age of 6 months than in older children. Pre-school children often eliminate medicines effectively, which is why they may require a higher dose per kilogram body weight and/or shorter dosage intervals than adults. For some medicines, genetic traits (genotype) or interaction with other medicines play an important role in the dose required. For certain medicines such as anti-epileptics, dosage may need adjusting based on measurements of the plasma concentration of the medicine.

Adverse Effects
The younger the child is, the harder it is to identify adverse effects. Children and adults differ in terms of physiologicaly and drug metabolism. That means that children may experience different side effects than adults. It is important to report suspected side effects to the MPA.

Practical Advice
Persuading infants to take their medicines can be hard. Compliance is affected by the child´s age and ability to participate in treatment, the motivation of the parent or carer, the dosage form of the medicine and the involvement of the physician and nurse.

- Try giving pills to children from around three years of age. Many solutions, particularly penicillins, have a bad taste. Parents often underestimate the child´s ability to swallow pills. It is an advantage if the child can try out medicines in the form of pills whilst still at the doctor´s office.
- It is easier to swallow a pill together with some viscous liquid containing solid pieces of something, e.g., fruit yoghurt. There are also products in the pharmacy, which provide pills with a thin, flavoured coating, which may make them easier to swallow. After the child has taken the pill, give it something tasty to drink.
- Some tablets may not be divided or crushed. There is a list of these under the heading ”To be swallowed whole” at www.apoteket.se (in Swedish). You can also find some brief information about breaking pills on www.fass.se.
- In the case of any inhalation treatment, let the child practice carefully before administrering the medicine and repeat the prodecure when revisiting the health clinic or hospital.

Dermatological and Venereal Diseases

Moisturizers

Indicated in diseases which are associated with dry skin.

Substance	Brand name/names
glycerol	Miniderm
urea	Canoderm
propylene glycol	Propyderm *cream*
propylene glycol	Propyless *cutaneous emulsion*

Glucocorticoids for External Use

GROUP I – MILD-ACTING	
hydrocortisone	Hydrocortisone CCS
hydrocortisone	Mildison Lipid

GROUP II – MEDIUM-STRONG ACTING	
hydrocortisonebutyrate	Locoid
clobetasone	Emovat

GROUP III – STRONG ACTING	
betamethasone	Betnovat
mometasone	Mometason …, Elocom, Elocon *cream* Ovixan *cream* Mometason …, Demoson, Elocon *lotion* Ovixan, Elocon *cutaneous solution* *once/day*

Cutaneous Mycoses

Yeast

Pityriasis Versicolor	
ketokonazol	Ketoconazole… *shampoo*

Candida Infection	
clotrimazole	Canesten
miconazole *+ hydrocortisone*	Cortimyk, Daktacort

Vaginitis, vaginosis page 44

Dermatophytes

terbinafine	Terbinafin ..., Terbisil *cream*

Nail Mycoses

Light Nail Involvement

Single nails with involvement of the distal half only.

amorolfine	Amorolfine ..., Finail, Loceryl *nail varnish*

Widespread Nail Involvement

Treat only in cases of significant symptoms and dermatophyte infection, which have been verified by laboratory testing.

Substance	Brand name/names
terbinafine	Terbinafin … *pill*

Oral terbinafine should be combined with local amorolfine for improved effect and less risk of recurrence.

Urticaria

Skin itching/swelling. Allergies may not be the only cause.

ANTIHISTAMINES

First-Line Treatment

desloratadine	Desloratadine ..., Aerius, Dasselta

Second-Line Treatment – if effect is insufficient

cetirizine	Cetirizine …, Cetimax, Vialerg

Tertiary Treatment – when sedation is desired

hydroxyzine	Hydroxyzine …, Atarax

Consider anticholinergic effects, particularly in the elderly.

Acne

Light-Medium Severity Acne

Local Treatment

adapalene	Differin
benzoyl peroxide	Basiron AC*
adapalene + *benzoyl peroxide*	Epiduo*

* Not included in the reimbursement scheme in Sweden.

Acne of Medium Severity – if local treatment is insufficient, add

lymecycline	Lymecycline ..., Tetralysal

The full dose should be given for three months. After antibiotic treatment is finished, the patient should continue with local treatment (without antibiotics) for a long time. For women in need of an oral contraceptive, local treatment may be combined with a suitable combined hormonal contraceptive instead.

Acne, see www.viss.nu (in Swedish)
Acne treatment, see www.mpa.se (in Swedish)

Rosacea

Rosacea of Light-Medium Severity

First-Line Treatment

azelaic acid	Finacea

Second-Line Treatment – if azelaic acid is not tolerated

metronidazole	Robaz, Rozex

Rosacea of Medium-Strong Severity

If local treatment alone is not sufficient

Substance	Brand name/names
lymecycline	Lymecycline ..., Tetralysal

Rosacea, see www.viss.nu (in Swedish)

Psoriasis

Glucocorticoids for External Use page 21

calcipotriol	Daivobet, Dovobet *lotion*
+ betamethasone	Daivobet, Dovobet, Xamiol *gel for the scalp*

Psoriasis, see www.viss.nu (in Swedish)
Medicine Treatment of Psoriasis, see www.mpa.se (in Swedish)

Atopic Eczema

First-Line Treatment
Glucocorticoids for External Use page 21

Specialised Care	
Second-Line Treatment	
*pimecrolimus**	Elidel *cream*
tacrolimus	Protopic *lotion*
* Limited reimbursement, see www.tlv.se (in Swedish)	

Medicine Treatment of Atopic Eczema, see www.mpa.se (in Swedish)

Seborrheic Eczema

ketokonazol	Ketoconazole… *shampoo*
miconazole	
+ hydrocortisone	Cortimyk, Daktacort

Seborrheic Eczema in Adults, www.viss.nu (in Swedish)

Actinic Keratosis

All patients seeking or undergoing treatment for actinic keratoses should be given advice about sun protection (www.stralsakerhetsmyndigheten.se/In-English/About-the-Swedish-Radiation-Safety-Authority1/) and recommended sunscreen with a minimum SPF of 15. Primary care physicians can treat actinic keratosis with imiquimod if the diagnosis can be determined with a high degree of accuracy. If there is diagnostic uncertainty or insufficient efficacy is observed when controlling treatment, refer to the dermatologist.

imiquimod	Zyclara

Head Lice

Medical products are first line treatment due to increased resistance in head lice towards medicines. These products may be purchased in the pharmacy. Preparations containing dimetikon should be preferred.

Treatment of Head Lice, see www.mpa.se

Scabies

Scabies should be identified before treatment is initiated.

Substance	Brand name/names
benzyl benzoate + disulfiram	Tenutex*

* Not included in the reimbursement scheme in Sweden

Sexually Transmitted Diseases

Chlamydia

doxycycline	Doxycycline …, Doxyferm

In pregnancy, see www.medscinet.se/infpreg (in Swedish).

Condyloma

podophyllotoxin	Wartec

Podophyllotoxin is contraindicated during pregnancy.

Mycoplasma Genitalium

azitromycin	Azithromycin …, Azitromax

Mycoplasma Genitalium, see www.viss.nu (in Swedish)
Genital Herpes page 52
Impetigo page 52
Skin and Soft Tissue Infections page 51

Ear Diseases

External Otitis

Systemic antibiotics should be avoided in cases of uncomplicated external otitis. Tamponade and rinsing using rubbing alcohol can be used as initial treatment to reduce swelling.

First-Line Treatment

Substance	Brand name/names
oxytetracycline *+ hydrocortisone* *+ polymyxin B*	Terracortril med polymyxin B *suspension*

Cleansing treatment may be required before application.

Second-Line Treatment	
hydrocortisonebutyrat	Locoid c*utaneous solution, group II*
betamethasone	Diproderm *ear drops, group III*

Acute Otitis Media page 48
Motion sickness page 39

The Elderly and Medicines

General Recommendations

Always give the patient an updated medication list.

At group level, the age 75 and above is often cited when the topic of medicine use in the elderly is discussed. At the individual level, the individual´s biological age is more important.With increasing age and comorbidity, it is especially important to individualize therapy and periodically evaluate the effects as well as reassessing indications. Polypharmacy increases the risk of both side effects and medicine interactions. The lowest effective dose should be sought. Older people are more sensitive to many medicines, such as those affecting the central nervous system or those leading to orthostatism. Measure your patients' blood pressure even while standing during treatment with antihypertensive medicines.

Estimate and consider renal function in the selection and dosing of medicines.

Renal function decreases with age and with increased morbidity. Therefore, medicines that are largely excreted in the urine should be administered at a dose according to renal function. Some medicines, such as COX inhibitors, further impair renal function. Keep in mind that renal function may deteriorate acutely, and that the risk of adverse effects of medicines then increases.

Several commonly used medicines have adverse effects that affect nutrition negatively by way of e.g., appetite loss, dry mouth and nausea. This should especially be considered in multimorbid patients. Many elderly patients have difficulty swallowing medicines. Some tablets must not be broken or crushed. A list of these is available at Swallow Whole, see www.apoteket.se (in Swedish). Brief information on tablet splitting is also available on www.fass.se (in Swedish).

Do not treat asymptomatic bacteriuria (ABU) in the elderly and only perform urine cultures after urinary tract symptoms.

Medicines to be Avoided in the Elderly Unless there are Special Reasons to use them

Medicines with Anticholinergic Effects

Medicines with pronounced anticholinergic effects should be avoided mainly due to the risk of cognitive disturbances and confusion. Some examples of such medicines are sedative antihistamines such as hydroxyzine and promethazine, certain antipsychotic medicines and tricyclic antidepressants.

Indicators for good medicine therapy in the elderly, appendix 1, see www. socialstyrelsen.se (in Swedish)

Avoid giving tramadol and propiomazine to the elderly.

Propiomazine

Propiomazine is unsuitable for older people due to the risk of daytime fatigue and extrapyramidal side effects.

Tramadol

Tramadol is unsuitable for older people due to the risk of side effects such as nausea and confusion. Tramadol should not be combined with antidepressants e.g., SSRI due to the increased risk of serotonergic side effects.

Codeine

Codeine is not recommended for the elderly due to the large interindividual variation in metabolism to morphine, the active metabolite. In addition, the combination of codeine and paracetamol entail the risk of an insufficient opioid effect, as the recommended maximum dosage of paracetamol to older people is 3g/day.

Medicines which should be Administered to the Elderly with Caution

Benzodiazepines

Benzodiazepines can cause cognitive impairment and increase the risk of falling and hence fractures in older people. Long-acting benzodiazepines (diazepam, nitrazepam and flunitrazepam) should be avoided. Only oxazepam can be recommended to older people.

Anti-Psychotic Medicines

Treatment with anti-psychotic medicines should be limited to psychotic symptoms, which disturb the patient and engender significant anxiety and/or aggressivity. Before treatment is initiated, possible somatic causes of the symptoms should be ruled out and non-pharmacological treatment be considered. Doses should be low and the effects evaluated continuously.

Diabetes Medicines

Older people are at increased risk of rapid deterioration of renal function, e.g.due to dehydration or acute disease. Hence, treatment with metformin may be unsuitable at estimated GFR <60 ml/min, due to the risk of lactate acidosis. Sulphonyl urea may cause serious hypoglycemias and the risk is increased when renal function is impaired. More frequent follow-up of renal funuction is important in the elderly.

Diabetes, see www.viss.nu (in Swedish)

Pain

Nociceptive Pain

PARACETAMOL

Substance	Brand name/names
paracetamol	Paracetamol …, Alvedon, Pamol, Panodil, Paracut, Pinex

Recommended max dose to older people is 1 g x 3.

COX INHIBITORS (NSAID)

Impaired renal function, hypertension and heart failure are more common in older people and these conditions constitute relative contraindications against COX inhibitors (including COX-2 inhibitors). The risks of gastrointestinal, cardiovascular and renal side effects are dose-dependent. We recommend administrering medicines at the lowest effective dose as needed. Ulcer prophylaxis using proton pump inhibitors should not be prescribed without individual assessment of risk.

naproxen	Naproxen ..., Alpoxen, Pronaxen

A suitable starting dose is 125–250 mg x 1–2.

ibuprofen	Ibuprofen …, Brufen, Ibumax, Ibumetin, Ipren

A suitable starting dose is 200 mg x 1–3.

Ibuprofen has a shorter half-life than naproxen, which can be an advantage in older people. Ibuprofen can counteract the antithrombotic effect of aspirin.

The combination of low dose aspirin and ibuprofen should be avoided, see www.janusinfo.se (in Swedish)**.**

OPIOID ANALGESICS
Treatment with opioids should be given after careful consideration and only when the pain is opioid-sensitive. It is important to separate opioid-induced sedation from analgesia. Individually adjusted dosing increases the chance of achieving the desired effect and reduces the risk of side effects, i.e. sedation, cognitive disturbances and urinary retention.

Effect duration is prolonged in older people due to impaired renal function. Begin with a low dose and adjust the dose to avoid accumulation. Effects and side effects should be evaluated continuously.

Substance	**Brand name/names**
morphine	Morfin ... *short-acting pill, injection*
morphine	Dolcontin *long-acting*
oxycodone	Oxycodone ..., OxyNorm *short-acting pill, injection*
oxycodone	Oxycodone ..., Oxikodon Depot …, OxyContin *long-acting*
buprenorphine	*Norspan plaster*

In cases of non-acute opioid sensitive pain, treatment can start with a low dose of long-acting morphine 5–10 mg x 2, long-acting oxycodone 5 mg x 2 or buprenorphine 5 µg/h.

Opioid-induced constipation page 64
Opioid-induced nausea page 64

Neuropathic Pain

First-Line Treatment	
amitriptyline	Amitriptyline …, Saroten

Start with 5–10 mg at night, may be increased once a week/weekly by 5–10 mg. The dose is titrated individually based on effect and side effects. For most of the patients, 10-30 mg is enough. Consider the risk of cognitive and cardiac side effects.

Second-Line Treatment	
gabapentin	Gabapentin Teva

A suitable starting dose is 100 mg x 1, which should be increased step-wise based on the renal function. Consider the risk of cognitive side effects.

Anxiety

Short-term anxiety and possibly initially in combination with SSRI therapy	
oxazepam	Oxascand, Sobril

Long-term anxiety	
escitalopram	Escitalopram …, Cipralex, Entact, Esertia, Seroplex, Prilect

The recommended max dose of escitalopram is 10 mg in patients over 65 due to dose-dependent QT-interval prolongation. SSRI's increase the risk of bleeding.

Only for continuation of therapy, not for new prescribing	
citalopram	Citalopram …

The recommended max dose of citalopram is 20 mg in patients over 65 due to dose-dependent QT-interval prolongation. SSRI involves an increased risk of bleeding.

Depression

The effect of antidepressive medicines sets in later in older people than in younger.

National guidelines for care of depression and anxiety syndrome, see www.socialstyrelsen.se/nationalguidelines/nationalguidelinesforcareincasesofdepressionandanxietydisorders

First-Line Treatment

Substance	Brand name/names
escitalopram	Escitalopram …, Cipralex, Entact, Esertia, Seroplex, Prilect

The recommended maximum daily dose of escitalopram is 10 mg in patients over 65 due to dose-dependent QT-interval prolongation. SSRI's increase the risk of bleeding.

Only for iteration, not when prescribing de novo	
citalopram	Citalopram …

The recommended maximum daily dose of citalopram is 20 mg in patients due to dose-dependent prolongation of the QT interval. SSRI's increase the risk of bleeding.

Second-Line Treatment	
mirtazapine	Mirtazapin ..., Mirtin

Sleep Disturbances

Rule out medicine side effects as well as somatic and mental causes of the sleep disturbances. Try non-pharmacological treatment first. If you prescribe medicines, aim for short treatment length. Intermittent treatment reduces the risk of the patient developing tolerance.

zopiclone	Zopiklon …, Imovane

Alzheimer´s Disease

Before initiating therapy, an investigation should be made in order to rule out treatable causes of cognitive impairment. Medicine therapy that can affect cognition should be excluded.

The treatment should always involve activation, verification of the patient´s sense of social security and management of psychological disorders. If the use of dementia medicines is initiated, a physician with a good knowledge of dementia diseases should prescribe them initially.

Th effect should be evaluated on an individual basis after 3-6 months for possible dose adjustment and then at least annually. Replacement or discontinuation of therapy may be recommended if they are not effective or there are side effects. The patient's condition should be evaluated no later than 3 weeks after discontinuation.

Evaluation of treatment outcomes should include information from family members and/or caregivers.

Symptomatic Treatment of Mild-Moderate Alzheimer's Disease

The effect on cognition and function is small and similar, but there are clinical differences in tolerability between different cholinesterase inhibitors.

Cholinesterase inhibitors may have vagotonic effects on heart rate, with the risk of cardiac complications in predisposed patients. Patients with vascular dementia should not be treated with cholinesterase inhibitors.

CHOLINESTERASE INHIBITORS

First-Line Treatment

Substance	Brand name/names
donepezil	Donepezil ..., Aricept, Azepezil

Second-Line Treatment

rivastigmine	Exelon, Orivast *patch*

In cases of cholinesterase inhibitor intolerance or containdication, memantine may be tried.

Symptomatic Treatment of Severe Alzheimer´s Disease

Donepezil and memantine have similar effects on cognition, ADL and behaviour in patients with severe Alzheimer´s Disease, but there are clinical differences in tolerability between them.

First-Line Treatment
CHOLINESTERASE INHIBITORS

donepezil	Donepezil ..., Aricept, Azepezil

Second-Line Treatment
NMDA RECEPTOR ANTAGONIST

memantine	Memantin ..., Axura, Ebixa, Mentixa, Nemdatine

Behavioural and Psychological Symptoms in Dementia (BPSD)

In BPSD, somatic causes as well as side effects of medicines should be excluded. Primarily, non-pharmacolocial treatment should be tried, such as caring measures and providing stimulation. In cases, where non-pharmacological treatment is insufficient, medicines should be tried. In general, the objective should be to aim for short treatment length, evaluating effect within two weeks as well as regularly reassessing the need for dose adjustments. People with Lewy body dementia should not be given antipsychotic medicines.

Antipsychotic medicines should be avoided for patients with dementia, see www.janusinfo.se (in Swedish)
Behavioural and psychological symptoms in dementia diseases (BPSD), see www.mpa.se (in Swedish)
National guidelines for care and caring in dementia disease, www.socialstyrelsen.se (in Swedish)

Endocrinology

Diabetes Mellitus

All diabetes mellitus patients should receive advice about suitable diets and information about the importance of daily physical exercise, stop smoking and, if overweight, losing weight. Lifestyle changes are the basis of cardiovascular prevention.
Nicotine Addiction page 73

Target for HbA1c
In order to reduce symptoms of hyperglycemia/hypoclycemia and prevent diabetic complications, it is important to maintain good glucose control. The target for glucose control is HbA1c ≤52 mmol/mol. The target should be individually adjusted. At diagnosis and the first years after, the target might be lower, at ≤42 mmol/mol. Consider the risk of hypoglycemia. Higher HbA1c is desirable in older and seriously ill patients, for whom the main focus is not on preventing diabetic complications.

Multifactorial Treatment
Cardiovascular disease is common in diabetes. In addition to glucose control it is important to achieve satisfactory blood pressure control (target <140/85 mmHg), however this should be done with caution with neuropathy/ortostatism and in the elderly. ACE inhibitors or ARB are first-line medicines of choice in diabetes mellitus featuring microalbuminuria. Statin treatment is often indicated. For more precise risk assessment, we recommend the risk engine of The National Swedish Diabetes Registry NDR at www.ndr.nu/risk (in Swedish).

Cardiovascular disease, page 9

Medicine Treatment in Type 2 Diabetes, see www.mpa.se (in Swedish)
Atherosclerotic Cardiovascular Disease, see www.mpa.se
National Guidelines for Diabetes Care, see the Swedish National Board of Health and Welfare website at www.socialstyrelsen.se (in Swedish)

Diabetes Mellitus Type 2

First-Line Treatment

Substance	Brand name/names
metformin	Metformin …

Metformin treatment should be discontinued when there is a risk of dehydration and before x-ray with contrast. Patient information is available on www.janusinfo.se (in Swedish).

If metformin is contraindicated (e.g., in the elderly, in patients with reduced renal function or other organ failure), we recommend first-line treatment with insulin.

Second-Line Treatment
If the effect of metformin is insufficent, insulin or alternatively glimepride or repaglinide may be added.

Insulins
In type 2 diabetes, insulin treatment is often necessary to achieve acceptable glucose control. The insulin dosage should be adjusted to reach treatment target levels. See **Diabetes** at www.viss.nu (in Swedish).

MEDIUM LONG-ACTING HUMAN INSULIN	
insulin human	Humulin NPH
insulin human	Insulatard
insulin human	Insuman Basal

MIXED INSULINS	
insulin aspart	NovoMix
insulin lispro	Humalog Mix

DIRECT-ACTING INSULIN ANALOGS

Substance	Brand name/names
insulin aspart	NovoRapid
insulin glulisine	Apidra
insulin lispro	Humalog

INSULIN RELEASERS

glimepiride	Glimepiride …, Amaryl
*repaglinide**	Repaglinid …, Novonorm

* Limited reimbursement, see www.tlv.se (in Swedish)

Only for iteration, not new prescriptions

*glibenclamide**	Glibenclamide …, Daonil

* Limited reimbursement, see www.tlv.se (in Swedish)

Specialised Care

Tertiary Level
For patients with BMI >35 kg/m^2 and unsatisfactory metabolic control despite treatment with metformin, insulin releaser or insulin.

GLP-1-AGONIST

*liraglutide**	Victoza

* Limited reimbursement, www.tlv.se (in Swedish)

Treatment should be evaluated after 3 months and terminated after 6 months if HbA1c has not decreased by ≥10 mmol/mol and weight loss is ≥3 %. We do not recommend doses above 1.2 mg per day.

Diabetes Mellitus Type 1

DIRECT-ACTING INSULIN ANALOGUES

insulin aspart	NovoRapid
insulin glulisine	Apidra
insulin lispro	Humalog

MEDIUM-LONG-ACTING HUMAN INSULIN

insulin human	Humulin NPH
insulin human	Insulatard
insulin human	Insuman Basal

LONG-ACTING INSULIN ANALOGUE
Insulin glargine can be a treatment option in patients with frequent nighttime hypoglycaemia during treatment with medium-long-acting human insulin.

*insulin glargine**	Lantus (in Swedish)

* Limited reimbursement, see www.tlv.se (in Swedish)

In Emergency Situations in Hospitalized Patients with Diabetes type 1 and 2

insulin human	Humulin Regular

Severe Hypoglycemia/Insulin Coma

Substance	Brand name/names
glucagon	Glucagon Novo Nordisk

Treatment with glibenclamide, glimepiride and other sulphonylurea preparations can result in serious and long-lasting hypoglycaemia requiring hospitalization.

Diabetes Aids

Recommendations for self-measurent of glucose in diabetes mellitus, see www.janusinfo.se (in Swedish)

Diseases of the Thyroid

Diagnosis and treatment of diseases of the thyroid, see Tyreoideasjukdomar, www.viss.nu (in Swedish)

THYROID HORMONE	
levothyroxine	Levaxin

Specialised Care

ANTI-THYROID MEDICINES May cause neutropenia and severe liver damage. In case of fever/infection, immediately check neutrophile granulocytes. Monitor liver enzymes regularly, particularly with propylthiouracil treatment.	
thiamazole	Thacapzol
For pregnant women and when there exists intolerance towards thiamazole.	
propylthiouracil	Tiotil

Vitamin D Deficiency

Vitamin D Deficiency (S-25-OH-vitamin D <25 nmol/L) is a large global problem, but the extent of the problem in Sweden is not well known. Risk factors include lack of exposure to sunshine, dressing in clothes which cover a large part of the body, dark skin, advanced age and malabsorption.

Vitamin D Deficiency, see www.viss.nu (in Swedish)

VITAMIN D	
cholecalciferol	Divisun

When calcium intake is also low	
calcium carbonate *+ cholecalciferol*	Kalcipos-D forte *tablet* Calcichew-D3 Forte, Kalcipos-D forte, Recikalc-D Forte *chewable tablet*

Specialised Care

Adrenocortical Hormone Deficiency

The early symptoms are diffuse – fatigue, loss of appetite, concentration difficulties, hypotension and non-specific pain. Chronic adrenal insufficency is a rare but important differential diagnosis in cases of cardiovascular shock. Rapid diagnosis and treatment are lifesaving. Chronic adrenal insufficiency may also occur after steroid treatment.

GLUCOCORTICOIDS	
hydrocortisone	Hydrocortisone Nycomed *tablet*
hydrocortisone	Solu-Cortef *injection*

Specialised Care

MINERAL CORTICOID

Substance	Brand name/names
fludrocortisone	Florinef

Hyperprolactinemia

Medical investigation at a specialist endocrinology and/or gynaecology clinic is called for. For women, see also **Gynaecology and obstetrics**, page 46.

DOPAMIN AGONISTS

bromocriptine	Parlodel, Pravidel
cabergoline	Cabergoline …, Dostinex

Male Hypogonadism

TESTOSTERONE

testosterone	Tostrex *gel*
testosterone	Nebido *injection*

Testosterone Deficiency in Men (Male Hypogonadism), see www.viss.nu (in Swedish).

Eye Diseases

Bacterial Conjunctivitis

In general, a case of infectious conjunctivitis will heal spontaneously within a week and usually does not warrant medicine treatment. Often it is sufficient to wash with lukewarm water or saline solution. In particular, this holds true for conjunctivitis cases occurring in connection with an upper respiratory infection.

Substance	Brand name/names
fusidic acid	Fucithalmic

Allergic Conjunctivitis

If symptoms are mild and as an adjunct to pharmacological treatment, cold, wet compresses and tear substitutes can provide relief. Sodium cromoglycate does not have an immediate effect, and so treatment should preferably start before an allergy is expected.

First-Line Treatment	
sodium cromoglicate	Lecrolyn, Lomudal

Second-Line Treatment – with insufficient effect	
emedastine	Emadine

Dry Eyes

Most patients with dry eyes can be recommended self-care. Prescriptions for tear substitutes should be reserved for patients with defined eye disease such as keratitis sicca.

Guidelines for treatment of dry eyes (also contains patient information to print out), see www.janusinfo.se.

Specialised Care

Chronic Open-Angle Glaucoma

The goal of treatment is to prevent the disease from progressing and the patient´s quality of life from deteriorating. As first choice of therapy, select medical treatment to lower the pressure in the eye.

PROSTAGLANDIN ANALOGUE	
latanoprost	Latanoprost ..., Xalatan

BETA BLOCKERS	
timolol	Timolol ..., Optimol

If systemic side effects from short-acting betablockers	
timolol	Timosan *long-acting*

Guidelines for treating open-angle glaucoma, see www.janusinfo.se (in Swedish)

Fluid Therapy and Nutrition

Specialised Care

Fluid Therapy

When oral/enteral fluid therapy is insufficient, we primarily recommended intravenous crystalloid solutions. For children, see local guidelines.

CRYSTALLOID SOLUTION

Substance	Brand name/names
balanced electrolyte solution	Ringer-Acetat Baxter Viaflo

In cases of therapy failure, the patient should benefit from multidisciplinary care.

For added electrolytes, see Infusion concentrate below.

Limit the clinical use of hydroxy ethyl starch (HES), see www.janusinfo.se

Enteral Nutrition

Enteral nutrition is initiated when any dehydration and circulatory disturbances have been managed, and when oral/enteral nutrition is insufficient. See local guidelines concerning children.

Basic Glucose Supply

GLUCOSE SOLUTION

glucose solution + electrolytes	Glukos Braun 50 mg/ml Na40+K20

Nutritional Treatment

These recommendations apply to acute and chronically ill with the exception of intensive care patients. Severely malnourished patients require specialist advice at the initiation of nutrition therapy. Enteral nutrition is the first choice for nutritional therapy. Parenteral nutrition is only indicated when the gastrointestinal tract is non-functioning or oral food intake is inadequate. If the patient is deemed malnourished, nutrition therapy should be initiated promptly. Otherwise, the administration of glucose solution containing electrolytes can be enough for 3-4 days. B vitamin deficiency is common in several patient groups. Mild deficiency requires the addition of Soluvit to glucose while pronounced deficiency requires replacement therapy, intravenously or intramuscularly.

Parenteral nutrition solutions/three-chamber bags contain glucose, amino acid solutions and fat emulsion, and are available for delivery via peripheral or central vein.

Trace elements and vitamins are added to parenteral nutrition. Electrolytes should be added according to individual patient needs. Electrolyte free solutions should normally be used.

Nutrition solution/three-chamber bags are prescribed based on the patient's fluid and energy needs. The basic fluid need of adults is 30 ml/kg/day. The energy requirement for bedridden patients is 20-25 kcal/kg /day and for ambulatory patients 25-30 kcal/kg/day.

Nutrient solutions/three-chamber bags differ primarily with respect to fat emulsion. There is no evidence that the choice of parenteral nutrition solution affects morbidity and mortality.

Specialised Care

Fish oil/omega-3 fatty acids are incompletely studied with respect to effects, side effects and dosage and are not recommended for routine use.

For detailed information regarding nutritional treatment for different patient categories, please refer to www.espen.org, Education, Espen guidelines. www.espen.org/education/espen-guidelines

3-CHAMBER BAG

Substance	**Brand name/names**
amino acid solution *lipid emulsion* *glucose + electrolytes*	Kabiven Kabiven Perifer
amino acid solution *lipid emulsion* *glucose + electrolytes*	Nutriflex Lipid Peri Nutriflex Lipid Plus Nutriflex Lipid Special
amino acid solution *lipid emulsion* *glucose + electrolytes*	Olimel Olimel perifer

We do not recommend substances containing fish oil/omega-3 fatty acids.

For total parenteral nutrition, electrolytes, vitamins and trace elements should be added.

VITAMINS

Water-soluble	
vitamins	Soluvit

Fat-soluble	
vitamins	Vitalipid Adult

TRACE ELEMENTS	
trace elements	Addaven

INFUSION CONCENTRATE – additives	
potassium chloride	Addex-Kaliumklorid
magnesium sulphate	Addex-Magnesium
sodium glycerophosphate	Glycophos
sodium chloride	Addex-Natriumklorid

Gastro-Intestinal System

Gastro-Esophageal Reflux Disease

In the case of prolonged reflux symptoms, prescribing acid-blocking medicines should be considered. The lowest possible dose should be aimed for. If there is any doubt about the diagnosis, a gastroscopy should be done in the first instance. The diagnostic yield of endoscopy deteriorates significantly when there is ongoing treatment with proton pump inhibitors.

In cases of moderate symptoms, in self-care or waiting for gastroscopy

Substance	**Brand name/names**
*ranitidine**	Ranitidin … *as needed*

* Not part of the medicine reimbursement scheme and not switchable at the pharmacy

In cases when symptoms are pronounced	
omeprazole	Omeprazol …, Omecat, Omestad, Omezolmyl

Gastric Ulcer Disease

Helicobactor Pylori (HP) Positive Duodenal and Gastric Ulcer

omeprazole	Omeprazol …, Omecat, Omestad, Omezolmyl
+	
metronidazole	Flagyl
+	
clarithromycin	Klacid

Omeprazole20 mg x 2 + metronidazole 400 mg x 2 + clarithromycin 250 mg x 2 for 7 days.
After that, gastric ulcer is treated with omeprazole20 mg x 1 until ulcer has healed as verified by gastrocopy.

In cases of therapy failure	
omeprazole	Omeprazol …, Omecat, Omestad, Omezolmyl
+	
amoxicillin	Amoxicillin …, Amimox
+	
clarithromycin	Klacid

Omeprazole20 mg x 2 + amoxicillin 500 mg 2 x 2 + clarithromycin 500 mg x 2 for 7 days.
After that, gastric ulcer is treated with omeprazole20 mg x 1 until gastrocopy-verified healing.

HP Negative Duodenal and Stomach Ulcer

omeprazole	Omeprazol …, Omecat, Omestad, Omezolmyl

Duodenal ulcer: 20 mg x 1 for 2 weeks.
Stomach ulcer: 20 mg x 1 until gastrocopy-verified healing.

Helicobacter Pylori (HP)

Eradication of HP is not suitable in cases of abdominal pains, which have not been the subject of medical investigation, in functional dyspepsia (abdominal symptoms without identifiable organic cause) or gastroesophagal reflux disease. In ulcer disease, HP diagnosis is relevant, however, and then primarily together with gastroscopy.

Symptoms of dyspepsia, see www.viss.nu (in Swedish)

Ulcer Prophylaxis

In patients with a history of ulcer, prophylaxis with proton pump inhibitors may be considered for treatment with low-dose ASA or long-term treatment with COX inhibitors. Glucocorticoid treatment alone does not justify prophylaxis with proton pump inhibitors. The risk of ulcer is not elevated in previously HP positive patients who have undergone successful eradication treatment.
Bleeding gastric ulcer, see www.sbu.se.

Treatment with Proton Pump Inhibitors (PPI)

Treatment with proton pump inhibitors is not advisable in the case of stomach pains of unknown cause.

Indications for PPI:

- Gastroesophageal reflux disease
- Ulcer disease
- Ulcer prophylaxis

Terminating PPI treatment may entail symptoms of elevated acid secretion (rebound), which the patient should be informed about. PPI treatment has been associated with an increased risk of pneumonia, fractures and severe infection of the gut (Clostridium difficile).

Oral Candidiasis

Substance	Brand name/names
nystatin	Mycostatin

Specialised Care

Esophageal Candidiasis

fluconazole	Fluconazol …, Diflucan *capsule*

Nausea

metoclopramide	Metoklopramid …, Primperan

Motion Sickness

Preventative

meclozine	Postafen

Nausea induced by chemotherapy page 61
Nausea in connection with pregnancy page 67
Migraine page 58
Opioid-induced nausea page 64
Post-operative nausea page 6

Diarrhoea

loperamide	Loperamid …, Dimor, Imodium

Choleretic Diarrhoea

cholestyramine	Quantalan, Questran Questran Loc

Meteorism

No medication is recommended, as there are no medicines with documented effect. **Meteorism – treatment recommendation,** see www.janusinfo.se (in Swedish)

Constipation

First-Line Treatment – also for long-term use

Substance	Brand name/names
ispaghula	Vi-Siblin Vi-Siblin S
lactulose	Lactulose …, Duphalac *Even for children*
sterculia	Inolaxol

Second-Line Treatment	
makrogol *+ electrolytes*	Lacrofarm, Laxido, Laxiriva, Movicol, Moxalole, Omnicol
makrogol *+ electrolytes*	Movicol Junior *For children from the age of 2*

Adjunct Treatment as Needed	
laurylsulfat	Microlax
sodium picosulphate	Cilaxoral

Opioid-induced constipation page 64
Treatment of constipation in children, see www.viss.nu (in Swedish)

IBS (Irritable Bowel Syndrome)

IBS with constipation as dominant bowel symptom, IBS-C

First-Line Treatment – even long-term	
ispaghula	Vi-Siblin Vi-Siblin S
sterculia	Inolaxol

Second-Line Treatment	
makrogol *+ electrolytes*	Lacrofarm, Laxido, Laxiriva, Movicol, Moxalole, Omnicol

Specialised Care **Adjunct Treatment if the Effect is Insufficient**	
linaclotide	Constella

IBS with Diarrhoea as Dominant Bowel Symptom, IBS-D

loperamide	Loperamid …, Dimor, Imodium

Abdominal Pain

amitriptyline	Amitriptyline …, Saroten

Start with 10 mg at night, and then slowly increase until the required effect has been achieved. Amitriptyline may cause constipation and is unsuitable in cases of IBS-C. Take other anticholinergic effects into account, particularly in the elderly.

Anal Pain Conditions

Before symptomatic treatment of anal pain, any underlying serious disease should be ruled out.
Symtomatic treatment

Substance	Brand name/names
lidocaine *+ hydrocortisone*	Xyloproct* *ointment*

* Not included in the Swedish reimbursement scheme

Chronic Pancreatic Insufficiency

pancreatic enzymes	Creon 25000 Creon 40000

Specialised Care

Colonic Cleansing Prior to Colonic X-ray and Coloscopy

First-Line Treatment

makrogol *+ elektrolytes*	Laxabon

Second-Line Treatment

sodium picosulphate combination	CitraFleet
sodium picosulphate combination	Picoprep

Contraindicated in cases of cardiac or renal failure.

Inflammatory Bowel Disease

The patient should quit smoking. Offer patients with Crohn´s disease a structured smoking cessation plan.

Nicotine Addicition page 73

First-Line Treatment

5-ASA

mesalazine	Asacol, Lixacol *pill* Asacol, Mesasal *suppository*
mesalazine	Pentasa *pill, rectal suppository, suppository,granulate*
mesalazine	Salofalk *foam, entero/depot granules*

STEROIDS

betamethasone	Betapred *injection*
prednisolone	Prednisolon Klysma Unimedic
prednisolone	Prednisolon *... pill*

Second-Line Treatment

azathioprine	Azathioprine …, Imurel
budesonide	Budenofalk *entero capsule*

Tertiary Treatment

adalimumab	Humira
infliximab	Remicade

Gynaecology and Obstetrics

Contraception

Guidelines for treatment with hormonal methods, see www.janusinfo.se (in Swedish)
Anticonception, see www.mpa.se (in Swedish)

Combined Hormonal Contraception

This is a highly effective method of contraception offering almost one hundred percent protection against unwanted pregnancies. Combined pills usually contain the synthetic oestrogen ethinyl estradiol and a gestagen. When prescribing for the first time, the first choice is monophasic low-dos oral contraceptives with levonorgestrel, but adjusting the regimen to the individual is important for good patient compliance. Whether breastfeeding or not, women may begin this treatment no earlier than 6-8 weeks after delivery.

Health Benefits

- Reduced pain during menstruation.
- Reduced bleeding, which reduces the incidence of iron deficiency anemia.
- Regular bleeding.
- Decreased incidence of functional ovarian cysts.
- Fertility is maintained better.
- Reduced risk of ovarian, endometrial and colorectal cancer.

Adverse Effects

- Increased risk of venous thromboembolism (VTE).
  The oestrogen component accounts for the increased blood clot risk and the gestagen component modifies the risk. Combined oral contraceptives containing levonorgestrel give a lower risk of venous thrombosis than preparations with other progestogens. The annual incidence of thrombosis in healthy women of childbearing potential not using the pill is 2/10 000. For pill users, the corresponding figure is 5-12/10 000 compared with the incidence in pregnancy which is 10-30/10 000.

- The progestogen content varies with different preparations, accounting for the bulk of the side effects experienced, such as breast engorgement, mood effects and dysphoria.

First-Line Treatment

Substance	Brand name/names
levonorgestrel *+ ethinylestradiol*	Erlibelle, Prionelle Abelonelle 28, Anastrella 28, Prionelle 28

Second-Line Treatment

drospirenone *+ ethinylestradiol*	Cleonita*, Eloine*, Yaz*
etonogestrel *+ ethinylestradiol*	NuvaRing** *vaginal insert*
nomegestrol *+ estradiol*	Zoely*

* Not included in the reimbursement scheme in Sweden, not subsidised by Stockholm County Council for women under 26 years of age and not exchangeable at the pharmacy.

** Not included in the reimbursement scheme in Sweden, but subsidised by SCC to women under 26 years of age.

Combined monophasic methods of contraception may be used without interruption to reduce symptoms related to menstruation. If bleeding arises, a pause may be made without compromising the preventive effect, see www.janusinfo.se (in Swedish).

Gestagen Contraception

Different gestagens vary in their contraceptive safety. There is no increased risk of thrombosis. All non-estrogen methods may commence any time after delivery, regardless of breastfeeding.

LOW-DOSE GESTAGEN METHODS

Mini pills offer women over 40 a good contraceptive effect. The contraceptive safety is lower than for combined hormonal contraceptives and is therefore not recommended as First-Line Treatment to young women.

Substance	Brand name/names
norethisterone	Mini-Pe*

* Not included in the Swedish pharmaceutical reimbursement scheme and not subsidised by the Stockholm County Council for women under 26 years of age.

The hormonal IUD causes less bleeding, less anemia and less risk of cervical cancer. The use of a hormonal IUD may initially cause minor bleeding and subsequently minor bleeding or amenorrhea.

levonorgestrel	Mirena *hormonal coil*

MEDIUM-DOSED GESTAGEN METHODS

The contraceptive effect of medium-dose pills and contraceptive implants is comparable to that of combined contraceptive pills. The most common side effects are irregular bleeding, mood swings, breast engorgement, weight gain and acne.

desogestrel	Desogestrel ..., Cerazette, Gestrina
etonogestrel	Nexplanon *implant*

HIGH-DOSE GESTAGEN METHODS

High-dose, long-acting gestagens provide highly effective protection against pregnancy. Endogenous estrogen production drops so low, that long-term use involves a risk of reduced bone density, which should be taken into consideration in teenagers and women over 45 years of age. Amenorrhea and irregular periods are common.

medroxyprogesterone	Depo-Provera *injection*

Non-Hormonal Methods of Contraception

THE COPPER INTRAUTERINE DEVICE (IUD)

The copper IUD may be recommended to women regardless of whether they have been pregnant or not. In very young women, it is not a first-line alternative but it may still be considered after an individual assessment. The copper IUD can cause a heavy period and dysmenorrhea.

Emergency Contraception

First-Line Treatment	
ulipristal	ellaOne* *Rx*

Second-Line Treatment

Substance	Brand name/names
levonorgestrel	Norlevo* *OTC*

* Not included in the reimbursement scheme in Sweden

Emergency contraception should be initiated as soon as possible after unprotected intercourse. A single dose of EllaOne is effective for up to 5 days after intercourse. A single dose of Norlevo is effective up to 3 days after intercourse. The protective effect may be shorter for women who weigh more. The copper IUD is effective if inserted within 5 days after intercourse.

Dysmenorrhea

naproxen	Naproxen ..., Alpoxen, Pronaxen

Even combined hormonal contraceptives and the IUD Mirena have well documented effect. Combined monophasic methods of contraception may be used without interruption to reduce menstruation related symptoms. If bleeding occurs, a pause of 3-4 days may be made without compromising the contraceptive effect, see www.janusinfo.se.

Heavy Periods

levonorgestrel	Mirena *hormonal IUD*
tranexamic acid	Tranexamsyra …, Cyklokapron, Cyklonova, Tranon

Even combined hormonal contraceptives have well documented effects and naproxen has some effect on heavy periods.

Investigation and treatment of gynaecological bleeding disorders, see www.janusinfo.se

Vaginitis, Vaginosis

Candida Infection

fluconazole	Fluconazol …, Diflucan capsule
clotrimazole	Canesten* *pessary*

* Not included in the reimbursement scheme in Sweden

For pregnant women, clotrimazole is recommended as First-Line Treatment.

Bacterial Vaginosis

clindamycin	Dalacin *vagitorium, vaginal cream*
metronidazole	Flagyl *tablett, ovule* *Also for trichomonas*

Diagnosis and treatment of diseases of the vulva and vagina, see www.janusinfo.se (in Swedish)

Pre-Menstrual Dysphoric Disorder

Pre-Menstrual Dysphoric Disorder (PMDS) is a condition affecting 3–5 % of women of fertile age and involves severe pre-menstrual symptoms, mainly irritability, dysphoria, tenseness and moodiness, which significantly affect their daily lives. The condition completely subsides during the first week after the period. Diagnosis is based on the presentation of five cycle-related symptoms, of which at least one should be on the list of above-mentioned symptoms. The diagnosis is confirmed by daily assessments of symptoms during two consecutive menstrual cycles.

SSRI treatment has shown very good effects in PMDS in placebo-controlled studies. Various SSRI agents appear to be equal in effects. Medicine treatment exclusively during the luteal phase seems to be as effective as continuous treatment.

Substance	Brand name/names
escitalopram	Escitalopram …, Cipralex, Entact, Esertia, Seroplex, Prilect *(10-)20 mg/day*
sertraline	Sertralin ..., Oralin, Sertrone, Zoloft *50–100 mg/day*

Pre-Menstrual Dysphoric Disorder, see www.janusinfo.se (in Swedish)

Menopausal Symptoms

Hormonal treatment of menopausal symptoms is very effective and the risk-benefit ratio is clearly advantageous, if treatment is initiated close to the time of menopause and limited to about 5 years. Three in ten menopausal women have such severe symptoms (sweating, hot flashes and sleep problems), that they want treatment. These symptoms usually last for a few years before and after the last menstruation, menopause. Hormone therapy can be recommended to women with symptoms that affect quality of life. Oestrogen therapy with systemic effects provides very good symptom relief for hot flashes and sweating. When a woman only has urogenital symptoms of vaginal dryness due to estrogen deficiency, local treatment with estrogen has a good effect. Women with menopause before the age of 45 should, regardless of symptoms, always be offered replacement therapy with potent estrogen agents to the expected menopausal age if there are no contraindications.

All women treated with medium potency oestrogen preparations who are not hysterectomised should have progestagen to protect the endometrium.

Contraindications to substitution with medium potency estrogens are breast or uterine cancer, previous deep vein thrombosis, pulmonary embolism, angina pectoris, myocardial infarction, stroke, and severe liver disease.

The treatment goal is to use the lowest effective dose for a limited time. Prolonged treatment with medium potency estrogen preparations results in a slightly increased risk of breast cancer that is measurable after five years of treatment. The risk is greater with combination therapy (estrogen + gestagen) compared to estrogen alone.

For women aged 50-59 years, the treatment has several positive health effects, including a beneficial effect on bone mineral density and reduced fracture risk, and it appears to reduce the risk of cardiovascular disease. The treatment should be evaluated and reviewed regularly.

Guidelines for estrogen treatment for menopausal symptoms, see www.janusinfo.se (in Swedish)

GESTAGEN-ESTROGEN COMBINATIONS

First-Line Treatment – fixed combination for improved compliance

Sequential treatment

norethisterone + estradiol	Novofem

Continuous treatment

medroxyprogesterone + estradiol	Indivina
norethisterone + estradiol	Activelle, Cliovelle

Second-Line Treatment – individual combination estrogen + gestagen

OESTROGEN

oestradiol	Femanest
oestradiol	Estradot *patch*

GESTAGENS

Substance	Brand name/names
levonorgestrel	Mirena *hormonal IUD*
medroxyprogesterone	Provera
norethisterone	Primolut-Nor

Vaginal Dryness

ESTROGENS FOR LOCAL TREATMENT

Used without addition of gestagen. Does not increase the risk of breast cancer.

estradiol	Oestring *vaginal ring*
estradiol	Vagifem* *vaginal pill*
estriol	Ovesterin *vaginal cream, ovule*

* Not included in the reimbursement scheme in Sweden

Specialised Care

Pre-Operative Myoma Treatment

ulipristal	Esmya

Hyperprolactemia

bromocriptine	Parlodel, Pravidel
cabergoline	Cabergoline …, Dostinex

Pre-Term Contractions and Emergency Premature Delivery

atosiban	Atosiban Sun
terbutaline	Bricanyl *injection*

Prevention of Rh-Immunisation

immunoglobulin anti-D	Rhophylac

Cervical Maturation

dinoprostone	Minprostin
misoprostol	Cytotec

Stimulates Contractions

oxytocine	Oxytocin Pilum

Bleeding During Labour and Abortion

First-Line Treatment

oxytocin	Oxytocin Pilum

Second-Line Treatment

carboprost	Prostinfenem
methylergometrine	Methergin

Specialised Care

Medical Abortion

Substance	Brand name/names
mifepristone	Mifepristone Linepharma
misoprostol	Cytotec

Fertility Treatment

Stimulates Ovulation

First-Line Treatment

clomifene	Pergotime

Second-Line Treatment – FSH agents

Induction of Ovulation After Stimulation of Ovulation

chorionic gonadotrophin alfa	Ovitrelle

Down-Regulation of Gonadotropins

nafarelin	Synarel, Synarela *nasal spray*

Gonadotropin Antagonist

ganirelix	Orgalutran *injection*

Support During Luteal Phase

progesterone	Lutinus *vaginal pill*

Infections

Overuse of antibiotics is a problem, particularly in upper respiratory infections, asymptomatic bacteriuria and venous leg ulcers.

Treatment Management Programme for Various Types of Infections and Suspected Allergy to Penicillin, see Strama, www.janusinfo.se (In Swedish)

Penicillin Allergy

Allergy towards penicillin refers to an IgE- and histamine-mediated rapid hypersensitivity reaction, which manifests as e.g., asthma, urticaria or anaphylaxis. This is unusual but should always be investigated using a diagnostic testing method. Skin manifestations without itching and gastointestinal disturbances are common during antibiotic treatment but are not associated with true allergy to penicillin. In cases where the patient history is uncertain, and there is cause to suspect a mild allergy to penicillin, consider using a test dose.

Upper Respiratory Tract Infections

Acute Otitis Media

For children 1–12 years old, a strategy of ”active expectancy” is recommended, i.e. to wait and see for 2-3 days. An exception is made if there is systemic involvement, perforated otitis or in the case of children under 2 years of age with bilateral otitis.

Empirical Treatment

phenoxymethylpenicillin (PcV) 25 mg/kg x 3 for 5 days (max 1.6 g x 3)

Discharge from the Ears of Children Treated With Tympanoplasty Tubes

Terracortril with polymyxin B 3–5 drops x 3 for 5 days

Therapy Failure in Acute Otitits Media

amoxicillin 20 mg/kg x 3 for 10 days (max 750 mg x 3)

Alternatively according to results of culture.

Recurrent Acute Otitis Media – within 4 weeks

phenoxymethylpenicillin (PcV) 25 mg/kg x 3 for 10 days (max 1.6 g x 3)

amoxicillin 20 mg/kg x 3 for 10 days (max 750 mg x 3)

Alternatively according to result of culture.

Allergy to Penicillin type 1

Ery-Max 10 mg/kg x 4 i 7 days (max 1 g/day) *mixture/granulate for oral suspension*

Acute Streptococcal Sore Throat (Bacterial Tonsillitis)

phenoxymethylpenicillin (PcV) 12,5 mg/kg x 3 for 10 days (max 1 g x 3)

Recurrent Streptococcal Sore Throat – within 4 weeks

Verify the diagnosis

clindamycin adults 300 mg x 3 for 10 days, children 5 mg/kg x 3 for 10 days (max 300 mg x 3)

*cefadroxil** adults 500 mg x 2 for 10 days, children 15 mg/kg x 2 for 10 days (max 1 g x 2)

* Restrictive use to reduce the risk of selection for ESBL producing bacteria, see www.strama.se.

Management of Pharyngeal Tonsillitis in Outpatient Care, see www.mpa.se (in Swedish)

Acute Maxillary Sinusitis

We recommend to ”wait and see” for symptoms <10 days in cases of a head cold with purulent discharge and moderate pain over the sinuses.

phenoxymethylpenicillin (PcV) 25 mg/kg x 3 for 7 days (max 1.6 g x 3)

Penicillin Allergy Type 1 and >8 years

doxycycline 200 mg x 1 for 3 days, after that 100 mg x 1 for 4 days

Lower Respiratory Infections

Do not treat uncomplicated acute bronchitis with antibiotics.

Acute Bronchitis

Do not give antibiotics to patients with otherwise healthy lungs, regardless of the etiology (virus, mycoplasma, other bacteria).

Pneumonia in Children

Children 0–5 years

amoxicillin 20 mg/kg x 3 for 5 days

Children >5 years

phenoxymethylpenicillin (PcV) 25 mg/kg x 3 for 7 days (max 1.6 g x 3)

Suspected Mycoplasma or Type 1 Penicillin Allergy

Ery-Max 10 mg/kg x 4 for 7 days *mixture/granulate for oral suspension*

Children >8 years

doxycycline 2 mg/kg x 1 for 7 days (max 100 mg x1)

Pneumonia in Adults

phenoxymethylpenicillin (PcV) 1 g x 3 for 7 days

Suspected Mycoplasma or Type 1 Penicillin Allergy

doxycycline 200 mg x 1 for 3 days, then 100 mg x 1 for 4 days

Underlying Chronic Obstructive Pulmonary Disease (COPD)

amoxicillin 500 mg x 3 for 7 days

Exacerbation of Chronic Obstructive Pulmonary Disease (COPD)

Increased sputum production, increased purulence of sputum and increased shortness of breath (at least two criteria).

First-Line Treatment

amoxicillin 500 mg x 3 for 5–7 days

Second-Line Treatment

doxycycline 200 mg x 1 for 3 days, then 100 mg x 1 for 4 days

Influenza

Treatment and Prophylaxis of Influenza Using Antivirals, see www.mpa.se (in Swedish).

Urinary Tract Infections (UTI)

Do not treat asymptomatic bacteriuria in the elderly and only culture from urine if the patient is experiencing urinary tract symptoms.

Alternate between different antibiotics to reduce the risk of developing resistance.

Cystitis in Women

nitrofurantoin 50 mg x 3 for 5 days (not in renal failure)

pivmecillinam 200 mg x 3 for 5 days

pivmecillinam 400 mg x 2 for 3 days (<50 years of age with sporadic UVI)

Alternative in the case of a sensitive strain verified by culture

trimethoprim 160 mg x 2 for 3 days

Bacteriuria and Cystitis in Pregnant Women

First take a culture.

nitrofurantoin 50 mg x 3 for 5 days (not in renal failure, or during delivery)

pivmecillinam 200 mg x 3 for 5 days

*cefadroxil** 500 mg x 2 for 5 days

* Restrictive use to reduce the risk of selecting for ESBL producing bacteria, see www.strama.se.

Cystitis in Men

First take a culture. It is recommended to monitor the result and identify any resistance.

nitrofurantoin 50 mg x 3 for 7 days (not in renal failure)

pivmecillinam 200 mg x 3 for 7 days

Cystitis in Children <2 years

All children <2 years with a UTI should be investigated and treated as cases with pyelonephritis regardless of their CRP or whether or not they are running a fever and should be referred to the child emergency department.

Cystitis in Children ≥2 years

First take a culture.

*nitrofurantoin** 1,5 mg/kg x 2 for 5 days (not in renal failure) (max 50 mg x 3)

pivmecillinam 200 mg x 3 for 5 days (children over 30 kg)

*cefadroxil*** 12,5 mg/kg x 2 for 5 days (max 500 mg x 2)

Alternative when there a sensitive strain verified by culture.

trimethoprim 3 mg/kg x 2 for 3 days (max 160 mg x 2)

* Tablets can be crushed and mixed into liquids or food.
** Restrictive use to reduce the risk of selecting for ESBL producing bacteria, see www.strama.se.

Pyelonephritis in Children

All children <2 years with urinary tract infection should be investigated and treated as pyelonephritis cases regardless of their CRP and whether they are running a fever or not. Children 2-15 years old with acute pyelonephritis should be referred to a children´s emergency department for investigation and treatment.

Pyelonephritis in Adults

First take a culture. It is recommended to monitor the result and identify any resistance.

ciprofloxacin 500 mg x 2 for 7 days (women), 10–14 days (men)***
trimethoprim + sulfamethoxazole 160 mg/800 mg x 2 for 10–14 days***

*** Adjust dose according to renal function.

Cystitis, see www.viss.nu (in Swedish)
UTI in Children and Adolescents, see www.viss.nu (in Swedish)

Skin and Soft Tissue Infections

Pharmacological Treatment of Bacterial Skin and Soft Tissue Infections, see www.mpa.se (in Swedish).

Borrelia (Solitary Erythema Migrans)

Adults

phenoxymethylpenicillin (PcV) 1 g x 3 for 10 days

In type 1 penicillin allergy, multiple erythema or concomitant fever

doxycycline 100 mg x 2 for 10 days

Children

phenoxymethylpenicillin (PcV) 25 mg/kg x 3 for 10 days

In type 1 penicillin allergy, multiple erythema or concomitant fever, see **Medicine Treatment in Borrelia Infection**, www.mpa.se (in Swedish).

Infected Bite Wounds from Dog, Cat or Humans.

First take a culture. Describe the type of bite wound on the referral document. Clindamycin, erythromycin, oral cephalosporins and flucloxacillin (isoxazolylpenicillin) are not effective against Pasteurella multocida, the main pathogen in bites from cats and dogs.

Bite Wounds from Dog and Human Beings.

Adults

amoxicillin + clavulanic acid 500 mg x 3 for 10 days

Children

amoxicillin + clavulanic acid 20 mg/kg x 3 for 10 days (max 500 mg x 3)

Wounds from Cat Bites

Adults

phenoxymethylpenicillin (PcV) 1 g x 3 for 10 days

Children

phenoxymethylpenicillin (PcV) 25 mg/kg x 3 for 10 days (max 1.6 g x 3)

Type 1 Penicillin Allergy

Adults

trimethoprim + sulfamethoxazole 160 mg/800 mg x 2 for 10 days

Children

trimethoprim + sulfamethoxazole 8 mg/ml + 40 mg/ml 0,4 ml/kg x 2 for 10 days
(max 160 mg/800 mg x 2)

Post-Traumatic or Post-Operative Wound Infections

Redness and moderate secretion are part of the normal wound healing process. Take a culture before any treatment with antibiotics.

Adults

flucloxacillin 750 mg–1 g x 3 for 7–10 days

Impetigo

Minor lesions
Soap and water

Moderate lesions

retapamulin (Altargo) ointment x 2 for 5 days

Widespread lesions

Children

flucloxacillin 25 mg/kg x 3 for 7–10 days (max 750 mg x 3)

*cefadroxil** 12,5 mg/kg x 2 for 7–10 days (max 1 g x 2)

* Restrictive use to reduce the risk of selecting for ESBL producing bacteria, see www.strama.se.

Adults

flucloxacillin 750 mg x 3 for 7–10 days

Infected Arterial or Venous Leg Ulcers

In the case of arterial ulcers, circulation should be assessed and optimised. In the case of venous ulcers, effective compression is the appropriate treatment. Leg ulcers are rarely infected, so use antibiotics sparingly.

Antibiotics only speed up healing when there are clear clinical signs of infections such as increasing local redness, pain, purulent secretion and fever. Take a culture first and do not treat gram-negative bacteria.

Streptococcus infection

phenoxymethylpenicillin (PcV) 1 g x 3 for 10–14 days

Stafylococcus infection

flucloxacillin 750 mg x 3 for 10–14 days

Erysipelas

Erysipelas is caused by betahemolytic streptococci. Acute symptoms are a high fever and well-defined redness and burning skin. The redness often spreads after treatment, whereas the fever drops quickly.

phenoxymethylpenicillin (PcV) 1 g x 3 for 10–14 days (2 g x 3 for body weight > 90 kg)

Herpes Zoster in the Immune Competent

All patients above 50 years and those with complicated shingles e.g., zoster oticus or opthalmicus should be treated. Treatment should commence within 72 hours of the first symptoms of a rash. In cases of zoster ophtalmicus, contact an eye specialist.

valaciclovir 500 mg 2 x 3 for 7 days

Reduced dose in cases of renal impairment.

Genital Herpes

valaciclovir 500 mg x 2 for 5–10 days in cases of primary infection and for 5 days in cases of recurrent, periodic onset.

Pharmacotherapy in herpes simplex-, varicella- and herpes zoster infections, see www.mpa.se (in Swedish).

Endocarditis Prophylaxis

Antibiotic prophylaxis is no longer routinely recommended in oral operations. Having previously had endocarditis, having an artifical heart valve or congenital cardiac disorders normally do not justify giving prophylaxis. Prophylaxis may still be called for in patients undergoing particularly risky operations.

Indications for antibiotic prophylaxis in dental care, see www.mpa.se (in Swedish).

Oral Antibiotics

Substance	Brand name/names
amoxicillin	Amoxicillin …, Amimox
amoxicillin + clavulanic acid	Amoxicillin/Clavulanic acid ..., Bioclavid, Spektramox
*cefadroxil**	Cefadroxil …
*ciprofloxacin**	Ciprofloxacin …
doxycycline	Doxycycline ..., Doxyferm
erytromycin	Ery-Max
fenoximetyl-penicillin (PcV)	Phenoxymethylpenicillin ..., Avopenin, Kåvepenin, Tikacillin
flucloxacillin	Flucloxacillin …, Heracillin
clindamycin	Clindamycin …, Dalacin
metronidazole	Flagyl
nitrofurantoin	Furadantin
pivmecillinam	Penomax, Selexid
trimethoprim	Trimetoprim ..., Idotrim
trimethoprim + sulfamethoxazole	Bactrim Bactrim forte, Eusaprim forte

* Restrictive use of antibiotics to reduce the risk of selecting for ESBL producing bacteria, see www.strama.se (in Swedish)

Specialised Care

Intravenous Antibiotics

When using intravenous antibiotics for inpatient care, it is important to follow these principles:

- The immediate administration of bactericide antibiotics is crucial for prognosis in cases of acute life-threatening infection such as severe septicemia or bacterial meningitis.
- Always take a blood culture and other relevant cultures before giving antibiotics intravenously in order to optimise treatment after obtaining a result to culture. Problems with taking cultures should however not be allowed to delay antibiotic treatment in the case of life-threatening infections.
- Aim to reduce the use of cephalosporins. These may often be replaced by narrower spectrum antibiotics but if a broader coverage is desirable, a combination with aminoglycoside may be considered initially.
- Peroperative antibiotics prophylaxis should consist of one or a few doses and be administered within 24 hours at the most.

Swedish guidelines for the use of antibotics in inpatient care and specific residential care, Strama, www.janusinfo.se (in Swedish).

För information about medicines, which can be switched, please consult ”The Wise List - Recommended and tendered medicines with synonyms.” In order to avoid switches, prescribe the tendered medication. The current list of medicines is to be found in the ordering system Proceedo and at www.janusinfo.se.

Substance	**Brand name/names**
ampicillin anhydrous	Doktacillin
benzylpenicillin	Benzylpenicillin Panpharma
*cefotaxime**	Cefotaxime Stragen
*ceftazidime**	Fortum
*ciprofloxacin**	Ciprofloxacin Fresenius Kabi
gentamicin	Gensumycin
imipenem + *cilastatin*	Tienam
clindamycin	Dalacin
cloxacillin	Cloxacillin Stragen
meropenem	Meropenem Hospira
metronidazole	Metronidazole Braun
piperacillin + *tazobactam*	Piperacillin/Tazobactam Fresenius Kabi
trimethoprim + *sulfamethoxazole*	Eusaprim
vancomycin	Vancomycin Hospira

* Restrictive use to avoid the risk of selecting for ESBL producing bacteria, www.strama.se.

Antiviral Medicines

valaciclovir	Valaciclovir …, Valtrex *pill*

Herpes zoster in the immunocompetent page 52
Genital herpes page 52

Specialised Care	
aciclovir	Aciclovir Hospira *infusion*

Antimycotics For Systemic Use

Substance	Brand name/names
fluconazole	Fluconazole …, Diflucan *capsule*

Specialised Care	
fluconazole	Fluconazol Fresenius Kabi *infusion*

Vaccinations

Vaccinating children, see www.janusinfo.se (in Swedish)
Conjugate vaccine for vaccinating children over 5 years of age and adults with high risk of pneumococci infection, see www.janusinfo.se
Guide to the use of vaccine against shingles, see www.janusinfo.se
Guide to the use of vaccination in adult patients before or after splenectomy, see www.janusinfo.se

For all other issues pertaining to vaccination, see **Vaccination**, www.smittskyddstockholm.se (in Swedish)

Neurology including Stroke

Stroke

Important lifestyle factors in prevention of TIA/stroke:

- Well-regulated blood pressure. **Hypertension** page 9
- Good metabolic control.
- Regular physical activity. Consider physical exercise on prescription, see www.viss.nu (in Swedish) or www.fyss.se/fyss-in-english/.
- Avoid excessive consumption of alcohol.
- Smoking cessation. **Nicotine Addiction** page 73

In atrial fibrillation, anticoagulation treatment should always be considered.
Recommendations on stroke prophylaxis with warfarin or new oral anticoagulants (NOAC) in atrial fibrillation, see www.janusinfo.se

If TIA/stroke is suspected, acute hospital examination and investigation should be performed immediately. The sooner treatment can be initiated, the better the prognosis. Thrombolytic treatment can be given within 4.5 hours of symptom onset, but other treatment, such as thrombectomy may be relevant even later. Even if more than 4.5 hours have passed, or if the exact time of onset is unknown, it is important for the patient to receive emergency medical care immediately.

Specialised Care

Acute Treatment in Ischemic Stroke

Treatment should be initiated as soon as possible, but at the latest within 4.5 hours of symptom onset.

Substance	Brand name/names
alteplase	Actilyse

Acute Prophylactic Antithrombotic Treatment

acetylsalicylic acid	Trombyl *300–500 mg as bolus dose*

If thrombolysis (alteplase) has been given, intracerebral hemorrhage should be excluded with neuro-immaging 24 hours after the treatment and before antiplatelet therapy is given. If the patient is hypersensitive to aspirin, clopidogrel can be used, the loading dose in such cases is 600 mg.

Acute Treatment of Intracerebral Hemorrhage in Patients on Warfarin Treatment

PROTROMBIN COMPLEX CONCENTRATE	
coagulation factors II, VII, IX, X	Confidex

VITAMIN K	
phytomenadione	Konakion Novum *injection*

Prothrombin complex is the first choice for serious bleeding during warfarin therapy and should usually be given withphytomenadione. See also **Prophylaxis and reversal of bleeding caused by anti-vitamin K (AVK) – Medicines,** see www.mpa.se.

Secondary Prevention after TIA/Ischemic Stroke without Atrial Fibrillation

Risk factors should be assessed and addressed at the onset of each cerebrovascular episode. Antihypertensive therapy is indicated after TIA/stroke except in cases of hypotension.

Secondary Prevention in Non-embolic Ischemic Stroke/TIA

Combine

Substance	Brand name/names
acetylsalicylic acid	Trombyl 75 *mg x 1*
+	
dipyridamole	Persantin Depot *200 mg x 2*

Alternatively monotherapy

clopidogrel	Clopidogrel …, Cloriocard, Grepid, Plavix *75 mg x 1*

Aspirin (ASA) with a loading dose is well documented as acute prophylaxis in TIA/ischemic stroke.

After TIA/ischemic stroke, dipyridamole in combination with ASA can have an enhanced secondary prophylactic effect, as compared with ASA monotherapy, on the overall risk of vascular death, stroke, MI, and severe bleeding. Clopidogrel monotherapy has a more favorable side-effect profile and is an alternative to combination therapy with ASA and dipyridamole. If none of these treatments can be tolerated, ASA monotherapy can be administered.

Because of the risk of severe bleeding, combination therapy with clopidogrel and ASA is not recommended except for a limited time, e.g., after stenting.

Hypertension page 9
Lipid-lowering medicines page 9

Secondary Prevention after TIA/ischemic Stroke in Cases of Cardioembolic Source

Risk factors should be assessed and addressed at the onset of each stroke/TIA episode. Antihypertensive therapy is indicated after TIA/stroke except in cases of hypotension. Anticoagulants should always be considered.

warfarin	Waran *contains blue dye, indigo carmine*
warfarin	Warfarin Orion

For safety reasons, a separate pill organizer, e.g., Dosett, should be used for white warfarin pills, so that they can be distinguished from other pills. It is important that medicine records be updated when medicine therapy is changed, so that dual therapy with Waran and Warfarin Orion can be prevented.

The recommended therapeutic range for warfarin therapy is PK-INR 2.0 - 3.0. For some patients, self-testing may be an option.

Information for prescribers on self-testing and self-care during treatment with warfarin, see www.janusinfo.se (in Swedish).

In cases of TIA, anticoagulants can be started immediately. In cases of more extensive cerebral infarction, anticoagulation should be initiated after 1-2 weeks because of the risk of hemorrhagic transformation. Old age is not in itself a contraindication to anticoagulation therapy; on the contrary, the risk of embolic events increases with age. More patients, especially women and elderly, should be offered anticoagulants. When the source of the embolism is atrial fibrillation, new oral anticoagulants may be considered. Which one is chosen depends on patient characteristics and patterns of adverse events. Initiating medicine treatment after stroke should be done in consultation with a specialist.

Anticoagulant treatment - for dosing high-risk patients and procedures for the temporary discontinuation of warfarin, see www.viss.nu (in Swedish)
Antithrombotic therapy in atrial fibrillation, see www.janusinfo.se (in Swedish)
Pharmacological treatment of intracerebral hemorrhage and cerebral infarction/TIA, see www.janusinfo.se (in Swedish)

Thromboembolic prophylaxis page 16
Atrial fibrillation, atrial flutter page 16
Hypertension page 9
Lipid-lowering medicines page 9

Sequelae of Stroke

Depression affects at least one third of stroke patients, see page 71.

Epilepsy affects approximately 5% of stroke patients, see focal seizures with or without generalization page 59.

Migraine

Use preventative treatment in patients who suffer from three or more monthly migraine attacks, which require treatment.

Treating Migraine Attacks

First-Line Treatment

Substance	Brand name/names
paracetamol	Paracetamol …, Alvedon, Pamol, Panodil, Paracut, Pinex
acetylsalicylic acid	Magnecyl effervescent tablet* *From 18 years of age*

* Not included in the reimbursement scheme in Sweden

Second-Line Treatment – when the effect is insufficient	
naproxen	Naproxen …, Alpoxen, Pronaxen *For adults and children over 12 years of age and for children who weigh >50 kg*
ibuprofen	Ibuprofen …, Brufen, Ibumax, Ibumetin, Ipren *For adults and children*

Adjunct therapy in cases of nausea	
metoclopramide	Metoklopramid …, Primperan

Tertiary Treatment – when the effect is insufficient	
sumatriptan	Sumatriptan … *Recommended dose for adults 50 mg*
sumatriptan	Imigran *nasal spray* *For children 12–18 years*

Migraine Prophylactic Treatment

metoprolol succinate	Metoprolol ..., Metomylan, Seloken ZOC *For adults*
propranolol	Propranolol …, Inderal *For children and adolescents* *Dosing 2-3 times daily*

Titrate up the dose and evaluate over time.

Specialised Care

Second-Line Treatment

topiramate	Topamac, Topimax

Topiramate has teratogenic effects and entails risks of depression, cognitive effects and weight loss.

Recommendations for migraine treatment, see www.janusinfo.se (in Swedish)
Migraine, see www.viss.nu (in Swedish)

Epilepsy

Focalseizures with or without generalisation

First-Line Treatment

Substance	Brand name/names
carbamazepine	Tegretol Retard

Specialised Care

Second-Line Treatment

lamotrigine	Lamotrigine Actavis, Lamotrigine Ebb
levetiracetam	Levetiracetam Actavis
oxcarbazepine	Trileptal *For children and adolescents*

Generalised Epileptic Seizures

First-Line Treatment

valproic acid	Ergenyl Depakine Retard, Ergenyl Retard

Other alternatives should be considered for children under the age of 2 and for women who might become pregnant.

Specialised Care

Second-Line Treatment

lamotrigine	Lamotrigine Actavis, Lamotrigine Ebb

Emergency Treatment Outside Hospital

diazepam	Diazepam Desitin, Stesolid *rectal solution*
midazolam	Buccolam *oromucosal solution* *For children*

Specialised Care

Treating children under the age of 2 is a matter for specialists. For recommendations on alternative treatment of epilepsy with focal seizures with or without geralisation and epilepsy with generalised seizures, respectively, see **Recommendations in epilepsy**, see www.janusinfo.se (in Swedish).

Status Epilepticus, Initial Treatment in Adults

diazepam	Stesolid novum *injection*
levetiracetam	Keppra *infusion*
valproic acid	Ergenyl *injection*

To be administered while monitoring respiration and circulation:

Step 1: Diazepam 10 mg IV. Use half the dose, 5 mg IV in patients >75 years. Do not wait more than 2 min for a seizure to pass before starting on step 2. If the patient has already received diazepam in the ambulance or the ward, go straight to step 2.

Step 2: Give a slow (5 min) IV injection of valproic acid 15–30 mg/kg. Contraindications: liver failure, known coagulation disorder, porphyria or mitochondrial disease. Ongoing anticoagulant treatment is not, however, a contraindication for acute treatment. Levetiracetam 1000-3000 mg IV as an infusion during 15 min is an alternative to valproic acid.

Specialised Care

Status Epilepticus, Initial Treatment in Children

Substance	Brand name/names
midazolam	Midazolam Panpharma *injection*

While monitoring respiration and circulation, administer:
Step 1: Midazolam 0,2 mg/kg IV.
Step 2: If the seizure do not stop, contact the pediatric emergency department for further management.

Guidelines for the treatment of convulsive status epilepticus in adults and children, see www.janusinfo.se (in Swedish)

Parkinson´s Disease

levodopa *+ benserazide*	Levodopa/Benserazide ...*, Madopark* Madopar Quick, Madopark Quick Madopar Depot, Madopark Depot
levodopa *+ carbidopa*	Sinemet* Levocar*, Sinemet Depot*

* The expert committee recommends specifying ”May not be exchanged” on the prescription.

Specialised Care

For treatment alternatives, see **Recommendations for the Treatment of Parkinson´s Disease, see** www.janusinfo.se (in Swedish).

Restless Legs (RLS)

Mild-Moderate RLS

Only for intermittent use due to the risk of so called augmentation (worsening of symptoms). Recommended dose of levodopa is 50–100 mg in the evening as needed.

levodopa *+ benserazide*	Levodopa/Benserazide ..., Madopark Madopar Quick, Madopark Quick
levodopa *+ carbidopa*	Sinemet

Moderately Severe-Severe RLS

pramipexole	Pramipexol …, Derinik, Oprymea

Risk of involuntary, sudden spells of falling asleep and disturbed impulse control.

Treatment of restless legs, see www.janusinfo.se (in Swedish)

Specialised Care

Multiple Sclerosis (MS)

Acute Treatment of Recurrent Episodes

methylprednisolone	Solu-Medrol
prednisone	Deltison

Several of the new oral medicines for preventing recurrent episodes are subject to the Stockholm County Council program of orderly introduction of new medicines.
Wise protocols page 85

Oncology

Specialised Care

There are national and/or regional guidelines for all the major groups of tumours. In addition to this, there are summaries on www.janusinfo.se. (in Swedish)

Patients with cancer should receive multidisciplinary and multiprofessional management. Treatment is given as inpatient care or day care in the disciplines of oncology, hematology, pulmonary medicine, urology, gynecology and pediatric oncology.

Prostate Cancer – Endocrine Therapy

Locally Advanced Disease

ANTI ANDROGEN

Substance	**Brand name/names**
bicalutamide	Bicalutamide …, Bicalustad, Casodex

Radiation of the mamillaries should be considered before treatment.

Metastatic Disease

For patients who do not undergo surgical castration.

First-Line Treatment

GnRH AGONIST

leuprorelin	Leuprorelin Sandoz *implant* *1 respective 3 mths dosage interval*
leuprorelin	Enanton Depot Dual, Procren Depot *subcutaneous injection* Enanton Depot Set *subcutaneous injection* *6 mths dosage interval*

Second-Line Treatment

ESTROGEN

polyestradiol phosphate	Estradurin *240 mg/month intramuscular*

Radiation of the mamillaries should be considered before treatment.

Breast Cancer – Endocrine Therapy

For low-risk patients

tamoxifen	Tamoxifen …, Nolvadex

For high-risk patients

anastrozole	Anastrozole …, Anastelb, Arimidex

Prevention of Skeletal Lesions and Tumor-Induced Hypercalcemia

pamidronic acid	Pamidronat …, Pamidronatdinatrium …, Pamifos
zoledronic acid	Zoledronsyra …, Zoledronic acid ..., Zometa

Chemotherapy-Induced Nausea

ondansetron	Ondansetron ..., Zofran *injection* Ondansetron ..., Zofran, Zofron *pill*

Osteoporosis

Important lifestyle factors/measures for prevention and treatment of osteoporosis:

- Smoking cessation. **Nicotine Addiction** page 73
- Well-balanced diet and normal body weight (low BMI is a risk factor for osteoporotic fracture).
- Regular physical activity. Consider physical activity on prescription, see www.viss.nu (in Swedish) or http://www.fyss.se/fyss-in-english/.
- Avoid excessive intake of alcohol.
- Prevention of accidents through falling.

Osteoporosis, see www.viss.nu (in Swedish)
National guidelines for musculoskeletal disorders, see www.socialstyrelsen.se (in Swedish)

CALCIUM + VITAMIN D
Give supplements only in patients with inadequate calcium intake and/or risk of vitamin D deficiency, as well as to those treated with cortisone or with therapy for osteoporosis . For others, it is not shown that the medical advantages outweigh the risks.

Substance	**Brand name/names**
calcium carbonate *+ cholecalciferol*	Kalcipos-D *pill* Calcichew-D3 *chewing pill*

When the vitamin D deficiency is more pronounced than the calcium deficiency	
calcium carbonate *+ cholecalciferol*	Kalcipos-D forte *pill* Calcichew-D3 Forte, Kalcipos-D forte, Recikalc-D forte *pill*

BISPHOSPHONATES
In combination with calcium and vitamin D in patients at high risk for fracture. For the assessment of fracture risk the WHO FRAX tool may be used, see www.viss.nu (in Swedish). Reconsider therapy after 3-5 years as the risk of atypical fractures increases with duration of treatment. Intake of oral bisphosphonate and calcium should be at different times not to impair the absorption of bisphosphonate.

For patients over 80 years of age with a high fracture risk and who are not considered suitable for treatment with bone resorption inhibitor, calcium and vitamin D may be sufficient.

First-Line Treatment	
alendronic acid	Alendronic acid … weekly pill, Alenat weekly pill, Fosamax weekly pill

Second-Line Treatment
In cases of gastro-intestinal intolerance and problems following the treatment regimen for alendronic acide. Only for patients with a GFR over 35 ml/min.

zoledronic acid	Zoledronsyra …, Aclasta *infusion*

Specialised Care

For patients who are intolerant towards all bisfosphonate medication or who have a GFR below 35 mL/min and for patients in poor general condition in which a flu reaction is deemed medically risky. Observe the risk of hypocalcemia in severe renal impairment (GFR below 35 mL/min).

OTHER BONE-RESORPTION INHIBITORS	
denosumab	Prolia *injection*

Pain and Inflammation

All pain treatment should be adjusted to the individual patient. The lowest effective dose should be used. The effect should be continuously evaluated and treatment re-evaluated if the treatment target is not achieved.

Nociceptive Pain

Pain from tissue damage, with or without inflammation.

PARACETAMOL

Substance	Brand name/names
paracetamol	Paracetamol …, Alvedon, Pamol, Panodil, Paracut, Pinex

Paracetamol may be combined with both COX inhibitors and opioids.

COX INHIBITORS (NSAID)

First-Line Treatment

naproxen	Naproxen ..., Alpoxen, Pronaxen

Second-Line Treatment

*ibuprofen**	Ibuprofen ..., Brufen, Ibumax, Ibumetin, Ipren Brufen Retard
ketoprofen	Orudis Retard

* Ibuprofen may counteract the antithrombotic effect of aspirin. Avoid combining low dose ASA with ibuprofen, see www.janusinfo.se (in Swedish)

For prophylaxis of gastric ulcers when treating with COX inhibitors, see page 39.

Specialised Care

For Parenteral Use

ketorolac	Toradol
paracetamol	Paracetamol Fresenius Kabi* *infusion*

* Intravenous paracetamol should only be used if paracetamol is considered to have a significant effect and it cannot be administered in any other way.

OPIOID ANALGESICS

All pain is not sensitive to opioids and all medicines, including codeine, involve the risk of dependence. The aims of opioid treatment are functional improvement and enhanced quality of life. If these treatment goals are not achieved, treatment should be discontinued. The physician who initiates opiod treatment is in charge of continued treatment until it is stopped or until this responsibility has been transferred to a colleague.

morphine	Morfin … *short-acting pill, injection*
morphine	Dolcontin *long-acting*
oxycodone	Oxycodone ..., OxyNorm *short-acting pill, injection*
oxycodone	Oxycodone ..., Oxikodon Depot ..., OxyContin *long-acting*
buprenorphine	Norspan *patch*
codeine *+ paracetamol*	Paracetamol/Codeine …, Citodon, Codalvonil, Panocod *Only for short-time use*

Treatment of pain which is not acute and which is sensitive to opioids may begin with a low dose of long-acting morphine 5–10 mg x 2, long-acting oxycodone 5 mg x 2 or buprenorphine 5 µg/h.

The analgetic effect of buprenophine 5 µg/h is considered to correspond to an oral daily dose of 10 mg oxycodone.

Codeine is not an analgesic in itself; the effect is due to transformation to morphine, which occurs to a varying degree. Codeine 30 mg is transformed to approximately 3 mg of morpine in most adults but it may vary from 0 to 30 mg morphine. Codeine is not recommended to children, breastfeeding women and the elderly.

Opioid treatment in long-term, non-cancer-related pain, see www.janusinfo.se (in Swedish), www.viss.nu (in Swedish)

Specialised Care

In cancer-related pain when oral opioid treatment cannot be given

Substance	**Brand name/names**
fentanyl	Fentanyl …, Durogesic, Matrifen *patch*
hydromorphone	Palladon *injection, infusion*

Pain treatment with transdermal fentanyl, www.janusinfo.se

Pain treatment in the elderly page 27

Opioid-Induced Constipation

Prophylactic treatment of constipation should be considered from the first day of treatment.

Basic treatment	
makrogol + electrolytes	Lacrofarm, Laxido, Laxiriva, Movicol, Moxalole, Omnicol

Adjunct treatment Motor-stimulating laxatives as needed.	
sodium picosulphate	Cilaxoral

Opioid-Induced Nausea

Consider prophylactic treatment of nausea from the first day of treatment. When the nausea stops, usually within 7-14 days, attempts at phasing out can be made.

meclozine	Postafen

Phasing Out Opioids

Phasing out should be done slowly to reduce the risks of withdrawal symptom. **Phasing out opioids,** see www.janusinfo.se (in Swedish)

Generalised Pain Conditions

As an isolated measure, medicine treatment is seldom successful in generalised pain conditions, e.g., fibromyalgia. If medicine treatment is indicated, trycyclic antidepressants may be tried in the framework of a multiprofessional team management approach.

amitriptyline	Amitriptyline …, Saroten

Start with 10 mg in the evening, gradually increase until the desired effect is achieved. Be observant for anticholinergic effects, particularly in the elderly.

Neuropathic Pain

The recommendation relates to peripheral pain (e.g., diabetic polyneuropathy, post-herpetic neuralgia) and central neuropathic pain (e.g., after stroke). **Pharmacological treatment of neuropathic pain,** see www.mpa.se (in Swedish).

First-Line Treatment

Substance	Brand name/names
amitriptyline	Amitriptyline …, Saroten

Start with 10 mg in the evening; gradually increase until the desired effect is achieved. Be observant for anticholinergic effects, particularly in the elderly.

Second-Line Treatment

gabapentin	Gabapentin Teva

Pain treatment in the elderly page 27

Trigeminal Neuralgia

carbamazepine	Tegretol Tegretol Retard

Inflammatory System and Joint Diseases

STEROID FOR INTRA- AND EXTRA-ARTICULAR INJECTION

methylprednisolone	Depo-Medrol

STEROID FOR INTRA-ARTICULAR INJECTION

triamcinolone	Lederspan

ORAL STEROID
In specific inflammatory states, e.g., polymyalgia reumatica

prednisolone	Prednisolon ...

Specialised Care

Reumatoid Arthritis, Psoriasis Arthritis and Ankylosing Spondylitis

methotrexate	Methotrexate ..., Metotab *pill*
methotrexate	Metoject *injection* Metojectpen *injection*

TNF INHIBITOR

golimumab	Simponi
infliximab	Remicade

We recommend combining TNF inhibitor and methotrexate.

Gout

Acute Treatment

First-Line Treatment

Substance	Brand name/names
naproxen	Naproxen …, Alpoxen, Pronaxen

Second-Line Treatment – when COX inhibitors are unsuitable or fail to provide a sufficient effect.

prednisolone	Prednisolon ...

Prophylaxis

allopurinol	Allopurinol …, Zyloric

Lightly elevated levels of urate without any identified urate crystals in the synovial liquid do not need to be treated.

Gout, see www.viss.nu (in Swedish)

Medicines and the Elderly, page 26
Migraine, page 58

Pregnancy and Breastfeeding

A risk-benefit assessment should always be made when initiating medicine treatment during pregnancy and breastfeeding. In many cases, the benefit of a medicine is greater than the potential risk.

Pregnancy and Medicine Treatment

The dose and time of exposure to a medicine during the fetal development is of great importance. The risk of malformations is greatest during the first trimester, while medicine treatment during late pregnancy may affect organ maturation, growth and the central nervous system. Exposure in late pregnancy may cause withdrawal symptoms or affect the child during the neonatal period in other ways.

Both acute and chronic diseases as well as pregnancy-related disorders often require pharmacological treatment. An untreated illness may involve a greater risk to the child than the increased risk caused by medicine exposure during the fetal development. The physiological changes that occur during pregnancy often affect drug metabolism and excretion. Dose adjustments may be required. It may be useful to determine the concentration of medicine in plasma when possible.

Nausea During Pregnancy

First-Line Treatment

Substance	Brand name/names
meclozine	Postafen

Second-Line Treatment – if the effect is insufficient

propiomazine *+ caffeine + ephedrine*	Lergigan comp*

* Not included in the reimbursement scheme in Sweden

Breastfeeding and Medicine Treatment

When breastfeeding, the risk of pharmacological effects on the child are dependent on many different factors e.g., the amount of medicine in the milk, the age and general condition of the child, and the ability of the child to absorb and eliminate the medicine. Premature infants and children who are ill are more senstive to medicine effects. Since side effects in infants often are non-specific, it is important to be particularly observant when prescribing and using medicines during breastfeeding.

Specialised Care

Stopping Breastfeeding	
cabergoline	Cabergoline …, Dostinex

For information on the effects of specific medicines:
Medicines and Effects on the Fetus, see www.janusinfo.se (in Swedish- this knowledge database presented in article by Nörby U et al (8).
Medicines and Breastfeeding, see www.janusinfo.se (in Swedish)

For questions on medicines in pregnancy and breastfeeding, contact the Karolinska Drug Information Center at Department of Clinical Pharmacology, Karolic; call 585 810 60, karolic@karolinska.se. This patient-related drug information service has been summarized and presented in several international publications (8-10).

Preoperative Care

Discontinuation of antiplatelet medicines and oral anticoagulants

Routine examination of the patient's medicine therapy is part of preoperative planning. For some medicines, treatment must be interrupted or doses changed before surgery and anesthesia. This applies in particular to medicines with anti-hemostatic effects. The following recommendations include oral medicines with clinically important effects on hemostasis. In these cases, there is often need for an individual assessment. The risk of recurrence of thromboembolic episodes during treatment must be weighed against the risk of a bleeding complication in the current intervention. In cases where a flexible range is listed below, the longer interval refers to procedures where even minor bleeding may have serious consequences, such as neurosurgery, certain eye surgery, urological surgery and spinal anesthesia.

Oral antithrombotic medicines in cases of bleeding and pre-surgically, see www.janusinfo.se (in Swedish)

Aspirin and COX inhibitors (NSAIDs)

Patients treated with low-dose aspirin (≤320 mg/day) as secondary prophylaxis after myocardial infarction, PCI, CABG, stroke, etc. should discontinue aspirin therapy only during the day of surgery. Patients with low cardiovascular risk taking low-dose aspirin (primary prophylaxis) may stop treatment three days preoperatively. For nonselective COX inhibitors, the time of preoperative discontinuation should be at least 5 drug half-lives. In most cases (e.g.ibuprofen) 24 hours is enough but in some cases (piroxicam and tenoxicam) the break should be for 14 days. Selective COX-2 inhibitors have no explicit antiplatelet effects, but should be avoided during coronary artery surgery because of increased risk of postoperative cardiovascular complications.

ADP Receptor Inhibitors

Clopidogrel, prasugrel (Efient) and ticagrelor (Brilique) require 5-7 days of treatment interruption before surgery for normalization of platelet function. For patients treated with ADP receptor inhibitors, alone or in combination with aspirin after myocardial infarction, PCI, CABG surgery or stroke, shorter treatment interruption than 5 days may be desirable because of the particularly high risk of thrombosis. This requires good planning in consultation with the treating surgeon, anesthesiologist and cardiologist.

Warfarin

For major surgery and in the case of epidurals, a PK-INR level below 1.5 is generally required. This level is normally reached 3-4 days after discontinuation of treatment in a patient whose prothrombin time or INR is within the therapeutic range (2-3), provided that the patient has a normal intake of vitamin K (dietary or otherwise). For minor dental procedures, superficial surgery etc. with little risk of bleeding complications, higher prothrombin time or INR values over 1.5 is acceptable. Consult with the anesthesiologist in charge if an epidural is needed.

When warfarin treatment is discontinued for more than 2-3 days, there is in certain cases, such as in patients with mechanical heart valve, a need for bridging treatment with low molecular weight heparin (LMWH).

Anticoagulant treatment with coumarin and LMWH, see www.viss.nu (in Swedish)

Direct-Acting Factor Xa Inhibitors

Treatment with apixaban (Eliquis) and rivaroxaban (Xarelto) should be discontinued 1-4 days preoperatively. Bridging therapy with low molecular weight heparin may be considered in cases where there is a high risk of thrombosis and in cases of longer treatment interruption, in consultation with the treating physician.

Questions and answers about apixaban and **Questions and answers about rivaroxaban**, see www.janusinfo.se (in Swedish).

Direct Acting Thrombin Inhibitor

Treatment with dabigatran (Pradaxa) should be discontinued 1-5 days preoperatively, dependent on the nature of the procedure and the patient's renal function. Bridging with low molecular weight heparin may be considered, in consultation with the physician in charge, in cases of high risk thrombosis and when treatment is interrupted for longer periods.

For more detailed recommendation, go to **Questions and answers about dabigatran,** see www.janusinfo.se (in Swedish).

Reversal of Anti-Hemostatic Effect

The effect of aspirin and COX inhibitors can be partially reversed with desmopressin (OCTOSTIM). During treatment with the ADP receptor inhibitors clopidogrel and prasugrel, platelet concentrates may have a good effect, while this is more doubtful of treatment with the reversible inhibitor ticagrelor. In all cases above, the treatment can be supplemented with tranexamic acid (Cyklokapron).

Recommendations for the treatment of coronary artery disease with ADP receptor inhibitor, see www.janusinfo.se (in Swedish).

When prothrombin time or INR is unfavorably high, the effect of warfarin may be reversed with vitamin K, which however has a slow effect. In severe bleeding, prothrombin complex is also administered in order to achieve instantaneous hemostasis.

There is no well-tested antidote for thrombin inhibitors and factor Xa inhibitors. Prothrombin Complex Concentrate can be tried to reverse the impact of factor Xa inhibitors. In severe bleeding during treatment with dabigatran, isolated cases of hemodialysis for 2-3 hours have been tried with some success.

Psychiatry

Temporary Treatment of Anxiety States

Substance	Brand name/names
alimemazine	Theralen
hydroxyzine	Hydroxyzine …, Atarax
oxazepam	Oxascand, Sobril

Alimemazine and hydroxyzine should generally speaking be avoided in the elderly due to anticholinergic side effects. Benzodiazepines increase the risk of confusion and falling accidents as well as cognitive impairment with long-term use.

Anxiety in the Elderly page 28

Specialised Care

Temporary Anxiety – for Children and Adolescents

alimemazine	Theralen
hydroxyzine	Hydroxyzine …, Atarax

Anxiety Syndrome

Generalised anxiety syndrome, panic syndrome, post-traumatic stress syndrome, social phobia and obsessive-compulsive syndrome.

The various selective serotonine reuptake inhibitors (SSRI) are considered as having equivalent effects in anxiety diseases.

First-Line Treatment	
sertraline	Sertralin ..., Oralin, Sertrone, Zoloft

Second-Line Treatment	
escitalopram	Escitalopram …, Cipralex, Entact, Esertia, Seroplex, Prilect
mirtazapine	Mirtazapin…, Mirtin

Tertiary Treatment	
clomipramine	Clomipramine ..., Anafranil Anafranil Retard

Consider anticholinergic effects, particularly in the elderly.

Anxiety in the elderly page 28

Anxiety syndrome, see www.psykiatristod.se (in Swedish)
National guidelines for care of depression and anxiety syndromes, see www.socialstyrelsen.se (in Swedish)
Treatment of anxiety syndrome, see www.sbu.se

Depression

Treat depression to complete remission.

The various selective serotonin reuptake inhibitors (SSRI) may be regarded as having equivalent antidepressive effects. Remission is the treatment goal. Treatment should be followed using validated symptom rating scales. In cases of insufficient effect despite dosage titration and treatment for an appropriate length of time, consider changing medication.

Combining SSRI with anticoagulants or thrombocytic inhibitors involves an increased risk of bleeding.

First-Line Treatment

Substance	Brand name/names
escitalopram	Escitalopram …, Cipralex, Entact, Esertia, Seroplex, Prilect
sertraline	Sertralin ..., Oralin, Sertrone, Zoloft

Second-Line Treatment

mirtazapine	Mirtazapin ..., Mirtin
venlafaxine	Venlafaxin ...

Depression in the elderly page 29
Depression, see www.psykiatristod.se (in Swedish)
National guidelines for care of depression and anxiety syndromes, see www.socialstyrelsen.se/english

Specialised Care

clomipramine	Clomipramine ..., Anafranil Anafranil Retard

Consider anticholinergic effects, particularly in the elderly.

Tertiary Treatment
Lithium as an adjunct (long-term treatment)

lithium	Lithionit

Depression in Children and Young People

Early follow-up of treatment is particularly important in children and adolescents due to the increased initial risk of suicidal thoughts. In general, children should be treated in child and adolescent psychiatry.

First-Line Treatment

fluoxetine	Fluoxetine …

Second-Line Treatment

sertraline	Sertralin ..., Oralin, Sertrone, Zoloft

Bipolar Disease

In bipolar disease, the prevailing general principle is preventive pharmocological treatment. A psychiatric specialist should manage treatment. These recommendations also apply to children and adolescents.

Preventative Maintenance Treatment

First-Line Treatment

Substance	Brand name/names
lithium	Lithionit

There is stronger evidence for lithium in the prevention of mania than in depression.

Second-Line Treatment – add on

quetiapine	Quetiapin ... Seroquel Depot
valproic acid	Ergenyl Depakine Retard, Ergenyl Retard

Valproic acid should not be administered to women of reproductive age.

In Depression or Mania with Periodic Onset

In depression or mania with periodic onset, lithium therapy should be reinitatied or initiated, the dosage adjusted, if applicable, and quetiapine treatment initiated.

Substance	Brand name/names
lithium	Lithionit
quetiapine	Quetiapin ... Seroquel Depot

A majority of the patients need combination treatment with lithium and quetiapine.

Pharmacological Treatment and Prophylaxis of Mania and Depression in Bipolar Syndrome, see www.janusinfo.se (in Swedish)
Bipolar Disease, see Disease, see www.psykiatristod.se (in Swedish)

Psychosis

Antipsychotic medicines should be used on clear indication and the dosing should be carefully titrated. The evaluation should take place after dose titration with adequate follow-up time for each dose. During long-term treatment, follow-up should involve structured symptom evaluation and annual monitoring of side effects.

There is a risk of weight gain, impaired glucose tolerance and elevated blood lipids, especially when treating with olanzapine or clozapine. All antipsychotics may cause extrapyramidal symptoms. Always strive for the lowest effective dose, especially when treating young people and the elderly.

During long-term treatment, prolonged injection is often preferred, however not for the elderly.

First-Line Treatment

risperidone	Risperidon …, Abriact, Risperdal *pill* Risperdal Consta, Rispolept Consta *injection*
zuclopenthixol	Cisordinol-Acutard, Clopixol-Acutard *injection* *In cases of agitation*
aripiprazole	Abilify Abilify Maintena *injection*

Second-Line Treatment

olanzapine	Olanzapin …, Zalasta, Zyprexa

Specialised Care

Tertiary Treatment

Substance	Brand name/names
clozapine	Clozapine ...

Medicine Treatment in Schizofrenia, see www.mpa.se (in Swedish)
National guidelines for antipsychotic medicine treatment in schizophrenia or schizophrenia-like conditions,
www.socialstyrelsen.se/nationalguidelines/nationalguidelinesforantipsychoticdrugtherapyforschizophreniaorschizophrenia-typeconditions

Sleep Disorders

Hypnotics should only be used in the short term. Short treatment and intermittent therapy reduces the risk of developing tolerance. When sleep disorders persist for a long time, underlying causes should be assessed before treatment is chosen.

zopiclone	Zopiklon ..., Imovane

If there is risk of dependence

propiomazin	Propavan

Propiomazine is inappropriate for the elderly because of the increased risk of daytime sleepiness and extrapyramidal side effects. There is insufficient evidence to support treating children and adolescents with hypnotics.

Sleep Disturbances in the Elderly page 29
In the case of prolonged sleep disorders, see www.janusinfo.se (in Swedish)

Nicotine Addiction

Advice and support for smoking cessation is an important form of health promotion, which the health care system can provide. Advice and motivational interviewing are the most important measures, but several different types of nicotine replacement therapy can be used as support to achieve abstinence.

If nicotine replacement therapy is used, it is important that the initial doses are high enough to minimize nicotine withdrawal. A combination of long acting (e.g., patches) and short acting (e.g., chewing gum) is more effective than monotherapy and should be tried before another medicine is prescribed.

If Smoking Cessation is Not Achieved with Nicotine Replacement Therapy

First-Line Treatment

bupropion	Bupropion ..., Zyban

May be combined with nicotine replacement therapy. Should be avoided for risk groups such as people with a history of epilepsy and patients with risk of developing delirium tremens.

Second-Line Treatment

*varenicline**	Champix

Watch out for psychiatric symptoms of recent origin.
* Limited reimbursement in Sweden, see www.tlv.se (in Swedish)

www.slutarokalinjen.org (in Swedish)
www.1177.se (in Swedish)

National guidelines for disease preventive methods, see www.socialstyrelsen.se/english.

Alcohol Disease

Increase the use of medicines to prevent relapse in alcohol dependence and follow up on treatment.

Relapse Prevention Treatment

Relapse-prevention treatment is of general usefulness in health care (not just in substance dependence care) in combination with follow-up, including medical advice and support.

First-Line Treatment

Substance	Brand name/names
acamprosate	Aotal, Campral
naltrexone	Naltrexon ...

Second-Line Treatment – aversion treatment	
disulfiram	Antabus

Medicine treatment of alcohol dependence, see www.mpa.se (in Swedish)

Treatment of Withdrawal Syndromes

oxazepam	Oxascand, Sobril

Treatment of alcohol withdrawal, see www.mpa.se.

Vitamin B1 Deficiency

thiamine	Vitamin-B1 ratiopharm *injection (available on license)*

Oral substitution is not recommended due to poor absorption.

Specialised Care

ADHD

The duration of action varies for the different medicines, which makes it easier to adjust treatment to the individual patient. Patients with complicating comorbidity, e.g., ongoing substance abuse, bipolar disease, developmental disorder or autism spectrum disorder, should be treated by a physician with experience of these conditions.

Specialist physicians in psychiatry, child and adolescent psychiatry, forensic psychiatry and child and adolescent neurology with habilitation are the only physicians who may prescribe narcotic medicines used for the treatment of ADHD.

ADHD, see www.psykiatristod.se (in Swedish)
Recommendations in ADHD, see www.janusinfo.se (in Swedish)
Medicine treatment in ADHD, see www.mpa.se (in Swedish)

First-Line Treatment

methylphenidate	Methylphenidate …, Concerta *long-acting*
methylphenidate	Ritalin, Ritalina *medium-long acting, depot capsule* Equasym Depot *medium-long acting, depot capsule*
methylphenidate	Medikinet, Ritalin *short-acting, pill*

Specialised Care

Second-Line Treatment

Substance	**Brand name/names**
atomoxetine	Strattera *In cases of dependence risk*
lisdexamfetamine	Elvanse *If the effect of methylphenidate is insufficient*

Renal Diseases

Estimate and consider renal function in the selection and dosing of medicines.

Bear in mind that renal function may suddenly deteriorate and that the risk of negative medicine effects will then increase.

Renal Protection in Medical Renal Disease

In patients with renal disease (including renal transplant patients), the general goal is to reach a blood pressure of <140/90 mmHg. In patients with manifest albuminuria (urine-albumine/creatinine ratio >30 mg/mmol), a target blood pressure of <130/80 mmHg may be justified.

Albuminuria and/or reduced GFR indicates increased risk of CVD. It is important to provide patients with renal disease CVD prevention.

Albuminuria must be reduced as far as possible by RAAS blockade. Start with low doses and escalate slowly in cases of severely impaired renal function (GFR <30 ml/min). Monitor eGFR and plasma potassium. Double RAAS block is a matter for specialists, as it involves an increased risk of hypercalemia and impacts on renal function.

For older and fragile patients, treatment should be individualised with special attention to tolerability (e.g., orthostatism, impact on renal function). Higher blood pressure levels are then acceptable.

ACE INHIBITORS

Substance	Brand name/names
enalapril	Enalapril …, Renitec
ramipril	Ramipril …, Triatec

ANGIOTENSIN RECEPTOR BLOCKERS (ARB)

losartan	Losartan …, Losarstad, Losatrix
*candesartan**	Candesartan …, Amias, Candesarstad, Candexetil, Kairasec, Kandrozid

* Limited reimbursement in Sweden, see www.tlv.se (in Swedish)

Fluid and Salt Retention

furosemide	Furosemide …, Furix, Impugan
furosemide	Lasix Retard

Metabolic Acidosis

sodium hydrogen carbonate	Natriumbikarbonat Recip

Vitamin D Deficiency

Vitamin D deficiency (S-25-OH-vitamin D <25 nmol/L) is common in chronic renal disease. Early treatment may prevent/delay the development of metabolic bone disease and secondary hyperparathyreoidism in renal disease.

VITAMIN D

cholecalciferol	Divisun

Hyperkalemia

Substance	Brand name/names
sodium polystyrene sulfonate	Resonium

Disturbed Calcium-Phosphate Metabolism

Prophylaxis and treatment of secondary hyperparathyroidism

D VITAMIN ANALOGUE

alfacalcidol	Alfacalcidol ..., Etalpha

PHOSPHATE BINDER

calcium carbonate	Calcitugg, Kalcidon *chewing tablet*
calcium carbonate	Kalcipos *tablet*
sevelamer	Renvela

Renal Anemia

ERYTHROPOETIC STIMULATOR

Target for treatment with erythropoetic stimulator is B-Hb 100–120 g/L

First-Line Treatment

epoetin zeta	Retacrit *short-acting*

Second-Line Treatment

darbepoetin alfa	Aranesp *moderate long-acting*

IRON

In treatment using single doses ≤200 mg

iron sucrose	Venofer

If the total dose exceeds 200 mg, it must be split up into several doses.

In the need of single doses ≥500 mg

dextriferron	Ferinject*

* Limited reimbursement in Sweden, see www.tlv.se (in Swedish)

Immunosuppression in Renal Transplantation

mycophenolate mofetil	Mycophenolate mofetil Sandoz**
tacrolimus	Adport**

** Please note that none of these medicines may be exchanged by the pharmacist.

Respiratory Tract

For long-term nasal and sinus symptoms, rinsing the nasal cavity with saline daily has a beneficial effect. Information about suitable rinse/wash kits is available at the community pharmacy. Nasal steroids may be used during pregnancy and breastfeeding.

Allergic Rhinoconjunctivitis

For nasal congestion, nasal steroids are more effective than oral antihistamines.

ANTIHISTAMINE

Substance	Brand name/names
desloratadine	Desloratadine …, Aerius, Dasselta

NASAL STEROID

Aim for the lowest possible maintenance dose.

mometasone	Mometasone …, Mommox, Nasomet, Nasonex

EYE DROPS

Cold, damp compresses and tear substitutes can provide relief for mild symptoms and as an adjunct to pharmacological treatment. Sodium cromoglicate does not work immediately, so the treatment should ideally be initiated before exposure to an expected allergen.

First-Line Treatment

sodium cromoglicate	Lecrolyn, Lomudal

Second-Line Treatment – if the effect is insufficient

emedastine	Emadine

Persistent Non-Allergic Rhinitis

NASAL STEROID

Aim for the lowest possible maintenance dose.

mometasone	Mometasone …, Mommox, Nasomet, Nasonex

LOCAL ANTICHOLINERGIC MEDICINE

For hypersecretion

ipratropium	Atrovent Nasal

Nasal Polyposis

NASAL STEROID

mometasone	Mometasone …, Mommox, Nasomet, Nasonex

Recurrent Rhinosinusitis

In patients with recurrent acute episodes of rhinosinusitis, try using a nasal steroid.

NASAL STEROID

mometasone	Mometasone …, Mommox, Nasomet, Nasonex

Acute maxillary sinusitis page 49
Acute Streptococcal Tonsillitis page 48
Recurrent Streptococcal Tonsillitis page 48

Croup

Substance	Brand name/names
betamethasone	Betapred

Specialised Care	
adrenaline	Adrenaline Mylan *1 mg/ml* *Dilute for inhalation in nebulisator*

Asthma in Adults

The goal of asthma treatment is good asthma control, which means freedom from symptoms and normal lung function. As the asthma disease varies in intensity over time, treatment should be monitored and adjusted accordingly. Asthma is treated in the same way during pregnancy and breastfeeding.

A spacer may be prescribed as an aid in aerosol device treatment.
Choice of spacer, see www.janusinfo.se (in Swedish)

Asthma in adults, see www.viss.nu (in Swedish)
Pharmacological treatment of asthma, see www.mpa.se (in Swedish)

Step 1

Asthma symptoms no more than twice a week

SHORT-ACTING BETA-2 AGONISTS

First-Line Treatment	
salbutamol	Buventol Easyhaler
salbutamol	Airomir *spray (with spacer)* *If the patient finds it hard to use a dry powder inhaler*

Second-Line Treatment	
terbutaline	Bricanyl Turbuhaler

Step 2

Continuous or recurring asthma symptoms (>twice weekly)
Addition to step 1

INHALED GLUCOCORTICOIDS

First-Line Treatment	
budesonide	Giona Easyhaler

Second-Line Treatment	
ciclesonide	Alvesco* *spray (with spacer)* *If the patient finds it hard to use a dry powder inhaler*

* Limited reimbursement; www.tlv.se

Step 3

Persistent asthma symptoms

It is important to evaluate the effect of inhaled steroids before long-acting beta-2 agonists are added. Inhaled steroids should always be continued when long-acting beta-2 agonists are added.

FIXED COMBINATIONS – steroid and long-acting beta-2 agonists (LABA)
First-Line Treatment

Substance	Brand name/names
budesonide *+ formoterol*	Bufomix Easyhaler

Second-Line Treatment

fluticasone *+ salmeterol*	Seretide Diskus, Seretide Diskus, Veraspir Diskus
fluticasone *+ formoterol*	Flutiform spray *(with spacer)* *If the patient finds it hard to use a dry powder inhaler*

Asthma in Children

The goal of the asthma treatment is to achieve symptom relief and normal lung function. Because the disease varies in severity over time, treatment should be monitored and adjusted accordingly.

A spacer may be prescribed as an aid in treatment with aerosol devices. For children under 4 years of age, a mask is needed. To choose a spacer, go to www.janusinfo.se.

Asthma/obstructive bronchitis in children and young people, see www.viss.nu (in Swedish)
Pharmacological treatment of asthma, see www.mpa.se (in Swedish)

Infants and Children 6 Months - 6 Years of Age

Mild symptoms triggered by infection

salbutamol	Airomir spray *(with a spacer)*

Episodic asthma (approx 10 days treatment)

fluticasone	Flixotide Evohaler, Flutide Evohaler *spray (with spacer)* *From the age of 1*
montelukast	Montelukast …, Singulair

Evaluate the effect of treatment. If the child still has obstructive symptoms after 7 to10 days, or if treatment is needed more than four times per year, a pediatrician should be consulted.

Children 7 - 17 Years Old – Step 1

Asthma symptoms at the most once a week.

SHORT-ACTING BETA-2 AGONISTS

salbutamol	Buventol Easyhaler
salbutamol	Airomir *spray (with a spacer)* *If the child has trouble handling a dry powder inhaler*

Children 7 - 17 Years Old – Step 2

Continuous or persistent asthma symptoms (>twice weekly)

Addition to Step 1
INHALED GLUCOCORTICOIDS OR LEUKOTRIENE RECEPTOR ANTAGONIST

First-Line Treatment

budesonide	Giona Easyhaler
montelukast	Montelukast …, Singulair

Evaluate the effect of treatment

Second-Line Treatment

Substance	Brand name/names
fluticasone	Flixotide Evohaler, Flutide Evohaler *spray (with a spacer)* *If the child has trouble handling a powder inhaler*

Children 7 - 17 Years Old – Step 3

Consult a pediatrican if symptoms are persistent.

Emergency Treatment/Short-Term Treatment in Adults and Children

BRONCHODILATING MEDICINES	
ipratropiumbromide	Ipratropiumbromid ..., Atrovent, Ipraxa *Solution for nebulizer*
salbutamol	Salbutamol ..., Airomir, Ventoline, *Solution for nebulizer*

ORAL STEROIDS	
betamethasone	Betapred
prednisolone	Prednisolon ...

Specialised Care **BRONCHODILATING MEDICINES**	
theophylline	Teofyllamin Meda
terbutaline	Bricanyl *injection*

Chronic Obstructive Pulmonary Disease (COPD)

Quitting smoking halts the progress of disease and is the single most important intervention. **Nicotine Addiction,** page 73

Physical activity is important in all stages of the disease, see www.fyss.se/fyss-in-english/

Long-acting bronchodilators are the foundation of medicine therapy. The objective of the treatment is to reduce symptoms, prevent exacerbations and improve quality of life.

COPD Chronic Obstructive Pulmonary Disease, see www.viss.nu (in Swedish)
Medicine Treatment in Chronic Obstructive Pulmonary Disease (COPD), see www.mpa.se (in Swedish)

Bronchodilating Medicines, Taken as Required

SHORT-ACTING BETA-2 AGONIST	
salbutamol	Buventol Easyhaler

SHORT-ACTING ANTI-CHOLINERGIC AGENT	
ipratropium	Atrovent
Should not be used together with a long-acting anticholinergic agent	

Bronchodilating, Maintenance Treatment for Symptoms

First-Line Treatment

LONG-ACTING ANTICHOLINERGIC MEDICINE	
tiotropium	Spiriva Handihaler

Second-Line Treatment
LONG-ACTING BETA-2 AGONIST (LABA)

Substance	Brand name/names
formoterol	Oxis Turbuhaler
salmeterol	Serevent Diskus

Consider combining tiotropium and LABA.

For Frequent Exacerbations and when FEV1 <50 % of the Expected Value

FIXED COMBINATIONS – steroid and long-acting beta-2 agonist (LABA)	
budesonide + formoterol	Bufomix Easyhaler
fluticasone + salmeterol	Brisomax Diskus forte, Seretide Diskus forte

Emergency Treatment/Short-Term Treatment

BRONCHODILATORS	
ipratropium	Ipratropiumbromid ..., Atrovent, Ipraxa *Solution for nebulizer*
salbutamol	Salbutamol ..., Airomir, Ventoline *Solution for nebulizer*

ORAL STEROIDS	
betamethasone	Betapred
prednisolone	Prednisolon ...

Specialised Care

BRONCHODILATING MEDICINES	
theophylline	Teofyllamin Meda
terbutaline	Bricanyl *injection*

Lower Respiratory Infections page 49

Urology

LUTS and Benign Hyperplasia

Generally, two medicine types are used in the treatment of LUTS (Lower Urinary Tract Symptoms) and BPH (Benigh Hyperplasia), alpha-1 receptor blockers and 5-alpha reductase inhibitors.

Alpha-1 receptor blockers facilitate urine drainage by relaxing muscles in the prostate and bladder neck and act quickly.

5-alpha reductase inhibitors affect the size of the gland, which shrinks an average of 20 percent. Hence, 5-alpha reduktase inhibitors are recommended in verified cases of enlarged prostate. Transrectal ultrasound is a reliable method of measuring the prostate. The treatment effect can only be evaluated after 3-6 months.

Combining alpha-1 receptor blockers and 5-alpha reductase inhibitors may be necessary in certain cases.

ALPHA-1 RECEPTOR BLOCKERS

Substance	Brand name/names
alfuzosin	Alfuzosin …, Danafusin, Lafunomyl, Xatral OD

5-ALFA REDUCTASE INHIBITORS

finasteride	Finasteride …

In cases of verified prostate enlargement (>40 ml eller PSA >1,4-1,6 µg/L).

Specialised Care

Prostate Cancer

Oncology page 61

Urgency, Urge Incontinence

These recommendations are for both women and men. Medicines for urgency and urge incontinence have a modest effect. Treatment should last 4-6 weeks before evaluation, provided that no serious side effects occur earlier. A micturition diary should be kept before and during treatment to evaluate the effect. Some anticholinergic medicines may cause cognitive impairment in the elderly, but this has not been demonstrated for tolterodine. In men with residual urine, consider the risk of impaired bladder voiding capactity at the beginning of treatment.

MUSCARINE RECEPTOR ANTAGONIST

tolterodine	Tolterodin ..., Detrusitol *pill* Tolterodin ..., Detrusitol SR *depot capsule*

Effort Incontinence

Guidelines for the treatment of urinary incontinence and **Guidelines for the treatment of urinary incontinence in women,** see www.janusinfo.se (in Swedish)**.**

Erectile Dysfunction

PDE5 INHIBITOR

Taking these together with nitrates is counterindicated. Patients with certain diseases of the optic nerve (NAION) should avoid PDE5 inhibitor treatment.

The duration of effect is approximately 6 hours for sildenafil and 36 hours for tadalafil.

First-Line Treatment

Substance	Brand name/names
sildenafil	Sildenafil …*, Idilico*, Viagra*

* According to the Medical Products Agency, the medicines are exchangeable. However, they are not included in the reimbursement scheme and so they may not be exchanged in the pharmacy. The Swedish system of free pricing means that prices may vary in different pharmacies.

Second-Line Treatment

tadalafil	Cialis**

** Not included in the reimbursement scheme. Free pricing means the price may vary in different pharmacies.

PGE1 ANALOGUE

alprostadil	Bondil *urethral rod*

Specialised Care	
alprostadil	Caverject *injection* Caverject Dual *injection*

Other Urology

LOCAL ANAESTHETIC

lidocaine	Xylocain *gel*

Wise Protocols

– Introduction and Follow-up of New Medicines within Stockholm County Council

New medicines are a priority area within the medicine strategy of Stockholm County Council. Some new medicines may offer significant benefits for patients, while the utility and safety is less clear for others. Our goal is a wise introduction of new medicines.

Regional decisions are required in order to ensure the satisfactory introduction and monitoring of all new medicines/new indications. The Stockholm County Council Drug and Therapeutics Committee makes medicine recommendations on the basis of efficacy, safety and cost. Effective and safe medicines that cure, relieve or prevent disease should be recommended to treat the right patients in the right context.

Medicine treatment is assessed in comparison with other forms of care and technologies - in addition or as an alternative.

Criteria for a medicine to be included in the process for introduction and follow-up

- Documentation is available and the application has been submitted to/approved by regulatory authorities (including cost-benefit issues).
- It represents an important therapy area.
- There remain unanswered questions as to the medicine's benefits for patients and possible added value such as increased survival and improved health-related quality of life.
- It may bring to the fore the need for making statements regarding e.g., ethical values, cost effectiveness, horizontal priority and/or funding.

For selected new medicines, so called **Wise Protocols** will be launched in order to establish introduction and monitoring. Wise Protocols can highlight one or more of the following aspects: overview of the medicine, indication, patient population, prescriber category, cost, assessment of value compared to established therapy, budgetary impact, training needs, communication and follow-up methods.

A recommendation is included of which patients should be considered for treatment and what follow-up is required during the introductory phase.

The Stockholm County DTC and its expert panels evaluate and make recommendations concerning new medicines. The following are some of the therapeutic areas/groups of medicines to be considered in 2015 and beyond:

- Anticoagulants
- Diabetes mellitus
- Inflammatory diseases
- Multiple sclerosis
- Tumour diseases

For more information, see www.janusinfo.se/nyalakemedel (in Swedish) and the concept as presented (2, 11).

Medicine Information Sources

www.janusinfo.se/In-English/

The website Janusinfo is produced by the Health and Hospital Administration and is the Stockholm County Council (SCC) website for medicine information. Here, you will find a wide range of non-commercial information and knowledge-based IT services and information for the health care system. Among these, Janusinfo.se contains information about the SCC Drug and Therapeutics Committee and its expert panels.

- **The Wise List**
  klokalistan.janusinfo.se/
  The justifications behind the recommendations as well as references.

- **Treatment Recommendation**
  www.janusinfo.se/Behandling/
  Recommendations from the expert committees of the SCC Drug Therapeutics Committee as well as from Strama, the Swedish Strategic Programme Against Antibiotic Resistance. Here you will also find the treatment program Emergency internal medicine.

- **Medicine News**
  www.janusinfo.se/Nyheter/Nyhetslista/

- **New Medicines**
  www.janusinfo.se/Behandling/Nya-lakemedel/Granskning-av-nya-lakemedel/
  Assessments of new medicines with recommendations as to their appropriate place in therapy.

- **Environmental Effects of Pharmaceuticals**
  www.janusinfo.se/Beslutsstod/Miljo-och-lakemedel/About-the-environment-and-pharmaceuticals/
  List of environmentally classified medicines and information on the effects of medicines on the environment.

- **Drug-drug Interactions** (publication 12)
  www.janusinfo.se/Beslutsstod/Interaktioner/Interaktioner-Sfinx/
  The Sfinx database mainly contains pharmokinetic interactions between medicines, certain herbals, foodstuffs, alcohol and tobacco. A user account can be obtained via the webpage.

- **Renal Function**
  The NjuRen service contains assessments and recommendations about medicine treatment in cases of impaired renal function. NjuRen is available within internal network SLLnet in Stockholm.

- **Medicines and their Impact on the Fetus** (publication 8)
  www.janusinfo.se/Beslutsstod/Lakemedel-och-fosterpaverkan/
  Assessments of the possible impacts of medicines on the fetus. Lists all medicines on the Swedish market.

- **Medicines and Breastfeeding**
  http://www.janusinfo.se/Beslutsstod/Lakemedel-amning/
  Information as to whether various medicine treatments are compatible with breastfeeding.

- **Sex, Gender and Drugs**
  http://www.janusinfo.se/Beslutsstod/Om-tjansten11/In-English/
  Structured information concerning sexual and gender aspects of medicine treatment.

Drug Information Centre (Reference 2,9,10)
If you have any drug-related questions concerning effects, interactions, side effects, pregnancy or breastfeeding, contact Karolic at Department of Clinical Pharmacology, ph. +46 8 585 810 60, karolic@karolinska.se.

Environmental Effects of Pharmaceuticals

www.janusinfo.se/environment

Most used pharmaceuticals eventually end up in the sewer, unchanged or as metabolites. Pharmaceutical residues can then reach watercourses and groundwater despite passing through wastewater treatment plants. Pharmaceuticals are often designed to resist biodegradation, and can therefore remain in the environment for a long time.

Some pharmaceuticals have been detected at low levels in drinking water, which is a warning sign that our approach to medication today can lead to health and environmental problems in the future. For this reason Stockholm County Council has decided that pharmaceuticals should be classified in terms of their environmental impact.

In the Wise List environmental impact is taken into account
Environmental classification is considered since 2005, if possible along with other environmental aspects, in choosing which pharmaceuticals should be recommended on the Wise List. When the pharmaceuticals being compared are equivalent in terms of medical efficacy, safety and pharmaceutical effectiveness, then their environmental impact and price is taken into account.

When possible other environmental effects are considered such as reduction in wastewater plants, environmental impact by manufacturing, availability of starter packs within the reimbursement system or environmentally friendly packaging. To obtain information about the environmental impact by manufacturing, Stockholm County Council has included this in the procurement process of pharmaceuticals. When a product is procured, the supplier must share information regarding certain environmental aspects of the production within six months.

A pharmaceutical substance with a small or moderate impact on the environment should be recommended before a substance lacking in environmental information in order to promote manufacturers who provide environmental information.

Environmental hazard refers to the environmentally harmful properties of the substance
The classification contains data of both the environmental hazard and the environmental risk. The term environmental hazard pertains to the environmentally harmful properties of the substance, its ability to resist degradation (persistence), capacity to accumulate in adipose tissue (bioaccumulation) and toxicity to aquatic organisms (toxicity) and will never change over time. The environmental hazard classification is performed by Stockholm County Council based largely on data from the drug manufacturers, but other research data is also taken into consideration when available. Today around 700 substances are classified.

Environmental risk refers to the probability of harmful concentrations occurring in waters in Sweden
Environmental risk is the likelihood of toxic effects on aquatic organisms from the use of the substance in its current magnitude. The environmental risk assessment is conducted by the Swedish Association of the Pharmaceutical Industry according to a model developed in collaboration with the Stockholm County Council, Apoteket AB (The former national Corporation of Swedish Pharmacies), the Swedish Medical Products Agency and the Swedish Association of Local Authorities and Regions. The risk may change during time, if the use increases so will the risk.

Both environmental hazard and environmental risk should be considered
When using the classification, both environmental hazard and environmental risk must be taken into consideration, because these concepts partially highlight different characteristics. The classification is available online and as a booklet. Other compiled environmental information will be published on a website (janusinfo.se) before long. For more detailed information, see www.janusinfo.se/environment.

The Stockholm Drug and Therapeutics Committee

The Stockholm County Council Drug and Therapeutics Committee (DTC) carries out its mandate according to Swedish Constitutanal Law, Act 1996:1157 on DTCs. The DTC is an advisory body of experts on medicine issues with the main task of promoting safe, efficient and cost-effective use of medicines. The DTC operates with the assistance of 21 expert panels in various therapeutic areas, consisting of experienced physicians involved in patient care, primary care as well as clinical pharmacologists and pharmacists. They offer expert advice based on high-level clinical and scientific expertise in their respective fields,

The Stockholm County Council Drug Therapeutics Committee and its expert panels have a common policy concerning conflicts of interest, where openness and transparency concerning any involvement or activities with pharmaceutical companies and other stakeholders is of central importance.

The Wise List is based on scientific evidence regarding efficacy and safety, pharmaceutical appropriateness, cost-effectiveness and environmental aspects. The expert panels submit proposals for recommendations to the Stockholm Country Council DTC that makes the decisions. The recommendations are reviewed annually or as needed.

The structure and function of Stockholm DTC and the Wise List concept are presented in international publications (1-4, 13).

Members of the Stockholm County Council Drug and Therapeutics Committee

Eva Andersén Karlsson, MD, Assoc Prof, Consultant, Head of Department, Chair,Health and Medical Care Administration

Johan Bratt, MD, Assoc Prof, Head Physican, Chair, Hospital Drug and Therapeutics Council at Karolinska University Hospital

Marja-Liisa Dahl, MD, Professor, Head of Department, Clinical pharmacologist
Department of Clinical Pharmacology, Karolinska University Hospital

Christine Fransson, Pharmacist, Pharmacy Secretary, Health and Medical Care Administration

Stina Fransson Sellgren, PhD, RN, Deputy Head of Nursing, Karolinska University Hospital

Jan Hasselström, MD, PhD, GP, Chair, Expert Panel on Family Medicine, Storvretens Primary Health Care Center

Roger Henriksson, MD, Professor, Head of Department, Chairperson, Expert Panel on Oncological and Hematological Diseases, Regional Cancer Center Stockholm County

Paul Hjemdahl, MD, Professor, Chair, Expert Panel for Cardiovascular Diseases, Division of Clinical Pharmacology, Karolinska University Hospital

Thomas Kahan, MD, Professor, Consultant, Chair, Hospital Drug and Therapeutics Council at Danderyd Hospital

Inga Klarin, MD, PhD, Consultant, Chair, Expert Panel on Geriatric Diseases, Karolinska University Hospital

Synnöve Lindemalm, MD, PhD, Consultant, Pediatrician, Astrid Lindgren Children's Hospital, Karolinska University Hospital

Rickard Malmström, MD, Assoc Prof, Consultant, Representative for Karolinska Institutet
Department of Clinical Pharmacology, Karolinska University Hospital

Mussie Msghina, MD, Assoc Prof, Consultant, Chair, Expert Panel for Psychiatric Diseases, Karolinska University Hospital

Christer Norman, MD, GP, Salems Primary Health Care Center

Marie-Louise Ovesjö, MD, PhD, Consultant, Chair, Wise List Working Group, Chair, Hospital Drug and Therapeutics Council at Södersjukhuset (Stockholm South General Hospital)

Peter Persson, PhD in Pharmacy, Pharmacist, Chair, Hospital Drug and Therapeutics Council at Capio S:t Görans Hospital

Michael Runold, MD, PhD, Consultant, Chair, Expert Panel for Respiratory and Allergic Disease, Karolinska University Hospital

Marie Sundström, RN, Local Authority Senior Medicine Advisor, Stockholm Municipality

Björn Wettermark, Assoc Prof, Pharmacist, Head of Department, Monitoring and evaluation, Health and Medical Care Administration

Rumiana Zlatewa, MD, Specialist Physician in Private Practice, CityHeart Cardiology Practice

Expert Panels of the Stockholm County Council Drug and Therapeutics Committee

Chairpersons

General Practice
Jan Hasselström, MD, PhD, GP
Storvretens Primary Health Care Center

Analgesics and Rheumatological Diseases
Carl-Olav Stiller, MD, Assoc Prof, Consultant
Karolinska University Hospital

Anaesthetics, Fluid Therapy and Nutrition
Inga Tjäder, MD, PhD, Consultant
Karolinska University Hospital

Endocrinological and Metabolic Diseases
Charlotte Höybye, MD, Assoc Prof, Consultant
Karolinska University Hospital

Gastroenterological Diseases
Mikael Lördal, MD, PhD, Consultant
Karolinska University Hospital

Geriatric Diseases
Inga Klarin, MD, PhD, Consultant
Karolinska University Hospital

Cardiovascular Diseases
Paul Hjemdahl, MD, Professor, Consultant
Karolinska University Hospital

Dermato-Venereological Diseases
Harry Beitner, MD, Assoc Prof, Consultant
Karolinska University Hospital

Infectious Diseases
Paulina Dalemo, MD, Specialist Physician
Karolinska University Hospital

Respiratory and Allergy Diseases
Michael Runold, MD, PhD, Consultant
Karolinska University Hospital

Medical Kidney Diseases
Peter Bárány, MD, Assoc Prof, Consultant
Karolinska University Hospital

Neurological Diseases
Mia von Euler, MD, Assoc Prof, Consultant
Södersjukhuset (Stockholm South General Hospital)

Obstetrics and Gynechology
Angelica Lindén Hirschberg, MD, Professor, Consultant
Karolinska University Hospital

Oncological and Hematological Diseases
Roger Henriksson, MD, Professor, Head of Department
Regional Cancer Center Stockholm County

Plasma Products and Certain Antithrombotic Drugs
Margareta Holmström, MD, Assoc Prof, Consultant
Karolinska University Hospital

Psychiatric Diseases
Mussie Msghina, MD, Assoc Prof, Consultant
Karolinska University Hospital

Radiological Drugs
Peter Aspelin, MD, Professor, Consultant
Karolinska University Hospital

Orphan Drugs
Ricard Nergårdh, MD, Assoc Prof, Consultant
Astrid Lindgren Children's Hospital, Karolinska University Hospital

Urology
Tareq Alsaody, MD, Consultant, Specialist
Karolinska University Hospital

Vaccinations
Åke Örtqvist, MD, Assoc Prof, Infectious Disease Doctor
Infectious Disease Unit, Health and Medical Care Administration

Eye Diseases
Leif Tallstedt, MD, Assoc Prof, Consultant
St. Erik Eye Hospital

For contact information, see www.janusinfo.se (in Swedish)

Changes in Medicine Recommendations from Wise List 2014 to Wise List 2015

New additions

adrenaline	Emerade
apixaban	Eliquis
azitromycin	Azithromycin …, Azitromax
benzyl benzoate+disulfiram	Tenutex
budesonide+formoterol	Bufomix Easyhaler
bupropion	Bupropion ..., Zyban
dabigatran	Pradaxa
escitalopram	Escitalopram …, Cipralex, Entact, Esertia, Seroplex, Prilect
imiquimod	Zyclara
midazolam	Buccolam
mometasone	Ovixan kräm
propranolol	Propranolol …, Inderal
repaglinide	Repaglinid …, NovoNorm
varenicline	Champix
Specialised Care	
aripiprazole	Abilify, Abilify Maintena
amino acid solution+lipid emulsion+ glukose+elektrolytes	Olimel
amino acid solution+lipid emulsion+ glukoss+elektrolytes	Nutriflex
linaclotide	Constella
lisdexamfetamine	Elvanse
methotrexate	Metoject, Metojectpen inj
methylphenidate	Equasym Depot
midazolam	Midazolam Panpharma *inj*
mycophenolate mofetil	Mycophenolate mofetil Sandoz
prednisone	Deltison
progesterone	Lutinus
tacrolimus	Adport
testosterone	Nebido
testosterone	Tostrex
topiramate	Topamac, Topimax
ulipristal	Esmya

Removed substances

adrenaline	Jext
budesonide	Desonix
budesonide	Novopulmon Novolizer
budesonide	Pulmicort Turbuhaler
budesonide+formoterol	Assieme Turbuhaler, Rilast Turbuhaler, Symbicort Turbuhaler
budesonide+formoterol	Symbicort forte Turbuhaler
formoterol	Formatris Novolizer
glipizid	Mindiab
imiquimod	Aldara
kloramfenikol	Chloromycetin
salbutamol	Ventilastin Novolizer
Specialised Care	
alanylglutamine concentrate	Dipeptiven
diazepam	Stesolid *pill*
mesalazine	Mesavancol, Mezavant
perphenazine	Trilafon dekanoat
progesterone	Crinone

Relevant References

– Added in the English Translated Version

1. Gustafsson LL, Wettermark B, Godman B, Andersén-Karlsson E, Bergman U, Hasselström J, Hensjö LO, Hjemdahl P, Jägre I, Julander M, Ringertz B, Schmidt D, Sjöberg S, Sjöqvist F, Stiller CO, Törnqvist E, Tryselius R, Vitols S, von Bahr C; Regional Drug Expert Consortium. The 'wise list'- a comprehensive concept to select, communicate and achieve adherence to recommendations of essential drugs in ambulatory care in Stockholm. Basic Clin Pharmacol Toxicol 2011;108:224-33. PubMed
2. Björkhem-Bergman L, Andersén-Karlsson E, Laing R, Diogene E, Melien O, Jirlow M, Malmström RE, Vogler S, Godman B, Gustafsson LL. Interface management of pharmacotherapy. Joint hospital and primary care drug recommendations. Eur J Clin Pharmacol 2013;69 Suppl 1:73-8. PubMed
3. Stichele RV. The 'wise list'- a comprehensive model for drug and therapeutics committees to achieve adherence to recommendations for essential drugs among prescribers? Basic Clin Pharmacol Toxicol 2011;108:221-3. PubMed
4. Sjöqvist F, Bergman U, Dahl ML, Gustafsson LL, Hensjö LO. Drug and therapeutics committees: a Swedish experience. WHO Drug Information 2002; 16:207-13.
5. Abernethy D, Birkett D, Brosen K, Cascorbi I, Gustafsson LL, Hoppu K, Maxwll S, Orme M, Rago L,Rawlins M Sir, Reidenberg M, Sjöqvist F, Smith T, Thuerman P, Walubo A. Clinical pharmacology in health care, teaching and research. Joint publication by WHO, CIOMS and IUPHAR (International Union of Pharmacology and Clinical Pharmacology) edited by Orme M, Sjöqvist F and Birkett D, Geneva 2012, Oct 8.
6. Bergman U, Popa C, Tomson Y, Wettermark B, Einarson TR, Aberg H, Sjöqvist F. Drug utilization 90%--a simple method for assessing the quality of drug prescribing. Eur J Clin Pharmacol 1998;54:113-8. PubMed
7. Molstad S, Cars O, Struwe J. Strama--a Swedish working model for containment of antibiotic resistance. Euro Surveill 2008;13:1-4. PubMed
8. Nörby U, Källén K, Eiermann B, Korkmaz S, Winbladh B, Gustafsson LL. Drugs and Birth Defects: a knowledge database providing risk assessments based on national health registers. Eur J Clin Pharmacol 2013;69:889-99. PubMed
9. Alván G, Ohman B, Sjöqvist F. Problem-oriented drug information: a clinical pharmacological service. Lancet 1983;2:1410-2. PubMed
10. Alván G, Andersson ML, Asplund AB, Böttiger Y, Elwin CE, Gustafsson LL, Öhman B, Törnqvist E. The continuing challenge of providing drug information services to diminish the knowledge--practice gap in medical practice. Eur J Clin Pharmacol 2013;69 Suppl 1:65-72. PubMed
11. Godman B, Malmström RE, Diogene E et al. Are new models needed to optimize the utilization of new medicines to sustain healthcare systems? Expert Rev Clin Pharmacol. 2015;8:77-94. PubMed
12. Böttiger Y, Laine K, Andersson ML, Korhonen T, Molin B, Ovesjö ML, Tirkkonen T, Rane A, Gustafsson LL, Eiermann B. SFINX-a drug-drug interaction database designed for clinical decision support systems. Eur J Clin Pharmacol. 2009;65:627-33. PubMed