Interakcije protimikrobnih zdravil z drugimi zdravili
Vir: baza LEXI-COMP

Opomba: Interakcije se nanašajo na 7 najpogosteje ambulantno predpisanih protimikrobnih zdravil v letu 2008: amoksicilin, azitromicin, sulfametoksazol/trimetoprim, ciprofloksacin, klaritromicin, metronidazol, doksiciklin

Antimicrobial agent	*Interacting members*	*Risk rating*	*Summary*	*Patient management*
Amoxicillin	**Tetracycline derivatives** (demeclocycline; doxycycline; minocycline; tetracycline)	D: Consider therapy modification	**Tetracycline derivatives may diminish the therapeutic effect of penicillins.** Penicillins exhibit optimal bacterial killing on dividing cells, which tetracyclines inhibit, thus reducing the efficacy of penicillins.	Monitor for decreased therapeutic effects of penicillin antibiotics, especially in the treatment of meningitis. Begin the penicillin at least 2 hours before the tetracycline. Higher doses of penicillin are less affected than lower doses.
Sulfamethoxazole, trimethoprim, azithromycin, ciprofloxacin	**Highest risk QTc-prolonging agents***	D: Consider therapy modification	**QTc-prolonging agents (indeterminate risk and risk modifying) may enhance the QTc-prolonging effect of highest risk QTc-prolonging agents.** The drugs listed in the indeterminate risk/risk modifier group have an uncertain effect on the QT interval, but have been associated with individual reports of QT prolongation, torsades de pointes (TdP), and/or are likely to increase the risk for QT prolongation and/or TdP via another mechanism.	Concomitant use may substantially increase the risk for serious toxicities, including TdP or other significant ventricular tachyarrhythmias. Patients with other risk factors present (e.g., older age, female sex, bradycardia, hypokalemia, hypomagnesemia, heart disease, and higher drug concentrations), would be at an even higher risk for these potentially life-threatening toxicities. The use of such a combination should be accompanied by close monitoring for evidence of QT prolongation or other alterations of cardiac rhythm.
Sulfamethoxazole, trimethoprim	**Methotrexate**	D: Consider therapy modification	**Sulfonamide derivatives and trimethoprim may enhance the adverse/toxic effect of methotrexate.** Trimethoprim/sulfamethoxazole appears to increase the concentration of free (unbound) methotrexate and reduces its excretion. Both trimethoprim/ sulfamethoxazole and methotrexate can contribute to folate deficiency (via suppression of dihydrofolate reductase) which could affect bone marrow activity.	Monitor for the development of signs and symptoms of methotrexate toxicity (eg, bone marrow suppression).
Sulfamethoxazole	**Vitamin K antagonists** (acenocoumarol; warfarin)	D: Consider therapy modification	**Sulfonamide derivatives may enhance the anticoagulant effect of vitamin K antagonists.** The following potential causes have been postulated: 1) sulfonamide displacement of warfarin from protein binding sites; 2) sulfonamide-associated reductions in GI flora responsible for production of vitamin K; and/or 3) sulfonamide-induced reductions in warfarin metabolism (via CYP2C9).	Monitor for increased INR/toxic effects of warfarin or other vitamin K antagonists if a sulfonamide is initiated/dose increased, or decreased INR/effects if a sulfonamide is discontinued/dose decreased. Consider reducing warfarin dose by 10-20% prior to starting the sulfonamide antibiotic and then monitoring INR closely to further guide dosing.

Doxycycline	**Antacids** (aluminum hydroxide; calcium carbonate; magaldrate; magnesium carbonate; magnesium hydroxide; magnesium trisilicate; sodium bicarbonate)	D: Consider therapy modification	**Antacids may decrease the absorption of tetracycline derivatives.** First, work in the 1950s demonstrated the formation of chelates between tetracyclines and aluminum, bismuth, calcium, and magnesium. The chelates have reduced solubility and thus reduced absorption from the GI tract. Second, tetracycline solubility is reduced in more alkaline environments (such as that produced by antacids) and, thus, absorption may be reduced. Finally, antibiotic adsorption onto the antacid compound might also result in reduced absorption.	To minimize the potential effects of interaction, administer tetracycline antibiotics at least 2 hours before, or 6 hours after, antacid administration. If a tetracycline is dissolved prior to administration, no precautions are needed with sodium bicarbonate administration. Consider using alternative acid-reducing agent in place of the antacid. Monitor for decreased therapeutic effects of tetracyclines if an antacid is initiated/dose increased. Doxycycline and minocycline are less likely to be of clinical concern.
	Penicillins	D: Consider therapy modification	**Tetracycline derivatives may diminish the therapeutic effect of penicillins.** Penicillins exhibit optimal bacterial killing on dividing cells, which tetracyclines inhibit, thus reducing the efficacy of penicillins.	Monitor for decreased therapeutic effects of penicillin antibiotics, especially in the treatment of meningitis. Begin the penicillin at least 2 hours before the tetracycline. Higher doses of penicillin are less affected than lower doses.
	Carbamazepine	D: Consider therapy modification	**Carbamazepine may decrease the serum concentration of Doxycycline.** The suspected mechanism of this potential interaction is induction of doxycycline metabolism or excretion by carbamazepine. The specific enzyme(s) and/or transporter(s) involved is uncertain, as most inducers like carbamazepine are capable of inducing several metabolic enzymes and transport proteins.	Monitor for decreased therapeutic effects of doxycycline if used concurrently with carbamazepine. Consideration might be given to increasing the dose of doxycycline at the initiation of carbamazepine, or use of another tetracycline derivative may be considered to avoid this interaction.
	Retinoic acid derivatives (acitretin; bexarotene; isotretinoin; tretinoin **Exceptions** adapalene; alitretinoin; tretinoin (topical))	X: Avoid combination	**Tetracycline derivatives may enhance the adverse/toxic effect of retinoic acid derivatives.** The development of pseudotumor cerebri is of particular concern. The mechanism of this interaction is unclear, but it is suspected that the interaction results from each agent's ability to independently increase intracranial pressure.	Due to the risk of developing pseudotumor cerebri (also known as intracranial hypertension), avoid this combination of drugs if possible. If used concomitantly, monitor for evidence of this interaction (eg, dizziness, diplopia, headache).
	Barbiturates (amobarbital; butabarbital; butalbital; methohexital; pentobarbital; phenobarbital*; secobarbital;	D: Consider therapy modification	**Barbiturates may decrease the serum concentration of doxycycline.** The suspected mechanism of this potential interaction is induction of doxycycline metabolism or excretion by the barbiturates. The specific enzyme(s) and/or transporter(s) involved is uncertain, as most inducers like phenobarbital are capable of inducing several metabolic enzymes and transport proteins.	Monitor for decreased therapeutic effects of doxycycline if used concurrently with a barbiturate. Use of another antimicrobial might be considered to avoid this interaction, or increasing the dose of doxycycline at the initiation of barbiturate therapy may be considered.

	thiopental)			
	Phenytoin	D: Consider therapy modification	**Phenytoin may decrease the serum concentration of doxycycline.** The suspected mechanism of this potential interaction is induction of doxycycline metabolism or excretion by phenytoin. The specific enzyme(s) and/or transporter(s) involved is uncertain, as most inducers like phenytoin are capable of inducing several metabolic enzymes and transport proteins.	Monitor for decreased therapeutic effects of doxycycline if used concurrently with phenytoin. Consideration might be given to increasing the dose of doxycycline at the initiation of phenytoin, or use of another tetracycline derivative may be considered to avoid this interaction.
Ciprofloxacin	**Antacids** (aluminum hydroxide; calcium carbonate; magaldrate; magnesium carbonate; magnesium hydroxide; magnesium trisilicate **Exceptions** sodium bicarbonate)	D: Consider therapy modification	**Antacids may decrease the absorption of quinolone antibiotics.** Of concern only with oral administration of quinolones. It is believed that the 3-carbonyl and 4-oxo functional groups on the antibiotic forms a chelate with the cations of the antacid resulting in inactive antimicrobials.1,2,3 This interaction appears most significant with aluminum and magnesium ions, to a lesser extent with calcium ions, and probably nonexistent with sodium ions.	Interactions can be minimized by administering oral quinolones at least 2 hours before, or 6 hours after, the dose of antacid. Consideration might also be given to the use of alternative, noninteracting acid reducers, such as histamine H2-antagonists. Monitor for decreased therapeutic effects of oral quinolones if administered with antacids.
	CYP1A2 substrates**	D: Consider therapy modification	Strong CYP1A2 inhibitors (ciprofloxacin) may decrease the metabolism of CYP1A2 substrates. Substrate clearance would decrease and serum concentrations would increase.	Consider an alternative for one of the interacting drugs in order to avoid toxicity of the substrate. Some combinations are specifically contraindicated by manufacturers. Suggested dosage adjustments are also offered by some manufacturers. Please review applicable package inserts. Monitor for increased effects of the CYP substrate if a CYP inhibitor is initiated/dose increased, and decreased effects if a CYP inhibitor is discontinued/dose decreased.
	Theophylline derivatives (aminophylline; theophylline **Exceptions** dyphylline)	D: Consider therapy modification	**Quinolone antibiotics may decrease the metabolism of theophylline derivatives.** The mechanism of these interactions is likely related to quinolone inhibition of CYP1A2 and/or CYP3A4 isoenzymes, thus limiting the metabolism of theophylline. In addition, it has been suggested that combined theophylline/quinolone therapy might augment the seizure-producing potential of each of the individual agents.	Consider an empiric reduction in the dosage of theophylline (25% to 50%) if ciprofloxacin is to be initiated to minimize the risk of theophylline toxicity. Consider using quinolones other than ciprofloxacin or enoxacin to reduce the risk of interaction. Monitor for toxic effects of theophylline preparations if a quinolone antibiotic is initiated/dose increased, or decreased effects if a quinolone antibiotic is discontinued/dose decreased.
	Tizanidine	X: Avoid combination	**Ciprofloxacin may decrease the metabolism of tizanidine.** Tizanidine is significantly metabolized by CYP1A2 enzymes. Ciprofloxacin is a strong inhibitor of these enzymes.	The manufacturer of ciprofloxacin contraindicates this combination of drugs. Monitor for increased effects of tizanidine if ciprofloxacin is initiated/dose increased.

Metronidazole	**Disulfiram**	X: Avoid combination	**Metronidazole may enhance the adverse/toxic effect of disulfiram**. Prescribing information for metronidazole notes that psychotic reactions have been reported in patients receiving metronidazole and disulfiram concurrently, and contains a warning to avoid the use of metronidazole in patients who have received disulfiram within the previous 2 weeks. Symptoms included acute psychoses, confusion, hallucinations, and/or delusions	Avoid the concomitant use of metronidazole and disulfiram. Avoid metronidazole use in patients who have received disulfiram within the previous 2 weeks.
	Vitamin K antagonists (acenocoumarol; warfarin)	D: Consider therapy modification	**Metronidazole may increase the serum concentration of Vitamin K antagonists**. The mechanism of this interaction has not been investigated. Metronidazole weakly inhibits CYP2C9, the primary enzyme responsible for S-warfarin metabolism. The impact of metronidazole on the pharmacokinetics/dynamics of acenocoumarol is unknown.	Consider alternatives to concomitant therapy with metronidazole and vitamin K antagonists. If concomitant therapy cannot be avoided, monitor for increased INR/bleeding risk if metronidazole is initiated/dose increased, or decreased effects if metronidazole is discontinued/dose decreased.
Clarithromycin	**Benzodiazepines**, metabolized by oxidation (alprazolam; bromazepam; chlordiazepoxide; clobazam; clonazepam; clorazepate; diazepam; estazolam; flurazepam; midazolam; nitrazepam; prazepam; quazepam; triazolam)	D: Consider therapy modification	**Macrolide antibiotics may decrease the metabolism of benzodiazepines (metabolized by oxidation).** The mechanism of these interactions appears to be related to macrolide inhibition of CYP3A4 isoenzymes. As such, benzodiazepines that do not undergo such metabolism (eg, lorazepam, oxazepam, and temazepam) would likely be safer alternatives. The manufacturer of midazolam recommends the use of lower-than-normal doses in patients receiving CYP3A4 inhibitors.	Consider using a noninteracting macrolide (azithromycin; fidaxomicin; spiramycin). Lower than normally recommended doses of midazolam should be used in patients receiving interacting macrolide antibiotics. Monitor for increased therapeutic/toxic effects of benzodiazepines if a macrolide antibiotic is already being received, is initiated, or the dose is increased, or decreased effects if a macrolide antibiotic is discontinued/dose decreased. If appropriate, consider using benzodiazepines which do not appear to be involved in this interaction (eg, lorazepam, oxazepam, and temazepam).
	HMG-CoA reductase inhibitors (atorvastatin; lovastatin*; pitavastatin; red yeast rice; simvastatin **Exceptions** fluvastatin; pravastatin; rosuvastatin)	D: Consider therapy modification	**Macrolide antibiotics may decrease the metabolism of HMG-CoA reductase inhibitors**. One mechanism appears to be macrolide-related ihibition of CYP3A4-mediated metabolism of specific HMG-CoA reductase inhibitors (simvastatin, lovastatin, atorvastatin). However, pitavastatin, which did interact with erythromycin to a significant degree, undergoes virtually no CYP3A4 metabolism, suggesting that another mechanism may be involved. Considering that pitavastatin disposition is largely dependent on the uptake transporter SLCO1B1 (OATP1B1), and possibly on ABCG2 (BCRP), and also somewhat dependent on	When coadministration of a macrolide antibiotic and an HMG-CoA reductase inhibitor is necessary, consider using a combination which appears to hold the lowest risk for the development of rhabdomyolysis. Lovastatin, simvastatin, atorvastatin, and pitavastatin all appear to represent a clinically significant degree of risk. Avoid use of lovastatin or simvastatin with erythromycin, clarithromycin, or telithromycin. Pitavastatin prescribing information recommends a maximum dose of 1 mg/day when used with erythromycin. Monitor for signs and symptoms of muscle toxicity/rhabdomyolysis when any macrolide antibiotic and HMG-CoA reductase inhibitor

			glucuronidation by UGT1A3 and UGT2B7, alterations in one or more of these processes may be at least somewhat responsible. Having negligible CYP3A4 effects, azithromycin and spiramycin may exert less of an affect the HMG-CoA reductase inhibitors.	are coadministered.
	Carbamazepine	D: Consider therapy modification	**Macrolide antibiotics may decrease the metabolism of carbamazepine**. The mechanism of these interactions appears to be related to the ability of macrolide antibiotics to inhibit the hepatic metabolism of carbamazepine.	Consider selecting a noninteracting macrolide. Monitor for toxic effects of carbamazepine if a macrolide antibiotic is initiated or the dose is increased. The dose of carbamazepine will likely need to be altered.
	Clozapine	D: Consider therapy modification	**Macrolide antibiotics may decrease the metabolism of clozapine.**	The potential severity of this interaction warrants consideration towards avoiding concurrent therapy with clozapine and macrolides. Azithromycin is likely a safe alternative in this class of antibiotics. If potentially interacting agents are used, monitor for toxic effects of clozapine if a macrolide antibiotic is initiated/dose increased, or decreased effects if a macrolide antibiotic is discontinued/dose decreased. Effects might include drowsiness, slurred speech, difficulty ambulating, and/or seizure.
	Ergot derivatives (bromocriptine; dihydroergotamine; ergoloid mesylates; ergonovine; ergotamine; methylergonovine **Exceptions** cabergoline)	D: Consider therapy modification	**Macrolide antibiotics may enhance the adverse/toxic effect of ergot derivatives.** Specifically leading the development of ergotism (characterized by cramping, pain, and ischemia in the extremities). The mechanism of these interactions are likely related to inhibition of CYP isoenzymes by the antibiotic, and reduced metabolism of the ergot derivative.	Monitor for toxic effects of ergot derivatives (specifically the signs and symptoms of ergotism: cramping, pain, and ischemia in the extremities) if used concomitant with a macrolide antibiotic. The concomitant use of telithromycin and ergot derivatives is contraindicated by the manufacturer. Azithromycin is not expected to negatively affect ergot derivatives, and therefore may be a safer alternative.
	Dronedarone	X: Avoid combination	**Strong CYP3A4 Inhibitors (clarithromycin) may increase the serum concentration of dronedarone** (CYP3A4 is the principle enzyme responsible for dronedarone metabolism).	Concurrent use of strong CYP3A4 inhibitors with dronedarone is contraindicated according to dronedarone prescribing information.
	Moderate risk QTc-prolonging agents***	D: Consider therapy modification	**Moderate risk QTc-prolonging agents may enhance the QTc-prolonging effect of other moderate risk QTc-prolonging agents.** Several drugs have been associated with the development of life-threatening ventricular arrhythmias, including most notably the polymorphic ventricular tachyarrhythmia torsades de pointes (TdP). Prolongation of the QT interval on the ECG is currently the best available biomarker to assess the risk for	The concomitant use of moderate risk QTc-prolonging agents with any other moderate risk QTc-prolonging agent should be avoided when possible. Concomitant use is expected to substantially increase the risk for serious toxicities, including the development of torsades de pointes (TdP) or other significant ventricular tachyarrhythmias. Patients with other risk factors present (e.g., older age, female sex, bradycardia,

			development of TdP or other ventricular tachyarrhythmias. Factors known to increase patient's risk include female sex, age over 65 years, bradycardia, hypokalemia, hypomagnesemia, underlying heart disease, higher concentrations of one or more QT-prolonging drugs, and genetic predisposition.	hypokalemia, hypomagnesemia, heart disease, and higher drug concentrations), would be at an even higher risk for these potentially life-threatening toxicities. The use of such a combination should be accompanied by close monitoring for evidence of QT prolongation or other alterations of cardiac rhythm.
	Systemic corticosteroids (betamethasone; corticotropin; cortisone; dexamethasone; fludrocortisone; hydrocortisone; methylprednisolone; mometasone; prednisolone; prednisone; triamcinolone)	D: Consider therapy modification	**Macrolide antibiotics may decrease the metabolism of corticosteroids (systemic).** The mechanism of these interactions is related to the ability of some macrolide antibiotics to inhibit CYP isoenzymes, and thus reduce the metabolism of various corticosteroids	Monitor for increased therapeutic/toxic effects of corticosteroids if an interacting macrolide antibiotic is initiated/dose increased, or decreased effects if an interacting macrolide antibiotic is discontinued/dose decreased. The dose of the corticosteroid may have to be reduced to avoid side effects. This interaction has been used at times to augment steroid effects in asthma patients. Azithromycin probably does not interact with corticosteroids.
	Calcium channel blockers (amlodipine; diltiazem; felodipine; isradipine; lacidipine; nicardipine; nifedipine; nilvadipine; nimodipine; nisoldipine; nitrendipine; verapamil **Exceptions** clevidipine)	D: Consider therapy modification	**Macrolide antibiotics may decrease the metabolism of calcium channel blockers.** The mechanism of this interaction appears to be inhibition of CYP3A4-mediated metabolism of calcium channel blockers by the macrolide antibiotics. Most macrolide antibiotics are moderate-to-strong CYP3A4 inhibitors (azithromycin reportedly lacks significant CYP3A4 inhibition), and most calcium channel blockers are CYP3A4 substrates. Inhibition of p-glycoprotein by the macrolide antiobiotic may also be involved for selected calcium channel blockers. Of note, verapamil and diltiazem are CYP3A4 and p-glycoprotein inhibitors, and may interact with at least some macrolides, possibly increasing macrolide concentrations/effects.	Consider using a noninteracting macrolide. Monitor for increased therapeutic effects of calcium channel blockers if an interacting macrolide antibiotic is initiated/dose increased, or decreased effects if a macrolide is discontinued/dose decreased.
	CYP3A4 inducers (strong) (aminoglutethimide; bosentan; carbamazepine; dexamethasone; efavirenz; etravirine; fosphenytoin; nafcillin;	D: Consider therapy modification	**CYP3A4 inducers (strong) may increase serum concentrations of the active metabolite(s) of clarithromycin.** Clarithromycin may increase the serum concentration of CYP3A4 Inducers (strong). CYP3A4 Inducers (strong) may decrease the serum concentration of Clarithromycin. The likely mechanisms for interactions are induction of the CYP3A enzyme that mediates the 14-hydroxylation of clarithromycin; clarithromycin	Consider alternative antimicrobial therapy for patients receiving a CYP3A inducer. Due to the different antimicrobial activities of clarithromycin and its active 14-hydroxy metabolite, drugs that enhance the metabolism of clarithromycin into 14-hydroxyclarithromycin may alter the clinical activity of clarithromycin, possibly impairing the intended therapeutic effectiveness of clarithromycin. Also,

	nevirapine; oxcarbazepine; pentobarbital; phenytoin; primidone; rifabutin; rifampin; rifapentine)		inhibition of CYP3A metabolism and/or p-glycoprotein transport/efflux.	monitor patients closely for evidence of CYP3A inducer (e.g., rifabutin, carbamazepine, etc.) toxicity.
	Sildenanfil	D: Consider therapy modification	**Strong CYP3A4 inhibitors (clarithromycin) may increase the serum concentration of sildenafil.** The mechanism of this interaction appears to be inhibition of the CYP3A4 metabolism of sildenafil, leading to increased sildenafil concentrations/exposure and possibly to greater effects and/or toxicity.	When sildenanfil is used for treatment of pulmonary arterial hypertension, concurrent use with strong CYP3A4 inhibitors is not recommended. When sildenafil is used for treatment of erectile dysfunction, consider using a lower starting dose of 25 mg in patients who are also taking a strong CYP3A4 inhibitor. Due to the particularly strong effects of ritonavir, sildenafil (for erectile dysfunction) doses greater than 25 mg per 48 hours are not recommended. Of note, the interaction between CYP3A4 inhibitors and sildenafil is predicted to be greater with orally administered than with injected sildenafil.
	Highest risk QTc-prolonging agents*	X: Avoid combination	**Moderate risk QTc-prolonging agents may enhance the QTc-prolonging effect of highest risk QTc-prolonging agents.** Several drugs have been associated with the development of life-threatening ventricular arrhythmias, including most notably the polymorphic ventricular tachyarrhythmia torsades de pointes (TdP). Prolongation of the QT interval on the ECG is currently the best available biomarker to assess the risk for development of TdP or other ventricular tachyarrhythmias. Factors known to increase patients' risk include female sex, age over 65 years, bradycardia, hypokalemia, hypomagnesemia, underlying heart disease, higher concentrations of one or more QT-prolonging drugs, and genetic predisposition	The concomitant use of highest risk QTc-prolonging agents with any other QTc-prolonging agent should be avoided. Many such combinations are listed contraindications for these drugs. Concomitant use is expected to substantially increase the risk for serious toxicities, including the development of torsades de pointes (TdP) or other significant ventricular tachyarrhythmias. Patients with other risk factors present (e.g., older age, female sex, bradycardia, hypokalemia, hypomagnesemia, heart disease, and higher drug concentrations), would be at an even higher risk for these potentially life-threatening toxicities.
	Theophylline derivatives (aminophylline; theophylline **Exceptions** dyphylline)	D: Consider therapy modification	**Macrolide antibiotics may decrease the metabolism of theophylline derivatives**. Azithromycin and clarithromycin appear to have little to no effect on the disposition of theophylline derivatives. The mechanism of this interaction is likely related to macrolide inhibition of CYP isoenzymes. In such case, clarithromycin would be expected to exhibit some effects.	Monitor for toxic effects of theophylline derivatives if a macrolide antibiotic is initiated or the dose is increased. This is of most concern with erythromycin or troleandomycin. Consider using a noninteracting macrolide. Other macrolides appear to have little to no effect on theophylline.
	CYP3A4 substrates**	D: Consider	**Strong CYP3A4 inhibitors (clarithromycin) may**	Consider an alternative for one of the interacting drugs

		therapy modification	**decrease the metabolism of CYP3A4 substrates.** Substrate clearance would decrease and serum concentrations would increase. Increased effects of the substrates would be expected.	in order to avoid toxicity of the substrate. Monitor for increased effects of the CYP substrate if a CYP inhibitor is initiated/dose increased, and decreased effects if a CYP inhibitor is discontinued/dose decreased.

*** Highest risk qtc-prolonging agents:** amiodarone; arsenic trioxide; artemether; asenapine; astemizole; cisapride; citalopram; disopyramide; dofetilide; dronedarone; escitalopram; flupentixol; halofantrine; ibutilide; iloperidone; lumefantrine; mesoridazine; mifepristone; nilotinib; paliperidone; pimozide; procainamide; quetiapine; quinidine; quinine; saquinavir; sotalol; sparfloxacin; telithromycin; terfenadine; tetrabenazine; thioridazine; toremifene; vandetanib; vemurafenib; ziprasidone; zuclopenthixol.

**** CYP1A2 substrates**: acenocoumarol; alosetron; aminophylline; asenapine; betaxolol; betaxolol (ophthalmic); betaxolol (systemic); bromazepam; caffeine; clomipramine; clozapine; cyclobenzaprine; dacarbazine; duloxetine; flutamide; fluvoxamine; guanabenz; lidocaine; lidocaine (systemic); lidocaine (topical); mexiletine; mirtazapine; olanzapine; pimozide; propranolol; ramelteon; rasagiline; ropinirole; ropivacaine; theophylline; thiothixene; tizanidine; trifluoperazine.

***** Moderate risk QTc-prolonging agents:** alfuzosin; chloroquine; chlorpromazine; clarithromycin; clozapine; crizotinib; degarelix; dolasetron; domperidone; droperidol; eribulin; erythromycin; erythromycin (systemic); flecainide; gemifloxacin; granisetron; haloperidol; indacaterol; lapatinib; levofloxacin; levofloxacin (systemic); methadone; moxifloxacin; moxifloxacin (systemic); ofloxacin; ofloxacin (systemic); ondansetron; pazopanib; pentamidine; perflutren lipid microspheres; propafenone; ranolazine; rilpivirine; risperidone; romidepsin; sunitinib; trazodone; voriconazole.

****** CYP3A4 substrates**: abiraterone acetate; alfentanil; alfuzosin; alprazolam; amiodarone; amlodipine; aprepitant; aripiprazole; armodafinil; atazanavir; atorvastatin; avanafil; axitinib; benzphetamine; bisoprolol; bortezomib; bosentan; bromocriptine; budesonide; budesonide (systemic, oral inhalation); buprenorphine; buspirone; busulfan; cabazitaxel; calcitriol; carbamazepine; chlordiazepoxide; chloroquine; chlorpheniramine; ciclesonide; ciclesonide (oral inhalation); cilostazol; cinacalcet; cisapride; citalopram; clarithromycin; clonazepam; clorazepate; cocaine; colchicine; conivaptan; crizotinib; cyclosporine; cyclosporine (systemic); cyproterone; dantrolene; dapsone; dapsone (systemic); darifenacin; darunavir; dasatinib; dexamethasone; dexamethasone (systemic); diazepam; digitoxin; dihydroergotamine; diltiazem; disopyramide; docetaxel; domperidone; doxorubicin; doxorubicin (liposomal); dronedarone; eletriptan; eplerenone; ergoloid mesylates; ergonovine; ergotamine; erlotinib; erythromycin; erythromycin (systemic); escitalopram; eszopiclone; ethosuximide; etoposide; etoposide phosphate; everolimus; felbamate; felodipine; fentanyl; fesoterodine; flurazepam; flutamide; fluticasone; fluticasone (oral inhalation); fosaprepitant; gefitinib; guanfacine; halofantrine; haloperidol; hydroxyprogesterone caproate; ifosfamide; imatinib; irinotecan; isosorbide dinitrate; isosorbide mononitrate; isradipine; ivacaftor; ixabepilone; ketamine; lacidipine; lapatinib; lidocaine; lidocaine (systemic); lidocaine (topical); lovastatin; lurasidone; maraviroc; mefloquine; methadone; methylergonovine; midazolam; mifepristone; mirtazapine; modafinil; nateglinide; nefazodone; nicardipine; nifedipine; nilotinib; nilvadipine; nimodipine; nisoldipine; nitrendipine; oxycodone; paclitaxel; paclitaxel (protein bound); pazopanib; phencyclidine; pimozide; pipotiazine; praziquantel; quetiapine; quinidine; quinine; ranolazine; repaglinide; rilpivirine; romidepsin; ruxolitinib; salmeterol; saxagliptin; sildenafil; silodosin; simvastatin; sirolimus; solifenacin; spiramycin; sufentanil; sunitinib; tacrolimus; tacrolimus (systemic); tadalafil; tamoxifen; tamsulosin; telaprevir; telithromycin; temsirolimus; teniposide; theophylline; tiagabine; tolterodine; tolvaptan; trabectedin; tramadol; trazodone; triazolam; trimipramine; vardenafil; venlafaxine; verapamil; vinblastine; vincristine; vinorelbine; zolpidem; zonisamide; zopiclone.

Interakcije protimikrobnih zdravil z drugimi zdravili
Vir: anonimizirana baza podatkov ZZZS o ambulantno predpisanih zdravilih

Opomba: Interakcije se nanašajo na 7 najpogosteje ambulantno predpisanih protimikrobnih zdravil v letu 2008: amoksicilin, azitromicin, ciprofloksacin, doksiciklin, klaritromicin, metronidazol, sulfametoksazol/trimetoprim

(številke v tabeli pomenijo frekvenco interakcij pri sočasnem predpisu para protimikrobno zdravilo-hkrati predpisano drugo zdravilo)

	Protimikrobno zdravilo							
Hkrati predpisano drugo zdravilo	Amoksicilin	Azitromicin	Ciprofloksacin	Doksiciklin	Klaritromicin	Metronidazol	Sulfametoksazol in trimetoprim	št. Interakcij
Escitalopram		437	226		274		499	1436
Bromazepam			563		331			894
Atorvastatin					654			654
Alprazolam					616			616
Simvastatin					552			552
Amlodipin					502			502
Citalopram		139	86		92		141	458
Amiodaron		59	252		38		94	443
Zolpidem					364			364
Teofilin			100		254			354
Bisoprolol					303			303
Kalcijev karbonat			260	19				279
Diazepam					270			270
Metilprednizolon					263			263
Kvetiapin		46	53		58		86	243
Lacidipin					198			198
Tramadol					183			183
Domperidon					148			148
Tamsulozin					134			134
Nifedipin					122			122
Karbamazepin				13	93			106
Propranolol			101					101
Varfarin						98		98
Verapamil					96			96

Tizanidin			92					92
Sotalol		24	11		11		29	75
Midazolam					72			72
Izosorbidmononitrat					60			60
Acenokumarol			58			2		60
Metotreksat							59	59
Mirtazapin			33		14			47
Flurazepam					38			38
Duloksetin			37					37
Doksiciklin	33							33
Lovastatin					28			28
Olanzapin			27					27
Aminofilin			16		9			25
Betaksolol			24					24
Diltiazem					20			20
Risperidon					19			19
Propafenon					19			19
Kalcitriol					16			16
Sildenafil					16			16
Eletriptan					15			15
Tamoksifen					14			14
Venlafaksin					14			14
Klonazepam					14			14
Klozapin			7		6			13
Fentanil					12			12
Repaglinid					11			11
Haloperidol					10			10
Solifenacin					9			9
Darifenacin					9			9
Moksifloksacin					8			8
Tolterodin					7			7
Oksikodon					7			7
Nitrazepam					6			6
Vardenafil					5			5
Darunavir					4			4
Aluminijev hidroksid			3	1				4

Ziprasidon							4	4
Nitrendipin					4			4
Dihidroergotamin					4			4
Primidon					4			4
Eritromicin					4			4
Razagilin			3					3
Flutamid			3					3
Flupentiksol		1					2	3
Izotretinoin				2				2
Levofloksacin					2			2
Ciklosporin					2			2
Paliperidon					2			2
Rifampicin					2			2
Ciproteron					2			2
Aripiprazol					2			2
Tadalafil					2			2
Bromokriptin					2			2
Zuklopentiksol		1					1	2
Klomipramin			2					2
Granisetron					1			1
Ropinirol			1					1
Aprepitant					1			1
Klobazam					1			1
Acitretin				1				1
Skupno število interakcij	33	707	1958	36	6053	100	915	9802