

DRUG INTERACTIONS II

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Potential risk induced by absolute contraindications

- Potential risk with induced exact CIs: ventricular arrhythmia-Torsade de Pointe,**
- Hypertension, coronary vasoconstriction,**
- Ergotism with the risk of necrosis of the extremities (inhibition of alkaloid metabolism),**
- Reduction of analgesic effect with receptor competitive block, risk of withdrawal syndrome,**
- Increased risk of hematological toxicity,**

Potential risk induced by absolute contraindications

- Increased hypoglycemic effect, hypoglycemia risk, coma,
- Serotonin syndrome: diarrhea, tachycardia, sweating, tremor, confusion, coma,
- Increased rhabdomyolysis and pharmacodynamic antagonism,
- Severe hemorrhage risk with metabolic inhibition and increased serum amount,
- Intracranial hypertension,
- Increased nephrotoxicity and ototoxicity,
- Severe or potentially fatal arrhythmia.

Potential risk induced by relative contraindications

Paroxysmal hypertension (occasional hypertension) and peripheral vasoconstriction syndromes,

Hypertension, coronary vasoconstriction with increased serotonergic effects,

Hemorrhage,

Hematological toxicity,

Hyperkalemia in fatal potential, especially in renal failure.

List of drugs with definite CI:

MEDICATION A	MEDICATION B	POTANTIEL RISK
Dopaminergic antiparkinsons	Dopamine receptor antagonists that prescribed as antipsychotic (excluding clozapine)	Reciprocal antagonism of dopaminergic antiparkinson drug and dopamine receptor antagonists
Dopaminergic antiparkinsons	Dopamine receptor antagonists that prescribed as antiemetic agents	Reciprocal antagonism of dopaminergic antiparkinson agents and dopamine receptor antagonists
Ergot alkaloids	Sumatriptan and its congeners (5-hydroxytryptamine receptor agonists)	Hypertension, coronary vasoconstriction
Ergotamine, dihydroergotamine	Macrolides (except spiramycin), ritonavir	Ergotism with risk of necrosis of the extremities (ergot alkaloids metabolism inhibition)
Taking drugs together that increase QT:	Amiodarone, erythromycin (injection), hydroquinidine, pentamidine, sotalol, pimozide phenothiazines, benzamides	Ventricular arrhythmias, i.e. Torsade de Pointes

List of drugs with definite CI:

MEDICATION A	MEDICATION B	POTANTIEL RISK
Digoxin	Calcium	Serious arrhythmia (potentially lethal)
Tramadol, pethidine, dextromethorphan	Nonselective MAO inhibitors, MAO-A inhibitors	Potential for serotonin syndrome : diarrhoea, tachycardia, sweating, tremor, confusion, coma
Aminoglycosides	Other aminoglycosides	Increased nephrotoxicity and ototoxicity
Retinoids (other than topical)	Tetracyclines (other than topical)	Intracranial hypertension
Opioid agonist analgesics	Mixed agonist/antagonist opioids	Decrease of the analgesic effect (competitive antagonism), risk of withdrawal syndrome

List of drugs with definite CI:

MEDICATION A	MEDICATION B	POTANTIEL RISK
Nonselective MAO inhibitors	Indirectly acting sympathomimetic drugs: amphetamines and its congeners (for depression of appetite and psychic effect); ephedrine and its congeners (topical and enteral), methylphenidate	Paroksimal hipertansiyon, hipertermi
Nonselective MAO inhibitors	Reserpine and its congeners (rauwolfia alkaloids)	Agitation, seizures, hypertension
Levodopa	Reserpine and its congeners (rauwolfia alkaloids)	Inhibition of levodopa effects
Levodopa	Nonselektif MAO inhibitörleri	Accentuation of the actions of levodopa and precipitation of life-threatening hypertensive crisis (inhibition of peripheral biotransformation)
Sumatriptan	Nonselective MAO inhibitors, MAO-A inhibitors, MAO-B inhibitors	Intracranial hypertension, of coronary vasoconstriction (additive effect)

List of drugs with definite CI:

MEDICATION A	MEDICATION B	POTANTIEL RISK
Combination oral contraceptives	Ritonavir	Concurrent use may render oral contraceptives less effective
Saquinavir	Enzyme activators : rifabutin, rifampin, anticonvulsants (carbamazepine, phenobarbital, phenytoin, primidone)	Decrease plasma levels and efficiency of the antiproteases (induction of hepatic biotransformation)
Cytotoxic drugs	Phenytoin	Seizures (decrease absorption of phenytoin)
Hyperkalemiant diuretics	Hyperkalemiant diuretics, potassium salt	Hyperkalemia (potentially lethal), especially in case of kidney failure (additive effect)
MAO-B inhibitors	Antidepressants: selective serotonin potentiating agents	Paroxysmic hypertension and symptoms of peripheral vasoconstriction

List of drugs with definite CI:

MEDICATION A	MEDICATION B	POTANTIEL RISK
Oral anticoagulants	Miconazole (oral administration and buccal gel)	Bleeding (inhibition of biotransformation)
Oral anticoagulants	High doses of salicylates (enteral and parenteral), phenylbutazone (enteral and parenteral)	Bleeding (displacement of oral anticoagulant from its plasma binding site)
Fibric acid derivates (hypolipidemic drugs)	Fibric acid derivates	Rhabdomyolysis (additive effects)
Sulfonylurea hypoglycaemic agents	Miconazole (oral administration and buccal gel)	Increase risk of hypoglycemia (risk of coma)
Methotrexate >15 mg/week	Salicylates	Increase haematologic toxicity of methotrexate

Some serious drug interactions

INTERACTION	POTENTIAL EFFECT	TIME TO EFFECT	RECOMMENDATION
Warfarin + ciprofloxacin, clarithromycin, erythromycin, metronidazole or trimethoprim-sulfamethoxazole	Increased effect of warfarin	Generally within 1 week	Select alternative antibiotic
Warfarin + acetaminophen	Increased bleeding, increased INR	Any time	Use lowest possible acetaminophen dosage and monitor INR
Warfarin + acetylsalicylic acid (aspirin)	Increased bleeding, increased INR	Any time	Limit aspirin dosage to 100 mg per day and monitor INR
Warfarin + NSAID	Increased bleeding, increased INR	Any time	Avoid concomitant use if possible; if coadministration is necessary, use a cyclooxygenase-2 inhibitor and monitor INR

Some serious drug interactions

INTERACTION	POTENTIAL EFFECT	TIME TO EFFECT	RECOMMENDATION
Fluoroquinolone+divalent / trivalent cations or sucralfate	Decreased absorption of fluoroquinolone	Any time	Space administration by 2–4 h
Carbamazepine + cimetidine, erythromycin, clarithromycin or Fluconazole	Increased carbamazepine levels	Generally within 1 week	Monitor carbamazepine levels
Phenytoin + cimetidine, erythromycin, clarithromycin or fluconazole	Increased phenytoin levels	Generally within 1 week	Monitor phenytoin levels
Lithium + NSAID or diuretic	Increased lithium levels	Any time	Decrease lithium dosage by 50% and monitor lithium levels

Some serious drug interactions

INTERACTION	POTENTIAL EFFECT	TIME TO EFFECT	RECOMMENDATION
Oral contraceptive pills + rifampin Avoid if possible.	Decreased effectiveness of oral contraception	Any time	If combination therapy is necessary, have the patient take an oral contraceptive pill with a higher estrogen content (>35 µg of ethinyl estradiol) or recommend alternative method of contraception
Sildenafil + nitrates (nitroglycerin, isosorbide mononitrate, isosorbide dinitrate)	Dramatic hypotension	Soon after taking sildenafil	Absolute contraindication
Sildenafil + cimetidine, erythromycin, itraconazole or ketoconazole levels	Increased sildenafil levels	Any time	Initiate sildenafil at a 25-mg dose

Some serious drug interactions

INTERACTION	POTENTIAL EFFECT	TIME TO EFFECT	RECOMMENDATION
Lovastatin + warfarin Lovastatin + warfarin	Increased effect of warfarin	Any time	Monitor INR
SSRI + TSA SSRI + tricyclic antidepressant	Increased tricyclic antidepressant level	Any time	Monitor for anticholinergic excess and consider lower dosage of tricyclic antidepressant
SSRI + selegiline or nonselective monoamine oxidase inhibitor initiation	Hypertensive crisis	Soon after	Avoid
SSRI + tramadol	Increased potential for seizures; serotonin syndrome	Any time	Monitor the patient for signs and symptoms of serotonin syndrome