Neuro.Wiki

Drugs that Lower the Seizure Threshold

Medications that commonly lower the seizure threshold, grouped by class and drug family. Risk rises with high doses, renal impairment (drug accumulation), and pre-existing epilepsy.

Category	Drugs that commonly lower the seizure threshold — grouped by family
Antibiotics	**Cephalosporins:** Cefepime (most implicated, esp. renal dysfunction); also Cefazolin, Ceftazidime **Carbapenems:** Imipenem (highest seizure risk), Meropenem, Ertapenem, Doripenem **(⚠ all lower valproate levels)** **Penicillins:** high-dose IV Penicillin G, Piperacillin/tazobactam, Ampicillin, Ampicillin/sulbactam (Unasyn) **(⚠ more with renal impairment)** **Fluoroquinolones:** Ciprofloxacin, Levofloxacin, Moxifloxacin, Ofloxacin **Others:** Isoniazid (overdose / pyridoxine deficiency), Metronidazole & Linezolid (prolonged use / toxicity)
Antipsychotics	**Atypical:** Clozapine (dose-related — highest risk); Olanzapine, Quetiapine (lower) **Typical / phenothiazines:** Chlorpromazine, Thioridazine
Antidepressants	**Aminoketone:** Bupropion (highest-risk antidepressant; max SR 400 / XL 450 mg/day; avoid in eating disorders & alcohol/benzo/AED withdrawal) **SNRI:** Venlafaxine (mainly in overdose) **Tricyclics:** Clomipramine (highest); Amitriptyline, Imipramine, Nortriptyline (mainly high-dose/overdose) **Tetracyclic / heterocyclic:** Maprotiline, Amoxapine
Mood stabilizer	**Lithium:** at toxicity / high levels
Analgesics	**Opioids:** Tramadol & Meperidine (highest); Tapentadol (lower); Fentanyl only high-dose/rapid/intrathecal
Immunosuppressants	**Calcineurin inhibitors:** Cyclosporine, Tacrolimus (neurotoxicity / PRES, hypomagnesemia — even at therapeutic levels)
Other	**Bronchodilators:** Theophylline, Aminophylline **Stimulants (intoxication/overdose):** Cocaine, Methamphetamine, Amphetamines; Methylphenidate (overdose) **Antihistamines (1st-gen, overdose):** Diphenhydramine, Dimenhydrinate **Other:** Flumazenil (benzo dependence), Local anesthetics (LAST — lidocaine, bupivacaine), Metoclopramide **Withdrawal states: Alcohol, Benzodiazepines, Barbiturates, Baclofen, abrupt antiseizure-med withdrawal — provoke seizures**

Although many drugs can *theoretically* lower the seizure threshold, most do so only rarely — e.g., all cephalosporins are implicated in theory, but **cefepime** is the one seen in practice (especially with renal impairment). Listed here are the agents that **commonly** provoke seizures. Highest-yield: cefepime, carbapenems, bupropion, clozapine, tramadol/meperidine, theophylline, and abrupt withdrawal from alcohol/benzodiazepines/barbiturates/baclofen.

Seizure Threshold — Quick Triage (Avoid vs. Caution)

Avoid where possible (high seizure risk) **Use with caution** (lower / relative — usually toxicity, high dose, or renal accumulation)

Category	Avoid — high risk	Caution — lower / relative
Antibiotics	Cefepime, Imipenem, high-dose IV Penicillin G	Fluoroquinolones, Meropenem, Ertapenem, Piperacillin/tazobactam, Metronidazole, Linezolid, Isoniazid
Antipsychotics	Clozapine	Chlorpromazine, Thioridazine, Olanzapine, Quetiapine
Antidepressants	Bupropion, Clomipramine	Amitriptyline, Imipramine, Nortriptyline, Maprotiline, Amoxapine, Venlafaxine
Analgesics	Tramadol, Meperidine	Tapentadol, Fentanyl (high-dose/intrathecal)
Stimulants	Cocaine, Methamphetamine	Amphetamines, Methylphenidate (overdose)
Bronchodilators	Theophylline, Aminophylline (toxicity)	—
Mood stabilizer	—	Lithium (toxicity / high levels)
Immunosuppressants	—	Cyclosporine, Tacrolimus
Other	—	Diphenhydramine (overdose), Flumazenil (benzo dependence), Local anesthetics (LAST), Metoclopramide
Withdrawal states	Alcohol, Benzodiazepines, Barbiturates, Baclofen, abrupt antiseizure-med withdrawal	—

Colour reflects **relative** seizure risk, not an absolute rule — most "caution" agents are safe at normal doses and become relevant with high dose, overdose, renal impairment, or pre-existing epilepsy. When in doubt, dose-adjust for renal function and monitor.