

List of safe drugs in acute porphyrias

(acute intermittent porphyria, variegated porphyria, hereditary coproporphyria)

This leaflet was not developed for HPU (hemopyrrololactamuria)

Main trigger factors for acute porphyria attacks:

1. Drugs that are not safe in acute porphyrias
2. Sex hormones (estrogens, gestagens), premenstrual phase
3. Reduced carbohydrate intake (fasting, strict weight loss programs)
4. Infections (e.g. flu or COVID)
5. Alcohol (in relevant quantities)
6. (psychological) stress

General recommendations: Patients with an acute porphyria should take as few drugs as possible. However, we also aim to avoid an insufficient treatment of medical conditions in patients with porphyria. This fact sheet is intended to help achieve a *lege artis* treatment with porphyria safe drugs. We generally do not recommend drug combinations. In case drug combinations are prescribed, please ensure that all components are safe in acute porphyrias. All drugs that are **completely not absorbed** and/or **entirely not metabolized** in the liver are considered safe in acute porphyrias.

In **complex treatment situations** such as oncological conditions or infections (e.g. tuberculosis), we recommend a consultation with our porphyria center to determine the optimal therapeutic approach.

Under **circumstances associated with a vital threat**, any life-saving drug should be administered, even if no information on the safety in acute porphyria is readily available. In this situation, switch to drugs known to be safe in porphyria at the earliest possible. Unlike allergic drug reactions, acute porphyria attacks develop with a latency of several days. Therefore, the porphyrin metabolism should be monitored. Please contact us for further information and to determine the optimal monitoring and treatment strategy. In case of an acute attack, heme-arginate can be administered.

Nutrition in acute porphyrias: We generally recommend a diet with a regular carbohydrate intake (at least two meals per day). During symptomatic periods or as a preventive measure in vulnerable patients, for instance in times of stress or in patients suffering from repeat porphyria attacks, a diet rich in carbohydrates is indicated. Depending on individual factors this diet should contain at least approx. 120-200g of carbohydrates distributed over 5-6 meals daily. In case of nausea, loss of appetite, or vomiting, the carbohydrates can also be taken as sweetened beverages (such as tea sweetened with dextrose or sugar, fruit juices, Coke/Sprite/Lemonade, or the like. Please note: "light" drinks are not suitable). If desired, a specialized nutritionist can also give individual dietary advice according to special dietary habits or intolerances.

Consultation: We are happy to help you and your physician. For further advice see contact information in the letterhead.

Important: This list is a recommendation based on clinical experience and theoretical knowledge. The administration/prescription of drugs remains the sole responsibility of the prescribing physician. The authors take no responsibility for errors, differing opinions, or for adverse events resulting from the use of this list. We strongly recommend limiting the use of drugs to the absolute necessary. **Please note that formularies for the guidance of drug prescription or the summary of product characteristics often do not report the drug safety regarding acute porphyrias correctly. Therefore, we strongly recommend an enquiry before administering any drug not listed below.**

Further information about drug safety: <http://www.drugs-porphyrria.org/>

Drugs compatible with acute porphyrias:

Indication	Substance
Acute porphyria attack	heme arginate 3-4 mg/kg bodyweight OD for 3-5 days, <i>in case of severe attacks maybe further doses. In case of the suspicion of an acute attack please contact us.</i>
Nausea, vomiting:	droperidol, granisetron, ondansetron, tropisetron, metoclopramide
Constipation:	lactulose, lactitol, neostigmine, macrogol & salts, rectally applied substances that are not absorbed. <i>Severe constipation is one of the typical symptoms of an acute porphyria attack: the constipation usually resolves after a successful treatment of the attack.</i>

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Antacids:	omeprazole, pantoprazole, lansoprazole
Allergic reaction:	cetirizine, cromoglicic acid, (nor-)adrenaline, corticosteroids.
Diarrhea:	loperamide, loperamide-simethicon
Epilepsy:	vigabatrin, lamotrigine, levetiracetam, lorazepam, midazolam, gabapentin - Acute seizure : 1 x 10 mg diazepam i.v. (only 1 dose), propofol
Art. hypertension:	- Ace inhibitors: lisinopril, enalapril, captopril, ramipril - Calcium channel blockers: felodipine, nifedipine - (α-)β-blockers: atenolol, propranolol, esmolol, metoprolol, bisoprolol, timolol, labetalol - ATII antagonists: candesartan, eprosartan, valsartan, losartan
Cardiovascular disease:	atropin, digoxin, (nor-)adrenaline, dopamine, dobutamine, glyceryl trinitrate (nitroglycerin), isosorbide dinitrate, isosorbide monohydrate, acetylsalicylic acid, milrinone
Tachycardia/ arrhythmia:	β -blockers, sotalol, magnesium sulfate. <i>Many antiarrhythmics are porphyrinogenic! However, life-threatening cardiac arrhythmias should be treated with the optimal antiarrhythmic drug. An acute porphyria attack can be treated with heme arginate. Please contact us immediately (see letterhead) to ensure the optimal treatment.</i>
Dyslipidemia:	simvastatin, pravastatin, rosuvastatin, ezetimibe
Anticoagulation:	phenprocoumon, (fractionated) heparin, rivaroxaban, apixaban, fondaparinux
Diuretics:	amiloride, hydrochlorothiazide, furosemide
Antibiotics:	- penicillins: Amoxicillin/ clavulanic acid, benzyl- or phenoxymethylpenicillin, piperacillin/tazobactam, - macrolides: azithromycin, spiramycin - aminoglycosides: amikacin, gentamicin, tobramycin - cephalosporins: cefuroxime, cefaclor, cefazolin, cefixime, cefpodoxime, ceftazidime, ceftibuten, ceftriaxone - quinolones: ciprofloxacin, levofloxacin, norfloxacin - carbapenems: ertapenem, imipenem/cilastatin, meropenem - others: vancomycin, fusidic acid, teicoplanin, fosfomycin, pentamidine
Fungostatics/-cides:	amphotericin B, flucytosine, caspofungin, micafungin, anidulafungin
Malaria prophylaxis:	<i>Information on compatibility is partly contradictory and incomplete. Please contact us. Probably compatible are:</i> Mefloquine, atovaquone/proguanil
Psychotropic drugs:	levomepromazine, haloperidol, fluphenazine, triazolam, temazepam
Pain/ anti-inflammation:	acetylsalicylic acid, paracetamol, ibuprofen, naproxen, indomethacin, buprenorphine, codeine, tramadol, pethidine, morphine, fentanyl, oxycodone/naloxone, TNF- α inhibitors
Insomnia :	zolpidem, oxazepam, lorazepam
Anesthetics :	<i>more detailed separate leaflet available on request</i> local: bupivacaine (\pm adrenaline), levobupivacaine, tetracaine, mepivacaine, prilocaine, oxybuprocaine, lidocaine, articaine (\pm adrenaline) for dental and small surgical procedures general: propofol, NO, fentanyl, suxamethonium, remifentanyl, non-depolarizing muscle relaxants
Vaccinations:	all vaccinations are considered tolerable, <i>flu and COVID vaccination recommended as preventive measures.</i>
Antidepressants:	citalopram, escitalopram, paroxetine, lithium salts, fluoxetine, venlafaxine, amitriptyline, nortriptyline, mianserin
Bone health:	vitamin D, calcium, bisphosphonates, denosumab, teriparatide
Hormone system/ endocrinology:	L-thyroxine, insulin, erythropoietin, cabergoline, corticosteroids, mineralosteroids, ACTH, hormonal IUDs (<i>other hormonal contraceptives should be avoided!</i>)
Diabetes:	insulin, metformin, liraglutide, empagliflozin, gliptins (DPP-IV inhibitors), pioglitazone
Oncology:	chlorambucil, mephalan, bendamustin, lomustin, methotrexate, cytarabine, all antibody-based treatments (biologicals). <i>Please contact us to ensure optimal treatment.</i>
Cough/ common cold:	acetylcysteine, codeine, dextromethorphan, pseudoephedrine, paracetamol, acetylsalicylic acid, vitamin C
Various:	vitamins, radiography and MRI contrast media, electrolyte and glucose infusions