

Drugs in acute porphyrias

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UK Porphyria Medicines Information Service



**Welsh Medicines
Information Centre**

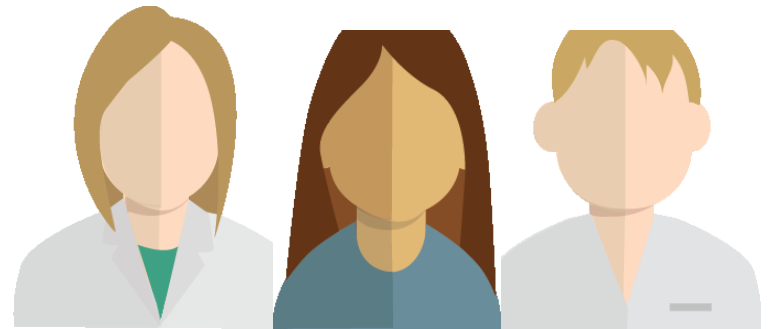
Timely, practical, evidence-based
advice for managing medicines

UKPMIS

- The UK Porphyria Medicines Information Service (UKPMIS) offers advice on the safe use of drugs in porphyria to patients and healthcare professionals in the UK.



Porphyria



UKPMIS

- Enquiry answering
 - 200 – 300 per year
- Safe list – updated annually
- Q&As for healthcare professionals
- Close links with Cardiff Porphyria Service and NAPS



2017 SAFE LIST: Drugs that are considered to be SAFE for use in the acute porphyrias

This safe list was produced jointly by UK Porphyria Medicines Information Service (UKPMIS) and Cardiff Porphyria Service and is supported by the National Acute Porphyria Service (NAPS). We gratefully acknowledge the clinical impact of the evidence-based drug safety assessments provided on the comprehensive Drug Database for Acute Porphyria (www.drugs-porphyria.org) on the range of available medicines for porphyria patients.

N.B. Some drugs may be included under their group name and not their individual drug name.

Abacimab	Cycloserine	Laxatives	Prampexole
Acamprosate	Dabigatran	Lidocaine	Pregabalin
ACE Inhibitors	Desferrioxamine	Lercanidipine	Prilocaine
Acetazolamide	Desflurane	Levetiracetam	Primidone
Acetylcysteine	Desloratadine	Levomopromazine	Prochlorperazine
Acidovir	Dextromethorphan	Levothyroxine sodium	Proguanil
Adenosine	Diamorphine	Lidocaine ²	Promethazine
Adrenaline	Diazepam	Linezolid	Propofol ¹
Aflentanil	Dicycloverine	Lithium salts	Propylthiouracil
Alginates	Digoxin	Loperamide	Proton Pump Inhibitors
Alopatholol	Dihydrocodeine	Loratadine	Pseudoephedrine
Aluminium salts	Dinoprostone	Lorazepam	Pyrazinamide
Amlodine	Diphendramine	Lymecycline	Pyridoxamine
Aminoglycosides	Dobutamine	Magnesium salts	Quinine
Amisulpride	Domperidone	Molindone ⁵	Quinolones ⁶
Amtriptiline	Dopamine	Mefloquine	Ranitidine
Amiodipine	Doxazosin	Melatonin	Remifentanyl
Amphotericin	Doxycycline	Meloxicam	Rivaroxaban
Angiotensin II inhibitors	Duloxetine	Memantine	Rivastigmine
Antimuscarinic bronchodilators	Epinephrine	Mepivacaine	Selective beta ₂ agonists
Antiplatelet drugs	Eplerenone	Mesalazine	Sevelamer
Apixaban	Epoetin & analogues	Metformin	SGLT-2 inhibitors ⁶
Articaine	Etanercept	Methadone	Sildenafil ¹
Aspirin	Ethambutol	Methotrexate	Sodium bicarbonate
Atomoxetine	Etoricoxib	Methylphenidate	Sodium fusidate
Atovaquone	Ezetimibe	Metoclopramide	Solfenacin
Atropine	Famciclovir	Metronidazole	SSRIs ⁶
Azathioprine	Felodipine	Midazolam ¹	Statins
Azithromycin	Fentanyl	Mirabegron	Strontium
Aztreonam	Fexofenadine	Mirtazapine	Suplind
Baclofen	Fibrates ¹	Mizolastine	Suxamethonium
Balsalazide	Fibrinolytic drugs	Monoclonal antibodies	Tacrolimus
Barium sulphate	Fucosylates	Morphine	Tadalafil
Bendroflumethiazide	Fiumazenil	Moxonidine	Tamsulosin
Beta-blockers	Fluphenazine	Muscle relaxants non-depolarising	Telocoplanin
Bile acid sequestrants	Fondaparinux	Mycophenolate salts	Temazepam
Bisphosphonates	Furosemide	Nifedipine	Terazosin
Bumetanide	Gabapentin	Nadolol	Terbinafine
Bupivacaine	Ganciclovir	Naloxone	Tetraosaccharide
Buprenorphine	G-CSF	Naproxen	Theophylline
Calcium salts	Gemprost	Neostigmine	Tirofiban
Carbapenems	Glipizide	Nicotine replacement therapy	Toiletrodine
Carbamazole	Glipitins ³	Nifedipine	Tramadol
Carboprost	Glucagon	Nimodipine	Tranexamic acid
Casopfungin	Glucosamine	Nitrous oxide	Trazodone
Celecoxib	Glycerol trinitrate	Noradrenaline/Norepinephrine	Trifluoperazine
Cephalosporins	Glycopyrronium	Nortriptyline	Triptans ³
Ceftriaxone	Granisetron	Ursodeoxycholic acid	Vaccines ⁷
Chloroquine	Haloperidol	Vaccines ⁷	Vaccines ⁷
Chlorphenamine	Heparin	Valaciclovir	Vaccines ⁷
Chlorpromazine	Heparin-low molecular weight	Valganciclovir	Vaccines ⁷
Closporon	Hyoscine salts	Valganciclovir	Vaccines ⁷
Cimetidine	Immunoglobulins	Vancomycin	Venlafaxine
Clobazam	Indometacin	Vigabatrin	Vitamin
Clozapem	Insulin	Vitamin	Warfarin
Clozapine	Iodine based contrast media	Warfarin	Zanamilvir
Co-amoxiclav	Iron	Penicillamine	Zinc preparations
Codine phosphate	Isotriamterol	Penicillins ⁴	Zonisamide
Colchicine	Isosorbide mononitrate	Pethidine	Zopiclone
Corticosteroids	Lacosamide	Phenytoin	
Cyclizine	Lamotrigine	Phosphate salts	
Cyclopenthiadiazide	Lamotrigine	Pliglitazone	

- Ciprofibrate has not been classified and should not be used
- Intravenous doses should be used with caution.
- Clinical safety has not been assessed for continuous use of these preparations.
- Pivmecillinam considered unsafe, temocillin and ticarcillin – not classified; conflicting safety advice for fusicoxacin. Contact UKPMIS for further advice. All topical preparations (including topical antifungals, lice treatments & eye drops) are considered safe, when applied to intact skin or mucosa.

- Nalidixic acid is unsafe and should not be used.
- Floratriptan has not been assessed as safe.

- An acute attack has been reported following yellow fever vaccine, so caution should be observed when using any live vaccine in adults.

³Glipitins = DPP-4 inhibitors = alogliptin, linagliptin, saxagliptin, sitagliptin, vildagliptin;
⁴SSRIs = Selective Serotonin Reuptake Inhibitor antidepressants

⁶SGLT-2 inhibitors = canagliflozin, dapagliflozin, empagliflozin;
 Written May 2017; Review May 2018

Anaesthesia & peri-operative drugs

Articaine
 Atropine
 Bupivacaine
 Desflurane
 Isoflurane
 Lidocaine²
 Mepivacaine
 Midazolam¹
 Muscle relaxants non-depolarising
 Neostigmine
 Nitrous oxide
 Prilocaine
 Propofol¹
 Remifentanyl
 Suxamethonium

Analgesics

Aflentanil
 Aspirin
 Buprenorphine
 Celecoxib
 Codeine phosphate
 Diamorphine
 Dihydrocodeine
 Etoricoxib
 Fentanyl
 Ibuprofen
 Indometacin
 Ketoprofen
 Meloxicam
 Methadone
 Morphine
 Naproxen
 Oxycodone
 Paracetamol
 Pethidine
 Tramadol

Antibacterial agents

Aminoglycosides
 Azithromycin
 Clazopline
 Fluphenazine
 Haloperidol
 Olanzapine
 Sulpride
 Trifluoperazine

Anticonvulsants

Clobazam
 Clonazepam
 Gabapentin
 Lacosamide
 Lamotrigine
 Levetiracetam
 Paraldehyde
 Pregabalin
 Vigabatrin
 Zonisamide

Antidepressants

Amtriptiline
 Duloxetine
 Mirazapine
 Nortriptyline
 SSRIs⁶
 Trazodone
 Venlafaxine

Antifungals/Antivirals

Aciclovir
 Amphotericin
 Caspofungin
 Famciclovir
 Flucytosine
 Ganciclovir
 Nystatin
 Osetamivir
 Terbinafine
 Valaciclovir
 Valganciclovir
 Zanamilvir

Antihistamines

Cetirizine
 Chlorphenamine
 Desloratadine
 Diphenhydramine
 Fexofenadine
 Loratadine
 Mizolastine
 Promethazine

Antipsychotics

Amisulpride
 Chlorpromazine
 Clozapine
 Fluphenazine
 Haloperidol
 Olanzapine
 Sulpride
 Trifluoperazine

Cardiovascular agents

Abacimab
 ACE Inhibitors
 Adenosine
 Amilorin
 Amlodipine
 Amiodipine
 Angiotensin II Inhibitors
 Antiplatelet drugs
 Bendroflumethiazide
 Beta-blockers
 Bumetanide
 Cyclopenthiadiazide
 Dabigatran
 Digoxin
 Dobutamine
 Dopamine
 Doxazosin
 Epinephrine
 Eplerenone
 Felodipine
 Furosemide

Glycerol trinitrate
 Isosorbide mononitrate
 Lercanidipine
 Mexonidine
 Nafidrofuryl
 Nifedipine
 Nimodipine
 Noradrenaline/Norepinephrine
 Rivaroxaban
 Terazosin
 Tirofiban

Gastro-intestinal drugs

Alginates
 Balsalazide
 Cimetidine
 Dicycloverine
 Laxatives
 Loperamide
 Mebeverine
 Mesalazine
 Proton Pump Inhibitors
 Ranitidine

Immunosuppressants

Azathioprine
 Ciclosporin
 Corticosteroids
 Methotrexate
 Monoclonal antibodies
 Mycophenolate salts
 Tacrolimus

Lipid lowering agents

Bile acid sequestrants
 Ezetimibe
 Fibrates¹
 Statins

Malaria Prophylaxis

Atovaquone
 Chloroquine
 Mefloquine
 Proguanil

Obs & Gynae Drugs

Carboprost
 Dinoprostone
 Gemprost
 Oxytocin

Other

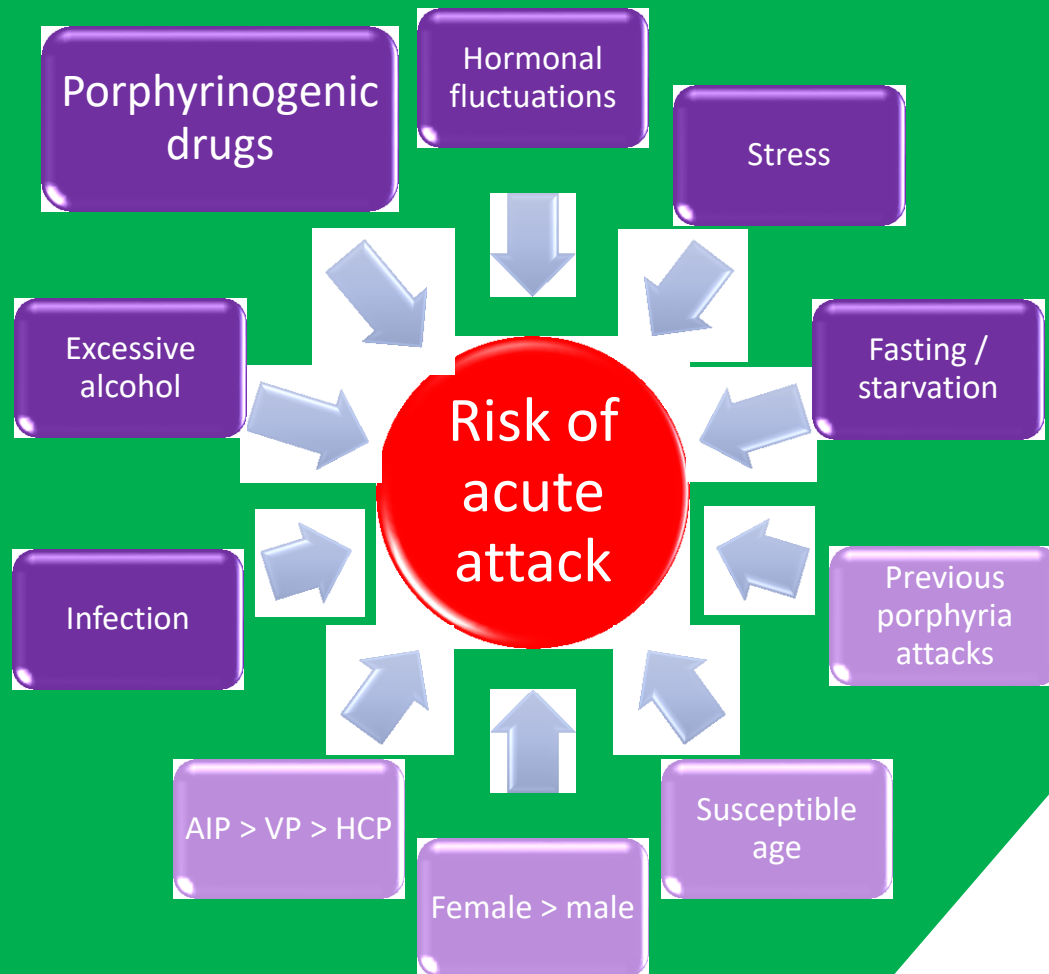
Acamprosate
 Acetazolamide
 Acetylcysteine
 Alogliptin
 Aluminium salts
 Antimuscarinic bronchodilators
 Apixaban
 Atomoxetine
 Baclofen
 Barium sulphate
 Bisphosphonates
 Calcium salts
 Carbimazole
 Clonidine
 Colchicine
 Desferrioxamine
 Dextromethorphan
 Diazepam
 Epoetin and analogues
 Etanercept
 Fibrinolytic drugs

Fiumazenil
 Fondaparinux
 G-CSF
 Glipizide
 Glipitins³
 Glucagon
 Glucosamine
 Glycopyrronium
 Heparin
 Heparin-low molecular weight
 Hyoscine salts
 Immunoglobulins
 Insulin
 Iodine based contrast media
 Iron
 Lefunomide
 Levomepromazine
 Levothyroxine sodium
 Lithium salts
 Lorazepam
 Magnesium salts
 Melatonin
 Memantine
 Metformin
 Methylphenidate
 Mirabegron
 Naloxone
 Nicotine replacement therapy
 Octreotide
 Orlistat
 Penicillamine
 Phenytoin
 Phosphate salts

See over the page for explanation of footnotes

This safe list is based on the best information available to us at the time of compilation and provides guidance on drugs to use first line. It is not intended to be comprehensive. Inclusion of a drug does not guarantee that it will be safe in all circumstances. For information on medication not listed and advice on the use of antiepileptics, anti-infectives or other complex treatment scenarios please contact UKPMIS by telephone (029 2074 3877), by fax (029 2074 3879) or see our website <https://www.wmhc.wales.nhs.uk/specialist-services/drugs-in-porphyria/>. Unfortunately we are unable to accept enquiries via e-mail. Healthcare professionals requiring clinical advice on management of acute porphyria attacks should contact NAPS on 029 2074 7747.

Precipitating / risk factors



What's the problem with drugs?

- Increased haem production so greater build up of haem precursors
- Increased or decreased action of certain liver enzymes
- Female sex hormones
- Side effects



How do we work out if a drug is safe or not?

- Complex process!
- Limited information for many drugs
- Lots of grey areas
- Limited knowledge of many healthcare professionals about porphyria



Considerations



- Individual risks
 - Type of porphyria
 - Gender
 - Age
 - History of attacks, especially drug induced
- Potential for the drug to cause attack
 - Information from several databases
 - Can vary in classification
 - Based on lab data, clinical experience, and an understanding of how drugs are processed by the body

Considerations

- Clinical need for the drug?
 - In serious or life-threatening situations necessary drugs should not be withheld on the basis of porphyria
- Is there a safer alternative?
- What needs to be monitored?



NAPOS



- <http://www.drugs-porphyria.org>
- 5 point classification:

Not porphyrinogenic (NP)
Probably not porphyrinogenic (PNP)
Possibly porphyrinogenic (PSP)
Probably porphyrinogenic (PRP)
Porphyrinogenic (P)

- Clinical explanation behind classification

What can I do?



- Encourage your healthcare professionals to talk to us about treatment options
- Take a copy of the UKPMIS safe list with you whenever seeing a healthcare professional
- If you want to double check, feel free to call and check with a UKPMIS specialist – 029 2074 2979

<https://www.wmic.wales.nhs.uk/>



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