

What are the restrictions on prescribing for patients with non-acute porphyria?

Background

The porphyrias can be split into two types according to whether they cause acute attacks or whether they have mainly skin effects. This advice is intended for patients with non-acute porphyria (congenital erythropoietic porphyria, erythropoietic protoporphyria or porphyria cutanea tarda). Patients with non-acute porphyria do not experience acute attacks. Skin lesions develop in these patients when porphyrins accumulate in their skin, absorb energy from the sun and release it, allowing it to damage lower layers of skin (1).

Answer

Erythropoietic protoporphyria and congenital erythropoietic porphyria

If patients have unequivocally been diagnosed as having congenital erythropoietic porphyria (CEP) or erythropoietic protoporphyria (EPP), there are **NO UNSAFE DRUGS** (1).

Porphyria cutanea tarda

In **active** porphyria cutanea tarda (active skin lesions associated with increased circulating plasma porphyrins), all drugs are considered to be **SAFE**.

However caution should be exercised when using:

- High-dose chloroquine (2) or hydroxychloroquine (3)

Chloroquine mobilises porphyrins from the liver (2), allowing them to be excreted in the urine (4). Chloroquine phosphate 125mg to 250mg twice weekly is therefore given as a treatment for active porphyria cutanea tarda (4,5). Hydroxychloroquine 200mg twice weekly has also been used to treat porphyria cutanea tarda but the resulting remission is shorter than with chloroquine (5).

In active porphyria cutanea tarda, it is not recommended that high doses of chloroquine or hydroxychloroquine are given (e.g. chloroquine phosphate 500mg once weekly for the prophylaxis of malaria). The rapid mobilisation of porphyrins from the liver that may be caused by high-dose chloroquine can lead to acute hepatitis (6). Once active porphyria cutanea tarda has been treated

and urine porphyrin excretion has returned to normal (i.e. patient is in remission), the patient can be given malaria prophylaxis safely (7).

- Oestrogens

As oestrogens have been implicated in the pathogenesis of porphyria cutanea tarda (2), they should be avoided in patients with active porphyria cutanea tarda. If hormone replacement therapy is strongly indicated, treatment with oestrogens can be prescribed when a patient with porphyria cutanea tarda is in remission (2).

Summary

- Non-acute porphyrias include congenital erythropoietic porphyria, erythropoietic protoporphyria and porphyria cutanea tarda.
- If a person has an unequivocal diagnosis of congenital erythropoietic porphyria or erythropoietic protoporphyria, all drugs are considered to be safe.
- If a person has been diagnosed with porphyria cutanea tarda, all drugs are considered to be safe excepting oestrogens and high-dose chloroquine or hydroxychloroquine when the porphyria is active.

Limitations

Porphyria cutanea tarda can be precipitated by a number of factors including hepatic iron overload, significant alcohol use, oestrogen exposure (e.g. initiating treatment with hormone replacement therapy or in males, as treatment for prostate cancer), viral infections (such as hepatitis C and HIV), chemical toxicity, liver dysfunction and systemic conditions such as systemic lupus erythematosus and lymphoma (2). It is important to determine how the illness has been acquired. There are individual case reports of porphyria cutanea tarda presenting in patients taking methotrexate (8), pravastatin (9), olmesartan (10), carbamazepine (11) and tamoxifen (12-13), which has partial oestrogenic activity. It has also been reported during post-marketing experience with ofatumumab (14). However, there is insufficient evidence to suggest that these drugs should be avoided by patients with porphyria cutanea tarda. Advice should be sought from a Porphyria Specialist before stopping the patient's medication. Further information on the safety of medicines in non-acute porphyria can be obtained from the UK Porphyria Medicines Information Service (UKPMIS); Tel: 029 21842251 or at: <https://www.wmic.wales.nhs.uk/specialist-services/drugs-in-porphyria/>.

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Search strategy

1. Embase (porphyria cutanea tarda/dm, pc, th OR erythropoietic protoporphyria/dm, pc, th OR congenital erythropoietic porphyria/dm, pc, th)
2. Medline (PubMed: "porphyria cutanea tarda" OR "erythropoietic protoporphyria" OR "congenital erythropoietic porphyria" AND (prevention OR management))
3. In-house database/ resources ("cutanea tarda" (title) "erythropoietic protoporphyria" (title) OR "congenital erythropoietic porphyria" (title))
4. Micromedex (Congenital erythropoietic porphyria; Erythropoietic protoporphyria; Porphyrin cutanea tarda, Drugs that cause porphyria cutanea tarda)
5. NICE Evidence (Porphyria cutanea tarda; Erythropoietic protoporphyria; Congenital erythropoietic porphyria)
6. Internet Search (Google; non-acute porphyria drug administration)

[Mae'r daflen hon hefyd ar gael yn Gymraeg.](#) This leaflet is also available in Welsh.

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