

DRUG-INDUCED PHOTOSENSITIVITY (Part 1 of 4)

DEFINITION AND CLASSIFICATION

Drug-induced photosensitivity: cutaneous adverse events due to exposure to a drug and either ultraviolet (UV) or visible radiation. Reactions can be classified as either photoallergic or phototoxic drug eruptions, though distinguishing between the two reactions can be difficult and usually does not affect management.

The following criteria must be met to be considered as a photosensitive drug eruption:

- Occurs only in the context of radiation
- Drug or one of its metabolites must be present in the skin at the time of exposure to radiation
- Drug and/or its metabolites must be able to absorb either visible or UV radiation

	Photoallergic drug eruption	Phototoxic drug eruption
Description	Immune-mediated mechanism of action. Response is not dose-related. Occurs after repeated exposure to the drug	More frequent and result from direct cellular damage. May be dose-dependent. Reaction can be seen with initial exposure to the drug
Incidence	Low	High
Pathophysiology	Type IV hypersensitivity reaction	Direct tissue injury
Onset	>24hrs	<24hrs
Clinical appearance	Eczematous	Exaggerated sunburn reaction with erythema, itching, and burning
Localization	May spread outside exposed areas	Only exposed areas
Pigmentary changes	Unusual	Frequent
Histology	Epidermal spongiosis, exocytosis of lymphocytes and a perivascular inflammatory infiltrate	Necrotic keratinocytes, predominantly lymphocytic and neutrophilic dermal infiltrate

DIAGNOSIS

Most cases of drug-induced photosensitivity can be diagnosed based on physical examination, detailed clinical history, and knowledge of drug classes typically implicated in photosensitive reactions. Specialized testing is not necessary to make the diagnosis for most patients. However, in cases where there is no prior literature to support a photosensitive reaction to a given drug, or where the diagnosis itself is in question, implementing phototesting, photopatch testing, or rechallenge testing can be useful.

PHOTOSENSITIZING DRUGS¹

Generic	Brand	Type of Reaction	Notes
ANTIMICROBIALS			
Antibiotics: Beta-Lactams			
cefotaxime	—	Photodistributed telangiectasia	
ceftazidime	Fortaz, Tazicef	Increased susceptibility to sunburn	
Antibiotics: Fluoroquinolones			
ciprofloxacin	Cipro	Mild phototoxic potential. Photo-induced purpura have been reported. Persistent sequelae from phototoxicity in lung-transplant recipient on long-term immunosuppressive therapy	Typically a return to baseline 1wk after drug discontinuation
levofloxacin	Levaquin	Mild phototoxic potential. Photo-induced purpura have been reported.	
moxifloxacin	Avelox	More photostable and least phototoxic	
ofloxacin	—	Moderate to severe sunburn reactions	
Antibiotics: Tetracyclines			
doxycycline ²	Doryx, Vibramycin	Mild sunburn-like reactions with erythema and burning in sun-exposed areas; photodermatitis; solar urticaria, actinic granuloma, lichenoid reactions, nail dystrophy with photo-induced onycholysis, dyschromia. Nail effects can be delayed in presentation up to 2wks following sun exposure	Severe doxycycline-induced photo-onycholysis can occur at doses as low as 20mg/day in children
minocycline	Minocin, Solodyn		Generally not considered to be significant cause
tetracycline ²	—		
Antibiotics: Others			
dapsone	—	Phototoxic and photoallergic drug eruptions	
trimethoprim	—	Photosensitivity	
Antifungals			
griseofulvin	—		Not a potent photosensitizer. UVA implicated in photosensitivity
itraconazole	Sporanox, Tolsura	Photosensitivity in predominantly phototoxic pattern. Erythema, edema, vesicles in sun-exposed areas	Side effects reported following 5-day course oral therapy for candidiasis
ketoconazole	—	Photodermatitis	
terbinafine	—	Solar urticaria	
voriconazole ²	Vfend	Classic phototoxicity patterns, cheilitis, pseudoporphyria, photo-onycholysis	Second most commonly reported culprit in phototoxicity reactions. More likely in patients receiving long-term prophylactic therapy. Photosensitive eruptions occur months after drug initiation. Acute photodermatitis usually resolves upon discontinuation, however, photoaging and development of melanoma and squamous cell carcinoma in previously affected areas have been reported (esp. in children).

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DRUG-INDUCED PHOTOSENSITIVITY (Part 2 of 4)

Generic	Brand	Type of Reaction	Notes
ANTIMICROBIALS (continued)			
Antimalarials			
atovaquone/proguanil	Malarone	Blisters and skin sloughing on sun-exposed areas	Occurred within hours of exposure and resolved within days of discontinuation. Confirmed by photopatch testing.
chloroquine	—	Drug-induced photodermatoses	Also used for photoprotective effects in photosensitivity conditions (eg, polymorphous light eruption, SLE). Occur within days to weeks of starting drug and resolve after discontinuation.
hydroxychloroquine	Plaquenil		
quinine	Qualaquin	Photoallergic and phototoxic reactions. Photosensitive dermatosis (edematous, eczematous, lichenoid); photo-onycholysis	Routinely confirmed by photopatch testing
Antiretrovirals			
efavirenz	Sustiva	Photosensitive eruptions (eg, polymorphous light eruption, porphyria cutanea tarda, actinic prurigo, chronic actinic dermatitis, photosensitive granuloma annulare, lichenoid photoeruption)	Photosensitive eruptions can occur in HIV patients, independent of drug
tenofovir	Vemlidy, Viread		
Antituberculosis			
isoniazid	—	Photosensitive dermatoses, lichenoid eruption	Confirmed by photopatch and re-challenge testing
pyrazinamide	—	Photosensitive dermatoses	Confirmed by re-challenge testing
CARDIOVASCULAR AGENTS			
Antihypertensives: ACE Inhibitors			
enalapril	Vasotec	Photosensitivity	
quinapril	Accupril		
ramipril	Altace		
Antihypertensives: Angiotensin Receptor Blockers			
candesartan	Atacand	Photosensitivity	
irbesartan	Avapro		
losartan	Cozaar		
olmesartan	Benicar		
telmisartan	Micardis		
valsartan	Diovan		
Antihypertensives: Diuretics			
furosemide	Lasix	Bullous eruptions (mimicking Brunsting-Perry-type presentation of localized bullous pemphigoid)	Chronic eczematous photosensitivity reported lasting months to years after discontinuation
hydrochlorothiazide	—	Exaggerated sunburn reactions, eczematous lesions in photodistributed pattern, lichenoid eruptions, photoleukomelanoderma	
indapamide	—	Photo-onycholysis	
triamterene	Dyrenium	Photosensitivity	Confirmed by photopatch testing
Antihypertensives: Calcium Channel Blockers			
amlodipine	Norvasc	Photodistributed facial telangiectasia	May cross react with nifedipine
diltiazem	Cardizem	Photodistributed hyperpigmentation, photosensitive dermatitis	May cross react with amlodipine
nifedipine	Procardia	Photodistributed facial telangiectasia, photodermatitis	
Antihypertensives: Others			
methyl dopa	—	Photosensitivity	
Antiarrhythmics			
amiodarone ²	—	Burning/tingling sensation in sun-exposed skin followed by development of erythema and eczema, pseudoporphyria; blue-grey hyperpigmentation on sun-exposed areas	Hyperpigmentation seen in long-term, high-dose therapy. Resolves within months of discontinuation; pigmentation fades over 1-2yrs.
	Nexterone		
dronedarone	Multaq	Photosensitivity	Significantly less phototoxic than amiodarone
quinidine	—	Eczematous dermatitis, lichenoid eruption, livedoid purpuric eruption, photoallergic reaction	
Cholesterol-Lowering Agents			
atorvastatin	Lipitor	Edematous erythema on sun-exposed areas	
fenofibrate	Tricor	Eczematous photosensitivity, lichenoid photosensitivity	
pravastatin	Pravachol	Photodistributed erythema multiforme	
simvastatin	Zocor	Persistent photodistributed dermatitis, photodistributed erythema multiforme	

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DRUG-INDUCED PHOTSENSITIVITY (Part 3 of 4)

Generic	Brand	Type of Reaction	Notes
CHEMOTHERAPY			
bicalutamide	Casodex	Photosensitivity	Seen in patients with prostate cancer
capecitabine	Xeloda	Photodistributed lichenoid eruptions	Less photosensitizing than fluorouracil. Alternative treatment for those unable to tolerate fluorouracil
crizotinib	Xalkori	Phototoxicity	
dacarbazine	—	Photosensitive eruptions	Can switch to temozolomide if unable to tolerate
doxorubicin	Doxil	Photosensitivity	
epirubicin	Ellence	Bullous eruption	
erlotinib	Tarceva	Photosensitivity	
fluorouracil	—	Photosensitive eruptions, enhanced sunburn reactions, photodistributed hyperpigmentation, polymorphous light eruption-like reactions	
flutamide	—	Photosensitivity	Seen in patients with prostate cancer
hydroxyurea	Droxia, Hydrea	Photodistributed dermatitis, photodistributed granulomatous rash	Seen in patients with chronic myeloid leukemia
imatinib	Gleevec	Exaggerated sunburn reactions, photo-induced dermatitis, pseudoporphyria	Seen in patients treated for chronic myelogenous leukemia. Dermatitis may resolve upon drug withdrawal and recur upon rechallenge
paclitaxel	Abraxane	Photodistributed erythema multiforme, onycholysis	Photosensitive reactions also reported for nab-paclitaxel
vandetanib	Caprelsa	Photodistributed erythematous, vesiculobullous eruption, erythema multiforme-like lesions, pigmentation in photo-exposed areas	Seen in patients treated for thyroid, lung, and hepatocellular carcinoma
vemurafenib ²	Zelboraf	Phototoxicity	Common culprit
vinblastine	—	Photosensitivity	
NSAIDS			
celecoxib	Celebrex	Photoallergic reactions and pseudoporphyria	
diclofenac	Arthrotec	Photo-onycholysis	
indomethacin	Indocin	Pseudoporphyria, erythema multiforme, lichenoid eruptions	
meclofenamate	—		
nabumetone	—		
naproxen ²	Aleve	Pseudoporphyria, erythema multiforme, lichenoid eruptions	Most photosensitizing potential
oxaprozin	Daypro	Pseudoporphyria, erythema multiforme, lichenoid eruptions	
piroxicam ²	Feldene	Vesiculobullous, eczematous, lichenoid reactions	
sulindac	—	Pseudoporphyria, erythema multiforme, lichenoid eruptions	
PSYCHOTROPIC AGENTS			
Antidepressants			
citalopram	Celexa	Photodistributed hyperpigmentation	
clomipramine	Anafranil	Photoallergy	
escitalopram	Lexapro	Erythroderma on sun-exposed areas	
fluoxetine	Prozac	Erythema, blisters	
fluvoxamine	—	Photosensitivity	
imipramine	Tofranil	Photodistributed erythema, blue-grey hyperpigmentation in photodistributed areas	Hyperpigmentation seen in long-term use
paroxetine	Paxil	Photosensitivity, photodistributed granuloma annulare	
phenelzine	Nardil	Clinical photosensitivity	
sertraline	Zoloft	Macular erythematous photoallergic reaction	
venlafaxine	Effexor XR	Photodistributed telangiectasia	
Antipsychotics			
aripiprazole	Abilify	Photo-onycholysis	
chlorpromazine ²	—	Exaggerated sunburn reactions, lichenoid reactions, bullous eruptions; photodistributed slate-grey to violaceous hyperpigmentation	Hyperpigmentation seen in long-term, high-dose therapy. Routinely confirmed by photopatch testing.
clozapine	Clozaril	Photosensitivity, vasculitis, erythema multiforme, skin pigmentation	
haloperidol	Haldol	Photosensitive dermatitis	
olanzapine	Zyprexa	Photo-onycholysis	
risperidone	Risperdal	Photosensitivity	
thioridazine ²	—	Photodistributed slate-grey to violaceous hyperpigmentation	Seen in long-term, high-dose therapy

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DRUG-INDUCED PHOTSENSITIVITY (Part 4 of 4)

Generic	Brand	Type of Reaction	Notes
PSYCHOTROPIC AGENTS (continued)			
Anxiolytics			
alprazolam	Xanax	Pruritic erythema in sun-exposed areas	
chlordiazepoxide	—	Photo-induced eczematous eruption	
OTHERS			
carbamazepine	Tegretol	Photosensitive eczematous eruptions, lichenoid eruptions	Carbamazepine-induced facial burns occurred in one patient due to prolonged use of a photocopier
clopidogrel	Plavix	Lichenoid photodistributed eruption	
diphenhydramine	Benadryl	Photosensitivity	
eculizumab	Soliris		
esomeprazole	Nexium	Photosensitive dermatitis	Resolved upon discontinuation
ethinyl estradiol	—	Photosensitive eruptions, erythematous vesicular eruptions	
glyburide	Diabeta, Glynase	Eczematous photodermatitis	
isotretinoin	Absorica, Amnesteem		No clinical or experimental evidence confirming isotretinoin-induced photosensitivity
leflunomide	Arava	Photosensitivity	
mesalamine	Lialda, Pentasa		
mesna	Mesnex		
metformin	Fortamet	Erythematous and eczematous photosensitivity eruptions	
pantoprazole	Protonix	Photosensitivity	
pirfenidone	Esbriet	Exfoliative erythema, photoleukmelanoderma	
ranitidine	—	Papulosquamous eruption on sun-exposed skin	Normalization upon discontinuation. No recurrence upon re-initiation
sitagliptin	Januvia	Prolonged photosensitive eruption	
tocilizumab	Actemra	Photosensitivity	

PREVENTION AND MANAGEMENT

- Caution patients of the potential reaction for drugs considered to be potent photosensitizers; monitor.
- Emphasize sun avoidance and sun protection upon treatment initiation.
- Discontinue offending drug once diagnosis of drug-induced photosensitivity is made. Implement secondary preventive measures (eg, sun avoidance esp. during peak daylight hours, use of sun protective clothing and sunscreens with both UVA and UVB protection) if drug discontinuation is not possible.
- Administer medication in the evening if appropriate.
- Use of topical or systemic corticosteroids may be helpful to treat drug-induced photosensitive eruptions in symptomatic patients.

NOTES

Key: ACE = angiotensin-converting enzyme; SLE = systemic lupus erythematosus

¹ Drugs that have been reported in medical literature to cause clinical photosensitivity are listed. Most of this literature consist of case reports and case series. Due to underreporting, it is difficult to ascertain the true incidence of photosensitivity reactions. Topically administered drugs that cause photosensitivity have been excluded, as well as drugs that cause photosensitivity as part of their desired mechanism of action.

² Considered to be potent and common causes of photosensitivity.

Not an inclusive list of medications and/or official indications. Please see drug monograph at www.eMPR.com and/or contact company for full drug labeling.

REFERENCES

Adapted from Blakely KM, Drucker AM, Rosen CF. Drug-Induced Photosensitivity - An Update: Culprit Drugs, Prevention and Management. *Drug Safety*. 2019; 42:827-847. <https://doi.org/10.1007/s40264-019-00806-5>.

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