6. Hale G, *et al.* Alemtuzumab (Campath-1H) for treatment of lymphoid malignancies in the age of nonmyeloablative conditioning? *Bone Marrow Transplant* 2002; **30:** 797–804.
7. Frampton JE, Wagstaff AJ. Alemtuzumab. *Drugs* 2003; **63:** 1229–43.
8. Keating M, *et al.* Management guidelines for use of alemtuzumab in B-cell chronic lymphocytic leukemia. *Clin Lymphoma* 2004; **4:** 220–7.
9. Faderl S, *et al.* The evolving role of alemtuzumab in management of patients with CLL. *Leukemia* 2005; **19:** 2147–52.
10. Morris PJ, Russell NK. Alemtuzumab (Campath-1H): a systematic review in organ transplantation. *Transplantation* 2006; **81:** 1361–7.
11. Magliocca JF, Knechtle SJ. The evolving role of alemtuzumab (Campath-1H) for immunosuppressive therapy in organ transplantation. *Transpl Int* 2006; **19:** 705–14.
12. Ravandi F, O'Brien S. Alemtuzumab in CLL and other lymphoid neoplasms. *Cancer Invest* 2006; **24:** 718–25.
13. Hillmen P, *et al.* Alemtuzumab compared with chlorambucil as first-line therapy for chronic lymphocytic leukemia. *J Clin Oncol* 2007; **25:** 5616–23.

Administration. Subcutaneous use of alemtuzumab has been investigated as a means of reducing adverse infusion reactions associated with intravenous dosage. Studies have found it to be safe and effective.[1,2] Similar blood concentrations are achieved to those after intravenous use, although accumulation in the blood took longer to achieve with subcutaneous use, and higher cumulative doses were required.[3] Prolonged treatment with subcutaneous low-dose alemtuzumab (10 mg three times weekly for 18 weeks) has been reported to be as effective as intravenous infusion in patients with chronic lymphocytic leukaemia and a poor prognosis.[4]

1. Montillo M, *et al.* Safety and efficacy of subcutaneous Campath-1H for treating residual disease with chronic lymphocytic leukemia responding to fludarabine. *Haematologica* 2002; **87:** 695–700.
2. Lundin J, *et al.* Phase II trial of subcutaneous anti-CD52 monoclonal antibody alemtuzumab (Campath-1H) as first-line treatment for patients with B-cell chronic lymphocytic leukemia (B-CLL). *Blood* 2002; **100:** 768–73.
3. Hale G, *et al.* Blood concentrations of alemtuzumab and antiglobulin responses in patients with chronic lymphocytic leukemia following intravenous or subcutaneous routes of administration. *Blood* 2004; **104:** 948–55.
4. Cortelezzi A, *et al.* A pilot study of low-dose subcutaneous alemtuzumab therapy for patients with hemotherapy-refractory [sic] chronic lymphocytic leukemia. *Haematologica* 2005; **90:** 410–12.

Preparations

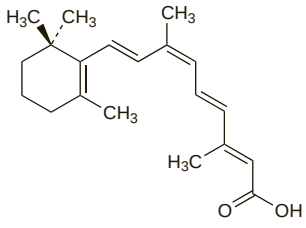
Proprietary Preparations (details are given in Part 3)
Arg.: Campath; ***Austria:*** MabCampath; ***Belg.:*** MabCampath; ***Braz.:*** Campath; ***Cz.:*** MabCampath; ***Denm.:*** MabCampath; ***Fin.:*** MabCampath; ***Fr.:*** MabCampath; ***Ger.:*** MabCampath; ***Gr.:*** MabCampath; ***Hung.:*** MabCampath; ***Irl.:*** MabCampath; ***Israel:*** MabCampath; ***Ital.:*** MabCampath; ***Malaysia:*** MabCampath; ***Neth.:*** MabCampath; ***Norw.:*** MabCampath; ***Pol.:*** MabCampath; ***Port.:*** MabCampath; ***Rus.:*** Campath (Кампас); ***S.Afr.:*** MabCampath; ***Singapore:*** MabCampath; ***Spain:*** MabCampath; ***Swed.:*** MabCampath; ***Switz.:*** MabCampath; ***UK:*** MabCampath; ***USA:*** Campath.

Alitretinoin *(BAN, USAN, rINN)*

AGN-192013; Alitretinoiini; Alitretinoína; Alitrétinoïne; Alitretinoinum; ALRT-1057; BAL-4079; LG-100057; LGD-1057; NSC-659772; 9-*cis*-Retinoic Acid. (2*E*,4*E*,6*Z*,8*E*)-3,7-Dimethyl-9-(2,6,6-trimethyl-1-cyclohexen-1-yl)-2,4,6,8-nonatetraenoic acid.

Алитретиноин

$C_{20}H_{28}O_2$ = 300.4.
CAS — 5300-03-8.
ATC — L01XX22.
ATC Vet — QL01XX22.



Adverse Effects and Precautions

Local skin toxicity may occur with topical application of alitretinoin, in particular erythema and oedema, and in some patients this may be dose-limiting. Pain, paraesthesia, rashes, pruritus, exfoliative dermatitis, and other skin disorders may also occur locally. Lymphadenopathy, phlebitis, cellulitis, and bacterial infections have been reported. Alitretinoin may have a weak photosensitising effect, and patients should minimise exposure of treated areas to sunlight or other ultraviolet light during therapy.

Interactions

Use of products containing diethyltoluamide is not recommended during alitretinoin therapy, as *animal* studies indicate an increase in diethyltoluamide toxicity with concurrent use.

Pharmacokinetics

Systemic absorption of topical alitretinoin is not considered to be extensive. *In-vivo* studies of oral doses indicate that alitretinoin is metabolised to 4-oxo-9-*cis*-retinoic acid.

Uses and Administration

Alitretinoin is a retinoid related to tretinoin (p.1618). It is used topically, as a 0.1% gel, in the management of cutaneous lesions in patients with AIDS-related Kaposi's sarcoma (p.675). It is applied directly to the lesions twice daily, increasing to up to 4 times daily if tolerated. Doses should be increased at intervals of at least 2 weeks. If local toxicity occurs, application frequency should be reduced, or treatment temporarily stopped, until the symptoms subside. EU licensed product information states that if no response is seen after 12 weeks, therapy should be stopped; however, US licensed product information states that some patients have required over 14 weeks to respond. Treatment may be continued as long as the patient responds. Oral formulations of alitretinoin are under investigation for the treatment of chronic hand dermatitis refractory to topical corticosteroids.

◊ References.

1. Cheer SM, Foster RH. Alitretinoin. *Am J Clin Dermatol* 2000; **1:** 307–14.
2. Bodsworth NJ, *et al.* Phase III vehicle-controlled, multi-centered study of topical alitretinoin gel 0.1% in cutaneous AIDS-related Kaposi's sarcoma. *Am J Clin Dermatol* 2001; **2:** 77–87.
3. Miles SA, *et al.* Antitumor activity of oral 9-cis-retinoic acid in HIV-associated Kaposi's sarcoma. *AIDS* 2002; **16:** 421–9.
4. Kurie JM, *et al.* Treatment of former smokers with 9-cis-retinoic acid reverses loss of retinoic acid receptor-beta expression in the bronchial epithelium: results from a randomized placebo-controlled trial. *J Natl Cancer Inst* 2003; **95:** 206–14.
5. Aboulafia DM, *et al.* 9-cis-Retinoic acid capsules in the treatment of AIDS-related Kaposi sarcoma: results of a phase 2 multicenter clinical trial. *Arch Dermatol* 2003; **139:** 178–86.
6. Ruzicka T, *et al.* Oral alitretinoin (9-cis-retinoic acid) therapy for chronic hand dermatitis in patients refractory to standard therapy: results of a randomized, double-blind, placebo-controlled, multicenter trial. *Arch Dermatol* 2004; **140:** 1453–9.
7. Ruzicka T, *et al.* Efficacy and safety of oral alitretinoin (9-cis retinoic acid) in patients with severe chronic hand eczema refractory to topical corticosteroids: results of a randomized, double-blind, placebo-controlled, multicentre trial. *Br J Dermatol* 2008; **158:** 808–17.

Preparations

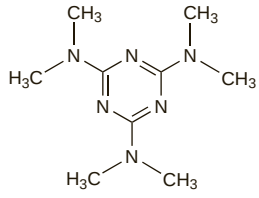
Proprietary Preparations (details are given in Part 3)
Arg.: Panretin; ***Cz.:*** Panretin; ***Fr.:*** Panretin; ***Ger.:*** Panretin; ***Gr.:*** Panretin; ***Neth.:*** Panretin; ***Port.:*** Panretin; ***USA:*** Panretin.

Altretamine *(BAN, USAN, rINN)*

Altretamiini; Altretamin; Altretamina; Altrétamine; Altretaminum; Hexamethylmelamine; HMM; NSC-13875; WR-95704. 2,4,6-Tris(dimethylamino)-1,3,5-triazine; N^2,N^2,N^4,N^4,N^6,N^6-Hexamethyl-1,3,5-triazine-2,4,6-triamine.

Альтретамин

$C_9H_{18}N_6$ = 210.3.
CAS — 645-05-6.
ATC — L01XX03.
ATC Vet — QL01XX03.



Pharmacopoeias. In *Chin.* and *US*.
USP 31 (Altretamine). A white crystalline powder. Insoluble in water; soluble in chloroform. Store in airtight containers.

Adverse Effects, Treatment, and Precautions

For a general outline see Antineoplastics, p.635, p.639, and p.641.

Bone-marrow depression is usually moderate, manifesting as leucopenia, thrombocytopenia, and anaemia, and may require dosage reduction; blood counts should be monitored regularly. Nausea and vomiting are common and usually moderate although they may be dose-limiting. Prolonged or high-dose therapy may be associated with neurotoxicity, both peripheral (neuropathies) and central (ataxia, depression, confusion, drowsiness, and hallucinations); neurological examination should be performed regularly and treatment interrupted or the dose reduced as appropriate. Renal toxicity may also be dose-limiting. Other rare adverse effects include rashes, alopecia, and hepatic toxicity.

Handling. Altretamine is irritant; avoid contact with skin and mucous membranes.

Interactions

For a general outline of antineoplastic drug interactions, see p.642. Pyridoxine appears to reduce the activity of altretamine.

Antidepressants. Severe and potentially life-threatening orthostatic hypotension developed in 3 patients who took *amitriptyline* or *imipramine* with altretamine and in a fourth patient who took *phenelzine* and altretamine.[1] One patient was able to tolerate the antineoplastic with *nortriptyline*.

1. Bruckner HW, Schleifer SJ. Orthostatic hypotension as a complication of hexamethylmelamine antidepressant interaction. *Cancer Treat Rep* 1983; **67:** 516.

Pharmacokinetics

Altretamine is well absorbed from the gastrointestinal tract after oral doses, but is rapidly demethylated in the liver producing variation in plasma-altretamine concentrations. The principal metabolites are pentamethylmelamine and tetramethylmelamine, which are excreted in urine. The elimination half-life has been reported to be 4 to 10 hours.

◊ References.

1. Damia G, D'Incalci M. Clinical pharmacokinetics of altretamine. *Clin Pharmacokinet* 1995; **28:** 439–48.

Uses and Administration

Altretamine is an antineoplastic agent structurally similar to the alkylating agent tretamine (triethylenemelamine) although its mode of action may be different. It is given orally and is licensed for use as a single agent in the palliative treatment of ovarian carcinoma (p.670). Altretamine has also been tried in lung cancer. The usual dose as a single agent in ovarian cancer is 260 mg/m^2 daily in four divided doses, for 14 or 21 consecutive days out of a 28-day cycle. Up to 12 cycles may be given. Therapy should be interrupted for at least 14 days, and subsequently restarted at a lower dose of 200 mg/m^2 daily, if the white cell count falls below 2000 cells/mm^3 or the platelet count below 75 000 cells/mm^3 or if neurotoxic or intolerable gastrointestinal symptoms occur. Lower doses are also used in combination regimens.

◊ Reviews.

1. Lee CR, Faulds D. Altretamine: a review of its pharmacodynamic and pharmacokinetic properties, and therapeutic potential in cancer chemotherapy. *Drugs* 1995; **49:** 932–53.
2. Manetta A, *et al.* Hexamethylmelamine as a single second-line agent in ovarian cancer: follow-up report and review of the literature. *Gynecol Oncol* 1997; **66:** 20–6.

Preparations

USP 31: Altretamine Capsules.

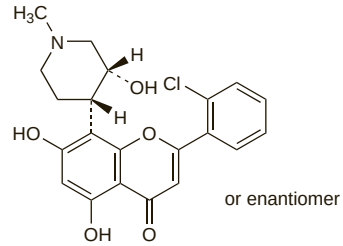
Proprietary Preparations (details are given in Part 3)
Austral.: Hexalen; ***Cz.:*** Tretax†; ***Neth.:*** Hexalen; ***Norw.:*** Hexalen†; ***NZ:*** Hexalen†; ***Rus.:*** Hexalen (Гексален); ***Swed.:*** Hexalen†; ***Thai.:*** Hexalen; ***USA:*** Hexalen.

Alvocidib *(rINN)*

Alvocidibum; Avodenib; Flavopiridol. (–)-*cis*-2-(2-Chlorophenyl)-5,7-dihydroxy-8-(3-hydroxy-1-methylpiperidin-4-yl)-4*H*-1-benzopyran-4-one.

Альвоцидиб

$C_{21}H_{20}ClNO_5$ = 401.8.
CAS — 146426-40-6.



Alvocidib Hydrochloride *(rINNM)*

Alvocidib *(USAN)*; Alvocidib, Chlorhydrate d'; Alvocidibi Hydrochloridum; Hidrocloruro de alvocidib; HL-275; HMR-1275; L-868275; MDL-107826A; NSC-649890. (–)-*cis*-2-(2-Chlorophenyl)-5,7-dihydroxy-8-(3-hydroxy-1-methylpiperidin-4-yl)-4*H*-1-benzopyran-4-one hydrochloride.

Альвоцидиба Гидрохлорид

$C_{21}H_{20}ClNO_5$,HCl = 438.3.
CAS — 131740-09-5.

Profile

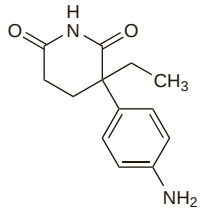
Alvocidib is an inhibitor of cyclin-dependent kinase that is under investigation as an antineoplastic for the treatment of chronic lymphocytic leukaemia.

Aminoglutethimide *(BAN, rINN)* ⊗

Aminoglutethimid; Aminoglutéthimide; Aminoglutethimidum; Aminoglutetimid; Aminoglutetimida; Aminoglutetimidas; Aminoglutetimidi; Aminoglythetimide; Ba-16038. 2-(4-Aminophenyl)-2-ethylglutarimide; 3-(4-Aminophenyl)-3-ethylpiperidine-2,6-dione.

Аминоглутетимид

$C_{13}H_{16}N_2O_2$ = 232.3.
CAS — 125-84-8.
ATC — L02BG01.
ATC Vet — QL02BG01.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *US*.

Ph. Eur. 6.2 (Aminoglutethimide). A white or slightly yellow, crystalline powder. Practically insoluble in water; freely soluble in acetone; soluble in methyl alcohol.

USP 31 (Aminoglutethimide). A white or creamy-white, fine, crystalline powder. Very slightly soluble in water; readily soluble in most organic solvents. It forms water-soluble salts with strong acids. The pH of a 0.1% solution in dilute methyl alcohol (1 in 20) is between 6.2 and 7.3.

Adverse Effects

The most frequent adverse effects reported with aminoglutethimide include drowsiness, lethargy, and skin rashes (sometimes with fever); these generally diminish after the first 6 weeks of therapy. Dizziness and nausea occasionally occur. Leucopenia, thrombocytopenia, agranulocytosis, or severe pancytopenia have occurred rarely. Adrenal insufficiency may rarely occur, and there have been reports of other endocrine disturbances including hypothyroidism, and virilisation. Other rare effects include ataxia, headache, depression, gastrointestinal disturbances, hypercholesterolaemia, and orthostatic hypotension.

Overdosage may lead to CNS depression and impairment of consciousness, electrolyte disturbances, and respiratory depression.

Effects on the liver. Aminoglutethimide has been associated with reports of cholestatic jaundice, accompanied by rash[1,2] and fever,[2] and probably due to an idiosyncratic hypersensitivity reaction.[1] It has been suggested that liver function tests should be carried out in patients receiving aminoglutethimide who develop fever and eruptions.[2]

1. Gerber SB, Miller KB. Cholestatic jaundice and aminoglutethimide. *Ann Intern Med* 1982; **97:** 138.
2. Perrault DJ, Domovitch E. Aminoglutethimide and cholestasis. *Ann Intern Med* 1984; **100:** 160.

Effects on the lungs. Pulmonary infiltrates in a patient who developed progressive dyspnoea on starting therapy with aminoglutethimide were found to be due to diffuse alveolar damage and haemorrhage; thrombocytopenia was present but prothrombin and bleeding times were normal. The patient's gas exchange and chest radiographs improved on stopping aminoglutethimide and giving corticosteroids.[1] Blood and pulmonary eosinophilia, which resolved on stopping aminoglutethimide therapy, has also been reported.[2]

1. Rodman DM, *et al.* Aminoglutethimide, alveolar damage, and hemorrhage. *Ann Intern Med* 1986; **105:** 633.
2. Bell SC, Anderson EG. Pulmonary eosinophilia associated with aminoglutethimide. *Aust N Z J Med* 1998; **28:** 670–1.

Lupus. SLE occurred in a patient who received aminoglutethimide, and resolved when the drug was withdrawn.[1] In another report, however, a patient with a lupus-like syndrome had a reduction in disease activity when tamoxifen therapy was changed to aminoglutethimide.[2]

1. McCraken M, *et al.* Systemic lupus erythematosus induced by aminoglutethimide. *BMJ* 1980; **281:** 1254.
2. Etherington J, *et al.* Effect of aminoglutethimide on the activity of a case of a connective tissue disorder with features of systemic lupus erythematosus. *Lupus* 1993; **2:** 387.

Precautions

Aminoglutethimide inhibits adrenal steroid production so supplementary glucocorticoid therapy with hydrocortisone must normally be given, although supplementation may not be necessary in patients with Cushing's syndrome. Some patients also require a mineralocorticoid. It has been suggested that aminoglutethimide should be temporarily withdrawn in patients who undergo shock or trauma, or develop intercurrent infection.

Blood pressure, blood counts, and serum electrolytes should be regularly monitored during aminoglutethimide therapy and periodic monitoring of liver and thyroid function is recommended.

Aminoglutethimide should not be given during pregnancy as pseudohermaphroditism may occur in the fetus.

Aminoglutethimide frequently causes drowsiness: patients so affected should not drive or operate machinery.

Porphyria. Aminoglutethimide has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Interactions

The rate of metabolism of some drugs is increased by aminoglutethimide; patients also taking warfarin or other coumarin anticoagulants, theophylline, tamoxifen, medroxyprogesterone, or oral hypoglycaemics, may require increased dosages of these drugs. The metabolism of dexamethasone is also accelerated, which limits its value for corticosteroid supplementation in patients receiving aminoglutethimide. Use with diuretics may lead to hyponatraemia, while alcohol may potentiate the central effects of aminoglutethimide.

◊ See also references to aminoglutethimide's interactions with *digitoxin* (p.1259), *theophylline* (p.1144), *progestogens* (p.2126), *tamoxifen* (see Antineoplastics, p.774), and *anticoagulants* (under Warfarin, p.1429).

Pharmacokinetics

Aminoglutethimide is well absorbed after oral doses, with peak plasma concentrations occurring after 1 to 4 hours. It is metabolised in the liver, primarily to *N*-hydroxylaminoglutethimide and *N*-acetylaminoglutethimide, and appears to induce its own metabolism. The half-life, which is reported to be about 13 hours after a single dose, is decreased to around 9 hours after about 2 weeks of continuous therapy. Aminoglutethimide is excreted in urine, about half a dose being excreted unchanged and the remainder as metabolites. Only about 20 to 25% of a dose is bound to plasma protein.

Half-life. A study in 17 patients showed that the plasma half-life of aminoglutethimide had a mean value of 15.5 hours after single doses but fell to 8.9 hours during multiple-dose therapy.[1] This marked reduction could largely be attributed to a decrease in the volume of distribution; auto-induction of metabolism might be of less importance in decreasing half-life than had been previously suggested.

1. Lønning PE, *et al.* Single-dose and steady-state pharmacokinetics of aminoglutethimide. *Clin Pharmacokinet* 1985; **10:** 353–64.

Uses and Administration

Aminoglutethimide is an analogue of glutethimide (p.1000) and was formerly used for its weak anticonvulsant properties. Aminoglutethimide blocks the production of adrenal steroids and acts as an aromatase inhibitor to block the conversion of androgens to oestrogens (the major source of oestrogens in women without ovarian function). It was used in the treatment of metastatic breast cancer (p.661) in postmenopausal or oophorectomised women and as palliative treatment in men with advanced prostatic cancer (p.671).

Aminoglutethimide has also been used in the treatment of Cushing's syndrome (p.2344). Usual oral doses range from 1 to 2 g daily, in divided doses.

The *dextro*-isomer of aminoglutethimide, dexaminoglutethimide has been investigated.

Preparations

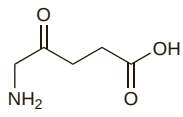
BP 2008: Aminoglutethimide Tablets;
USP 31: Aminoglutethimide Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Orimeten†; ***Austral.:*** Cytadren; ***Austria:*** Orimeten†; ***Belg.:*** Orimeten†; ***Braz.:*** Orimeten†; ***Chile:*** Orimeten†; ***Cz.:*** Orimeten†; ***Fr.:*** Orimetene†; ***Ger.:*** Orimeten†; ***Hong Kong:*** Orimetene; ***Ital.:*** Orimeten†; ***Malaysia:*** Orimetene†; ***Neth.:*** Orimeten†; ***NZ:*** Cytadren†; ***Rus.:*** Mamomit (Мамомит); Orimeten (Оримотен)†; ***S.Afr.:*** Orimeten†; ***Spain:*** Orimeten†; ***Switz.:*** Orimetene†; ***UK:*** Orimeten†; ***USA:*** Cytadren†.

5-Aminolevulinic Acid

ALA; 5-ALA; δ-Aminolaevulinic Acid; 5-Aminolaevulinic Acid; 5-Aminolevulínico, ácido. 5-Amino-4-oxopentanoic acid.

$C_5H_9NO_3$ = 131.1.
CAS — 106-60-5.
ATC — L01XD04.
ATC Vet — QL01XD04.



Aminolevulinic Acid Hydrochloride *(USAN)*

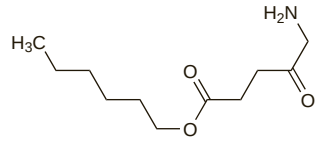
Aminolaevulinic Acid Hydrochloride; Aminolevulínico, hidrocloruro ácido. 5-Aminolevulinic acid hydrochloride.

$C_5H_9NO_3$, HCl = 167.6.
CAS — 5451-09-2.
ATC — L01XD04.
ATC Vet — QL01XD04.

Hexaminolevulinate Hydrochloride *(USAN)*

P-1026. Hexyl 5-amino-4-oxopentanoate hydrochloride.

$C_{11}H_{21}NO_3$,HCl = 251.8.
CAS — 140898-91-5.



(hexaminolevulinate)

Methyl Aminolevulinate Hydrochloride *(USAN)*

Methyl Aminolaevulinate Hydrochloride; Metilaminolevulinato, hidrocloruro de; P-1202. Methyl 5-amino-4-oxopentanoate hydrochloride.

$C_6H_{11}NO_3$,HCl = 181.6.
CAS — 79416-27-6.
ATC — L01XD03.
ATC Vet — QL01XD03.

Adverse Effects and Precautions

The mechanism of action of topical 5-aminolevulinic acid or its derivatives generally results in local phototoxicity, manifest as a localised burning or stinging sensation, erythema, oedema, pruritus, scabbing, or pain. Symptoms are usually mild to moderate, and transient. During treatment, patients should be advised to avoid sunlight or prolonged exposure to bright light.

Other common adverse effects on the skin include scaling or crusting, ulceration, suppuration, blistering, bleeding, sensation of heat, erosion or exfoliation, and skin infection. Urticaria, rash, and changes in skin pigmentation may also occur. Application site discharge, eczema, and allergic contact dermatitis have been reported. Other common adverse effects include paraesthesia and headache. Nausea, fatigue, eye swelling or eye pain, and wound haemorrhage have been reported.

Handling. US licensed product information warns that nitrile gloves should be worn during application and removal of methyl aminolevulinate hydrochloride cream; vinyl or latex gloves do not provide adequate protection.

Hypersensitivity. Allergic reactions to aminolevulinic acid[1] and methyl aminolevulinate[2] have been reported.

1. Gniazdowska B, *et al.* Allergic contact dermatitis from δ-aminolevulinic acid used for photodynamic therapy. *Contact Dermatitis* 1998; **38:** 348–9.
2. Wulf HC, Philipsen P. Allergic contact dermatitis to 5-aminolaevulinic acid methylester but not to 5-aminolaevulinic acid after photodynamic therapy. *Br J Dermatol* 2004; **150:** 143–5.

Porphyria. 5-Aminolevulinic acid and its derivatives are considered to be unsafe in patients with porphyria.

Interactions

Use with other known photosensitisers such as griseofulvin, thiazide diuretics, sulfonylureas, phenothiazines, sulfonamides, and tetracyclines might increase the photosensitivity reaction commonly seen with 5-aminolevulinic acid or its derivatives.

St John's wort. A patient taking St John's wort had a pronounced phototoxic reaction consisting of an erythematous rash and swelling of the face, neck, and hands, 6 hours after receiving oral aminolevulinic acid. Although both drugs have been associated with photosensitivity, the authors suggested a synergistic effect had occurred. Tests *in vitro* appeared to confirm this.[1]

1. Ladner DP, *et al.* Synergistic toxicity of δ-aminolaevulinic acid-induced protoporphyrin IX used for photodiagnosis and hypericum extract, a herbal antidepressant. *Br J Dermatol* 2001; **144:** 916–8.

Pharmacokinetics

After intravenous and oral doses of aminolevulinic acid hydrochloride equivalent to 100 mg of aminolevulinic acid, the mean half-life of aminolevulinic acid is stated to be about 0.83 hours and 0.7 hours, respectively; oral bioavailability is about 50 to 60%. *In-vitro* studies of dermal absorption found that the mean cumulative absorption of methyl aminolevulinate