

Fluorescein (BAN)

Fluoresceína; Fluoresceina; Fluorescine; Fluoresceinum. 3',6'-Di-hydroxyspiro[isobenzofuran-1(3H),9'(9H)xanthen]-3-one.

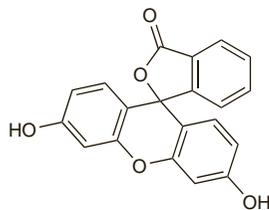
Флуоресцеин

C₂₀H₁₂O₅ = 332.3.

CAS — 2321-07-5.

ATC — S01JA01.

ATC Vet — QS01JA01.



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

Ph. Eur. 6.2 (Fluorescein). An orange-red, fine powder. Practically insoluble in water; soluble in hot alcohol. It dissolves in dilute solutions of alkali hydroxides. Protect from light.

USP 31 (Fluorescein). A yellowish-red to red, odourless powder. Insoluble in water; soluble in dilute alkali hydroxides. Store in airtight containers.

Fluorescein Dilaurate (BANM)

Fluoresceína, dilaurato de.

Флуоресцеина Дилаурат

C₄₄H₅₆O₇ = 696.9.

CAS — 7308-90-9.

ATC — S01JA01.

ATC Vet — QS01JA01.

Fluorescein Sodium (BANM)

CI Acid Yellow 73; Colour Index No. 45350; D & C Yellow No. 8; Fluorescein Natrium; Fluorescein sodná sůl; Fluoresceína sodíca; Fluorescine sodique; Fluoresceinnatrium; Fluoresceino natrio druska; Fluoresceinum natrium; Fluoresceinnatrium; Fluorescein Sodyum; Fluorescein-nátrium; Obiturin; Resorcinolphthalein Sodium; Sodium Fluorescein; Soluble Fluorescein; Uranin. Disodium fluorescein.

Флуоресцин Натрий

C₂₀H₁₀Na₂O₅ = 376.3.

CAS — 518-47-8.

ATC — S01JA01.

ATC Vet — QS01JA01.

NOTE. FLN is a code approved by the BP 2008 for use on single unit doses of eye drops containing fluorescein sodium where the individual container may be too small to bear all the appropriate labelling information. LIDFLN is a similar code approved for eye drops containing lidocaine hydrochloride and fluorescein sodium, and PROXFLN a code for eye drops containing proxymetacaine hydrochloride and fluorescein sodium.

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

Ph. Eur. 6.2 (Fluorescein Sodium). An orange-red, fine hygroscopic powder. Freely soluble in water; soluble in alcohol; practically insoluble in dichloromethane and in hexane. A 2% solution in water has a pH of 7.0 to 9.0. Store in airtight containers. Protect from light.

USP 31 (Fluorescein Sodium). An orange-red, hygroscopic, odourless powder. Freely soluble in water; sparingly soluble in alcohol. Store in airtight containers.

Adverse Effects and Precautions

The intravenous injection of fluorescein sodium may produce nausea and vomiting. Extravasation is painful. Hypersensitivity reactions range from urticaria to occasional instances of severe anaphylaxis. Cardiac arrests and fatalities have occurred rarely. Concern that impurities or a defect in manufacturing processes might be responsible for the serious reactions led to a review of the BP specification in the early 1980s and a reduction in the permitted level of impurities. Facilities for resuscitation should be available whenever fluorescein sodium is used intravenously.

The skin and urine may be coloured yellow but this is transient. Fluorescein sodium can stain skin, clothing, and soft contact lenses on contact. Intra-ocular fluorescein can produce transient blurring of vision.

Oral fluorescein dilaurate should not be given to patients with acute necrotising pancreatitis. Sulfasalazine may interfere with estimations of fluorescein in the fluorescein dilaurate test.

◇ Two large studies have examined the incidence of adverse reactions after intravenous fluorescein angiography. An international survey¹ collected information concerning 594 687 angiographic procedures; the incidence of serious reactions was 1 in 18 020, and that of fatal reactions, 1 in 49 557. Reactions included anaphylactic shock, cardiac arrest, myocardial infarction, and

shock with hypotension or respiratory distress. A US survey of 221 781 fluorescein angiograms² reported frequency rates of 1 in 63 for a moderate reaction (urticaria, syncope, thrombophlebitis, pyrexia, tissue necrosis, or nerve palsy) and 1 in 1900 for severe reactions (respiratory or cardiac events or tonic-clonic seizures); there was one death.

Individual reports of adverse reactions to intravenous fluorescein sodium include pancreatitis,³ painful crises in patients with sickle-cell disease,⁴ psoriasisiform drug eruption,⁵ and photoallergy⁶ and phototoxicity.⁷

- Zografos L. Enquête internationale sur l'incidence des accidents graves ou fatals pouvant survenir lors d'une angiographie fluoresceinique. *J Fr Ophthalmol* 1983; **6**: 495–506.
- Yannuzzi LA, et al. Fluorescein angiography complication survey. *Ophthalmology* 1986; **93**: 611–17.
- Morgan LH, Martin JM. Acute pancreatitis after fluorescein. *BMJ* 1983; **287**: 1596.
- Acheson R, Serjeant G. Painful crises in sickle cell disease after fluorescein angiography. *Lancet* 1985; **i**: 1222.
- Mayama M, et al. Psoriasisiform drug eruption induced by fluorescein sodium used for fluorescein angiography. *Br J Dermatol* 1999; **140**: 982–4.
- Hochsattel R, et al. Photoallergic reaction to fluorescein. *Contact Dermatitis* 1990; **22**: 42–4.
- Kearns GL, et al. Fluorescein phototoxicity in a premature infant. *J Pediatr* 1985; **107**: 796–8.

Breast feeding. The American Academy of Pediatrics¹ states that there have been no reports of any clinical effect on the infant associated with the use of fluorescein by breast-feeding mothers, and that therefore it may be considered to be usually compatible with breast feeding.

- American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108**: 776–89. Correction. *ibid.*; 1029. Also available at: <http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776> (accessed 02/06/04)

Uses and Administration

Fluorescein sodium stains damaged cornea and ocular fluids and is applied to the eye for the detection of corneal lesions and foreign bodies, as an aid to the fitting of hard contact lenses, and in various other diagnostic ophthalmic procedures. It is applied as a 1 or 2% solution as eye drops or as sterile papers impregnated with fluorescein sodium. It may also be given with a local anaesthetic, typically as a 0.25% solution with lidocaine hydrochloride, oxybuprocaine hydrochloride, or proxymetacaine hydrochloride.

Fluorescein sodium may be given by rapid intravenous injection, usually as a solution equivalent to fluorescein 10 or 25%, for retinal angiography. The usual dose is the equivalent of 500 mg of fluorescein. A dose of 7.5 mg/kg has been suggested for children. The oral route has also been tried for angiography. Other uses of intravenous fluorescein sodium have included the differentiation of healthy from diseased or damaged tissue and visualisation of the biliary tract.

Fluorescein dilaurate is given by mouth for the assessment of exocrine pancreatic function (see below). Pancreatic enzymes hydrolyse the ester and the amount of free fluorescein excreted in the urine can therefore be taken as a measure of pancreatic activity. A dose of 348.5 mg of fluorescein dilaurate, equivalent to 0.5 mmol of fluorescein, is given with a standard meal, and urine collected for the next 10 hours. The manufacturers give instructions concerning the type and amount of liquid and food which may be taken during this period. A control dose of 188.14 mg of fluorescein sodium, also equivalent to 0.5 mmol of fluorescein, is given on the next day under the same conditions.

Pancreatic function test. Studies of the fluorescein dilaurate test have considered it to be a useful noninvasive screening test for the exclusion of pancreatic exocrine failure in outpatients, particularly those presenting with steatorrhoea.^{1–3} The need for tests such as the pancreozymin–secretin test, which requires duodenal intubation, may thus be avoided. However, low specificity (a relatively high rate of false-positive responses) has been reported with the fluorescein dilaurate test in some patient populations,^{2,4} and the need for careful patient instruction in performance of the test has been emphasised.³ In order to avoid the prolonged collection of urine necessary in the standard test, serum concentrations of fluorescein may be measured several hours after taking the test substance.⁵

The test has been used successfully in children,⁶ particularly when the doses of fluorescein dilaurate and fluorescein sodium are reduced and fluid intake modified,⁷ although the manufacturers recommend that the commercially available test is not used for this age group. In children, a simplified, single-day test using dual markers, fluorescein dilaurate and mannitol, has been investigated with encouraging results.⁸ The fluorescein dilaurate test was found to be more sensitive than the faecal elastase I test for the diagnosis of mild-to-moderate exocrine pancreatic insufficiency in a study involving 40 patients.⁹

- Barry RE, et al. Fluorescein dilaurate—tubeless test for pancreatic exocrine failure. *Lancet* 1982; **ii**: 742–4.
- Boyd EJS, et al. Prospective comparison of the fluorescein-dilaurate test with the secretin–cholecystokinin test for pancreatic exocrine function. *J Clin Pathol* 1982; **35**: 1240–3.
- Gould SR, et al. Evaluation of a tubeless pancreatic function test in patients with steatorrhoea in a district general hospital. *J R Soc Med* 1988; **81**: 270–3.

- Braganza JM. Fluorescein dilaurate test. *Lancet* 1982; **ii**: 927–8.
- Dimagno EP. A perspective on the use of tubeless pancreatic function tests in diagnosis. *Gut* 1998; **43**: 2–3.
- Cumming JGR, et al. Diagnosis of exocrine pancreatic insufficiency in cystic fibrosis by use of fluorescein dilaurate. *Arch Dis Child* 1986; **61**: 573–5.
- Dalzell AM, Hear DP. Fluorescein dilaurate test of exocrine pancreatic function in cystic fibrosis. *Arch Dis Child* 1990; **65**: 788–9.
- Green MR, et al. Dual marker one day pancreolauryl test. *Arch Dis Child* 1993; **68**: 649–52.
- Leodolter A, et al. Comparison of two tubeless function tests in the assessment of mild-to-moderate exocrine pancreatic insufficiency. *Eur J Gastroenterol Hepatol* 2000; **12**: 1335–8.

Pediculosis. Infestation of the eye lashes or brows with pubic lice (p.2034) has been successfully treated with a single application of a 20% solution of fluorescein.¹

- Mathew M, et al. A new treatment of phthiasis palpebrarum. *Ann Ophthalmol* 1982; **14**: 439–41.

Retinal angiography. Fluorescein is usually given intravenously for retinal angiography, but a study in 20 healthy subjects concluded that an oral dose of fluorescein sodium 25 mg/kg could produce good quality retinal angiograms in the majority of subjects.¹ This study used specially prepared 500-mg capsules of fluorescein sodium; the authors commented that previous oral studies had used the liquid preparation intended for intravenous use. Only mild reactions, possibly due to hypersensitivity, appear to have been reported with oral fluorescein.

- Watson AP, Rosen ES. Oral fluorescein angiography: reassessment of its relative safety and evaluation of optimum conditions with use of capsules. *Br J Ophthalmol* 1990; **74**: 458–61.

Preparations

BP 2008: Fluorescein Eye Drops; Fluorescein Injection; **USP 31:** Fluorescein Injection; Fluorescein Sodium and Benoxinate Hydrochloride Ophthalmic Solution; Fluorescein Sodium and Proparacaine Hydrochloride Ophthalmic Solution; Fluorescein Sodium Ophthalmic Strips.

Proprietary Preparations (details are given in Part 3)

Arg.: Angiofluor; Fluorescite; RFG-Kit; **Austral.:** Disco-Plaque; Fluorescite; Fluorets; Ful-Glo; **Canad.:** Diofluor; Fluorescite; Fluorets; **Cz.:** Fluorescite; **Hong Kong:** Fluorescite; **India:** Fluore Stain Strips; **Irl.:** Fluorets; **Ital.:** Fluoralfa; **Malaysia:** Fluorescite; Fluorets; **Mex.:** Optifluor; **NZ:** Fluorescite; Fluorets; **Pol.:** Fluorescite; **Port.:** Fluorescite; **S.Afr.:** Fluorescite; Fluorets; **Singapore:** Fluorescite; Fluorets; **Thal.:** Fluorescite; **Turk.:** Fluorescite; **UK:** Fluorets; **USA:** Ak-Fluor; Fluor-I-Strip; Fluorescite; Fluorets; Ful-Glo; Funducise; Ophthifluor.

Multi-ingredient: **Austral.:** Fluress; **Austria:** Flurekain; Pancreolauryl-Test; **Canad.:** Fluoracaine; **Cz.:** Thilorbin; **Fin.:** Oftan Flurekain; **Ger.:** Pancreolauryl-Test N; Thilorbin; **NZ:** Fluress; **Port.:** Fluotest; **Spain:** Fluotest; Pancreolauryl; **Swed.:** Fluress; **USA:** Flu-Oxinate; Fluoracaine; Fluorox; Fluorat; Fluress; Fluorox; Healon Yellow.

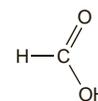
Formic Acid

Ácido amínico; Ácido formílico; Acidum Formicum; Ameisensäure; Aminic Acid; E236; E238 (calcium formate); E237 (sodium formate); Fórmico, ácido; Kwaz mrówkowy.

CH₂O₂ = 46.03.

CAS — 64-18-6.

ATC Vet — QP53AG01.



Pharmacopoeias. In *Pol.*

Profile

Formic acid resembles acetic acid in its properties (see p.2244) but is more irritating and pungent. The acid and its sodium and calcium salts are used as preservatives in food. Solutions containing about 60% formic acid have been marketed for the removal of lime scale from kettles. Formic acid has also been used for the removal of tattoos. It is an ingredient of some external preparations promoted for the relief of musculoskeletal and joint disorders, and has been used with benzyl alcohol to aid the removal of nits.

◇ In a report of 3 patients who swallowed descaling agents containing 40 or 55% formic acid, the major complications included local corrosive effects, metabolic acidosis, derangement of blood-clotting mechanisms, and acute onset of respiratory and renal failure.¹ All 3 patients died between 5 and 14 days after admission to hospital. A further report of 53 cases of formic acid ingestion included 15 fatalities.²

- Naik RB, et al. Ingestion of formic acid-containing agents — report of three fatal cases. *Postgrad Med J* 1980; **56**: 451–6.
- Rajan N, et al. Formic acid poisoning with suicidal intent: a report of 53 cases. *Postgrad Med J* 1985; **61**: 35–6.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: **Austria:** Acimont; Bergegist; **Ital.:** Rubjovit; **Switz.:** Fortalis.