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FOURTEENTH EDITION

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(Springer, New York, 1967) 164 pp; Hulet, Bode, "Separation Chemistry of the Lanthanides and Transplutonium Actinides" in *MTP Int. Rev. Sci.: Inorg. Chem., Ser. One* vol. 7, K. W. Bagnall, Ed. (University Park Press, Baltimore, 1972) pp 1-45; Moeller, "The Lanthanides" in *Comprehensive Inorganic Chemistry* vol. 4, J. C. Bailar, Jr. et al., Eds. (Pergamon Press, Oxford, 1973) pp 1-101; F. H. Spedding in *Kirk-Othmer Encyclopedia of Chemical Technology* vol. 19 (John Wiley & Sons, New York, 3rd ed., 1982) pp 833-854; *Chemistry of the Elements*, N. N. Greenwood, A. Earnshaw, Eds. (Pergamon Press, New York, 1984) pp 1423-1449. Brief review of properties: G. T. Seaborg, *Radiochim. Acta* 61, 115-122 (1993).

Body-centered cubic crystal lattice; d 5.244; mp 826°. bp 1429°. Heat of fusion: 9.221 kJ/mol. Heat of sublimation (25°): 144.7 kJ/mol. Sol in liq ammonia. Shows two reduction potentials -0.710 and -2.510 v. (referred to a normal calomel electrode); Noddack, Brukl, *Angew. Chem.* 50, 362 (1937); gives two definite series of salts, in one the metal is divalent, and in the other it is trivalent.

Sesquioxide. Eu₂O₃. Pink powder, d 7.42, prepd by heating the hydroxide, nitrate, oxalate or sulfate at 1600°. The oxide of the divalent metal is prepd by reduction of the sesquioxide at elevated temp.

Hydroxide. Eu(OH)₃. Prepd by adding ammonia or an alkali hydroxide to a soln of an europic salt.

Europic chloride. EuCl₃. Greenish-yellow needles; mp 623° in nitrogen (in a closed tube), d^{35} 4.471, prepd by passing sulfur chloride over the heated oxide at 200-500°. LD₅₀ of trichloride in mice: 550 mg/kg i.p.; 5 g/kg orally (Haley).

Europous chloride. EuCl₂. Prepd by reduction of EuCl₃ with hydrogen at 600°. White amorphous powder, sol in water.

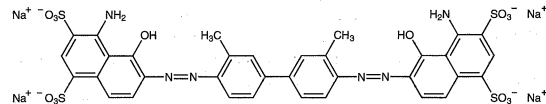
Europic sulfate. Eu₂(SO₄)₃. Octahydrate, a pinkish cryst solid, prepd by dissolving the oxide in sulfuric acid. Soly in water: 2.56 parts per 100 parts at 20°, 1.93 parts per 100 parts at 40°. On heating at 375° yields the anhydr sulfate.

Europic nitrate. Eu(NO₃)₃. Hexahydrate, mp 85° in its water of crystallization (sealed tube). LD₅₀ in rats (mg/kg): 210 i.p.; >5000 orally (Haley).

Europous sulfate. EuSO₄. Colorless crystals. Insol in water and in dil acids. Prepd by electrolytic reduction of europic salts.

USE: The salts in cathode ray tube coatings for color television receivers. Eu has a very high cross-section for the capture of thermal neutrons which is of value in the construction of electric atomic power stations. Organic derivs as shift reagents in NMR spectroscopy: C. C. Hinckley, *J. Am. Chem. Soc.* 91, 5160 (1969); R. E. Sievers, *Nuclear Magnetic Resonance Shift Reagents* (Academic Press, New York, 1973).

3905. Evan's Blue. [314-13-6] 6,6'-[(3,3'-Dimethyl[1,1'-bi-phenyl]-4,4'-diyl)bis(azo)]bis[4-amino-5-hydroxy-1,3-naphthalenedisulfonic acid] tetrasodium salt; C.I. Direct Blue 53; 4,4'-bis[7-(1-amino-8-hydroxy-2,4-disulfo)naphthylazo]-3,3'-bitolyl tetrasodium salt; C.I. 23860; T-1824; Azovan Blue. C₃₄H₂₄N₆Na₄O₁₄S₄; mol wt 960.81. C 42.50%, H 2.52%, N 8.75%, Na 9.57%, O 23.31%, S 13.35%. Prepd by coupling 1 mol of diazotized *o*-tolidine with 2 mols of Chicago acid (1-amino-8-naphthol-2,4-disulfonic acid): **DE 35341**; **DE 38802** *Frdl.* 1, 469, 488 (1877-1887); **DE 3949**; **DE 57327**; **DE 75469** *Frdl.* 3, 685, 687, 690 (1890-1894); Hartwell, Fieser, *Org. Synth. coll. vol. II*, 145 (1943). Diagnostic use: M. H. Nielsen, N. C. Nielsen, *Scand. J. Clin. Lab. Invest.* 14, 605 (1962); O. Linderkamp et al., *Eur. J. Pediatr.* 125, 135 (1977).



Blue crystals with bronze to green luster. Sol in water, alcohol, acids, alkalis. Indicator changing color near pH 10. Destroyed by strong oxidizing and reducing agents and precipitated from soln by strong concns of neutral salts. Rather stable in aq soln, and may be autoclaved at 15 lbs pressure for 30 min. Dye made up in physiological saline should not be autoclaved.

THERAP CAT: Diagnostic aid (blood volume determination).

3906. Evening Primrose Oil. EPO. Seed oil of the evening primrose, *Oenothera biennis* L., *Onagraceae*, which contains approx 72% linoleic acid and approx 9% γ -linolenic acid, *q.q.v.*; as the two main constituents. Unique among vegetable oils because of its high content of γ -linolenic acid. Effect on prostaglandin biosynthesis in rats: B. A. Schölkens et al., *Prostaglandins Leukotrienes Med.* 8, 273 (1982). Clinical studies in atopic eczema: C. R. Lovell et al., *Lancet* 1, 278 (1981); S. Wright, J. L. Burton, *ibid.* 2, 1120 (1982); P. L. Biagi et al., *Drugs Exp. Clin. Res.* 14, 285 (1988). Ingredient in cosmetics for aging skin: J. P. Marty, **DE 3447618** (1985 to Roussel-UCLAF), *C.A.* 103, 146984r (1985). Brief review including discussion of uses: A. J. Barber, *Pharm. J.* 240, 723-725 (1988).

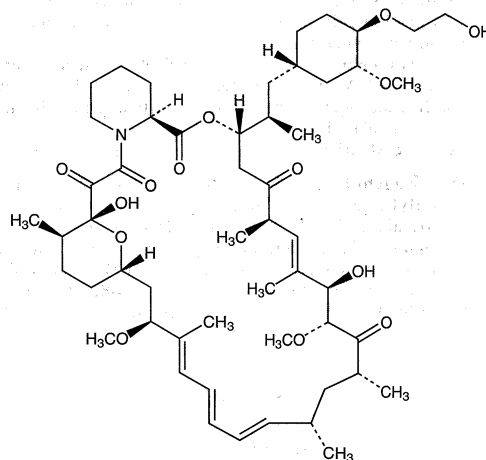
Clear, golden yellow oil. d_{15} 0.9283. n_D^{25} 1.4782. Sapon. no. 287.8. Iodine no. 154.8.

Note: Evening primrose oil products include *Efamol*, *Efamast*, *Epopam*.

USE: Dietary supplement.

THERAP CAT: In treatment of atopic eczema and mastaglia.

3907. Everolimus. [159351-69-6] 42-*O*-(2-Hydroxyethyl)-rapamycin; 40-*O*-(2-hydroxyethyl)rapamycin; RAD-001; SDZ RAD; Certican. C₅₃H₈₃NO₁₄; mol wt 958.22. C 66.43%, H 8.73%, N 1.46%, O 23.38%. Macrolide immunosuppressant; derivative of rapamycin, *q.v.* Inhibits cytokine-mediated lymphocyte proliferation. Prepn: S. Cottens, R. Sedrani, **WO 9409010**; *eidem*, **US 5665772** (1994, 1997 both to Sandoz). Pharmacology: W. Schuler et al., *Transplantation* 64, 36 (1997). Whole blood determ by LC/MS: N. Brignol et al., *Rapid Commun. Mass Spectrom.* 15, 898 (2001); by HPLC: S. Baldelli et al., *J. Chromatogr. B* 816, 99 (2005). Clinical pharmacokinetics in combination with cyclosporine: J. M. Kovarik et al., *Clin. Pharmacol. Ther.* 69, 48 (2001). Clinical study in prevention of cardiac-allograft vasculopathy: H. J. Eisen et al., *N. Engl. J. Med.* 349, 847 (2003). Review: F. J. Dumont et al., *Curr. Opin. Invest. Drugs* 2, 1220-1234 (2001); B. Nashan, *Ther. Drug Monit.* 24, 53-58 (2002).



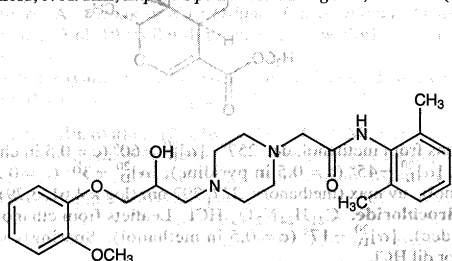
THERAP CAT: Immunosuppressant.

3908. Evodiamine. [518-17-2] 8,13,13b,14-Tetrahydro-14-methylindolo[2',3':3,4]pyrido[2,1-*b*]quinazolin-5(7*H*)-one. C₁₉H₁₇N₃O; mol wt 303.36. C 75.23%, H 5.65%, N 13.85%, O 5.27%. From *Evodia rutaecarpa* Hook. & Thoms and bark of *Zanthoxylum rhetsa* DC., *Rutaceae*: Y. Asahina, K. Kashiwaki, *J. Pharm. Soc. Jpn.* 1915, 1293, *C.A.* 10, 607 (1916); Gopinath et al., *Tetrahedron* 8, 293 (1960). Structure: Y. Asahina *J. Pharm. Soc. Jpn.* 1924, 1; Ohta, *J. Pharm. Soc. Jpn.* 65, 15 (1945), *C.A.* 45, 5697 (1951). Synthesis: Asahina, Ohta, *Ber.* 61B, 319 (1928); T. Kametani et al., *J. Am. Chem. Soc.* 98, 6186 (1976); *eidem*, *Heterocycles* 4, 23 (1976). Biosynthesis: M. Yamazaki et al., *Tetrahedron Lett.* 1966, 3221; 1967, 3317. Mass spec.: J. Tamas et al., *Acta Chim. Acad. Sci. Hung.* 89, 85 (1976).

Solid, mp 69-70°. **Hydrochloride**. [66357-59-3] AH-19065; Azantac; Melfax; Noctone; Raniben; Ranidil; Raniplex; Sostril; Taural; Terposen; Trigger; Ulcex; Ultidine; Zantac; Zantic. $C_{13}H_{22}N_4O_3 \cdot S \cdot HCl$; mol wt 350.86. Off-white solid, mp 133-134°. Freely sol in acetic acid and water, sol in methanol, sparingly sol in ethanol. Practically insol in chloroform.

Bismuth citrate. [128345-62-0] Ranitidine bismutrex; GR-122311X; Pylorid; Tritec. $C_{13}H_{22}N_4O_3 \cdot S \cdot C_6H_5BiO_7$; mol wt 712.48. Pharmacology and activity vs *Helicobacter* sp: R. Stables et al., *Aliment. Pharmacol. Ther.* **7**, 237 (1993).
THERAP CAT: Antilcerative.

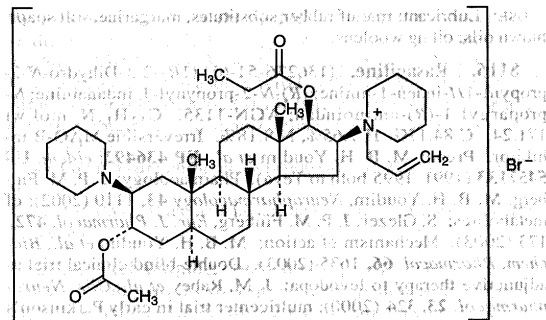
8111. Ranolazine. [95635-55-5] *N*-(2,6-Dimethylphenyl)-4-[2-hydroxy-3-(2-methoxyphenoxy)propyl]-1-piperazineacetamide; (\pm)-4-[2-hydroxy-3-(*o*-methoxyphenoxy)propyl]-1-piperazineacetamide; (\pm)-1-[3-(2-methoxyphenoxy)-2-hydroxypropyl]-4-[*N*-(2,6-dimethylphenyl)carbamoylmethyl]piperazine; Ranexa. $C_{24}H_{33}N_3O_4$; mol wt 427.54. C 67.42%, H 7.78%, N 9.83%, O 14.97%. Anti-ischemic agent which modulates myocardial metabolism. Prepn: A. F. Kluge et al., EP 126449; *idem*, US 4567264 (1984, 1986 both to Syntex). HPLC resolution of enantiomers: E. Delée et al., *Chromatographia* **24**, 357 (1987). Clinical trial in angina: B. R. Chaitman et al., *J. Am. Coll. Cardiol.* **43**, 1375 (2004). Review of pharmacology and clinical development: J. G. McCormack et al., *Gen. Pharmacol.* **30**, 639-645 (1998); R. S. Schofield, J. A. Hill, *Expert Opin. Invest. Drugs* **11**, 117-123 (2002).



Dihydrochloride. [95635-56-6] RS-43285. $C_{24}H_{33}N_3O_4 \cdot 2HCl$; mol wt 500.46. White crystalline powder from methanol/ether, mp 164-166°. Readily sol in water.
THERAP CAT: Antianginal.

8112. Ranpirnase. [133737-96-9] Ribonuclease (*Rana pipiens* reduced); P-30 protein; Onconase. Antitumor ribonuclease isolated from oocytes and early embryos of *Rana pipiens*. Single chain protein containing 104 amino acid residues; mol wt ~12 kDa. Description of cytotoxic activity: Z. Darzynkiewicz et al., *Cell Tissue Kinet.* **21**, 169 (1988). Amino acid sequence and identification as a ribonuclease: W. Ardelt et al., *J. Biol. Chem.* **266**, 245 (1991). Crystallization: S. C. Mosimann et al., *Proteins: Struct. Funct. Genet.* **14**, 392 (1992). Mechanism of action: Y. Wu et al., *J. Biol. Chem.* **268**, 10686 (1993). Prepn by recombinant technology: E. Notomista et al., *FEBS Lett.* **463**, 211 (1999). Clinical trial in malignant mesothelioma: S. M. Mikulski et al., *J. Clin. Oncol.* **20**, 274 (2002).
THERAP CAT: Antineoplastic.

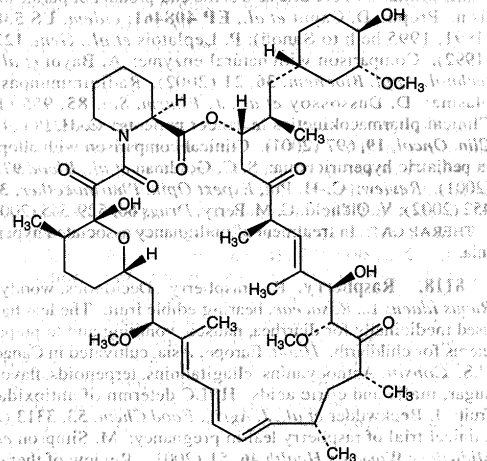
8113. Rapacuronium Bromide. [156137-99-4] 1-[(2 β ,3 α -5 α ,16 β ,17 β)-3-(Acetyloxy)-17-(1-oxopropoxy)-2-(1-piperidinyl)-androstan-16-yl]-1-(2-propenyl)piperidinium bromide; 1-allyl-2-(3 α ,17 β -dihydroxy-2 β -piperidino-5 α -androstan-16 β -yl)piperidinium bromide 3-acetate 17-propionate; Org-9487; Raplon. $C_{37}H_{61}N_2O_4 \cdot Br$; mol wt 677.80. C 65.56%, H 9.07%, N 4.13%, O 9.44%, Br 11.79%. Aminosteroid; competitive neuromuscular blocker. Prepn: T. Sleight et al., CA 2094457; *idem*, US 5418226 (both to Akzo). Clinical pharmacodynamics: P. M. C. Wright et al., *Anesthesiology* **90**, 16 (1999). Clinical trial in pediatric patients: R. F. Kaplan et al., *Anesth. Analg.* **89**, 1172 (1999). Review of pharmacology and use in endotracheal intubation: S. V. Onrust, R. H. Foster, *Drugs* **58**, 887-918 (1999).



Crystals from diethyl ether-acetone, mp 184°. $[\alpha]_D^{25} -12.7^\circ$ (c = 1.01 in $CHCl_3$).

THERAP CAT: Neuromuscular blocking agent.

8114. Rapamycin. [53123-88-9] Sirolimus; RAPA; RPM; AY-22989; NSC-226080; Rapamune. $C_{51}H_{79}NO_{13}$; mol wt 914.17. C 67.01%, H 8.71%, N 1.53%, O 22.75%. Triene macrolide antibiotic isolated from *Streptomyces hygroscopicus*. Name derived from the native word for Easter Island, Rapa Nui. Isolin: S. N. Sehgal et al., DE 2347682; *idem*, US 3929992 (1974, 1975 both to Ayerst McKenna Harrison); purification and characterization: C. Vézina et al., *J. Antibiot.* **28**, 721 (1975); S. N. Sehgal et al., *ibid.* **727**. Inhibition of immune response: R. R. Martel et al., *Can. J. Physiol. Pharmacol.* **55**, 48 (1977); of graft rejection in mice: C. P. Eng et al., *Transplant. Proc.* **23**, 868 (1991). Total synthesis: K. C. Nicolaou et al., *J. Am. Chem. Soc.* **115**, 4419 (1993); D. Romo et al., *ibid.* **7906**. Series of articles on therapeutic monitoring and pharmacokinetics: *Clin. Ther.* **22**, Suppl. 2, B1-B132 (2000); on pharmacology and clinical experience in transplantation: *Transplant. Proc.* **35**, Suppl. 1, S1-S233 (2003). Clinical trial in prevention of coronary restenosis: D. R. Holmes, Jr. et al., *Circulation* **109**, 634 (2004).



Colorless crystalline solid from ether, mp 183-185°. uv max (95% ethanol): 267, 277, 288 nm ($E_{1\%}^{1cm}$ 417, 541, 416). $[\alpha]_D^{25} -58.2^\circ$ (methanol). Sol in ether, chloroform, acetone, methanol and DMF; very sparingly sol in hexane and petr ether. Substantially insol in water. LD₅₀ in mice (mg/kg): =600 i.p.; >2,500 orally (Vézina).

USE: Tool for immunochemistry.

THERAP CAT: Immunosuppressant; antirestenotic.

8115. Rapeseed Oil. Colza oil. Oil expressed from seeds of *Brassica campestris* L.; *Cruciferae*. Pale yellow; rather viscid liq. d 0.913-0.917; n_D^{20} 1.4720-1.4752. Solidif = 2° to -10°. Sapon no: 170-177. Iodine no: 97-105. Sol in chloroform, ether, CS_2 .

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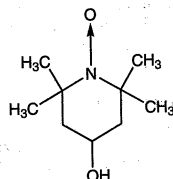
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USE: In organic chemistry as a radical trap, a catalyst and in polymerization mediation.

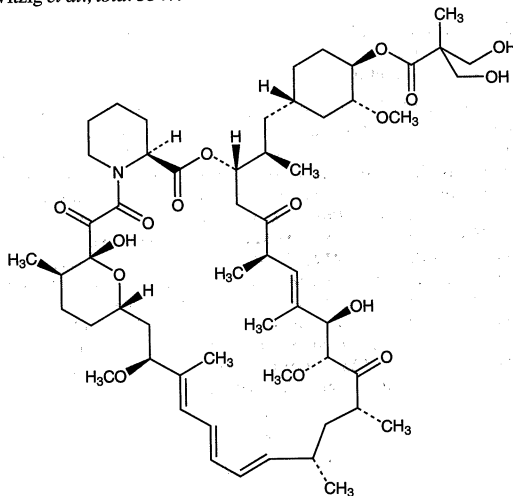
9141. TEMPOL. [2226-96-2] 4-Hydroxy-2,2,6,6-tetramethyl-1-piperidinyloxy; 4-hydroxy-TEMPO; 4-hydroxy-2,2,6,6-tetramethyl piperidine *N*-oxide; 4-hydroxy-2,2,6,6-tetramethylpiperidinyloxy. $C_9H_{18}NO_2$; mol wt 172.24. C 62.76%, H 10.53%, N 8.13%, O 18.58%. Stable nitroxyl radical; water-soluble analogue of TEMPO, *q.v.* Functions as a membrane-permeable radical scavenger. Prepn: E. G. Rozantsev, *Bull. Acad. Sci. USSR Div. Chem. Sci.* **12**, 2085 (1964). Energy transfer studies: N. N. Quan, A. V. Guzzo, *J. Phys. Chem.* **85**, 140 (1981). IR conformation study: W. A. Bueno, L. Degrève, *J. Mol. Struct.* **74**, 291 (1981). Solid state NMR spectra: C. J. Groombridge, M. J. Perkins, *J. Chem. Soc. Chem. Commun.* **1991**, 1164. LC/MS/MS determ: I. D. Podmore, *J. Chem. Res. Synop.* **2002**, 574. Use as a phase transfer catalyst: X.-Y. Wang *et al.*, *Synth. Commun.* **29**, 157 (1999). Review of effects in animal models for shock, ischemia-reperfusion injury, and inflammation: C. Thiemermann, *Crit. Care Med.* **31**, S76-S84 (2003).



Crystals from ether + hexane, mp 71.5°. uv max (hexane): 240, 450-500 ($\epsilon \sim 1800$, ~ 5). uv max (ethanol): 242, 435-455 ($\epsilon \sim 3800$, ~ 10). Sol in water.

USE: Spin label for EPR studies; phase transfer dehydration catalyst; antioxidant; inhibitor of olefin free radical polymerization.

9142. Temsirolimus. [162635-04-3] Rapamycin 42-[3-Hydroxy-2-(hydroxymethyl)-2-methylpropanoate]; rapamycin 42-ester with 2,2-bis-(hydroxymethyl)propionic acid; CCI-779. $C_{56}H_{87}NO_{16}$; mol wt 1030.29. C 65.28%, H 8.51%, N 1.36%, O 24.85%. Ester analog of rapamycin, *q.v.*; selectively inhibits mammalian target of rapamycin (mTOR). Prepn: J. S. Skotnicki *et al.*, *US 5362718* (1994 to Am. Home Prod.). Lipase-catalyzed synthesis from rapamycin: J. Gu *et al.*, *Org. Lett.* **7**, 3945 (2005). Clinical pharmacology: E. Raymond *et al.*, *J. Clin. Oncol.* **22**, 2336 (2004). Clinical study in advanced refractory renal cell carcinoma: M. B. Atkins *et al.*, *ibid.* 909. Clinical evaluation in glioblastoma multiforme: E. Galanis *et al.*, *J. Clin. Oncol.* **23**, 5294 (2005); in breast cancer: S. Chan *et al.*, *ibid.* 5314; in mantle cell lymphoma: T. E. Witzig *et al.*, *ibid.* 5347.

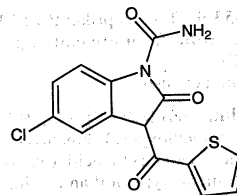


White solid. Sol in water. Lipophilic.
THERAP CAT: Antineoplastic.

9143. Tenecteplase. [191588-94-0] 103-L-Asparagine-117-L-glutamine-296-L-alanine-297-L-alanine-298-L-alanine-299-L-ala-

nineplasinogen activator (human tissue-type); TNK-tPA; Metalyse. Genetically engineered variant of human tissue plasminogen activator (t-PA), *q.v.*; expressed in Chinese hamster ovary cells. mol wt ~ 65 kDa. Constructed by oligonucleotide-directed mutagenesis at 3 specific sites. Prepn: W. F. Bennett *et al.*, *WO 9324635* (1993 to Genentech); B. A. Keyt *et al.*, *Proc. Natl. Acad. Sci. USA* **91**, 3670 (1994). Pharmacology: C. R. Benedict *et al.*, *Circulation* **92**, 3032 (1995). Clinical pharmacokinetics: N. B. Modi *et al.*, *Thromb. Haemostasis* **79**, 134 (1998). Clinical trial in acute myocardial infarction: ASSENT-2 Investigators, *Lancet* **354**, 716 (1999).
THERAP CAT: Thrombolytic.

9144. Tenidap. [120210-48-2] (Z)-5-Chloro-2,3-dihydro-3-(hydroxy-2-thienylmethylene)-2-oxo-1H-indole-1-carboxamide; 5-chloro-2,3-dihydro-2-oxo-3-(2-thienylcarbonyl)-1H-indole-1-carboxamide; 5-chloro-3-(2-thienyl)-2-oxindole-1-carboxamide; CP-66248. $C_{14}H_9ClN_2O_3S$; mol wt 320.75. C 52.42%, H 2.83%, Cl 11.05%, N 8.73%, O 14.96%, S 10.00%. Inhibitor of 5-lipoxygenase and interleukin-1 (IL-1) activity. Prepn: S. B. Kadin, *EP 156603*; *idem.*, *US 4556672* (both 1985 to Pfizer). Effect on 5-lipoxygenase activity *in vitro*: K. Fogh *et al.*, *Arch. Dermatol. Res.* **280**, 430 (1988). Effect on IL-1 activity in patients with rheumatoid arthritis: B. McDonald *et al.*, *Arthritis Rheum.* **31**, Suppl., S52 (1988). Clinical evaluation: P. Katz *et al.*, *ibid.* S52.



Fluffy, yellow crystals from acetic acid, mp 230° (dec).
Sodium salt. [119784-94-0] CP-66248-2. $C_{14}H_8ClN_2NaO_3S$; mol wt 342.73. Crystals from methanol-isopropanol, mp 237-238°. THERAP CAT: Anti-inflammatory.

9145. Teniposide. [29767-20-2] (5R,5aR,8aR,9S)-5,8,8a,9-Tetrahydro-5-(4-hydroxy-3,5-dimethoxyphenyl)-9-[[[4,6-O-[(R)-2-thienylmethylene]- β -D-glucopyranosyl]oxy]furo[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-6(5aH)-one]-4'-demethylepipodophyllotoxin 9-(4,6-O-2-thienylidene- β -D-glucopyranoside); 4'-demethylepipodophyllotoxin- β -D-thienylidene glucoside; ETP; NSC-122819; VM-26; Vehem-Sandoz; Vumon. $C_{32}H_{32}O_{13}S$; mol wt 656.65. C 58.53%, H 4.91%, O 31.67%, S 4.88%. Semi-synthetic derivative of podophyllotoxin, *q.v.* Prepn: A. Von Wartburg, *ZA 6607585*; C. Keeler-Juslen *et al.*, *US 3524844* (1968, 1970 both to Sandoz). Mechanism of action: H. Stählin, *Eur. J. Cancer* **6**, 303 (1970). Pharmacology: M. Hacker, D. Roberts, *Cancer Res.* **37**, 3287 (1977); S. M. Sieber *et al.*, *Teratology* **18**, 31 (1978); T. J. Vietti *et al.*, *Cancer Treat. Rep.* **62**, 1313 (1978). Metabolism: L. Allen, *Drug Metab. Rev.* **8**, 119 (1978); *Cancer Res.* **38**, 2549 (1978). Clinical studies: N. M. Gadel-Mawla *et al.*, *Cancer Treat. Rep.* **62**, 993 (1978); R. E. Bellet *et al.*, *ibid.* 445. Studies on delayed toxicity in mice after i.p. injections: M. Hacker, D. Roberts, *Cancer Res.* **35**, 1756 (1975); H. Stählin, *Eur. J. Cancer* **12**, 925 (1976). Review of pharmacology, pharmacokinetics and assay methods: P. I. Clark, M. L. Slevin, *Clin. Pharmacokinetics*, **12**, 223-252 (1987). Comprehensive description: J. J. Kettenes-van den Bosch *et al.*, *Anal. Profiles Drug Subs.* **19**, 575-600 (1990).

