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Osteoporosis. Treatment with folate and vitamin B_{12} can reduce elevated plasma homocysteine concentrations and may subsequently decrease the risk of osteoporosis and hip fracture, see Osteoporosis, under Vitamin B_{12}, p.1983.

Prophylaxis of malignant neoplasms. For reference to suggestions that folate supplements may be associated with reduced risk of certain cancers, see p.1927. However, folic acid may have dual modulatory effects on carcinogenesis, see Carcinogenicity, above.

Preparations

BP 2008: Ferrous Fumarate and Folic Acid Tablets; Folic Acid Tablets; ***USP 31:*** Folic Acid Injection; Folic Acid Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Acifol; Anemidox Folico; Anfolic; Azolac Folico; Biolfolic; Coflic; Conacid; Dupofol; Edulsan Folic; Egestan; Folaport; Foliagen; Folimax; Folinemic; Galfol; Livifol; Medifol; Ronfolic; Sojar Folico; Suprafol; ***Austral.:*** Megafol; ***Austria:*** Folsan; ***Belg.:*** Folavit; ***Braz.:*** Acfol†; Afopic; Endofolin; Enfol; Folacin; Folin†; Folital; Materfolic; Neo Folico; ***Chile:*** Folacid; Folifemin; Folisanin; ***Denm.:*** Folimet; ***Fin.:*** Folvite; ***Fr.:*** Speciafoldine; ***Ger.:*** DreisaFol; Fol-Asmedic†; Folarell; Folcur; Folgamma Mono; Folsan; Folverlan; Gravi-Fol; Lafol; RubieFol†; ***Gr.:*** Filicine; ***Hung.:*** Feroglobin-B12; Folsav; Huma-Folacid; ***India:*** Folet; Folvite; Ingafol; Rubraplex; Vitafol; ***Indon.:*** Folac; Folacite; Folacom; Folas; Folavit; Folaxin; Nufolic; ***Irl.:*** Cardioguard†; Clonfolic; ***Ital.:*** Fertifol; Folidex; Folina; Folingrav; Serengrav; ***Mex.:*** AF; Folivital; Materfol; Prinac Ac; ***Philipp.:*** Enhansid; Purifol; ***Pol.:*** Acifolik; Folacid; Folifem; Folik; Folimin; Folovit; ***Port.:*** Acfol; Dozefol; Folicil; ***Rus.:*** Folacin (Фолацин); ***Spain:*** Acfol; Zolico; ***Swed.:*** Folacin; ***Switz.:*** Andreafol; Drossafol; Foli-Rivo†; Folvite; ***Thai.:*** Foliamin; Folicare; Folivit; ***Turk.:*** Folbiol; ***UAE:*** Folicum; ***UK:*** Folicare; Lexpec; Preconceive; ***USA:*** Folvite; ***Venez.:*** Afoklin; Folac.

Multi-ingredient: ***Arg.:*** Acifol-B12; Anemidox-Ferrum; Anemidox-Solutab; Blastop; Egestan Hierro; Factofer B12; Fefol; Ferranin Complex; Ferretab Compuesto; Ferro Folic; Ferrocebrina; Folimax B; Hierro Dupofol; Hierro Folico; Hierro Plus; Hierroquick; ITE B12 Forte; Maltofer Fol†; Presterin; QX 10; Rubiron; Sideralce; Siderblut Folic; Tenvic; Vitalix Complex; Yectafer Complex; ***Austral.:*** Antioxidant Forte Tablets; Fefol; FGF Tabs; Pre Natal†; Vita-Preg†; ***Austria:*** Aktiferrin Compositum; Beneuran compositum; Ferretab Comp; Ferrograd Fol; Losferron-Fol; Tardyferon-Fol; ***Belg.:*** Gestiferrol; ***Braz.:*** Anemofer†; Betozone; Coraben†; Ferrini Folico; Ferroplex; Ferrotonico B12†; Ferrotrat; Ferrumvit†; Fol Sang; Folacin; Folifer; Iberin Folico; Iloban; Neutrofer Folico; Noripurum Folico; Vi-Ferrin; ***Canad.:*** Neo-Fer CF; Palafer CF; Slow-Fe Folic; ***Chile:*** Cronoferril†; Ferranem; Ferranim; Ferro F-500 Gradumet†; Ferro Vitaminico; Foli Doce; Folifer; Iberol Folico; Maltofer Fol; ***Cz.:*** Aktiferrin Compositum; Ferretab Compositum; Ferro-Folgamma; Ferrograd Folic†; Maltofer Fol; Tardyferon-Fol; ***Fin.:*** Obsidan comp; ***Fr.:*** Folio; Gynosoja; Tardyferon B ; ***Ger.:*** B Fol-Vicotrat†; Eryfer comp; Ferro sanol comp; Ferro sanol gyn; Ferro-Folgamma; Ferro-Folsan; Folgamma; Folicombin; Hamatopan F; Hepagrisevit Forte-N†; Kendural-Fol-500; Medivitan N; Medyn; MerSol†; Plastulen N; Selectafer N†; Tardyferon-Fol; ***Gr.:*** Dextrifer-Fol; Feofol; Fero-Folic; Ferrum Fol Hausmann; Gyno-Tardyferon; Hemafer fol; ***Hong Kong:*** Eurofer; Hepatofalk; Iberet-Folic; ***Hung.:*** Atherovit; Ferro-Folgamma; Ferrograd Folic; Maltofer Fol; Pregmag; Tardyferon-Fol; ***India:*** Anemidox; Blosyn; Cafe-Kit†; Carbofliot†; Cofol; Cofol Z; Conviron-TR; Dexorange; Elferri-Z; Fecontin-F; Fecontin-Z; Fefol; Fefol-Z; Fericip; Ferrochelate; Ferrochelate-Z; Fervit†; Fesovit; Genfol; Globac-Z; Hepasules; Hepatoglobine; Hepofer; Jectocos Plus; JP Tone-TR; Livogen Captab; Livogen Hemtonic; Livogen-Z; Livogen†; Maxiferon; Mumfer-Z†; Mumfer†; Plastules; Probofex; Raricap; Softeron; Softeron-Z; Tonoferon; Vitamon; ***Indon.:*** Adfer; Biosanbe; Folaplus; Hemobion; Iberet-Folic; Maltofer Fol; Natabion; Neogobion; Sangobion; Vomilat; ***Irl.:*** Fefol; Ferrocap F†; Ferrograd Folic; Galfer FA; Givitol; ***Israel:*** Aktiferrin-F; Ferrifol; Ferrograd Folic; Folex; Foric; Slow-Fe Folic; Tricardia; ***Ital.:*** Epargriseovit; Evafer; Ferrograd Folic; Folepar B12; ***Malaysia:*** Aktiferrin-F; Ferrovit; Iberet-Folic; Maltofer; Sangobion; ***Mex.:*** Dialeli AF; Ferlor AF†; Ferranina Fol; Ferricol; Ferro Folico; Forta; Intrafer; Intrafer F-800; Intrafer TF; Ironfol; Orafer Comp; Tardyferon-Fol; Uniferfol; Yemiferhe; ***NZ:*** Ferrograd Folic; ***Philipp.:*** Ameciron; Anemicon Plus; Anixon; Beniforte; Drexabion OB; Dupharon; Essenfer; Eurofer; Femina; Fergesol; Ferlin; Ferosal; Ferro-Folsan Plus; Foralivit; Foramefer; Fortifer FA; Harvifer; Hemobion; IBC; Iberet-Folic; Imefer; Irobon; Meganerv F-A; Micron-C; Molvite-OB; Nakaron; Sangobion; Terraferron; TriHEMIC; ***Pol.:*** Additiva Ferrum; Ferrograd Folic; Hemofer F; Tardyferon-Fol; ***Port.:*** Ferro-Folsan†; Ferrograd Folico; Ferrum Fol; Folifer; Maltoferfol; Neobefol; Tardyferon-Fol; ***Rus.:*** Aktiferrin Compositum (Актиферрин Композитум); Ferretab Comp (Ферретаб Комп); Ferro-Folgamma (Ферро-Фольгамма); Gyno-Tardyferon (Гино-тардиферон); ***S.Afr.:*** Fefol; Fefol-Vit; Fero-Folic; Ferrimed; Foliglobin; Hepabionta; Pregamal; ***Singapore:*** Aktiferrin-F; Eurofer; Iberet-Folic; Iron Melts; Neogobion; Saferon†; Sangobion; Tardyferon B †; Wanse; ***Spain:*** Foli Doce; Foliferron; Hepa Factor; Normovite Antianemico; ***Switz.:*** Actiferrine-F Nouvelle formule; Duofer Fol; Fero-Folic; Gyno-Tardyferon; Maltofer Fol; ***Thai.:*** Adnemic F†; Eurofer; Ferli-6; Ferosix; Orofer; Trinsicon†; ***Turk.:*** Blood Builder; Epargriseovit; Ferplex Fol; Ferro-Vital; Ferrum Fort Hausmann; Folic Plus; Gyno-Tardyferon; Gynoferon; Maltofer Fol; Vi-Fer; ***UAE:*** Folicron; ***UK:*** Fefol; Ferrograd Folic; Galfer FA; Hematinic; Ironorm; Lexpec with Iron-M†; Lexpec with Iron†; Meterfolic; Pregaday; Slow-Fe Folic†; SoyPlus; ***USA:*** ABC to Z; Berocca Plus; Bevitamel; Centurion A–Z†; Certagen; Cevi-Fer†; Chromagen FA; Chromagen Forte; Compete; Contrin; Fe-Tinic Forte; Feocyte; Fero-Folic; Ferotrinsic; Ferralet Plus†; Ferrex Forte; Ferrex Forte Plus†; Ferrogels Forte; FOLTX; Formula B Plus; Geriot; Geritol Complete; Gevral T; Hematinic; Hematinic Plus; Hemocyte Plus; Hemocyte-F; Iberet-Folic†; Icar-C Plus; Ircon-FA†; Iromin-G; Livitrinsic-f; Nephro-Fer Rx†; Niferex Forte; Nu-Iron V; Parvlex; Poly-Iron Forte; PremesisRx; Pronemia Hematinic; Slow Fe with Folic Acid; Tandem F; Thera Hematinic; Theragenerix-H; Theravee Hematinic; TriHEMIC; Trinsicon; Vitafol; Yelets; Zodeac; ***Venez.:*** Calcibon Natal; Cobalfer; Fefol; Ferganic Folic; Ferro-Folic; Folifer B-12; Hepafol con B-12; Herrongyn; Intaferfol; Maltoferfol.

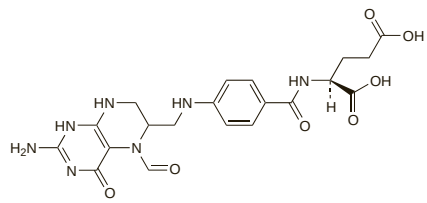
Folinic Acid *(BAN)*

Citrovorum Factor; Folínico, ácido; Leucovorin. 5-Formyltetrahydropteroylglutamic acid; *N*-[4-(2-Amino-5-formyl-5,6,7,8-tetrahydro-4-hydroxypteridin-6-ylmethylamino)benzoyl]-L(+)-glutamic acid.

Фолиновая Кислота

$C_{20}H_{23}N_7O_7$ = 473.4.

CAS — 58-05-9.



Calcium Folinate *(BANM, rINN)*

Calcii folinas; Calcii Folinas Hydricus; Calcium, folinate de; Calcium Folinate-SF; Calcium Leucovorin; Folinate de Calcium; Folinato cálcico; Kalcio folinatas; Kalciumfolinat; Kalcium-folinát; Kalcium-folinát hydrát; Kalsiumfolinaatti; Kalsiyum Folinat; Kalsiyum Lökovorin; Leucovorin Calcium; NSC-3590. The calcium salt of folinic acid (1:1).

Кальция Фолинат

$C_{20}H_{21}CaN_7O_7$ = 511.5.

CAS — 1492-18-8 (anhydrous calcium folinate); 41927-89-3 (calcium folinate pentahydrate); 6035-45-6 (calcium folinate pentahydrate).

ATC — V03AF03.

ATC Vet — QV03AF03.

Pharmacopoeias. In *Eur.* (see p.vii), *Int.*, *Jpn*, and *US*. *Chin.* includes the pentahydrate ($C_{20}H_{21}CaN_7O_7,5H_2O$ = 601.6).

Ph. Eur. 6.2 (Calcium Folinate). A white or light yellow, amorphous or crystalline powder. Sparingly soluble in water; practically insoluble in alcohol and in acetone. A 2.5% solution in water has a pH of 6.8 to 8.0. Store in airtight containers. Protect from light.

USP 31 (Leucovorin Calcium). A yellowish-white or yellow, odourless, powder. Very soluble in water; practically insoluble in alcohol. Protect from light.

Incompatibility. Calcium folinate and fluorouracil, with or without 5% glucose, were incompatible when mixed in various ratios and stored in PVC containers at various temperatures.[1]

1. Trissel LA, *et al*. Incompatibility of fluorouracil with leucovorin calcium or levoleucovorin calcium. *Am J Health-Syst Pharm* 1995; **52:** 710–15.

Calcium Levofolinate *(BAN, rINN)*

Calcii Levofolinas; Calcii levofolinas pentahydricus; Kalcio levofolinatas; Kalciumlevofolinat; Kalcium-levofolinát pentahydrát; Kalcium-levofolinát-pentahidrát; Kalciumlevofolinatpentahydrat; Kalsiumlevofolinaatti; Kalsiumlevofolinaattipentahydraatti; Levofolinate; Lévofolinate calcique pentahydraté; Lévofolinate de Calcium; Levofolinato de calcio; Levoleucovorin Calcium *(USAN)*. The calcium salt of the isomer of *S*-folinic acid (1:1).

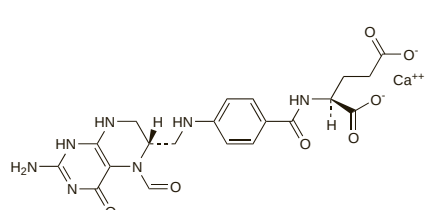
Кальция Левофолинат

$C_{20}H_{21}CaN_7O_7,5H_2O$ = 601.6.

CAS — 80433-71-2 (anhydrous calcium levofolinate).

ATC — V03AF04.

ATC Vet — QV03AF04.



(anhydrous calcium levofolinate)

Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Calcium Levofolinate Pentahydrate). A white or light yellow, amorphous or crystalline, hygroscopic powder. Slightly soluble in water; practically insoluble in alcohol and in acetone. A 0.8% solution in water has a pH of 7.5 to 8.5. Store in airtight containers. Protect from light.

Sodium Folinate

Disodium folinate *(BANM)*.

Натрия Фолинат

$C_{20}H_{21}N_7O_7Na_2$ = 517.4.
CAS — 42476-21-1 (monosodium folinate).
ATC — V03AF06.
ATC Vet — QV03AF06.

Adverse Effects

Occasional hypersensitivity, including anaphylactic reactions, has been reported; pyrexia has occurred rarely after injections. Gastrointestinal disturbances, insomnia, agitation, and depression have been reported rarely, after high doses.

Precautions

As for Folic Acid, p.1940.

Interactions

As for Folic Acid, p.1940.

Folinic acid should not be used with a folic acid antagonist such as methotrexate as this may nullify the effect of the antagonist. Folinic acid enhances the toxicity, as well as the antineoplastic action, of fluorouracil, especially on the gastrointestinal tract.

Pharmacokinetics

Calcium folinate is well absorbed after oral and intramuscular doses and, unlike folic acid (p.1941), is rapidly converted to biologically active folates. Sodium folinate is considered to be bioequivalent to calcium folinate. Folate is concentrated in the liver and CSF although distribution occurs to all body tissues. Folates are mainly excreted in the urine, with small amounts in the faeces.

◊ References.

1. McGuire BW, *et al.* Pharmacokinetics of leucovorin calcium after intravenous, intramuscular, and oral administration. *Clin Pharm* 1988; **7:** 52–8.
2. Wolfrom C, *et al.* Pharmacokinetic study of methotrexate, folinic acid and their serum metabolites in children treated with high-dose methotrexate and leucovorin rescue. *Eur J Clin Pharmacol* 1990; **39:** 377–83.
3. Zittoun J, *et al.* Pharmacokinetic comparison of leucovorin and levoleucovorin. *Eur J Clin Pharmacol* 1993; **44:** 569–73.
4. Mader RM, *et al.* Pharmacokinetics of rac-leucovorin vs [S]-leucovorin in patients with advanced gastrointestinal cancer. *Br J Clin Pharmacol* 1994; **37:** 243–8.
5. Schmitz JC, *et al.* Disposition of folic acid and its metabolites: a comparison with leucovorin. *Clin Pharmacol Ther* 1994; **55:** 501–8.

Uses and Administration

Folinic acid is the 5-formyl derivative of tetrahydrofolic acid, the active form of folic acid. Folinic acid is used principally as an antidote to folic acid antagonists, such as methotrexate (p.747), which block the conversion of folic acid to tetrahydrofolate by binding the enzyme dihydrofolate reductase. It does not block the antimicrobial action of folate antagonists such as trimethoprim or pyrimethamine, but may reduce their haematological toxicities. It is also used as an adjunct to fluorouracil in the treatment of colorectal cancer.

Folinic acid is given as calcium or sodium folinate, although doses are stated in terms of folinic acid. 1.08 mg of anhydrous calcium folinate, 1.27 mg of calcium folinate pentahydrate, or 1.09 mg of sodium folinate are each equivalent to about 1 mg of folinic acid. Calcium folinate can be given orally, by intramuscular injection, or by intravenous injection or infusion. It has been recommended that oral doses should not be greater than 50 mg, since absorption is saturable. Calcium levofolinate, the active laevo-isomer, is used similarly to calcium folinate; it is given in doses half those recommended for the racemic form. Sodium folinate is given by intravenous injection or infusion; sodium levofolinate is used similarly.

In cases of inadvertent **overdosage of a folic acid antagonist**, folinic acid should be given as soon as possible and preferably within the first hour. Doses equal to or greater than the dose of methotrexate have been recommended. Intravenous injections should be given over several minutes because of their calcium content; the maximum recommended rate is equivalent to folinic acid 160 mg/minute. Alternatively it has been stated that for large doses or overdoses of methotrexate, calcium folinate may be given by intravenous infusion in a dose equivalent to 75 mg of folinic acid within 12 hours, followed by 12 mg intramuscularly every 6 hours for 4 doses. Although vincristine is not a folic acid antagonist, folinic acid has also been proposed for some manifestations of vincristine toxicity overdosage—see p.787.

Folinic acid is used with high-dose methotrexate antineoplastic therapy to reduce the toxicity of the methotrexate (‘**folinic acid rescue**’; ‘calcium leucovorin rescue’). Calcium folinate rescue is necessary when methotrexate is given at doses exceeding 500 mg/m^2 and should be considered with methotrexate doses of 100 to 500 mg/m^2. It may sometimes be considered in patients who have received lower doses.

Dosage and duration of folinic acid rescue must be adapted according to the methotrexate regimen and the patient’s ability to clear the antineoplastic; many antineoplastic regimens include appropriate rescue protocols. In general, UK licensed drug information recommends that the first dose of calcium folinate is the equivalent of 15 mg folinic acid (6 to 12 mg/m^2) to be given 12 to 24 hours (usually the latter) after the beginning of methotrexate infusion. The same dose is given every 6 hours for 24 hours, initially by intramuscular injection or intravenous injection or infusion, but switching to the oral form after one or more parenteral doses. At the end of this time (48 hours after the start of the original methotrexate infusion) the residual methotrexate concentration should be measured. If this is *less* than a threshold concentration of 0.5 micromoles/litre, the same dose is continued usually for a further 48 hours. If it is *greater* than this value, further calcium folinate dosages should be adapted according to methotrexate concentration as follows, and given every 6 hours for a further 48 hours or until the serum-methotrexate concentration falls below 0.05 micromoles/litre (i.e. one-tenth of the threshold concentration):

- serum methotrexate > 0.5 micromoles/litre: calcium folinate equivalent to 15 mg/m^2 folinic acid
- serum methotrexate > 1 micromole/litre: calcium folinate equivalent to 100 mg/m^2 folinic acid
- serum methotrexate > 2 micromoles/litre: calcium folinate equivalent to 200 mg/m^2 folinic acid

The dose of sodium folinate in rescue therapy is also based on serum-methotrexate concentrations (as measured 24 to 30 hours after beginning methotrexate):

- serum methotrexate 0.01 to 1.5 micromoles/litre: sodium folinate equivalent to 10 to 15 mg/m^2 folinic acid every 6 hours for 48 hours
- serum methotrexate 1.5 to 5 micromoles/litre: sodium folinate equivalent to 30 mg/m^2 folinic acid every 6 hours until methotrexate concentration is less than 0.05 micromoles/litre
- serum methotrexate > 5 micromoles/litre: sodium folinate equivalent to 60 to 100 mg/m^2 folinic acid every 6 hours until methotrexate concentration is less than 0.05 micromoles/litre

In patients who have received doses of methotrexate below 100 mg, and in whom rescue therapy is considered appropriate, doses of folinic acid 15 mg by mouth every 6 hours for 48 to 72 hours may suffice.

In addition, measures to ensure the prompt excretion of methotrexate (maintenance of high urine output and alkalinisation of urine) are integral parts of rescue treatment. Renal function should be monitored daily.

Folinic acid is also used **with fluorouracil** to enhance the cytotoxic effect in advanced colorectal cancer. Both high-dose regimens (typically doses of folinic acid 200 mg/m^2, followed by fluorouracil) and low-dose regimens (20 mg/m^2) have been used—for details, see Uses and Administration of Fluorouracil, p.723. Sodium folinate has been used in similar doses. It may also be given at a dose equivalent to folinic acid 500 mg/m^2 by intravenous infusion over 2 hours. An intravenous injection of fluorouracil 600 mg/m^2 is given one hour after the start of the folinate infusion. Alternatively, a continuous infusion of fluorouracil 2.6 g/m^2 is given for 24 hours after the sodium folinate dose. Treatment is given weekly for 6 weeks, and may then be repeated after a 2-week interval; the number of cycles depends on the response of the tumour.

Folinic acid, like folic acid, is effective in the treatment of folate-deficient **megaloblastic anaemia** (see p.1982). Doses of 15 mg daily by mouth have been suggested. If given intramuscularly a dose of up to 1 mg daily has been recommended on the grounds that higher doses have not been proven to be any more effective. It is unsuitable for megaloblastic anaemia secondary to vitamin-B_{12} deficiencies.

Cardiovascular disease. For a report of the use of intravenous folinic acid to reduce levels of homocysteine in haemodialysis patients, see Cardiovascular Disease, under Folic Acid, p.1941.

Deficiency states. Cerebral folate deficiency has been defined as any neurological syndrome associated with low CSF concentrations of 5-methyltetrahydrofolate, the active metabolite of folic acid.[1,2] Neurodevelopmental disorders have been associated with this deficiency, manifest as irritability, sleep disturbances, cerebellar ataxia, spastic paraplegia, dyskinesia, epileptic seizures, and speech difficulties. Dramatic improvements in some symptoms have been noted with oral folinic acid;[1-3] 0.5 to 1 mg/kg folinic acid daily has been used.[1] Analysis of CSF folate metabolites is recommended for patients presenting with movement disorders, mental retardation, or autism.[2,3]

1. Ramaekers VT, Blau N. Cerebral folate deficiency. *Dev Med Child Neurol* 2004; **46:** 843–51.
2. Hansen FJ, Blau N. Cerebral folate deficiency: life-changing supplementation with folinic acid. *Mol Genet Metab* 2005; **84:** 371–3.
3. Moretti P, *et al.* Cerebral folate deficiency with developmental delay, autism, and response to folinic acid. *Neurology* 2005; **64:** 1088–90.

HIV infection and AIDS. Calcium folinate has been used to reduce the toxicity of pyrimethamine and trimethoprim in patients with HIV infection. However, oral calcium folinate given to patients with AIDS receiving co-trimoxazole for the treatment of pneumocystis pneumonia was associated with a higher rate of therapeutic failure and a decrease in survival and did not reduce the frequency of dose-limiting co-trimoxazole toxicity.[1] Calcium folinate also did not reduce the toxicity of co-trimoxazole being used for the primary prophylaxis of PCP.[2] Vitamin B_{12} and folinic acid supplementation in patients with HIV infection did not prevent or reduce zidovudine-induced myelosuppression.[3]

1. Safrin S, *et al.* Adjunctive folinic acid with trimethoprim-sulfamethoxazole for Pneumocystis carinii pneumonia in AIDS patients is associated with an increased risk of therapeutic failure and death. *J Infect Dis* 1994; **170:** 912–17.
2. Bozzette SA, *et al.* The tolerance for zidovudine plus thrice weekly or daily trimethoprim-sulfamethoxazole with and without leucovorin for primary prophylaxis in advanced HIV disease. *Am J Med* 1995; **98:** 177–82.
3. Falguera M, *et al.* Study of the role of vitamin B and folinic acid supplementation in preventing hematologic toxicity of zidovudine. *Eur J Haematol* 1995; **55:** 97–102.

Preparations

BP 2008: Calcium Folinate Injection; Calcium Folinate Tablets;
USP 31: Leucovorin Calcium Injection; Leucovorin Calcium Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Asovorin; Cromatonbic Folinico†; Elvefocal; Estroquin; Folinfabra; Leucocalcin; Novizet; Rontafor; ***Austria:*** FOLI-Cell; Isovorin; Rescuvolin; Sodiofolin; ***Belg.:*** Elvorine; Folina-Cell; Ledervorin; Rescuvolin; VoriNa; ***Braz.:*** Calfolin†; Folicorin; Isovorin†; Legifol CS; Lenovor†; Levorin; Nyrin†; Prevax; Rescuvolin†; Tecnovorin; ***Chile:*** Covorit; ***Cz.:*** Antrex†; Levofolic; Sanficinate†; VoriNa; ***Denm.:*** Isovorin; Rescuvolin†; ***Fin.:*** Antrex; Isovorin; Rescuvolin†; ***Fr.:*** Elvorine; Folinoral; Lederfoline; Osfolate; ***Ger.:*** DeGalin; FOLI-Cell; Lederfolat; Neofolin; *O*-folin; Oncofolic; Rescuvolin; Ribofolin; VoriNa; ***Gr.:*** Buateron; Calcifolin; Calcivoran; Claro; Durofolin; Esvorin; Fedolen; Folical; Foliment; Folinato; Folivoran; Folmigor; Foxolin; Isovorin; Lizocalcio; Reotan; Rescuvolin; Sanovein; Veravorin; Vivalcid; Zamenit; Zenemia; ***Hong Kong:*** Calciumfolinat; ***Hung.:*** VoriNa; ***India:*** Biovorin; ***Indon.:*** Rescuvolin; ***Irl.:*** Isovorin†; Lederfolin; ***Ital.:*** Calcifolin; Calfolex; Calinat; Citofolin; Divical†; Divifolin; Ecofol; Emovis†; Folanemin; Folaren; Foliben; Folicalgyn†; Folidar; Folinact†; Folinvit†; Foliplus†; Lederfolin; Levofolene; Osfolato; Resfolin†; Sanifolin; Sulton; Tonofolin; ***Jpn:*** Uzel; ***Malaysia:*** Nyrin; Rescu-