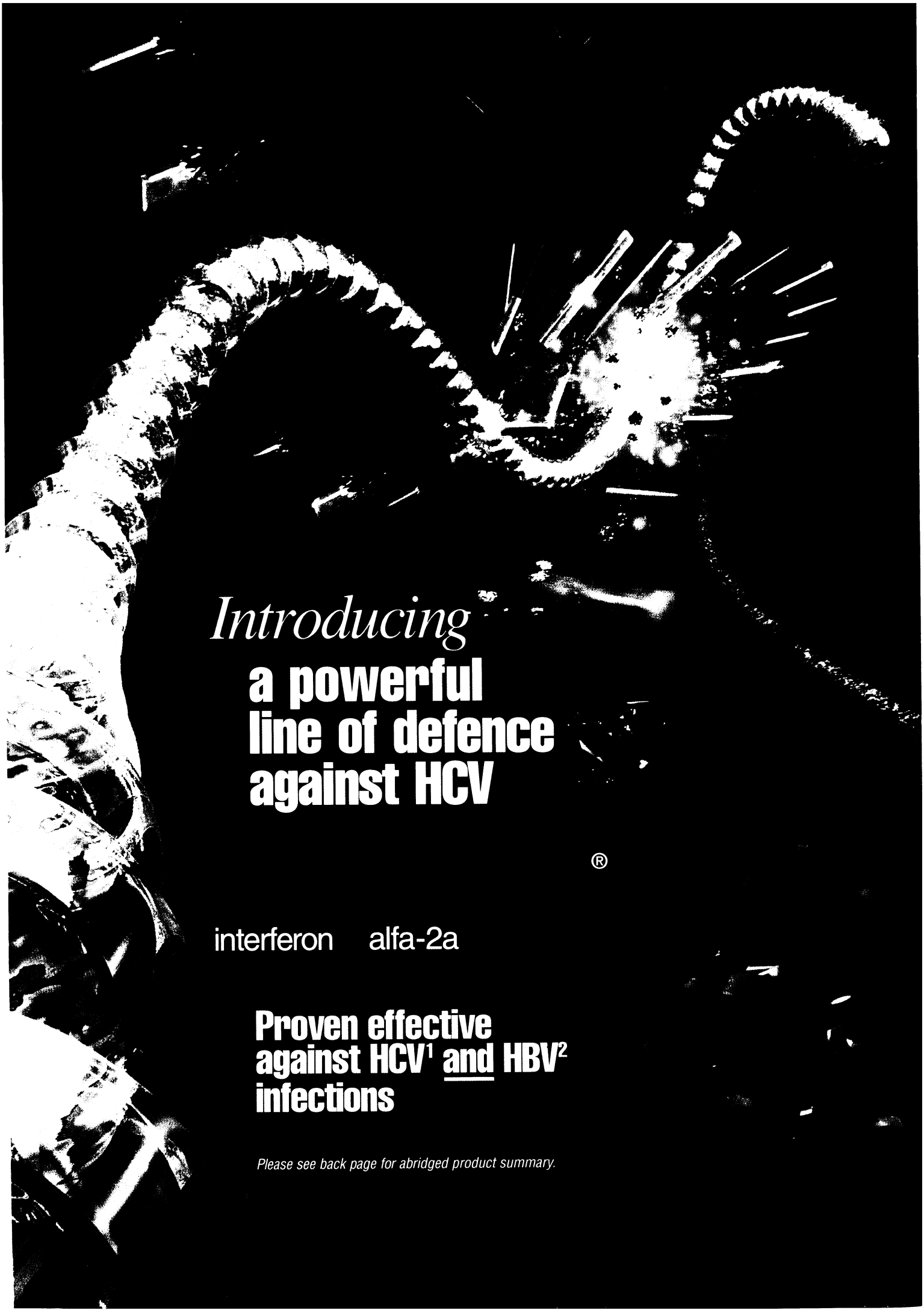
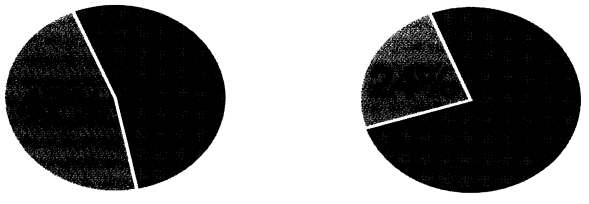

Introducing
a powerful line of defence against HCV
®
interferon alfa-2a
Proven effective against HCV[1] and HBV[2] infections
Please see back page for abridged product summary.

One line of defence for both HCV and HBV infections

Normalizes ALT in up to 83% of patients with chronic HCV infection[1,3]

IN A WORLDWIDE CLINICAL TRIAL PROGRAM, A TOTAL OF 1,831 PATIENTS WITH CHRONIC HCV INFECTION WERE TREATED WITH ROFERON-A.[1]

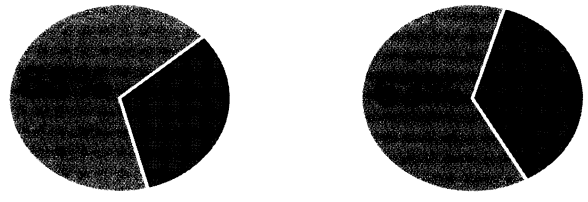
Responders*



Patients without cirrhosis | Patients with cirrhosis

ALT normalization was achieved in one study in 47% of patients (without cirrhosis) and in 24% of patients (with cirrhosis) with HCV when treated with ROFERON-A (6 MIU tiw for 3 months, then 3 MIU tiw for 3 months).[4]

Sustained Responders†



Patients without cirrhosis | Patients with cirrhosis

A normal ALT was sustained respectively in 68% (without cirrhosis) and 63% (with cirrhosis) of these responders 6 months after completion of therapy.[4]

Clears virologic markers in a significant number of patients with chronic HBV infection[2]

BOTH HBe ANTIGEN AND HBV-DNA WERE CLEARED IN 40% (55/136) OF PATIENTS WITH CHRONIC HBV INFECTION TREATED FOR 12 TO 24 WEEKS WITH 4.5, 9, OR 18 MIU‡ ROFERON-A TIW.[2]

ROFERON®-A
interferon alfa-2a

Roche

* At the end of the 6-month treatment period, 137 patients were evaluated.
† Six months after treatment was completed, 127 patients were evaluated.
‡ Statistically significant difference in response was seen between doses.

References:
1. Bernstein A, Chanéac M, Sullivan-Bolyaí J, Smith P, Facey K, Ryff J-C. Roferon®-A (Ro 22-8181) in chronic hepatitis non-A non-B: overall integrated summary of efficacy and safety. Research Report No. B-154'521. Data on file, F. Hoffmann-La Roche Ltd. **2.** Thomas HC, Lok ASF, Carreño V, et al. Comparative study of three doses of interferon-α2a in chronic active hepatitis B. *Journal of Viral Hepatitis.* 1994;1:139-148. **3.** Chemello L, Pontisso P, Rose KA, et al. The long-term response (LTR) to interferon-alfa (IFN-2a) in chronic hepatitis C is influenced by dose and duration of treatment and by the HCV serotype. *J Hepatol.* 1993;18:S10-S11. Abstract. **4.** Ouzan D, Skaf R, Andréani T, et al. French multicenter controlled trial of interferon alpha-2a (IFN) in chronic hepatitis C. Does an attack dose (6 MU) increase the response rate at 6 and 12 months? *J Hepatol.* 1993;18:S53. Abstract.

ROFERON-A

Composition: Interferon alfa-2a. **Indications:** Roferon-A is indicated for the treatment of hairy cell leukemia, cutaneous T-cell lymphoma (mycosis fungoides and Sézary syndrome), AIDS-related Kaposi's sarcoma, renal cell carcinoma, metastatic malignant melanoma, chronic myeloid leukemia in its chronic stage and essential thrombocytosis associated with myeloproliferative disease, chronic active hepatitis B and chronic hepatitis C. Registered indications may vary between different countries. **Dosage:** The approved dose for HCV is 3 to 6 MIU SC or IM tiw. Optimal dose and duration of treatment is still not known. Dosage recommendations for other indications are available on request. **Contraindications:** A history of hypersensitivity to recombinant interferon alfa-2a or any component of the preparation. Patients with severe cardiac disease or with any history of cardiac illness. Severe renal, hepatic or myeloid dysfunction. Seizure disorders and/or compromised central nervous system function. Chronic hepatitis with advanced, decompensated cirrhosis of the liver. Chronic hepatitis or recently been treated with immunosuppressive agents, excluding short-term 'steroid withdrawal'. CML who have an HLA-identical relative and for whom allogeneic bone marrow transplantation is planned or possible in the immediate future. **Precautions:** Roferon-A should be administered under the supervision of a qualified physician experienced in the management of the respective indication. When mild to moderate renal, hepatic or myeloid dysfunction is present, close monitoring of these functions is required. Careful periodic neuropsychiatric monitoring of all patients is recommended. In patients with severe myelosuppression. In transplant patients. In rare cases, severe hepatic dysfunction and liver failure have been reported. The safety and effectiveness of Roferon-A in children has not been established. The neurotoxic, hematotoxic or cardiotoxic effects of previously or concurrently administered centrally acting drugs may be increased by interferons. Men and women receiving Roferon-A should practice effective contraception. In pregnancy, Roferon-A should be administered only if the benefit to the woman justifies the potential risk to the fetus. It is not known whether this drug is excreted in human milk. A decision must be taken whether to suspend breast-feeding or to discontinue the drug. **Side effects:** *General symptoms:* The majority of the patients experienced *flu-like symptoms.* Reactivation of peptic ulcer and non-life-threatening gastrointestinal bleeding have been reported in isolated cases. In rare cases, hepatitis was reported. Severe somnolence, coma, cerebrovascular adverse events, transient impotence and ischemic retinopathy were rare complications. Rare cases of pulmonary edema, congestive heart failure, cardiorespiratory arrest and myocardial infarction have been reported. Cardiovascular problems are very rarely seen in patients with hepatitis B. Transient leukopenia occurred variably in about one third to over one half of the patients. In non-myelosuppressed patients, thrombocytopenia was less frequently seen, and decrease of hemoglobin and hematocrit occurred rarely. In myelosuppressed patients, thrombocytopenia and decreased hemoglobin occurred more frequently. Recovery of severe hematological deviations to pretreatment levels usually occurred within seven to ten days after discontinuing Roferon-A treatment. **Packs:** Vials containing 3, 4.5, 9 or 18 million IU + ampoules containing 1 ml sterile water for injections, 5's.
Registered indications and dosages may vary by country. Please consult your country's complete prescribing information before prescribing Roferon-A.

Printed in U.S.A.

The first UK approved treatment for chronic hepatitis C

ROFERON-A®

interferon alfa-2a (rbe)

BRIEF PRESCRIBING INFORMATION

Indications: Hairy cell leukaemia; AIDS-related Kaposi's sarcoma without prior opportunistic infection (as single agent); chronic active hepatitis B; Ph' positive chronic myelogenous leukaemia (adults >18 years); recurrent or metastatic renal cell carcinoma; refractory, progressive, cutaneous T-cell lymphoma; chronic hepatitis C. **Dosage:** Modify dose according to toxicity or pre-existing reduced bone marrow function. **Adults:** Hairy cell leukaemia - Induction with 3 million IU daily IM or SC for 16-24 weeks; maintenance with 3 million IU three times per week. AIDS-related Kaposi's sarcoma - Escalation from 3 million IU daily, SC or IM, to 18-36 million IU daily over 12 weeks, then maintenance with maximum tolerated dose (to maximum of 36 million IU) three times per week. Chronic active hepatitis B - Usually 2.5-5.0 million IU/m^2 SC for 4-6 months; escalation permitted in absence of response. Chronic myelogenous leukaemia - Escalation from 3 million IU daily to 9 million IU daily, SC or IM, over 12 weeks. Continue to complete haematological response, or maximum 18 months treatment, in responders. Complete haematological responders should continue with 9 million IU, daily (if tolerated) or three times per week, to achieve cytogenic response. Recurrent or metastatic renal cell carcinoma - Escalation from 3 up to maximum 36 million IU daily, IM, over 10 to 12 weeks (SC administration permitted for doses up to 18 million IU). Maintenance with 18-36 million IU three times per week. Refractory, progressive, cutaneous T-cell lymphoma - Escalation from 3 million IU to 18 million IU daily IM or SC for total 12 weeks, then maintenance with maximum tolerated dose (up to 18 MIU) three times per week for at least 8 weeks to determine response, and at least 12 months in responders. Chronic hepatitis C - Induction with 6 million IU three times weekly IM or SC for 3 months followed by maintenance with 3 million IU three times weekly for 3 months in responders (normalised ALT). **Elderly:** Caution; more susceptible to side-effects. Children: Safety and efficacy not established.

Administration: Reconstitute powder with 1 ml Water for Injections Ph.Eur. Reconstituted solution stable for 24 hours at 2-8°C, or 2 hours at room temperature. For subcutaneous or deep intramuscular injection (vary site for repeat injections).

Contra-indications: Hypersensitivity to interferons or Roferon-A excipients; severe cardiac, renal, hepatic or myeloid disease; epilepsy and/or compromised CNS function. Chronic hepatitis with advanced, decompensated liver cirrhosis; recent immunosuppressive therapy (excluding short term "steroid withdrawal"); CML immediate candidates for allogeneic bone marrow transplantation.

Pregnancy: Avoid (Use only where potential benefit outweighs risk in females). Contraception to be used in fertile males and females. Avoid in breast feeding. Known abortifacient in primates.

Precautions: Use under specialist supervision. Efficacy not shown in hepatitis B with HIV co-infection. Monitor renal, hepatic and myeloid function closely if pre-existing mild to moderate dysfunction. Neuropsychiatric monitoring, suicidal behaviour has been rarely observed (discontinuation recommended). Extreme caution in severe myelosuppression (monitor complete blood count), and transplant patients on immunosuppressants. Possible impairment of driving, machine operation, etc. Recurrence of Kaposi's sarcoma lesions possible on stopping treatment. Autoantibodies have been reported and autoimmune phenomena such as vasculitis, arthritis, haemolytic anaemia, thyroid dysfunction, and lupus erythematosus have been rarely observed.

Drug interactions: CNS active drugs and those metabolised by oxidative enzymes. Additive toxicity with neurotoxic, haemotoxic, or cardiotoxic agents. May reduce clearance of theophylline.

Side-effects and adverse reactions: General symptoms: Influenza-like symptoms (respond to paracetamol); severe anorexia and weight loss; GI tract: GI upset and rarely GI bleeds or reactivation of peptic ulcer. Liver function: Altered liver function tests; rare reports of hepatitis, and liver failure. CNS symptoms: Uncommonly, dizziness, vertigo, visual disturbance, forgetfulness, depression, drowsiness, confusion, nervousness, and sleep disturbances; rare reports of suicidal behaviour, ischaemic retinopathy, convulsions, severe somnolence, and coma. Peripheral nervous system: Occasionally sensory and motor neuropathies. Cardiovascular ~ pulmonary: Transient BP fluctuations; oedema; cyanosis; arrhythmias, palpitations, and chest pain. Rarely, myocardial infarction, congestive cardiac failure, pulmonary oedema, pneumonia, and cardiorespiratory arrest. Rarely coughing, mild dyspnoea. Skin, mucous membranes etc.: Rarely herpes labialis exacerbation, rash, pruritus, dryness, rhinorrhoea and epistaxis; reversible alopecia; rarely exacerbation/provocation of psoriasis. Renal: rarely renal impairment; electrolyte disturbances; proteinuria; interstitial nephritis; rare elevations in BUN, serum creatinine, and uric acid. Haematopoietic: Transient leucopenia; thrombocytopenia; rarely decreased haemoglobin and haematocrit. Severe changes normalise by 7-10 days post-treatment. Other: Inconsequential hypocalcaemia; hyperglycaemia; injection site reaction; menstrual irregularities in animals; development of neutralising antibodies: in patients with hepatitis C a trend for loss of response in responding patients who develop such antibodies has been seen, no other clinical sequelae clearly documented.

Legal category: POM.

Presentations and Basic NHS Cost: 1 vial containing 3 million IU of lyophilised interferon alfa-2a (rbe) accompanied by 1ml Water for Injections Ph.Eur. as solvent: £16.96. 1 vial containing 4.5 million IU of lyophilised interferon alfa-2a (rbe) accompanied by 1ml Water for Injections Ph.Eur. as solvent: £25.44. One vial containing 9 million IU of lyophilised interferon alfa-2a (rbe) accompanied by 1 ml Water for Injections Ph.Eur. as solvent: £50.88. 1 vial containing 18 million IU of lyophilised interferon alfa-2a (rbe) accompanied by 1ml Water for Injections Ph.Eur. as solvent: £101.77. Each presentation includes a disposable syringe for IM or SC injections.

Product Licence Numbers:

PL 0031/0201 (3 MIU vial), PL 0031/0295 (4.5 MIU vial), PL 0031/0215 (9 MIU vial)
PL 0031/0202 (18 MIU vial), PL 0031/0284 (Ampoules Water for Injections Ph.Eur.)

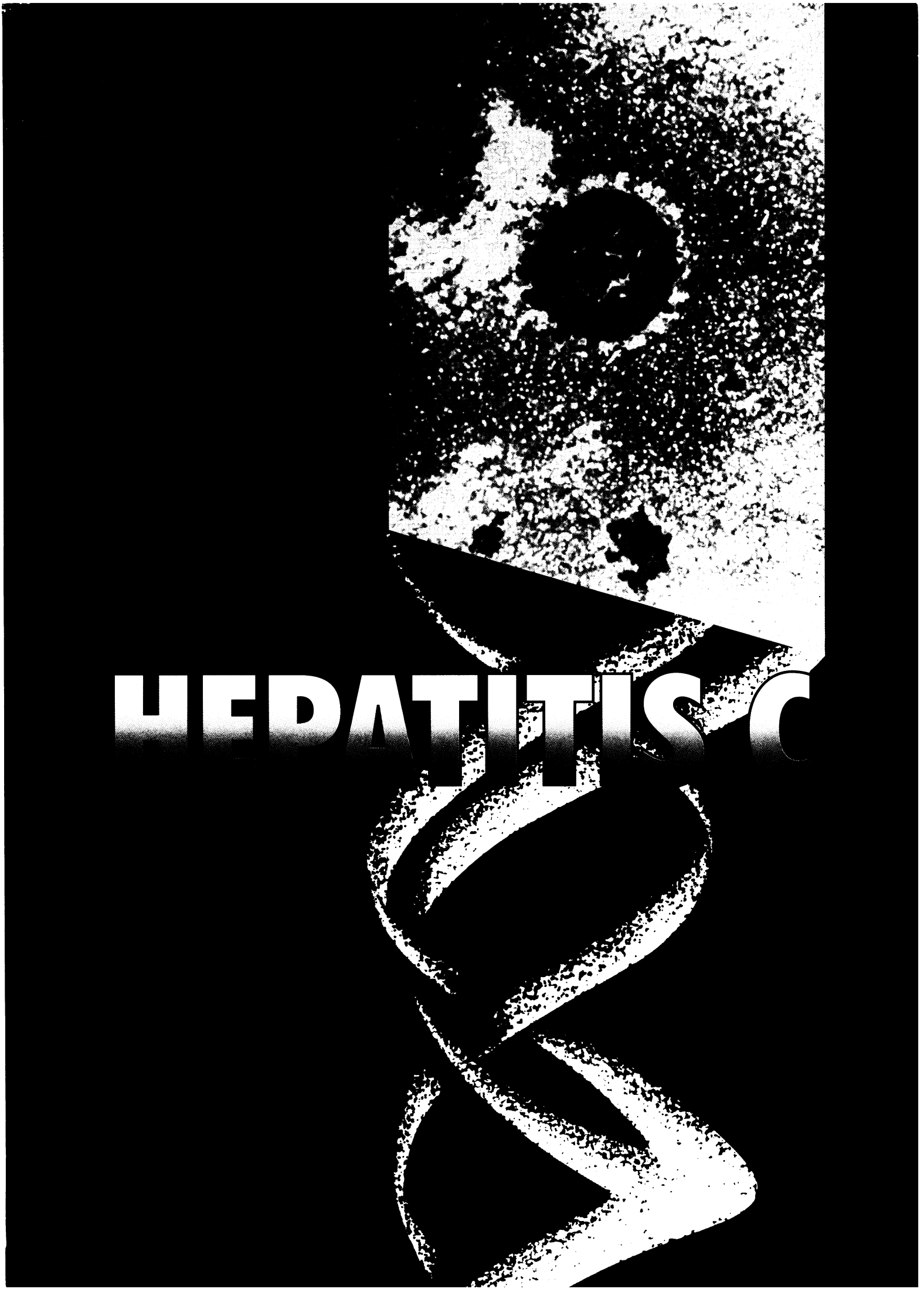
Product Licence Holder: Roche Products Limited, PO Box 8, Welwyn Garden City, Herts., AL7 3AY.

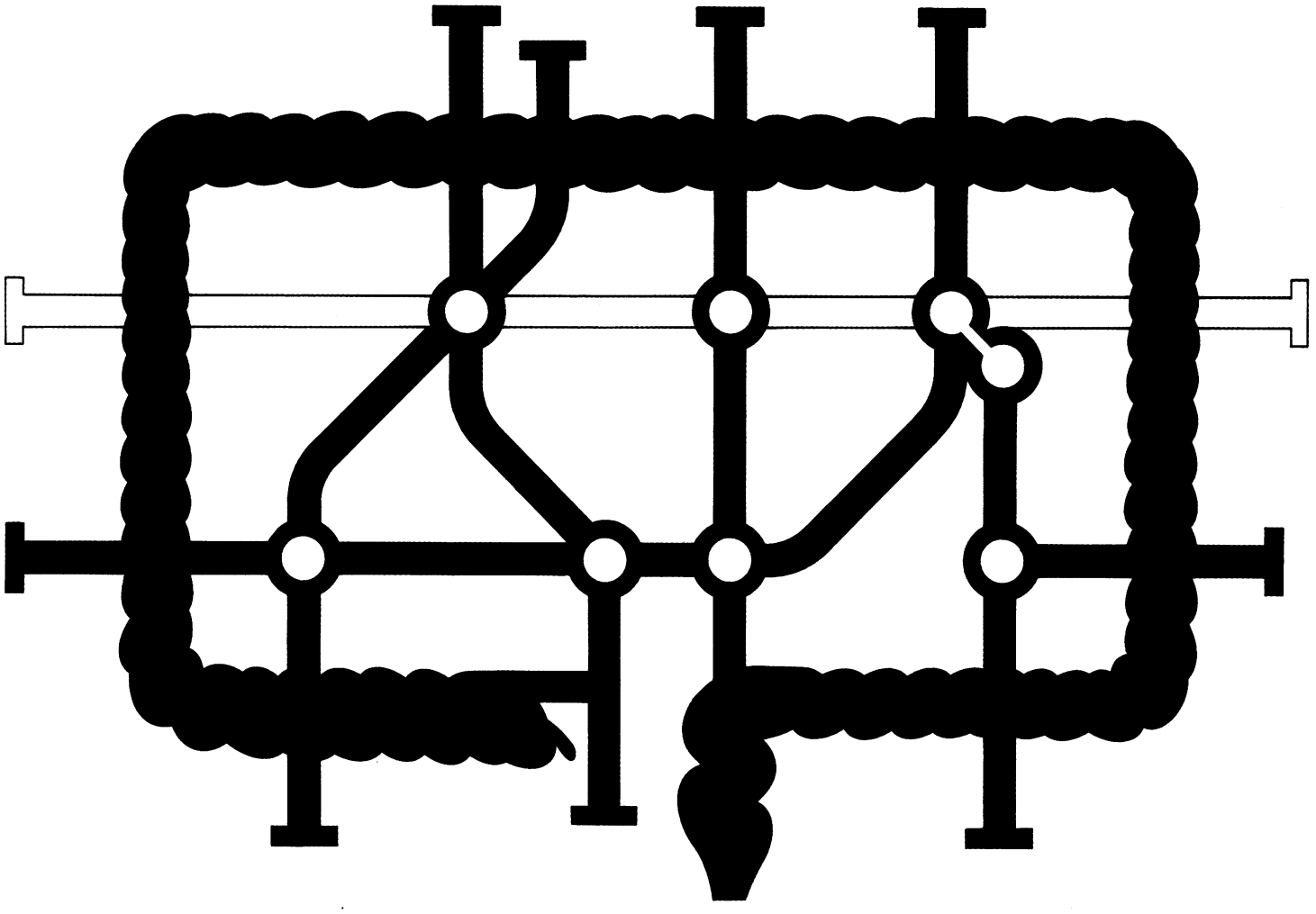
Full prescribing information available on request.

Roferon is a registered trademark.

Roche

J739190


HEPATITIS C



COLIFOAM

10% hydrocortisone acetate

FIRST CLASS TREATMENT WHICH TRAVELS TO WORK

- Colifoam is highly effective for distal ulcerative colitis.[1]
- The retrograde spread of Colifoam increases with the extent of disease.[2]
- Colifoam is easier to retain than liquid enemas and causes less interference with social, sexual and occupational activities.[1,3]

PRESCRIBED WITH CONFIDENCE FOR OVER 20 YEARS.

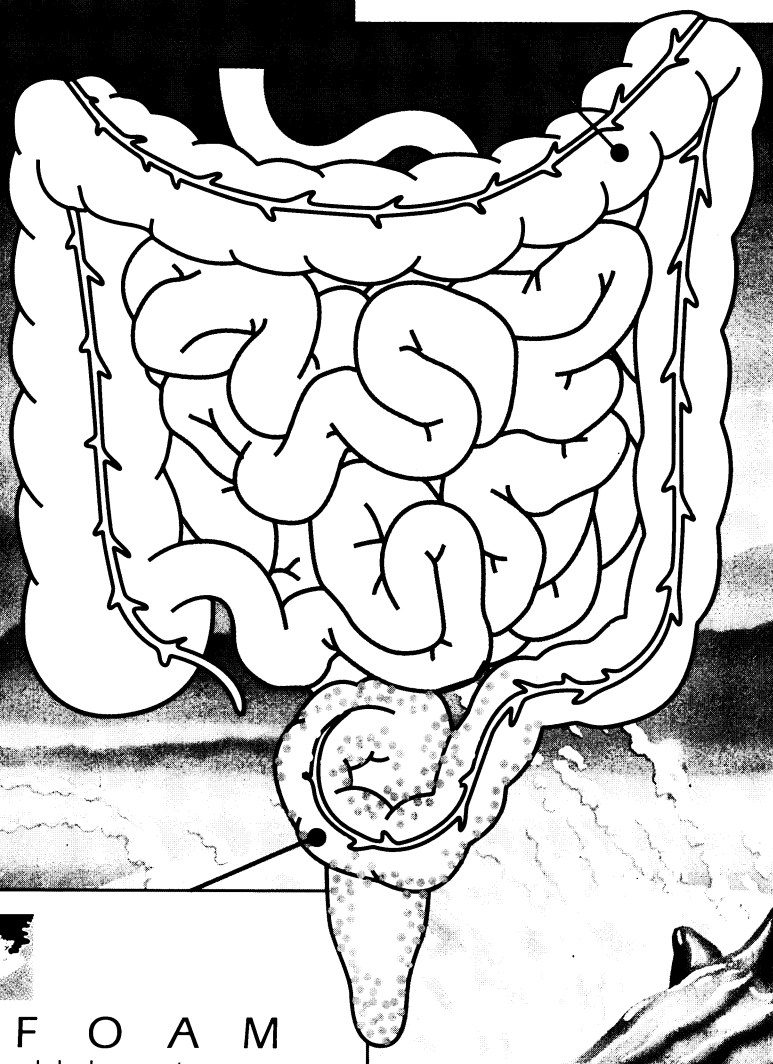
PRESCRIBING INFORMATION: Presentation: White odourless aerosol containing hydrocortisone acetate Ph Eur 10% w/w. **Uses:** Ulcerative colitis, proctosigmoiditis and granular proctitis. **Dosage and administration:** One applicatorful inserted into the rectum once or twice daily for two or three weeks and every second day thereafter. Shake can vigorously before use (illustrated instructions are enclosed with pack). **Contra-indications, warnings etc.:** Local contra-indications to the use of intrarectal steroids include obstruction, abscess, perforation, peritonitis, fresh intestinal anastomoses and extensive fistulae. General precautions common to all corticosteroid therapy should be observed during treatment with Colifoam. Treatment should be administered with caution in patients with severe ulcerative disease because of their predisposition to perforation of the bowel wall. Safety during pregnancy has not been fully established. **Pharmaceutical precautions:** Pressurized container. Protect from sunlight and do not expose to temperatures over 50°C. Do not pierce or burn even after use. Do not refrigerate. Keep out of reach of children. For external use only. **Legal category:** POM. **Package Quantity and Basic NHS cost:** 25g canister plus applicator, £7.07. **Further Information:** One applicatorful of Colifoam provides a dose of approximately 125mg of hydrocortisone acetate, similar to that used in a retention enema, for the treatment of ulcerative colitis, sigmoiditis and proctitis. **Product Licence No.:** 0036/0021 Colifoam is a registered trade mark. **References:** 1. Somerville KW et al. BMJ 1985;291:866. 2. Farthing MJG et al. BMJ 1979;2:822-824. 3. Ruddell WSJ et al. Gut 1980;21:885-889. Further information is available on request. Stafford-Miller Ltd., Professional Relations Division, Broadwater Road, Welwyn Garden City, Herts. AL7 3SP. **Code:** DO2665.

Calming the Colitic Colon

P R E D E N E M A

Prednisolone Metasulphobenzoate

Aqueous formulation for the effective treatment of extensive colitis.[1]



P R E D F O A M

Prednisolone Metasulphobenzoate

Metered dose foam formulation provides accurate and consistent dosing for the effective treatment of distal ulcerative proctocolitis.[2]

A complete local management system for ulcerative colitis

Abbreviated Prescribing Information.

Predenema: **Presentation:** Disposable enema 100ml aqueous solution containing prednisolone metasulphobenzoate sodium equivalent to 20 mg of prednisolone. A long tube version is available. **Uses:** Local treatment of ulcerative colitis. **Dosage and Administration:** Adults only: 1 enema nightly for two to four weeks extending the course where a good response is being obtained. **Contraindications, Warnings etc:** Conditions where infection might be masked or healing impaired. Prolonged continuous use is undesirable. There is inadequate evidence of safety in human pregnancy. **Legal categories and Product Licence Numbers:** POM PL 0108/5018 PA 100/7/1. **Packs and NHS Price:** Pack of 7 enemas long tube £9.45. Pack of 10 enemas, standard tube £8.00. Full prescribing information is available on request.

Predfoam Presentation: A foam enema containing prednisolone metasulphobenzoate sodium equivalent to 20mg of prednisolone per metered dose. **Uses:** Treatment of proctitis and ulcerative colitis. **Dosage and Administration:** Adults and Elderly patients: Once or twice daily for two weeks, extending treatment for a further two weeks when a good response is obtained. Children: Not recommended. **Contraindications, Warnings etc:** Conditions where infection might be masked or healing impaired. Prolonged continuous use is undesirable. There is inadequate evidence of safety in human pregnancy. **Legal categories and Product Licence Numbers** POM PL 0108/0101 PA 100/40/1. **Packs and NHS Price** Box containing one 14 dose canister, 14 disposable nozzles and 14 plastic bags:£7.06.Full prescribing information is available on request. **Date of preparation:** October 1994

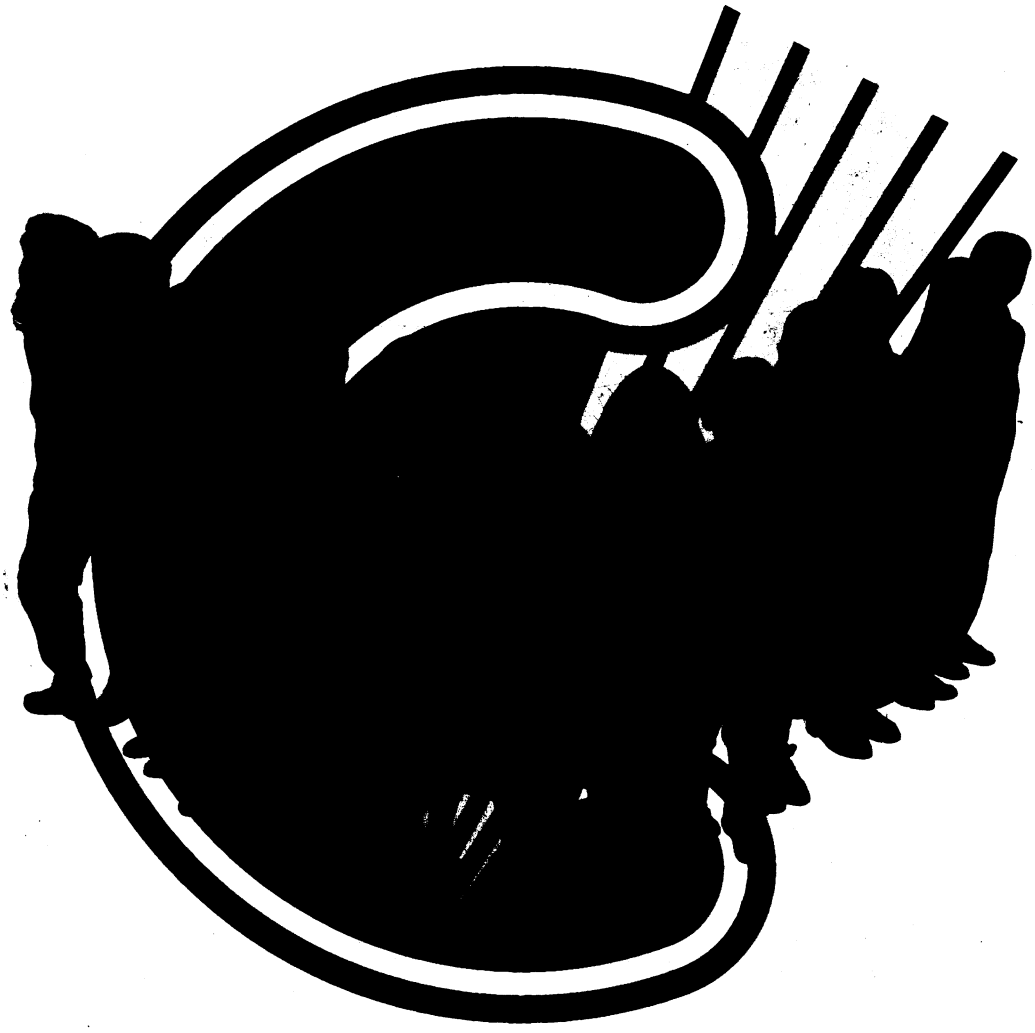
References. 1. Lee DAH, et al. Rectally administered prednisolone - evidence for a predominantly local action. 1980 Gut;21:215-218. **2.** Foster P, Atkinson M. Clinical evaluation of a prednisolone metasulphobenzoate rectal foam in the treatment of acute distal ulcerative colitis. Data on file.

Pharmax Limited Bexley Kent DA5 1NX

PHARMAX

EPFOA0688

The CF World has been turning to Creon for years



creon®
pancreatin

Because CF patients need all the help they can get

PRESCRIBING INFORMATION

Presentation 1. Creon - brown/yellow capsules containing enteric coated granules of pancreatin, equivalent to: 8,000 PhEur units of lipase; 9,000 PhEur units of amylase and 450 PhEur units (total) of protease (210 BP units). Available in packs of 100. Basic NHS price of £13.33. PL 5727/0001. 2. Creon sachets - unit dose sachets containing enteric coated granules of pancreatin, equivalent to: 20,000 PhEur units of lipase, 22,500 PhEur units of amylase and 1,125 PhEur units (total) of protease. Available in packs of 40. Basic NHS price of £13.33. PL 5727/0007.

Indication Pancreatic exocrine insufficiency.

Dosage and Administration: Adults and children: 1. Creon - initially one or two capsules with meals, then adjust according to response. 2. Creon sachets - initially the contents of one sachet with meals, then adjust according to response. (Note that two sachets of Creon granules are equivalent to five capsules of Creon.) The contents of each sachet can be taken from a spoon or tipped directly onto the tongue, and then washed down with a drink of water or other fluid. The granules contained in Creon capsules or sachets can also be sprinkled on soft food, which should then be swallowed without chewing. If the granules are mixed with food, it is important that they are taken immediately, otherwise dissolution of the enteric coating may result.

Contra-indications, Warnings etc. Contra-indications: substitution with pancreatic enzymes is contra-indicated in the early states of acute pancreatitis. Use in pregnancy: there is inadequate evidence of safety in use during pregnancy. **Warnings:** The product is of porcine origin. Rarely cases of hyper-uricosuria and hyper-uricaemia have been reported with very high doses of pancreatin. Perianal irritation, and rarely, inflammation, could occur when large doses are used.

Legal Classification: P

Name and Address of Licence Holder: Kali Chemie Pharma GmbH, Postfach 220, D-30173, Hannover 1, Germany.

Further information available from: Duphar Laboratories Limited, Gaters Hill, West End, Southampton SO18 3JD. Tel: 0703 472281.

Date of preparation August 1994

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SOLVAY DUPHAR LABORATORIES