Number 2
in a series

Gastric ulcer

reduce acid...improve healing

(Artist's impression of H_2 receptor antagonist acting on receptor site in the parietal cell in gastric mucosa.)

Healing

'Tagamet', by its unique action in selectively reducing gastric acid secretion, achieves remarkable results in the treatment of gastric ulcer.[1-6] In clinical trials, 79% of 'Tagamet'-treated patients have shown complete healing in 4-6 weeks compared with only 45% in the placebo group.[6] In addition, in a comparative controlled trial with carbenoxolone,[5] preliminary results have shown that 'Tagamet' produced healing in 73% of patients (11/15) compared with 50% in the carbenoxolone group (8/16).

Symptomatic Relief

In gastric ulcer, overall experience has shown that more rapid and greater relief of pain is experienced in those patients receiving 'Tagamet'.[6] However, symptomatic relief, whilst very good, is not as predictable in onset as it is in duodenal ulcer.[3,4] For patients who experience pain during the early stages of treatment, antacids should be made available.

Tagamet

H_2 reduces gastric acid secretion

References

1. Healing of gastric ulcer during treatment with cimetidine. (1976) Lancet, **i,** 337.
2. Treatment of gastric ulcer by cimetidine. (1977) Proceedings of the Second International Symposium on Histamine H_2-Receptor Antagonists. Excerpta Medica. p. 267.
3. A controlled trial of cimetidine in the treatment of gastric ulcer. (1977) Proceedings of the Second International Symposium on Histamine H_2-Receptor Antagonists. Excerpta Medica. p. 283.
4. Cimetidine in patients with gastric ulcer: a multicentre controlled trial. (1977) Brit. med. J., **2,** 795.
5. Double-blind trial comparing cimetidine with carbenoxolone in the treatment of benign gastric ulcer. (1977) Gut, **18,** A420.
6. Data on file. Smith Kline & French.

'Tagamet' (cimetidine) is available as 200mg film-coated tablets, 200mg 5ml syrup and 200mg 2ml ampoules.

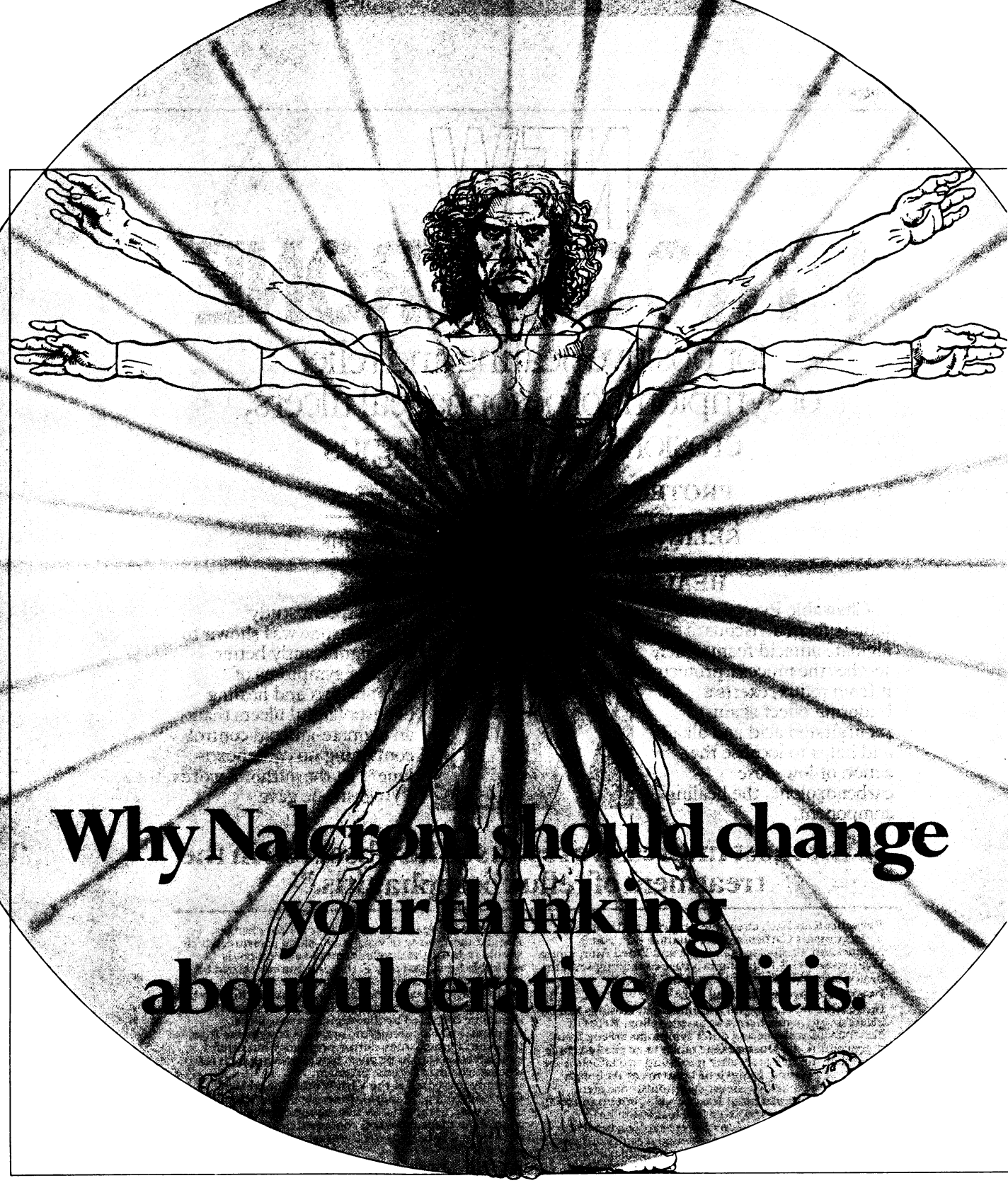
'Tagamet' is a trade mark.

Full prescribing information is available from:–

SK&F
a SmithKline company

Smith Kline & French Laboratories Limited
Welwyn Garden City
Hertfordshire AL7 1EY
Telephone: Welwyn Garden 25111

TG/AD28



Prescribing Information

PRESENTATION: Nalcrom is a presentation of sodium cromoglycate for oral use. It is presented in clear/clear hard gelatine capsules printed Fisons 101 in black. Each capsule contains 100mg sodium cromoglycate as a white powder.

USES: As an adjuvant in the treatment of ulcerative colitis, proctitis and proctocolitis. Sodium cromoglycate is considered to exert a stabilising effect upon mast cells capable of releasing mediators, thus preventing the local inflammatory reaction in the gastrointestinal tract.

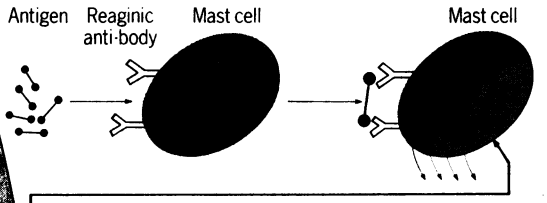
DOSAGE AND ADMINISTRATION: Dosage Adults: Two capsules four times daily.
Children: From 2–14 years; one capsule four times daily.
Nalcrom should not be used for children under two years.
Maintenance dosage To prevent relapses dosage should be maintained indefinitely at two capsules four times daily in adults and one capsule four times daily in children.
Administration The capsules may be swallowed whole or alternatively the powder contents may be dissolved in 20–30ml of water and swallowed.

Nalcrom offers a completely new approach to the management of ulcerative colitis.

And it could mean freedom from side effects often associated with the limited number of treatments now available.

Nalcrom is sodium cromoglycate.

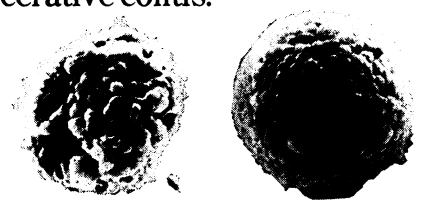
Sodium cromoglycate is the unique drug which is used successfully in the treatment of allergic diseases, such as asthma and rhinitis.



Sodium cromoglycate prevents the degranulation of mast cells caused by the interaction of antigens and reaginic antibodies.

It is a potent inhibitor of mast cell degranulation. It prevents the release of inflammatory agents into sub-mucosal tissue in the lung, nose and other organs. So it stops symptoms before they even start. And over ten years of clinical use has proved it to be a very effective drug with remarkably few serious side-effects.

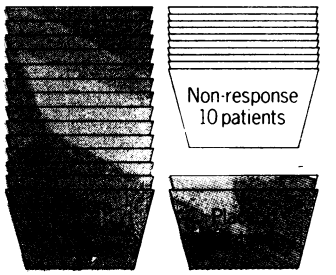
Now it offers hope as a new treatment for ulcerative colitis.



On left mast cell undergoing gross degranulation. On right mast cell stabilised after treatment with sodium cromoglycate. Photomicrographs prepared by: R & D Laboratories, Fisons Ltd., Pharmaceutical Division.

Why an anti-allergy drug?

Ulcerative colitis in its natural history and histological appearance has many features such as macrophages, mast cells and eosinophils that suggest that an allergic or immunological process may be involved. Sodium cromoglycate may have a clinically beneficial effect in these processes. So a double blind cross-over trial was carried out with 26 patients suffering from chronic proctitis[1]. The 14 responders to sodium cromoglycate had a high local eosinophil count which in most cases fell in the course of treatment.



In a double-blind cross-over trial of 26 patients, 14 responded to sodium cromoglycate, 10 didn't respond and 2 responded to placebo.

Another study of 12 patients with ulcerative colitis treated with sodium cromoglycate showed a significant improvement in sigmoidoscopic appearance. And again, rectal biopsies showed a significant reduction in eosinophil counts[2,3].

How to find out more about Nalcrom.

Specialist representatives are available at this stage to discuss Nalcrom with hospital doctors. Simply fill in and post the coupon or write to: Fisons Limited, Pharmaceutical Division, Loughborough, Leicestershire.

Nalcrom®
(Sodium Cromoglycate B.P.)

References 1. Heatley, R.V. et al, 1975, "Gut," **16**, 559 2. Mani, V. et al, 1976, "Lancet," **1**, 439 3. Mani, V. et al, 1977, "Gastro-enterology," **72**, 1093.

Please arrange for a specialist representative to call.

Name _____ Address _____

Further information is available on request from Fisons Limited, Pharmaceutical Division, Loughborough, Leicestershire.

®FISONS
Leaders in Allergy Research

G/N/3

CONTRA-INDICATIONS, WARNINGS, ETC: Contra-indications There are no specific contra-indications. The safety of Nalcrom during pregnancy has not yet been established.
Side-effects Nausea has been reported in a few cases.
Overdosage As Nalcrom is absorbed only to a very limited extent, no action other than medical observation should be necessary.
PHARMACEUTICAL PRECAUTIONS: Store in a dry place. Reclose the container tightly after use.
LEGAL CATEGORY: P.O.M.
PACKAGE QUANTITIES: Containers of 100 capsules.

FURTHER INFORMATION: 1. Nalcrom may be used in conjunction with steroid therapy and sulphasalazine in the treatment of acute relapses of proctocolitis and in maintaining remissions.
2. If steroid therapy is to be reduced or withdrawn this should be done cautiously.
3. Nalcrom may be used in patients with a history of hypersensitivity to or intolerance of sulphasalazine.
4. Dosages of 2000mg daily have been used in some cases of proctocolitis.
PRODUCT LICENCE NUMBER: PL 0113/0073.

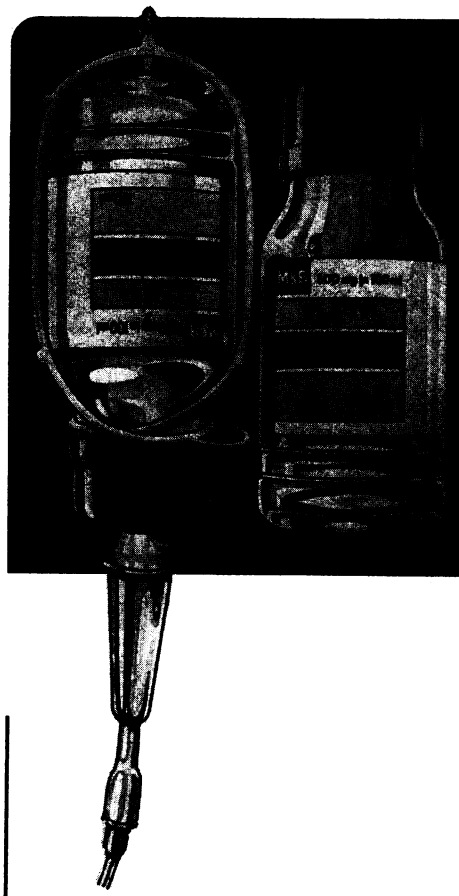
In abdominal and gynaecological surgery, Flagyl is revolutionising the treatment of infection...

and now

Flagyl Injection

for intravenous infusion

M&B May&Baker



Flagyl

cause-specific, effect...decisive

in most infections following abdominal or gynaecological surgery

Most of these infections are caused by anaerobes

Post-operative infection is a major complication of gastro-intestinal and gynaecological surgery.[1] After colonic surgery the incidence can exceed 50 per cent.[2]
In both the colon and the female genital tract, non-sporing obligate anaerobic bacilli are commonly occurring (and, in the colon, heavily preponderant) organisms of the normal bacterial flora.[2-4] Now, with greatly improved techniques of isolation, there is increasing awareness of their importance as the major pathogens in post-surgical infection involving these fields.[1, 2, 4-7]
"... it is now well established that most of these post-operative infections are due to anaerobes ..."[1]
"... aerobic bacteria are usually only of secondary importance in these clinical settings."[2]

Flagyl is specifically, intensely, consistently bactericidal to anaerobes...

'Flagyl' is unique as the only available antimicrobial agent with selective activity against obligate anaerobes.[2, 5] Experience shows it to be consistently, completely bactericidal to these organisms[8] – at serum and tissue concentrations well below those normally obtained in treatment.[1, 7] Bactericidal concentrations are also rapidly reached in most other body fluids.[1]

...and thus dramatically, uncompromisingly effective in clearing most of the infections

Incisively active against the primary pathogens, 'Flagyl' is spectacularly successful in providing effective antimicrobial therapy in most post-operative abdominal and gynaecological anaerobic infections.
"In all our infected patients the clinical and microbiological response to metronidazole was dramatic. Within 12-24 hours the

temperature and pulse-rate had usually returned to normal, the patient looked and felt better... There was a strikingly rapid disappearance of anaerobic bacteria from pathological discharges, which ceased to be purulent and offensive and quickly subsided."[2]

Even in cases of mixed anaerobic/aerobic aetiology, the use of 'Flagyl' alone, directed against the anaerobic component, has given excellent results.[7]

Moreover the results of preventative use are equally impressive:

"... considerable reduction in post-operative morbidity due to metronidazole prophylaxis... has lightened the nursing of patients with serious post-operative sepsis by virtually eliminating it."[6]

Flagyl does not have the drawbacks of agents previously used

Previously preferred antimicrobial agents such as chloramphenicol, lincomycin and clindamycin are not consistently bactericidal to anaerobes at readily attainable serum concentrations – nor completely bactericidal to all strains of the major species. They may also predispose to resistance of aerobic or facultatively anaerobic pathogens.[4, 5]

'Flagyl' reliably anaerobicidal and, through its specificity, incapable of inducing aerobic resistance,[2, 5, 9] does not have these disadvantages – which is why it is now revolutionizing the management of post-operative abdominal and gynaecological infections.

Flagyl injection provides a convenient new dosage form for the seriously ill

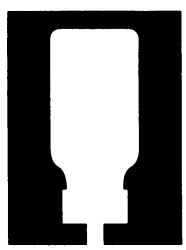
'Flagyl' injection for intravenous infusion answers the need for conveniently given, rapidly effective medication for sepsis following major surgery,[7] especially when the infection is well established. High blood levels can be very quickly obtained and adequately maintained[10] until the patient is well enough to transfer to oral or rectal therapy.

"We have found intravenous metronidazole to be safe, easy to administer, and well tolerated by patients..."[7]

- ★ **compatible in the body with other antibacterial agents when combined antimicrobial therapy is appropriate**[9]
- ★ **Seventeen years' well tolerated, widespread use in other major indications**
- ★ **now in oral, rectal and i.v. presentations**

references and full prescribing information overleaf

Flagyl Injection



the vital complement to surgical skill

Flagyl Injection

for intravenous infusion in postoperative abdominal and gynaecological infection

PRESCRIBING INFORMATION
(anaerobic infections)

N.B. Metronidazole has no useful direct activity against aerobic or facultatively anaerobic bacteria.

Presentation

Injection (for intravenous infusion) 0.5%w/v in 100ml bottles (500mg metronidazole per 100ml).

Uses

1. Treatment of infections in which anaerobic bacteria have been identified or are suspected as pathogens, particularly *Bacteroides fragilis* and other species of bacteroides and including other species for which metronidazole is bactericidal, such as fusobacteria, eubacteria, clostridia and anaerobic cocci.
'Flagyl' has been used successfully in: septicaemia, bacteraemia, brain abscess, necrotising pneumonia, osteomyelitis, puerperal sepsis, pelvic abscess, pelvic cellulitis, peritonitis and postoperative wound infection, from which one or more of these anaerobes have been isolated.

2. Prevention of postoperative infections due to anaerobic bacteria, particularly species of bacteroides and anaerobic streptococci.

Dosage and Administration

In patients with severe anaerobic infection for whom oral medication is not possible or is contra-indicated; it is particularly useful in emergencies and is indicated in patients needing surgery who:
– have or are believed to have anaerobic sepsis such as septicaemia, peritonitis, subphrenic or pelvic abscesses.
– at operation show signs of established or impending anaerobic sepsis.
– undergo operations in which contamination occurs with anaerobes from the gastro-intestinal or female genital tracts or the oropharynx.
In infants and other patients maintained on intravenous fluids, 'Flagyl' injection may be diluted with appropriate volumes of normal saline, dextrose-saline, dextrose 5% w/v or potassium chloride injections (20mmol and 40mmol).

1. Treatment:
Adults and children over 12 years:
100ml by intravenous infusion eight-hourly. The injection should be infused intravenously at the rate of 5ml per minute but may be administered alone or concurrently (but separately) with other bacteriologically appropriate antibacterial agents in parenteral dosage forms. Oral medication with 400mg three times daily should be substituted as soon as this becomes feasible. Treatment for seven days should be satisfactory for most patients but, depending upon clinical and bacteriological assessments, the physician might decide to prolong treatment e.g. for the eradication of infection from sites which cannot be drained or are liable to endogenous re-contamination by anaerobic pathogens from the gut, oropharynx or female genital tract.

Children under 12 years:
As for adults but the single intravenous dose is based on 1.5ml (7.5mg metronidazole) per kg bodyweight and the oral dose on 7.5mg per kg bodyweight.

2. Prevention:
Adults and children over 12 years:
100ml by intravenous infusion immediately before, during or after operation, followed by the same dose eight-hourly until oral medication (200 to 400mg three times daily) can be given to complete a seven-day course.
Children under 12 years:
As for adults but the single intravenous dose is based on 1.5ml (7.5mg metronidazole) per kg bodyweight and the oral dose on 3.7 to 7.5mg per kg bodyweight.

Contra-indications

There are no absolute contra-indications to the use of 'Flagyl' intravenous injection for anaerobic antibacterial therapy.

Precautions

The recommended dosages, frequencies of administration and durations of medication have been found effective and well tolerated in nearly all cases. However, regular clinical and biological surveillance are advised if administration of 'Flagyl' for more than 10 days is considered to be necessary.

Clinicians who contemplate continuous therapy, for the relief of chronic conditions, for periods longer than those recommended are advised to consider the possible therapeutic benefit against the risk of peripheral neuropathy.

Such evidence as is available suggests that patients with various degrees of renal impairment handle metronidazole like patients with normal renal function. Daily dosage may, however, be halved for patients with renal failure, if the clinician so wishes, as such dosage has been found effective.

Patients should be advised not to take alcoholic drinks during metronidazole therapy.

Metronidazole enhances the activity of warfarin and if 'Flagyl' is to be given to patients receiving this or other oral anti-coagulants the dosages of the latter should be recalibrated.

Pregnant women tolerate metronidazole well and no adverse effect on their offspring has been reported. As with all medicines 'Flagyl' should not be given during pregnancy or during lactation unless the physician considers it essential.

Side effects and adverse reactions

No serious adverse reactions have been encountered with the recommended regimes. There have been occasional reports of an unpleasant taste in the mouth, furred tongue, nausea, vomiting (very rarely) and gastro-intestinal disturbance. Drowsiness, dizziness, headache, ataxia, skin rashes, pruritus, inco-ordination of movement and darkening of the urine (due to a metronidazole metabolite) have been reported but very rarely. During intensive and/or prolonged metronidazole therapy, a few instances of peripheral neuropathy have been reported but in most cases the reaction disappeared after treatment was stopped or when dosage was reduced. A moderate leucopenia has been reported in some patients but the white cell count has always returned to normal before or after treatment has been completed. Transient epileptiform seizures have been reported in a few patients undergoing intensive, high-dosage metronidazole radio-sensitisation therapy.

Treatment of overdosage

There is no specific treatment for gross overdosage of 'Flagyl', but early gastric lavage is recommended. Uneventful recovery has followed attempts at suicide with quantities of 30 and 60 x 200mg tablets.

Pharmaceutical precautions

Protect from light.

Package quantities

Bottle of 100ml injection 0.5% w/v.

Further information

Other established indications for 'Flagyl' include urogenital trichomoniasis, giardiasis, all forms of amoebiasis, acute ulcerative gingivitis and acute dental infections. 'Flagyl' is also available as tablets and, in some territories, as suppositories.

References

1 *Scot.Med.J.*, **22**, 155, 1977
2 *Br.Med.J.*, **i**, 607, 1977
3 *Finegold, S.M.*, Anaerobic bacteria in human disease, p. 257, Academic Press Inc., New York, 1977
4 *Lancet*, **ii**, 997, 1975
5 *S.Afr.Med.J.*, **52**, 161, 1977
6 *Br.Med.J.*, i, 318, 1976
7 *Ibid.*, **ii**, 1418, 1976
8 *J.Infect.Dis.*, **131**, 417, 1975
9 *J.Antimicrob.Chemother.*, **1**, **387**, 1975
10 *Selkon, J.B., Hale, J.H., Ingham, H.R.*, Chemotherapy, vol. 1., p.277, Plenum Pub. Corp., New York, 1976.

'Flagyl' metronidazole

Tablets 200mg	PL 0012/5256
400mg	PL 0012/0084
Suppositories 500mg	PL 0012/0113
1gram	PL 0012/0114
Injection 0.5% w/v	PL 0012/0107

Further information is available on request
'Flagyl' is a trade mark
May & Baker Ltd Dagenham Essex RM10 7XS

M&B May & Baker

A member of the Rhone-Poulenc Group of Companies

Flagyl
the anaerobicide