"...the major cause of sepsis after surgery of the gastrointestinal tract or female genital tract".

Br.Med.J. i, 318. 1976



#### proves decisive in anaerobic infections

Only with recent improvements in bacterial culturing techniques has the pathogenic role of anaerobes in post-surgical infections been fully recognized. 
Now Flagy! Injection offers out decisive means of treating these infections—which are often life-threatening and often resistant to established antimicrobials. The response to 'Flagy!' Injection is rapid and degendable, as it is consistently bactericidal to pathogenic anaerobes at tissue concentrations easily achieved in treatment. Bacterial resistance is not a problem, and 'Flagy!' is highly acceptable—as eighteen years of use in other indications has established.

Dosage: Treatment: adults and children over 12 years: 100 ml by intravenous infusion eight-hourly, administered 5 ml per minute. Oral medication with 400 mg three times daily should be substituted as soon as this becomes feasible. Treatment for seven days should be satisfactory in most cases. Children under 12 years: as for adults but the single intravenous dose is based on 1.5 ml (7.5 mg metronidazole) per kg bodyweight and the oral dose on 7.5 mg per kg bodyweight. Prevention: adults and children over 12 years: 100 ml by intravenous infusion immediately before, during or after operation, followed by the same dose eighthourly until oral medication (200 to 400 mg 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 1,5 ml (7.5 mg metronidazole) per kg bodyweight and the oral dose on 3.7 to 7.5 mg per kg bodyweight. Precautions: pregnancy; lactation; clinical and biological surveillance if recommended duration of treatment exceeded; dosage may be halved for patients with renal failure; avoid alcohol; if 'Flagyl' is to be given to patients receiving oral anticoagulants the dosages of the latter should be recalibrated. Side effects and adverse reactions: occasionally an unpleasant taste, furred tongue, nausea, vomiting (very rarely), gastro-intestinal disturbance. Drowsiness, dizziness, headache, ataxia, skin rashes, pruritus, inco-ordination of movement, darkening of the urine very rarely. During intensive and/or prolonged therapy, peripheral neuropathy has been reported. A moderate leucopenia has been reported but the white cell count has always returned to normal before or after treatment has been completed. Transient epileptiform

seizures in a few patients undergoing intensive, high dosage metronidazole radiosensitization therapy.

'Flagyl' metronidazole Tablets 200 mg PL 0012/5256

400 mg PL 0012/0084 Suppositories 500 mg PL 0012/0113

1 gram PL 0012/0114 Injection 0.5% w/v PL 0012/0107 Basic N.H.S. cost (as at November 1978)

Injection for i.v. infusion Bottle of 100 ml £6.40.

References I. Willis, A.T. (1977) Scottish Medical Journal, 22, 155. 2. Willis, A.T. et al. (1977) British Medical Journal, i. 607. 3. Finegold, S.M. Anaerobic Bacteria in Human Disease, Academic Press Inc. New York, 1977. 4. Willis, A.T. et al (1975) Journal of Antimicrobial Chemotherapy, 1, 393, 1975.

Further information is available on request. 'Flagyl' is a trade mark. May & Baker Ltd., Dagenham,

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### PHARMACIA, THE MANUFACTURERS OF SALAZOPYRIN WISH TO DRAV THE ATTENTION OF ALL PRACTISING PHYSICIANS AND SURGEONS TO SOME IMPORTANT NEW INFORMATION

#### **Crohn's** Disease

Various clinical trials and publications 1.2.3.4.5 have now demonstrated that the benefits of Salazopyrin may be successfully extended to the management of active Crohn's Disease.

#### **Ulcerative** Colitis

Recent work has stressed that the ideal maintenance dose in ulcerative colitis is 2g per day,6 and that such maintenance should be extended indefinitely to minimise the risk of relapse? Cessation of therapy increases relapse risk four-fold regardless of time<sup>7,8</sup> since the acute. attack, or whether placebo<sup>7</sup> or high fibre diet8 are substituted.

## Salazopyrin

36 years of therapeutic management.

#### **Prescribing Information**

#### Dosage and Administration

Plain or FN Tablets: In acute moderate attacks 2:4 tablets At times a day. In severe attacks steroids should also be given.

After 2-3 weeks the dose may gradually be reduced to the
maintenance level of 3-4 tablets daily which should be given. indefinitely.

**Suppositories:** Two inserted morning and night, the dose being gradually reduced after 3 weeks as improvement occurs.

Children: Reduce the adult dose on the basis of body weight.

#### Contra-Indications, Warnings etc.

Contra-Indications: Contra-indicated in sensitivity to salicylates and sulphonamides. Infants under 2 years

Adverse Reaction: Side effects common to salicylates or sulphonamides may occur. Most commonly these are nausea, loss of appetite and raised temperature which may be relieved on reduction of dose, use of EN tablets or suppositories, If serious reactions occur the drug should be

discontinued.

Rarely the following adverse reactions have been reported. Haematological: eg. Heinz body anaemia, haemolytic anaemia leucopenia, agranulocytosis and aplastic anaemia.

Hypersensitivity: eq. Rash, fever, Gastrointestinal: eg. Impaired folate uptake, stomatitis. C.N.S.: eg. Headache, peripheral neuropathy. Renal: eg. Proteinuria, crystalluria.

Also, Stevens-Johnson syndrome and lung complications. eg. Fibrosing alveolitis.

#### Precautions

Care in cases of porphyria, allergic, renal or hepatic disease, glucose 6-PD deficiency. Blood checks should be made initially and periodically.

#### Pregnancy

The benefit to risk ratio must be carefully evaluated when the drug is given during pregnancy

#### References

Scand, J. Gastroenterol (1974) **9**, 549. Scand, J. Gastroenterol (1978) **13**, 161. Brit med. J. (1975) **2**, 297.

Brit med J. (1975) 2, 297.
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 Castroenterology (1977) 72, 1153.
 Cott, (1977) 18, 421.
 Cott, (1971) 14, 925.
 Brit med J. (1978) 1, 1524.

**Pharmacia** 

Salazopyrin (regd.), sulphasalazine, is a product of Pharmacia (Great Britain) Ltd., Prince Regent Road, Hounslow, Middlesex TW3 1NE. Telephone. 01-572 7321. Further information is available on request to the Company,

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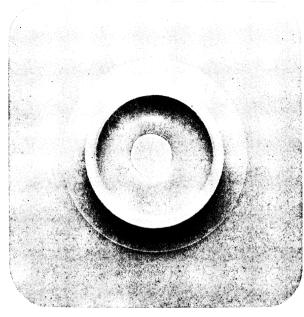
Surgicare<sup>TM</sup> System 2 saves the daily trauma of peeling off adhesive bags often resulting in irritation, soreness and discomfort. The Stomahesive<sup>TM</sup> with Flange can be left on the skin undisturbed for several days whilst pouches are replaced as often as necessary... so simply.

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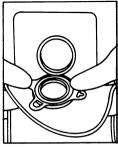
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The Stomahesive TM base will mould to irregular contours of the skin and is so easy to apply without wrinkling Comfort is derived not only from the feel of Stomahesive<sup>TM</sup> against the skin but from the confidence that the appliance will be secure and leak free irrespective of the condition of the skin.

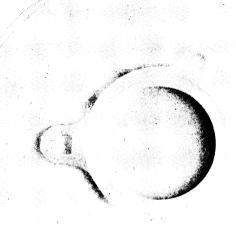


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When the patient is well nourished but unable to take food by mouth, FreAmine II—with or without calorific supplement—can be used for short-term administration to spare body protein.



# Freamine<sup>®</sup> II Amino Acids for Intravenous Nutrition

Presentation
FreAmine II is a sterile, non-pyrogenic solution containing crystalline amino acids and electrolytes. Each 100 ml contains FreAmine II Amino Acid Mixture (Lysine Acetate and Cysteine Hydrochloride, HyO added) 8.5g. Phosphoric Acid NF 0.115g. Sodium Bisulphite USP less than 0.10g and Water for Injection USP to 100 ml.

The approximate concentration of amino acids in grams per 100 ml is Essential amino acids: L Isoleucine 0.59, L Leucine 0.77, L. Lysine Acetate 0.87 (free base 0.62), Methionine 0.45, L. Phenylalamine 0.48, L. Threonine 0.34, L. Tryptophan 0.13, L. Valine 0.56.

L Valine U. 56.

Non-essential amino acids: L Alanine 0.60, L Arginine 0.31, L Histidine 0.24,
L Proline 0.95, L Serine 0.50, Aminoacetic Acid (Glycine) 1.7, L-Cysteine Hydrochloride H<sub>2</sub>0 less
than 0.02. Alpha amino nitrogen greater than 80% of total nitrogen present.

than U.2. Alpha aimon introgen greater than doz o total nitrogen present.

No peptides or glutamic or aspartic acid, which can cause nausea and vomiting, are included in the formulation.

The concentration of electrolytes in mimols per litre is. Sodium 10, Phosphate 10.

The pH of the solution is approximately 6.6 and the calculated osmolarity is approximately 850 m0sm per litre 4.500 m lunit of FreAmine II provides 39g of protein equivalent and 6.25g of

#### Uses

FreAmine II provides, in concentrated form, a physiological ratio of biologically utilizable amino acids for protein synthesis. Gene with concentrated sources of calories such as hyperform destrose or fat emulsions and with electrolytes, vitamins and minerals, provides total parenterial nutrition. Administered pervisionally, alone as an isotomic Soliton 12.8% or with minimal caloric supplementation such as 5% dextrose, FreAmine II provides nutritional support and spares body protein

Parenteral nutrition with FreAmine II is indicated when there is a requirement to

Parentiera nutrition with rearmine is indicated wind there is a requirement to prevent introgen loss or to treat negative introgen balance in patients where [1] the oral, gastrostomy or rejunostomy routes should not or cannot be used [2] gastro-intesting all absorption of protein is impaired [3] protein requirements are substantially increased, as in patients with

#### **Dosage and Administration**

The total daily dose of FreAmine II will depend upon protein requirements and the response of the patient as determined by clinical judgement and laboratory data such as

response of the patient as determined by clinical judgement and laboratory data such as mitrogen balance.

1987, kg of body weight and, for healthy, growing infants and children, 2 g, kg of body weight however, timus to be brine in mind that, in trainmatised or under nourished patients, the protein and caloric requirements may be substantially increased in such cases, daily amino acid dosen approximately 10 to 15 g, kg of body weight for adults and 2 to 3g, kg of 3g, kg

#### **Central Venous Nutrition**

For severely catabolic, depleted patients or those requiring long term total parenteral nutrition, administration of FreAmine II with hypertonic dextrose solutions by central venous infusion should be considered

#### Peripheral Parenteral Nutrition

For the moderately catabolic or depleted patient for whom the central venous route of administration is not indicated, FreAmine II may be mixed with dextrose 5% solutions and infused by peripheral ven. supplemented, if necessary, by fat emulsion.

Protein Sparing Nutrition
In the well nourshed, mildly catabolic patients (such as routine post surgical patients reguing short term parenter an furtifion only) protein sparing can be achieved by peripheral ntusion of FreAmine II with or without dextrose

#### Contra-indications, Warnings, etc.

Contra-Indications, Warnings, etc.

Amino acids are contra indicated in patients with renal failure or severe liver disease.

Warnings: The administration of amino acids to a patient with hepatic insufficiency may result in blood aminonia, administration in the presence of impaired renal function may augment an increasing blood urea introgen and also presents the danger's associated with electrolyte disturbances. The safety of the use of amino acid solutions in pregnant women has not been established.

Precautions: Frequent evaluation and laboratory determinations should be carried and disturbances. Sudderchald the distribution of user corrier protons before and

Precautions: Frequent evaluation and laboratory determinations should be carried out during parenteral nutrition. Studies should include blood sugar, serum proteins, kidney and liver function tests, electrolytes, haemogram, carbon dioxide content, serum osmolarities, blood cultures and blood ammonia levels. Should hyperammonaemia develop, administration of amino acids should be discontinued and the patient's clinical state re evaluated (This is particularly important in infants). Care should be taken to avoid circulatory overload, particularly in patients with cardiac insufficiency. In myocardial infanction, amino acids should be given with dextrose.

oe given with dextrose.

Strongly hypertonic amino acid solutions and associated hypertonic dextrose solutions should be administered only by continuous infusion through a central venous catheter with the tip located in the vena cava.

Side-effects: Prolonged infusion of hypertonic solutions may cause phlebotrombosis extending from the site of infusion.

Pharmaceutical Precautions

Avoid freezing and excessive heat; store at temperatures between 2°C and 25°C. Protect from light. Do not use a solution unless clear and a vacuum is present. Legal Category

#### Package Quantities

FreAmine II: 500ml Intravenous Infusion Bottle

FreAmine II Hyperalimentation Kit (140% Dextrose): Consists of one 500ml bottle of FreAmine II and one 1000ml bottle containing 500ml of 40% Dextrose injection with Transfer Set and Additive Cap.
FreAmine II Hyperalimentation Kit (50% Dextrose): Consists of one 500ml bottle of FreAmine II and one 1000ml bottle containing 500ml of 50% Dextrose): Consists of one 500ml bottle of FreAmine II and one 1000ml bottle containing 500ml of 50% Dextrose injection with Transfer Set and

#### Product Licence Numbers

FreAmine II: PL2737/0001 FreAmine II Hyperalimentation Kit (40% Dextrose): PL2737/0002 FreAmine II Hyperalimentation Kit (50% Dextrose): PL2737/0003

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## **DUODENAL ULCERATION.** WHAT COMES NATURALLY

'Tagamet' has been shown to be unequalled in the short-term treatment of duodenal ulceration. inducing early and dramatic symptomatic relief. rapid healing and subsequent remission.12

In addition, 'Tagamet' has been shown to prevent relapse during longer-term maintenance therapy: 3-5 the only drug so far proven to have this property.

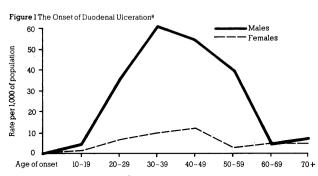
However, experience to date tends to suggest that for many patients the natural history of the disease remains unaltered despite medical intervention<sup>6</sup> and the question inevitably arises will patients with a severe condition require medical treatment for the rest of their lives?

This can only be answered when the natural history of duodenal ulcer disease is fully understood. Some aspects of the natural history of the disease, however have been well recognised for some vears.

It is a naturally relapsing condition: in fact, it has been estimated that 75-80% of patients have at least one recurrence within 5 years of the initial episode,7 some relapsing several times in one year.

The onset of duodenal ulceration is related to age, as shown in Figure 1. The initial episode is most likely in the 30-39 age group for males and slightly later in life for females.

Of greater interest is the natural development of the disease following its onset. Figure 2 demonstrates how the disease tends to 'burn itself out' after a certain period of time.8 In a group of duodenal ulcer patients who were followed for 15 years, the symptoms tended to peak in severity

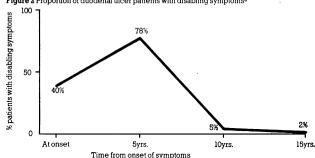


after 5 years and then progressively remit until at 10 years no more than 5% of patients had severe symptoms.

This finding has been recently substantiated by workers in Denmark who found in a retrospective study that the disease is present for a finite time.9

The workers concluded ... most patients with duodenal ulceration will need only intermittent or continuous cimetidine treatment for a limited period.

Figure 2 Proportion of duodenal ulcer patients with disabling symptoms<sup>8</sup>



#### Prescribing Information

Presentations
"Tagamet' Tablets PL0002/0063 each containing 200mg cimetidine. 100, £13.22; 500, £64.75. "Tagamet' Syrup PL0002/0073 containing 200mg cimetidine per 5ml syrup. 200ml, £6.29. Indication

Duodenal ulcer.

Adults: 200mg tds with meals and 400mg at bedtime (1.0g/day) for at least 4 weeks (for full instructions see Data Sheet).

To prevent relapse, 400mg at bedtime or 400mg morning and evening for at least 6 months.

Impaired renal function: reduce dosage (see Data Sheet). Potentiation of oral anticoagulants (see Data Sheet). Prolonged treatment: observe patients periodically. Avoid during pregnancy and lactation.

Adverse reactions

Unique control of gastric acid secretion

Diarrhoea, dizziness, rash, tiredness. Rarely, mild gynaecomastia, reversible liver damage, confusional states (usually in the elderly or very ill), interstitial

- 1. Oral cimetidine in severe duodenal ulceration.
- (1977) Lancet, i, 4.
  2. Cimetidine in the treatment of active duodenal and prepyloric ulcers. (1976) Lancet, ii, 161.

  3. Maintenance treatment of recurrent peptic ulcer by
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  4. Prophylactic effect of cimetidine in duodenal ulcer disease. (1978) Brit.med.J., 1, 1095.
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- Gastroenterology. (In Press). 6. Cimetidine for duodenal ulcer. (1978) Lancet, ii, 1237. The natural history of duodenal ulcer disease. (1976) Surg. Clin. N. Amer., 56, 1235.
- 8. Peptic ulcer: a profile. (1964) Brit med. J. 2, 809.
  9. Long-term prognosis of duodenal ulcer: follow-up study and survey of doctors' estimates.
  (1977) Brit med. J., 2, 1572.

Full prescribing information is available from



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# Recorded Colifoam

hydrocortisone acetate foam

A remarkable new study<sup>1</sup> carried out in the gastroenterology department of St. Bartholomew's Hospital now provides firm evidence of the extent to which 'Colifoam' penetrates into the colon – and how long it remains in situ.

The study involved 14 patients with ulcerative colitis. 'Colifoam' labelled with a radioactive marker was administered in the normal recommended dosage, and its penetration recorded by gamma photography.

In all of the patients with active disease the foam reached the mid-sigmoid colon, and in 78% the foam reached the proximal sigmoid colon.



These photographs illustrate results in a typical case:

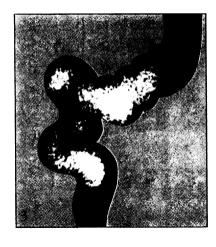
- 1. Immediately after instillation.
  There is already good
  penetration through the
  rectum.
- 2. After 1 hour. 'Colifoam' has now reached the sigmoid colon.
- 3. After 6 hours. 'Colifoam' is present in high concentration throughout the sigmoid colon, including the proximal segment.



This study confirms the relevance of 'Colifoam' therapy in patients with ulcerative colitis throughout the sigmoid colon: that means a high proportion of new cases, and a significant proportion of all ulcerative colitis sufferers. Indeed, it is noteworthy that retrograde spread of the foam was greatest in patients with more extensive disease.

'Colifoam' offers these patients the benefits of anti-inflammatory therapy

# Delivery



in a form that is much more acceptable than the outmoded retention enema.

"Of the twenty patients, 19 found Colifoam easy to use and more comfortable to insert than a steroid enema..."<sup>2</sup>



#### References

 Paper presented at Meeting of British Society of Gastro-enterology. Hull. 1979. March 29-30.

2. Practitioner (1977) 219: 103

# In ulcerative colitis Colifoan gets to the point

#### Presentation

White odourless aerosol foam containing hydrocortisone acetate 10% with inert propellants. **Uses** 

Anti-inflammatory corticosteroid therapy for the topical treatment of ulcerative colitis, proctosigmoiditis and granular proctitis.

#### **Dosage and Administration**

One applicatorful inserted into the rectum once to twice daily for two or three weeks and every second day thereafter. Shake can vigorously before use (illustrated instructions are enclosed in each pack).

Satisfactory response usually occurs within five to seven days.

One applicatorful of Colifoam provides a dose of approximately 90-110mg of hydrocortisone acetate, similar to that used in a retention enema, for the treatment of ulcerative colitis, sigmoiditis and proctitis.

#### Contra-indications and Warnings, etc.

Local contra-indications to the use of intrarectal steroids include obstruction, abscess, perforation, peritonitis, fresh intestinal anastomoses and extensive fistulas

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 diseases because of their predisposition to perforation of the bowel wall.

Safety during pregnancy has not been fully established.

#### **Package Quantities**

Aerosol canister containing 20g (14 applications) plus a plastic applicator and illustrated leaflet. Basic NHS cost £6.27

#### Product Licence No.

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Further information is available on request. **Stafford-Miller Ltd.,** Professional Relations Division, Hatfield, Herts.

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1. Double blind controlled trial on 37 patients treated for 8 weeks. Curr. med. Res. Opin. (1978), 5:638.



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which protects it from
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action of a low but
effective dose of the
healing agent
carbenoxolone.

Formula. Each chewable, strawberry flavoured tablet contains carbenoxolone sodium B.P. 20 mg, magnesium trisilicate B.P. 60 mg and dried aluminium hydroxide gel B.P. 240 mg in a base containing alginic acid B.P.C. 600 mg and sodium bicarbonate B.P. 210 mg. Presentation. Cartons of 4 x 25 tablets in foil strips. Basic NHS cost. One day's treatment (5 tablets) 56p. Indications. For the treatment of oesophageal inflammation, erosions and ulcers due to hiatus hernia or other conditions causing gastric reflux; and for the relief of heartburn, flatulence and other symptoms associated with reflux oesophagitis. Dosage. (Adults). One to be chewed immediately after meals 3 times a day, and two to be chewed at bedtime. Safety factors. Pyrogastrone should not be prescribed for patients suffering from severe cardiac, renal or hepatic failure, or for patients on digitalis glycosides, unless serum electrolyte levels are monitored at weekly intervals to detect promptly the development of hypokalaemia. Special care should be exercised with patients predisposed to sodium and water retention, potassium loss and hypertension (e.g. the elderly and those with cardiac, renal or hepatic disease) since the carbenoxolone content of Pyrogastrone can induce

similar changes. Regular monitoring of weight and blood pressure, which should indicate the development of such effects, is advisable for all patients. A thiazide diuretic should be administered if oedema or hypertension occurs (spironolactone should not be used because it hinders the therapeutic action of carbenoxolone). Potassium loss should be corrected by the administration of oral supplements. No teratogenic effects have been reported with carbenoxolone sodium, but careful consideration should be given before prescribing Pyrogastrone for women who may become pregnant.

\*The Pyrogastrone tablets used in this trial contained the same low dose of carbenoxolone (20 mg) but only one third the alginate and antacid now available in Pyrogastrone. The control tablets contained the same base, but without carbenoxolone.

Pyrogastrone is a registered trade mark. Made under licence from Biorex Laboratories. Brit. Pat. Nos. 843133 and 1390683. PL 0071/0138.

Full prescribing information is available on request from Winthrop Laboratories, Surbiton-upon-Thames, Surrey. WINTHROP

# In dyspepsia, antacids only cloud the issue. Maxolon

clears it.



Maxolon protects the gastric mucosa from over-long exposure to gastric acid<sup>1</sup> by promoting normal peristalsis and gastric emptying.<sup>2,3</sup> This action contrasts with that of antacids.

By restoring the stomach's normal control, symptoms described by the patient as fullness, pain. heartburn and discomfort can be effectively treated and their recurrence prevented.

To the patient, Maxolon is the simple and convenient therapy to replace his repetitive antacid prescriptions.

#### Prescribing Information

Indications

Dyspepsia, heartburn and flatulence associated with the following conditions e.g., Reflux oesophagitis, Gastritis, Hiatus hernia, Peptic ulcer.

Adult Dosage (oral)

Adults 19sage (19th)
Adults 19mg
1 tablet or 10ml syrup 3 times a day,
Young adults (15-20 years) 5-10mg
½-1 tablet or 5-10ml syrup 3 times a day
commencing at the lower dosage.

Note: Total daily dosage of Maxolon, especially for children and young adults should not normally exceed 0.5mg/kg

#### Side-effects and Precautions

There are no absolute contra-indications to the use of Maxolon.

Various extra-pyramidal reactions to Maxolon. Usually of the dystonic type, have been reported. The incidence of these reactions in children and young adults may be increased if daily dosages higher than 0.5mg/kg body-weight are administered. The majority of reactions occur within 36 hours of starting treatment and the effects usually disappear within 24 hours of withdrawal of the drug Should treatment of a reaction be required, an anticholinergic anti-Parkinsonian drug e.g. benapryzine, or a benzodiazepine may be used. Since extra-pyramidal symptoms may occur with both

Maxolon and phenothiazines, care should be exercised in the event of both drugs being prescribed concurrently.

Raised serum prolactin levels have been observed during metoclopramide therapy; this effect is similar to that noted with many other compounds.

Maxolon's action on the gastro-intestinal tract is antagonised by anticholinergics. Although animal tests in several mammalian species have shown no teratogenic effects. treatment with Maxolon is not advised during the first trimester of pregnancy.

Following operations such as pyloroplasty or gut anastomosis Maxolon therapy should be withheld for three or four days as

vigorous muscular contractions may not help healing.

Availability and NHS Prices Tablets 10mg (£5.84 per 100). Syrup 5mg/5ml (£2.42 for 200ml)

A paediatric liquid presentation and ampoules for injection are also available.

Avarage daily cost of Mayolon tablets

Average daily cost of Maxolon tablets (ex. 500 pack) 17p. Prices correct at January 1979. Further information is available on request to the company.

Maxolon (metoclopramide) is a product of
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PL 0038/0095 0098 5040 5041

1.Gut.(1969), 10.678-680 2.Postgrad.med J..(1973), 49.(Suppl), 29 3.Gut.(1974), 15, 462-467 4.Brit med J..(1971), 2.25

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Morgan AG et al (1978) BMJ, 2, 1323-1326

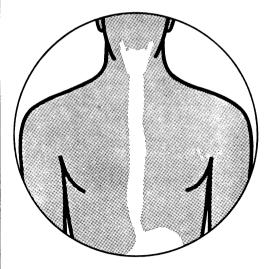
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