

Nizoral

TRADEMARK

ketoconazole

The first
oral anti-fungal
effective against
all pathogenic
fungi

dosage:

vaginal candidosis:	all other superficial and systemic fungal infections:
2 tablets once daily (with food) for 5 days	1 tablet daily (with food) until complete symptomatic and mycological cure is obtained

PRESCRIBING INFORMATION

Presentation: white, flat, half scored uncoated tablets marked "Janssen" on one side and k/200 on the reverse. Each tablet contains 200 mg ketoconazole. **Uses:** Nizoral is an orally active antimycotic for the treatment in adults, of vaginal candidosis, superficial and systemic mycoses including dermatophyte and yeast infections of the skin, hair and nails, yeast infections of the mouth and G.I. tract. Also maintenance treatment of systemic mycoses and chronic mucocutaneous candidosis and prophylaxis in "at risk" patients. In children: systemic mycoses and severe local infections where previous topical treatment has failed. **Side-effects, precautions, contra-indications:** contra-indicated in pregnancy. For maximal absorption Nizoral should be taken with meals. The use of agents which reduce gastric acidity (anti-cholinergic drugs, antacids, H2 blockers) should be avoided and, if indicated, such drugs should be taken not less than two hours after Nizoral. Nausea, skin rash, headache and pruritus may occasionally be observed. Alterations in liver function tests have occurred in patients on ketoconazole, these changes may be transient. Cases of hepatitis have been reported with an incidence of about 1 per 10,000 patients. Some of these may represent an idiosyncratic adverse reaction to the drug. This should be borne in mind in patients on long-term therapy. If a patient develops jaundice or any symptoms suggestive of hepatitis, treatment with ketoconazole should be stopped.

Not all indications are as yet approved in all countries.

Janssen Pharmaceutica
B-2340 Beerse, Belgium



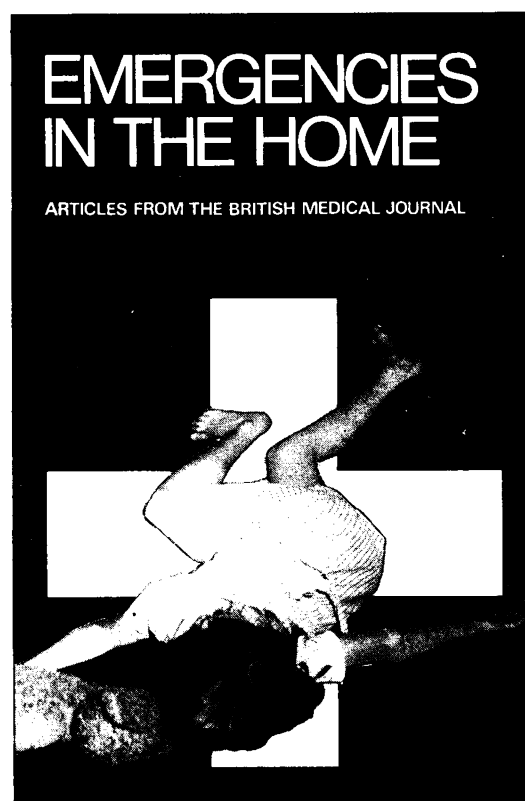
EMERGENCIES IN THE HOME

General practitioners are often the first doctors to see acutely ill patients, and often in difficult circumstances. This book tells general practitioners straightforwardly what they need to know to deal with such emergencies—both the common and the less common. A specialist and a general practitioner have co-operated on each chapter, making each both authoritative and practical.

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TODAY'S TREATMENT/4

The drugs that we use today are increasingly potent, dangerous, and expensive, and every doctor should have some understanding of clinical pharmacology and drug-induced diseases. Both these subjects, which have been badly taught in medical schools, are covered comprehensively in this new book, which consists of articles taken from the *BMJ*. Also included are articles that provide a clear and up-to-the-minute introduction to anaesthetics.

Price: Inland £4.50; Overseas US\$20.50*
(Inland £4.00; Overseas US\$19.00* for BMA members)

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PRESCRIBING INFORMATION

PRESENTATION

Maxolon 'High Dose' Ampoules: Clear, colourless solution. Each 20ml ampoule contains Metoclopramide Hydrochloride B.P. equivalent to 100mg of the anhydrous substance.

USES

Maxolon 'High Dose' is indicated for the treatment of nausea and vomiting associated with intolerance to cytotoxic drugs.

DOSEAGE AND ADMINISTRATION

Maxolon 'High Dose' may be given in doses of up to 2mg/kg body weight by IV infusion suitably diluted. The initial dose should be given prior to commencement of cytotoxic chemotherapy. Dosage may be repeated two-hourly up to a maximum of 10mg/kg body weight in any 24 hour period. It is recommended that each dose be added to at least 50ml of an appropriate diluent (see below), and infused over at least 15 minutes.

The cytotoxic agent should be administered as a separate infusion. Note: The high dose ampoule presentation is not suitable for multidose use.

Stability in intravenous fluids.

Intravenous solutions should be prepared as near as possible to the time of infusion. However, Maxolon has been shown to be stable in the solutions listed below for at least 24 hours at room temperature.

Intravenous infusions.

Sodium Chloride Intravenous Infusion B.P. (0.9% w/v)
Dextrose Intravenous Infusion B.P. (5% w/v)
Sodium Chloride and Dextrose Intravenous Infusion B.P.
(sodium chloride 0.18% w/v; dextrose 4% w/v)
Compound Sodium Lactate Intravenous Infusion B.P.
(Ringer-Lactate Solution; Hartmann's Solution)

CONTRA-INDICATIONS, WARNINGS, ETC.

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

When given at high dose in association with cancer chemotherapy, Maxolon has been found to be well tolerated with few adverse effects, the most common being mild sedation.

Various extrapyramidal reactions to Maxolon, usually of the dystonic type, have been reported. Studies to date of Maxolon given up to 10mg/kg body weight/day by IV infusion report a low incidence of extrapyramidal reactions of less than 10%.

Reactions to Maxolon have included: Spasm of the facial muscles, trismus, rhythmic protrusion of the tongue, a bulbar type of speech, spasm of extra-ocular muscles including oculogyric crises, unnatural positioning of the head and shoulders and opisthotonos. There may be a generalised increase in muscle tone. 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, or a benzodiazepine may be used. Since extrapyramidal 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.

FURTHER INFORMATION

Maxolon 'High Dose' is specifically for use in the management of cytotoxic intolerance. It is not intended for use in the wider range of indications for which Maxolon at standard dose is indicated. The Maxolon Data Sheet should be consulted for such cases.

AVAILABILITY AND NHS PRICE

(Price correct at November 1982)

'High Dose' Ampoules (100mg/20ml) £26.90 for 10

References

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A new approach to the treatment of nausea and vomiting associated with cancer chemotherapy.

Maxolon metoclopramide 'High Dose'

Introduction

Nausea and vomiting commonly occur after the administration of a variety of chemotherapeutic agents used for the treatment of cancer and frequently constitute a major problem resulting from such treatment. This is especially true when cisplatin is used either alone¹ or in combination with other anti-neoplastic drugs including dacarbazine, doxorubicin and cyclophosphamide.² An otherwise effective treatment regime is often extremely difficult for patients to tolerate and for these reasons some patients miss appointments or delay prescribed courses of chemotherapy, thus affecting their chance of cure.³

Routinely used antiemetic agents, such as the phenothiazines and antihistamines appear to be of only marginal value against strongly emetic agents.^{4, 5, 6}

A New Approach

In 1979, several antiemetics, administered parenterally in high doses were tested in dogs receiving intravenous cisplatin at 5mg/kg.⁷

Metoclopramide [Maxolon] resulted in 72% and 99% protection against cisplatin-induced emesis when given at doses of 1.0mg/kg and 3.0mg/kg respectively. The antiemetic efficacy of metoclopramide [Maxolon] was superior to that of chlorpromazine (3.0mg/kg—57%), haloperidol (1.0mg/kg—54%), nabilone (0.1mg/kg—20%) and saline control.

Recent clinical trials, in patients receiving cytotoxic chemotherapy, have demonstrated the effectiveness of high dose intravenous metoclopramide [Maxolon] in the control of vomiting.

Results

High dose metoclopramide [Maxolon] has been shown to be effective in controlling nausea and vomiting associated with many antineoplastic regimes⁸⁻¹³; cisplatin, either alone or in combination (eg with doxorubicin, lomustine and cyclophosphamide)⁸⁻¹¹; also mixtures of other commonly used agents (eg cyclophosphamide/etoposide/methotrexate and vincristine/doxorubicin/procarbazine).¹²

Some of the trials of metoclopramide [Maxolon] in cisplatin chemotherapy have been double blind with placebo, prochlorperazine, (10mg IM: total dose 50mg) or

Δ^9 tetrahydrocannabinol (THC) (10mg orally every 3 hours: total dose 75-100mg).^{8, 13} High dose metoclopramide [Maxolon] reduced the average number of episodes of emesis to one or two, compared to 10.5 with placebo, 12.0 with prochlorperazine and 8.0 with THC.

In the majority of studies, an initial dose of metoclopramide [Maxolon] (usually in the range 1-2mg/kg body weight) was given over 15 minutes, half an hour prior to commencement of cytotoxic chemotherapy. Further doses were given at two or three hourly intervals.

Patients receiving cisplatin at doses greater than 100mg/sq m had an improved clinical response when the higher dose level of metoclopramide (2mg/kg body weight) was used⁹; although 1mg/kg gave adequate protection in patients receiving less than 100mg/sq m cisplatin.^{10, 11} The total metoclopramide dosage per course was usually in the range 5-10mg/kg body weight.

Tolerance

In these trials, the most commonly occurring side effect was mild sedation.

The majority of studies quote a low incidence of extrapyramidal reactions. In several extended trials involving a total of 300 patients, such reactions occurred in 3% of patients overall; however, they were significantly more frequent in patients aged below 30.¹³ When extrapyramidal symptoms did occur many settled quickly and did not require treatment; the others responded promptly to diphenhydramine or diazepam.

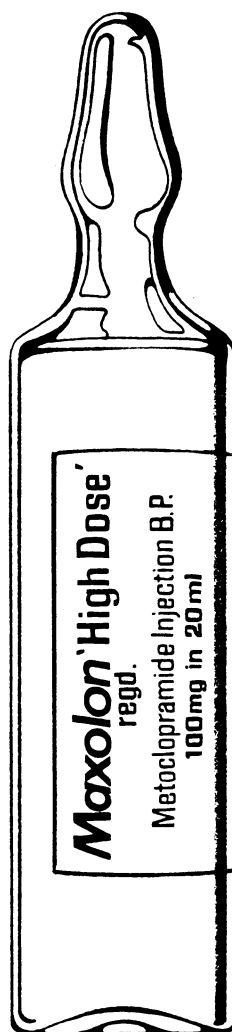
Increased perspiration occurred in some patients.

An increased frequency of bowel movements has been noted in cisplatin clinical studies with high intravenous doses of metoclopramide. However, in a double blind trial the mean number of stools during the 24 hour observation period was no higher in metoclopramide-treated patients than in those who received placebo or prochlorperazine.⁸

Conclusion

At high dosage intravenous metoclopramide [Maxolon] has been found to be effective against nausea and vomiting induced by cytotoxic chemotherapy. In clinical trials it has been found to be well tolerated, the most common side effect being mild sedation.

MAXOLON 'HIGH DOSE' AMPOULES (100mg/20ml) FOR INTRAVENOUS INFUSION ARE NOW AVAILABLE



Further information is available on request from

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Brentford, England

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Prescribing Information

Uses Management of Diabetes mellitus.

Dosage and administration Dosage to be determined by the physician. Site of injection to be changed according to suitable routine. Avoid unintentional intravascular injection.

Neusulin, Soluble Insulin: Administered s.c., i.m. or i.v. S.c., onset of action within 30-60 minutes, duration 6-8 hours. I.m., onset is faster and duration is shorter. I.v. administration has fastest onset and shortest duration, usually reserved for investigational use or diabetic ketoacidosis.

Neuphane, Neulente: Administered s.c. or i.m. *Not to be given i.v.* S.c., onset of action within 2 hours, duration (Neuphane) 20-24 hours, duration (Neulente) 24-28 hours. I.m., onset is faster and duration shorter. Mix well by gently inverting the vial several times before use.

Mixing: Neusulin may be mixed in the syringe, on medical advice, with Neuphane or Neulente if required, *provided the mixture is injected immediately*. However, it is preferable to avoid mixing insulins of different pH. See data sheet for procedure.

Contra-indications Hypoglycaemia.

Precautions Dosage requirement may alter with variation of lifestyle, infection, pregnancy and with change in species, type or purity of insulin.

Hypo- and hyperglycaemia may be enhanced by drugs which interact with insulin. Beta-blockers may affect insulin requirement and mask hypoglycaemia. MAO inhibitors may potentiate insulin.

Side-effects Hypoglycaemia. Possible altered visual refraction. Transient local reactions at the site of injection.

Storage Store at 2-8°C. *Do not freeze.* Avoid direct sunlight.

Presentation Neusulin, Neuphane and Neulente are available in strengths of 40 and 80 units per ml in vials of 10 ml.

Basic NHS costs

Neusulin			Neuphane		
40 units/ml	PL3/0137	£2.31	40 units/ml	PL3/0139	£2.31
80 units/ml	PL3/0138	£4.14	80 units/ml	PL3/0140	£4.47
Neulente					
40 units/ml	PL3/0141	£2.28			
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ABC OF 1 TO 7

Dr. Bernard Valman's series of *BMJ* articles, the ABC of 1 to 7, covered the diseases, emotional problems, and developmental disorders that tax doctors (and parents) in the early years of childhood, giving straightforward advice with emphasis on practice rather than theory. These articles have been collected together in this book, which provides a worthy sequel to Dr. Valman's *First Year of Life*.

Price: Inland £7.50; Abroad US\$25.25 (including air mail postage).

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In recent years alcohol problems have increased dramatically and the thinking on them has undergone a revolution. *Alcohol Problems* brings together two recent series of articles published in the *BMJ*—the *ABC of Alcohol*, with its emphasis on straightforward advice for the clinician, and *Alcohol and Alcoholism*, Dr. Richard Smith's more discursive survey of current thinking and controversies. Together they cover both the clinical aspects of managing alcohol problems and the social and political factors that surround them.

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SEX PROBLEMS IN PRACTICE

Patients increasingly are bringing their sex problems to doctors, many of whom have had no training in managing such problems. This book provides straightforward advice on what general practitioners and other front-line health workers can and cannot do. Most problems can be managed with simple advice and counselling, but some need referral.

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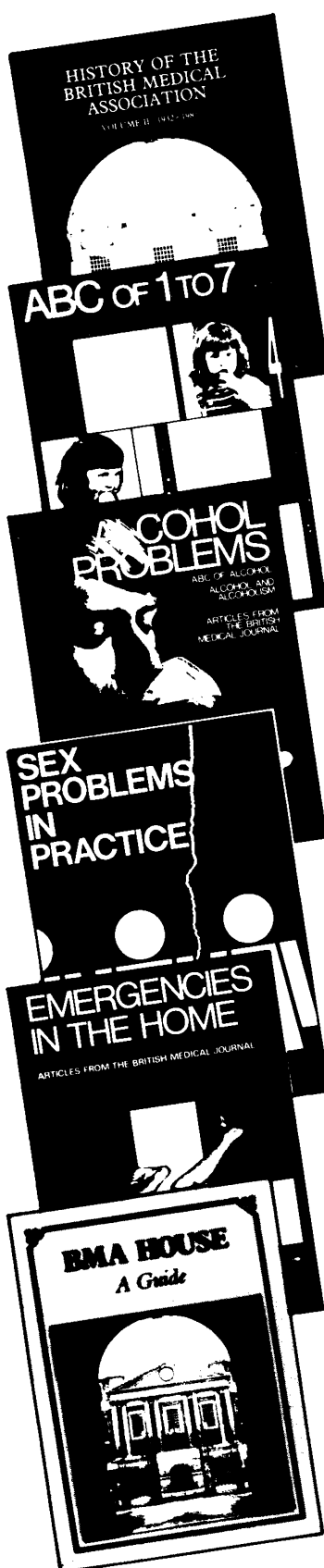
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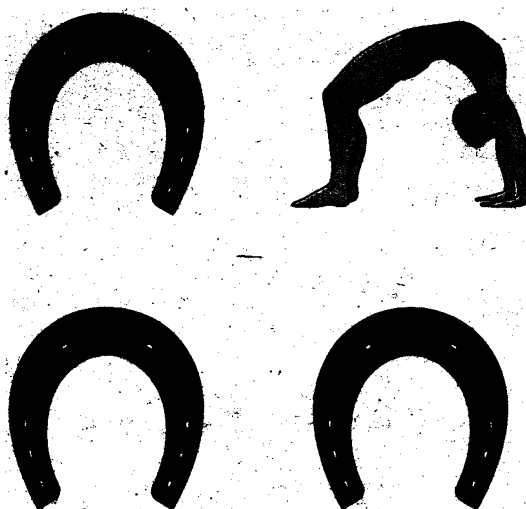
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