

Nizoral

REG. TRADE MARK

ketoconazole

oral therapy for all common fungal infections

Vaginal candidosis:	In all dermatological and in 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

Not all indications are as yet approved in all countries.

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.



Janssen Pharmaceutica
B-2340 Beerse, Belgium

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.

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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.

DOSAGE 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 3mg/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 regimes⁸⁻¹⁵; 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.

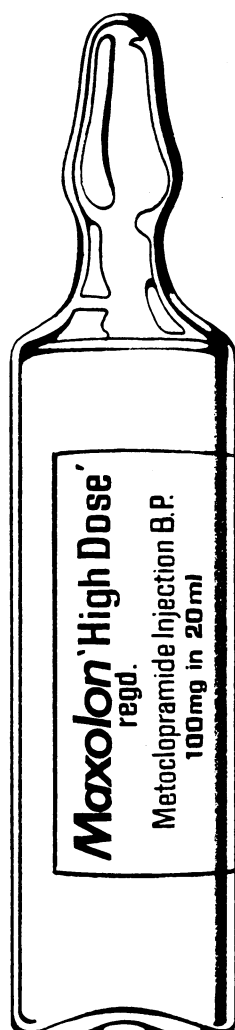
Increased perspiration occurred in some patients.

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



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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	PL 3/0137	£2.31	40 units/ml	PL 3/0139	£2.31
80 units/ml	PL 3/0138	£4.14	80 units/ml	PL 3/0140	£4.47
Neulente					
40 units/ml	PL 3/0141	£2.28			
80 units/ml	PL 3/0142	£3.90			

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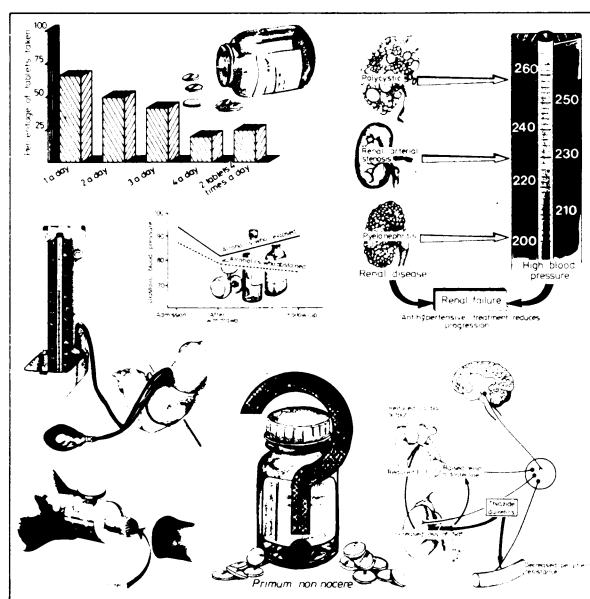
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ABC OF HYPERTENSION

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The British Council International Medical Courses

CHILD DEVELOPMENT: NORMAL AND ABNORMAL

12-24 June 1983 in London

This course will provide information about the methods currently available in Britain for studying and evaluating child development and in doing so will review the characteristics of child development. The Director of Studies will be **Professor Kenneth S Holt**, Head of the Department of Developmental Paediatrics, Institute of Child Health, University of London.

The course is intended for paediatricians studying or teaching child development or concerned with the evaluation and management of the development of disabled children.

Fee £695 (Residential), £405 (Non-residential).

NUTRITION AND GROWTH

26 June-8 July 1983 in Cambridge/London

This course is designed to cover a wide range of theoretical and practical aspects of nutrition in relation to growth with particular emphasis on the early years of life and recent advances in this field will be presented. The Directors of Studies will be **Professor J T Harries**, Department of Paediatric Gastroenterology, Institute of Child Health, University of London and **Dr W P T James**, recently Assistant Director, Medical Research Council Dunn Nutrition Unit, Cambridge. The course is designed for doctors and nutritionists with 5-10 years' experience who have a special interest in nutrition in early life.

Fee £695 (Residential), £405 (Non-residential).

PAEDIATRIC NURSING

3-15 July 1983 in London

The purpose of this course, which is based at the Charles West School of Nursing, Hospital for Sick Children, Great Ormond Street, London is to provide an up-to-date review of special areas of paediatric nursing and the changing pattern of care. The Directors of Studies will be **Miss B M Barchard**, Chief Nursing Officer and **Miss S Barlow**, Director of Nurse Education.

The course is open to senior nurses involved in the clinical, managerial and teaching aspects of paediatric nursing.

Fee £545 (Residential), £320 (Non-residential).

NEONATAL SURGERY

6-19 July 1983 in Liverpool/London

This course is designed to provide an up-to-date review of current practice in neonatal surgery. The aetiology, pathology, diagnosis and treatment of individual conditions demanding urgent surgery in the first few days of life will be considered in detail, and special attention will be directed to the problems of management of children with multiple anomalies and of the increasing numbers of children of very low birth weight who survive as a result of aggressive neonatal intensive care. The Director of Studies will be **Professor James Lister** of the Department of Paediatric Surgery, University of Liverpool.

The course is intended for experienced surgeons at or near consultant level with a major interest in paediatric surgery.

Fee £715 (Residential), £415 (Non-residential).

PAEDIATRIC CARDIOLOGY

10-22 July 1983 in Cambridge

This course on the management of congenital heart disease will cover pre- and post-operative care, atrioventricular septal defects, univentricular hearts, truncus arteriosus, total anomalous pulmonary venous drainage, atrial isomerism, interrupted aortic arch, pulmonary atresia with and without ventricular septal defect, tetralogy of Fallot, complete and corrected transposition, double outlet right ventricle and arrhythmias. The Director of Studies will be **Professor Fergus Macartney**, Vandervell Professor of Paediatric Cardiology, Institute of Child Health, University of London.

The course is intended for doctors with several years' experience in the field of paediatric cardiology or paediatric cardiac surgery.

Fee £690 (Residential), £405 (Non-residential).

PROBLEMS IN DIAGNOSTIC ORAL PATHOLOGY

31 July-12 August 1983 in Sheffield

The aim of this course is to provide participants with the opportunity for discussion and guidance on difficult problems encountered in the microscopic diagnosis of pathological conditions associated with the tissues in and adjacent to the mouth. Much of the course will involve the study of prepared specimens with the light microscope. The Director of Studies will be **Professor Colin Smith**, Professor of Oral Pathology at the University of Sheffield. The course will be held at the Medical and Dental Schools of the University of Sheffield. Every participant will be expected to be familiar with, and practised at, the recognition of the common and typical features of oral pathological conditions. Applicants should have had at least five years' experience in the microscopical diagnosis of oral lesions.

Fee £595 (Residential), £345 (Non-residential).

CURRENT CONCEPTS IN ANAESTHESIA AND INTENSIVE CARE

11-23 September 1983 in Glasgow

This course is being organised by the University Department of Anaesthesia at the Royal Infirmary in Glasgow. The aim is to review important recent advances and current concepts in anaesthesia and intensive care, with lectures, discussion groups and workshops for participants. The Director of Studies will be **Professor Donald Campbell**. The course is designed for specialists in anaesthesia and intensive care of consultant standing.

Fee £645 (Residential), £375 (Non-residential).

TUBERCULOSIS

18-30 September 1983 in London

This seminar is to provide an understanding of the pathogenesis, epidemiology and treatment of tuberculosis and other mycobacterial diseases. Main topics that will be covered are pathogenesis, immunology, BCG vaccination as well as the epidemiological, clinical and laboratory aspects of case-finding and treatment of tuberculosis, including the organisation of national programmes. The Directors of Studies will be **Professor Wallace Fox**, Director of the Medical Research Council Tuberculosis and Chest Diseases Unit and **Professor D A Mitchison**, Honorary Director at the Medical Research Council Unit for Laboratory Studies of Tuberculosis, Royal Postgraduate Medical School. The seminar is intended for chest physicians, clinical epidemiologists and public health administrators interested in tuberculosis and leprosy and laboratory workers with a specialist interest in mycobacterial diseases.

Fee £695 (Residential), £405 (Non-residential).

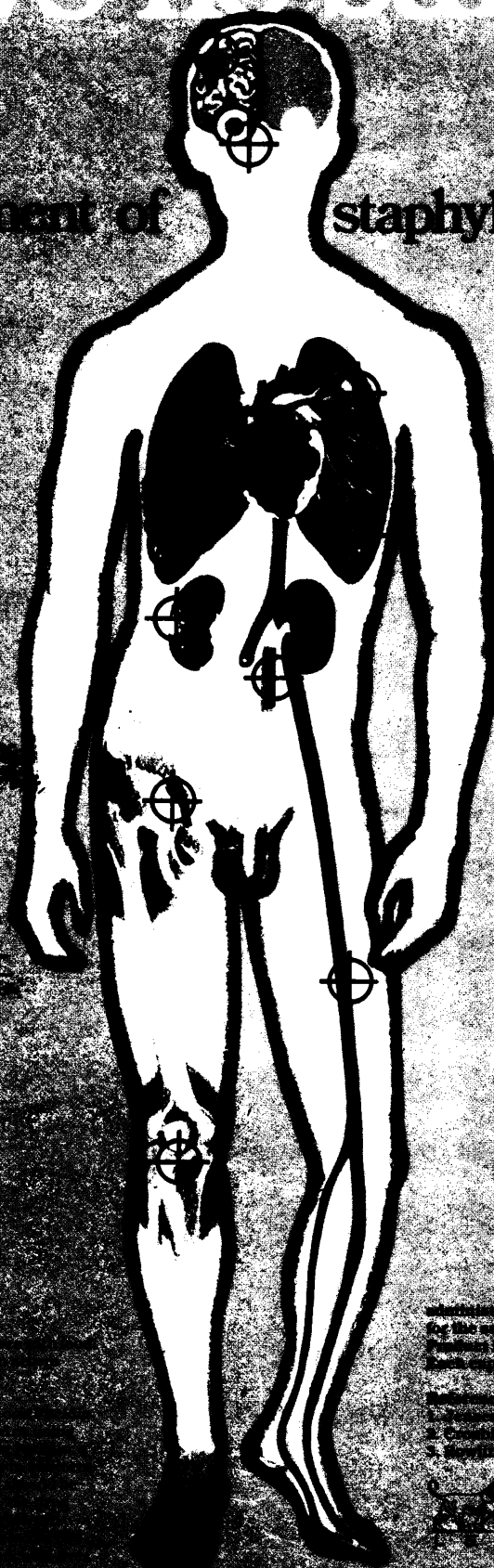
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- Empyema
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- Deep wound infection
- Septic arthritis
- Foreign bodies ^{osteal} prostheses
- Osteomyelitis
- Diabetic gangrene

Contraindications:
Fucidin is contraindicated in patients with known hypersensitivity to sodium fusidate or to any of the excipients. It should also be avoided in patients with severe renal impairment (creatinine clearance < 10 ml/min) and in patients with severe hepatic impairment (bilirubin > 3 mg/dl).
Warnings:
Fucidin should be used with caution in patients with moderate renal impairment (creatinine clearance 10-30 ml/min) and in patients with moderate hepatic impairment (bilirubin 1-3 mg/dl).
Precautions:
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