COMMITTEE ON SAFETY OF MEDICINES

CURRENT PROBLEMS

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*AN OCCASIONAL SERIES OF LEAFLETS

CONTENTS

INTRODUCTION

This series of leaflets is intended to draw attention to problems being considered by the Committee on Safety of Medicines which are not urgent enough to need the issue of a warning in the yellow 'Adverse Reactions Series'. The subjects included may be such that a definitive statement is not possible on the basis of the data available at the time of publication.

Starting with the January 1976 issue, some of the products listed in MIMS are marked with a new symbol ▼ . This is to draw attention to the fact that the product is one recently introduced to the British market and therefore one on which the Committee is especially anxious to collect reports of suspected adverse reactions, even if quite minor. There is not, of course, less interest than hitherto in reports for older drugs. All serious or unusual reactions should be reported whether or not the product is marked with the new symbol. The length of time for which the new symbol will be retained in MIMS for any particular product will be determined by the use of that product. For drugs with very restricted use, a long time may elapse before a significant number of patients have been exposed to any possible hazard.

ADVERSE REACTIONS TO PRACTOLOL AND OTHER BETA BLOCKERS

Prescribers are reminded that the recommended uses of practolol (Eraldin) are restricted to certain acute cardiac dysrrhythmias in hospitalised patients. The Committee cannot, however, be sure that these recommendations are being observed. It is therefore taking this opportunity of reminding doctors that the hazards of practolol make it unsuitable for the treatment of angina or hypertension.

The Committee is particularly interested to receive reports of any suspected adverse reactions to other beta blockers and the importance of early reporting of any suspicions of such reactions is emphasised.

A NOTE ON REPORTING

We continue to receive obsolete yellow cards which can be recognised by the fact that they are addressed to Queen Anne's Mansions.

A supply of new yellow cards may be obtained from:

The Secretary
Committee on Safety of Medicines
Finsbury Square House
33-37A Finsbury Square
LONDON EC2A 1PP

The new format allows for more information to be included. Data such as the time interval between starting treatment and the development of a possible adverse reaction can be very important. Inclusion of all relevant facts helps us to provide a better service.

ADVERSE REACTIONS TO INTRAVENOUS ANAESTHETIC AGENTS

It is interesting to note the different patterns of reported adverse reactions to three relatively recently introduced intravenous anaesthetic agents. Reports relating to propanidid (Epontol) show that flushing of the skin, urticaria, and hypotension occur commonly. In the case of ketamine (Ketalar) reports of mental disturbances during recovery from anaesthesia predominate. The reports relating to a mixture of alphadalone and alphaxalone (Althesin) show a preponderance of reactions affecting the respiratory and cardio-vascular systems. A characteristic picture is frequently described with this agent consisting of severe bronchospasm, profound hypotension and widespread erythema or cyanosis. These features are often accompanied by cardiac dysrrhythmias, oedema of the face and profuse sweating. There seems to be no satisfactory way of predicting a reaction of this type in any particular patient. Two of the reports relating to Althesin have concerned fatal reactions, and nearly a quarter describe patients who required intensive care during recovery.

COLITIS ASSOCIATED WITH CLINDAMYCIN AND LINCOMYCIN THERAPY

Reports continue to be received of serious colitis following administration of clindamycin (Dalacin C) or lincomycin (Lincocin, Mycivin). Examination of the reports shows that the indications for using these agents are not always clearly defined either clinically or bacteriologically.

LACTIC ACIDOSIS AND PHENFORMIN

Reports continue to come in of the occurrence of this serious, and often fatal, adverse reaction in patients receiving phenformin (Dibotin, Meltrol, Dipar). In many cases the pathogenesis of the condition is complex; excessive alcohol intake, renal or hepatic dysfunction and circulatory failure being also involved.

It is likely that this problem is common to all the biguanides although this is not clearly established by reports submitted to the Committee.

DRUG INTERACTION AND UNINTENDED PREGNANCY IN ORAL CONTRACEPTIVE USERS

We occasionally receive reports of cases of unintended pregnancy occurring in patients taking oral contraceptives who are receiving other concurrent medication. In some of these the reporting doctor mentions his suspicion of a causal relation.

There is an increasing amount of evidence that some drugs can render oral contraceptives ineffective. The Committee is interested in obtaining any information on unintended pregnancy occurring in patients receiving oral contraceptives.

MAPROTILINE (LUDIOMIL) AND CONVULSIONS

Maprotiline is a tetracyclic anti-depressant which has been on the market since 1975. The Committee has received seven reports of convulsions in patients, treated with maprotiline at the recommended dose. These patients had no predisposing abnormality.

INSULIN PREPARATIONS

The introduction of a number of new preparations of insulin may have led to some confusion and it looks as if there are more preparations yet to come. The Committee hopes that the following notes may therefore be helpful.

It is important to know exactly what preparation diabetic patients are currently using. If a change is contemplated the possible effect on dose should be borne in mind. Many diabetics are satisfactorily controlled on existing preparations of insulin but some may develop insulin antibodies or have local reactions at the injection site.

All insulin preparations are now labelled with the source of animal origin and this enables prescribers to specify beef or pork insulin if there is some special reason to do so.

Neutral Insulin Injection BP may cause fewer local reactions than the acidic Insulin Injection BP (Soluble Insulin) but it is important to note that if neutral insulin is required, it should be specifically prescribed.

Insulins described as "Pro-Insulin Freed" can be directly substituted for conventional insulins without change of dosage requirements. The dose needed may be found to decrease gradually when conventional preparations have been used previously.

Pro-Insulin Freed Preparations

Name	Type	Animal Sou
Semilente (Novo)	Insulin Zinc Suspension (Amorphous)	pork
Lentard	Insulin Zinc Suspension	pork and beef
Rapitard	Biphasic Insulin	pork and beef
Ultratard	Insulin Zinc Suspension (Crystalline)	beef

The purer preparations described as Monocomponent (MC: Novo) or Rarely Immunogenic (RI: Nordisk) cannot be treated as clinically inter-changeable with conventional preparations of the same release characteristics. Because the new preparations may be less antigenic than previously available insulins, a dose reduction may be required when they are first prescribed. A current problem is that experience to date is insufficient to allow accurate estimation of the reduction necessary. Further changes in dose may be required depending on the response of the patient.

MC/RI Preparations made from highly purified pork pancreas

Name	Description	Duration
*Actrapid MC) Leo Neutral RI)	Neutral Insulin	Short
Semitard MC	Insulin Zinc Suspension Amorphous	Intermediate
Leo Retard RI	Isophane Insulin	Intermediate
Monotard MC	Insulin Zinc Suspension	Intermediate-Long

*This is the only preparation of Actrapid Insulin available

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