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COMPENDIUM

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Data Sheet Compendium

1980-81



Datapharm Publications Limited
162 Regent Street London W1R 6DD

The compendium

22 OCT 1980

The data sheets in this Compendium are prepared independently by each participating company and each proof is checked and the text confirmed as correct by the participant concerned. Neither Datapharm Publications Limited nor the Association of the British Pharmaceutical Industry (ABPI) give any guarantee whatsoever as to the accuracy of the information contained in the data sheets and accept no liability whatsoever in respect of any loss, damage or expense arising from any such information or for any error or omission in the data sheets and in particular (but without prejudice to the generality of the foregoing) shall not be liable for any consequential damages or expenses or any loss of profit or any liability to third parties incurred by anyone relying on the information contained in the data sheets appearing in this Compendium.

Indexes

An alphabetical index of products, an index of non-proprietary names and a directory of participating companies (together with their telephone numbers) are provided in the tinted section at the back of the compendium.

Data sheets

Data sheets are supplied to practitioners in order to comply with the requirements of the Medicines Act 1968.

They are prepared by the individual companies concerned and, in consequence, vary somewhat in style. All follow, however, the requirements which are laid down by 'The Medicines (Data Sheet) Regulations 1972'.

Participation in the compendium is open to all companies manufacturing medicinal products intended for use under medical supervision.

Further information

The regulations which relate to data sheets restrict the scope of the material which may be given under the heading 'Further information' and require insertion of the word 'Nil' in any data sheet where there is no entry under that heading. Manufacturers are, of course, none the less always willing to provide additional information on their products upon request.

Enquiries should be directed to the companies concerned.

Date of preparation

The data sheets included in this compendium were prepared or reviewed during the first quarter of 1980 and the compendium itself was published in July 1980.

Trade marks

An asterisk by the name of a product indicates that the name is a trade mark. The company symbols which appear in certain participants' sections are also trade marks.

Legal category

The following abbreviations are used under the heading 'Legal category' in entries in the Compendium.

- GSL A preparation which is included in the General Sale List.
- P A pharmacy sale medicine which can be sold only from a retail pharmacy.
- POM A prescription only medicine.
- MDA A preparation containing a substance included in Schedule 2 to the Misuse of Drugs Regulations 1973 (Misuse of Drugs Act 1971).

Doctors are reminded that the Misuse of Drugs Regulations 1973 lay down special requirements relating to the writing of prescriptions for products coming within Schedule 2.



The reporting of adverse reactions

One of the functions of the Committee on Safety of Medicines is to collect and study reports of adverse reactions to medicines. All doctors and dentists in the United Kingdom are encouraged to report toxicity or side-effects that they observe or suspect.

Certain products, which are marked ▼ are recent introductions, and doctors are therefore particularly requested to report details of all suspected adverse reactions to the Committee on Safety of Medicines, preferably on the yellow card issued by the Committee. They are asked to continue to report serious or unusual reactions to all other products.

Even incomplete reports can be helpful and practitioners should not be deterred from reporting because some details are not known.

Special postage-paid forms ('yellow cards') are provided for reports. Supplies of these can be obtained from the Committee at Market Towers, 1 Nine Elms Lane, London SW8 5NQ, telephone 01-720-2188.

The above statement and the symbols marking certain products have been included in the compendium at the request of the Medicines Division of the Department of Health and Social Security.

The individual companies concerned would find it helpful to be informed by practitioners of any adverse reactions to their products which are reported.

Code of Practice for the Pharmaceutical Industry

Fifth edition (December 1978)

For many years members of the Association of the British Pharmaceutical Industry have voluntarily agreed to observe the principles set out in a *Code of Practice for the Pharmaceutical Industry*; a Code which regulates the standards of conduct to be followed in the marketing of medicines intended for use under medical supervision.

The Code was first published in 1958 and has been regularly revised to take account of changes in marketing practices. A fifth edition was introduced in 1978, publication following consultation with the British Medical Association and the Department of Health and Social Security. The Code embodies the basic principles and procedures which the pharmaceutical industry believes to be essential for the conduct of its marketing activities and for the maintenance of standards which are in the interests alike of the public, the medical and allied professions and the industry.

On occasion, the criticism has been made that members of the medical profession were not aware of the provisions of the Code and, consequently, that the Code had been less effective than might otherwise have been the case. To ensure that these provisions become better known, the fifth edition of the Code has been reproduced in its entirety below.

Those who feel that the promotion of a medical speciality product has fallen below the standards which are required by the Code may write, if they so wish, to the Secretary, Code of Practice Committee, Association of the British Pharmaceutical Industry, 162 Regent Street, London W1R 6DD, and ask that the matter be investigated.



INTRODUCTION

- a This Code of Practice for the Pharmaceutical Industry has been drawn up after consultation with the British Medical Association, and the Department of Health and Social Security.
- b The Code owes its origin to the determination of the Association of the British Pharmaceutical Industry to secure the acceptance and adoption of high standards of conduct in the marketing of medical products designed for use under medical supervision.
- c Medical products usually owe their existence to research carried out by their manufacturers or to the development by them of results of academic research. Before a medical product is placed on the market the manufacturer will have accumulated considerable toxicological, pharmacological and clinical evidence and will have met all the statutory requirements for the testing, manufacture, and marketing of that product. Comprehensive legislation has been introduced to safeguard the public by ensuring that all products meet standards of quality, efficacy and safety which are acceptable in the state of present knowledge and experience.
- d It is necessary, however, for the manufacturer operating as he does in a keenly competitive industry and serving professions for which freedom of choice is essential, to draw attention to the existence and nature of a particular product; for example, by appropriate promotional measures and the dissemination of further knowledge and experience gained in wide-spread use.
- e While it is possible to legislate satisfactorily for the testing, manufacture and control of medical products, the Association believes that appropriate standards of marketing conduct cannot be defined by the same means. For this reason, members of the Association have concurred in the promulgation of the Code of Practice and submitted to its restraints.
- f The Code emphasises the importance in the public interest of providing the medical and allied professions with accurate, fair and objective information on medical products so that rational prescribing decisions can be made. Moreover, the Code accepts the principle that such information should be presented in a form and by ways and means which conform not only to legal requirements but also to ethical standards and canons of good taste.
- g The industry recognises its obligation to provide information about medical products to the pharmaceutical profession and the principles set out in this Code, therefore, apply equally to communications addressed to that profession. However, there may be instances where compliance with every provision of the Code would be inappropriate; for example in connection with promotional material the purpose of which is to convey information of a commercial nature to pharmacists or pharmaceutical distributors.
- g The Code, therefore, represents an act of self-discipline. Acceptance and observance of its provisions are a condition of membership of the Association of the British Pharmaceutical Industry. Member companies also acknowledge that the Code itself is to be applied in the spirit, as well as in the letter.
- h Pharmaceutical companies outside the Association are invited to accept and observe the Code because it is considered that high ethical standards should be followed throughout the whole industry if it is to maintain the confidence of all the interests which it serves.

The Code is administered by a Committee established by the Board of Management of the Association. The Committee, with an independent legally qualified Chairman from outside the industry, consists of two independent members who are medically qualified persons not engaged in the industry, and twelve members who are drawn from the senior management of member companies, including at least four medical directors or medically qualified persons of equivalent status.

The Chairman has general authority to obtain expert assistance in any field, and has an original and a casting vote.

The Committee meets regularly to deal with complaints, to secure compliance with the Code, and to make such recommendations as it deems fit for the amendment of the provisions of the Code.

An outstanding feature has been the success of voluntary compliance with the provisions of the Code and acceptance of the rulings of the Committee. It has not been found necessary to apply sanctions to secure compliance because members of the Association are anxious to ensure that their marketing activities conform to the highest standard.

It is important, therefore, that the Code should accurately reflect that standard and for this reason it is kept under constant review by the Board of Management and amended from time to time where necessary to clarify it and bring it up to date. Notes for the guidance of member companies are issued periodically to keep them informed of the rulings and recommendations of the Committee and of any alterations to the Code.

This edition of the Code supersedes all previous editions and is the fifth edition since the Code was established in 1958. It embodies the basic principles and provisions which the pharmaceutical industry believes are essential for the conduct of its marketing activities and for the maintenance of standards which are in the interests alike of the public, the medical and allied professions and the industry.

PROVISIONS OF THE CODE

The supplementary text, which appears in italics, is intended to give guidance as to the interpretation of the Code.

Definition of certain terms

The term 'promotion' means those informational and marketing activities, undertaken by the product licence holder or with his authority, the purpose of which is to induce the prescribing, supply or administration of his medical products. It includes, for example, the activities of representatives; various aspects of sales promotion such as journal and direct mail advertising; the use of films and other audio-visual material and exhibitions; and the provision of samples, gifts or hospitality.

The term 'promotion' does not extend to:

(i) Replies made in response to enquiries from particular doctors or to replies in response to a specific communication, whether of enquiry or comment, including letters published in a medical journal.

(ii) Announcements of pack changes, adverse reactions, warnings or recall of products provided they contain no product claims.

(iii) 'Trade advertisements' as defined in the Medicines (Advertising of Medicinal Products) Regulations 1975, i.e. catalogues, price lists or other documents issued with a view to wholesale dealing but not containing any reference to product usage other than a therapeutic classification.

By 'wholesale dealing' is meant the sale of a product to a person who, during the course of his business or professional practice, buys it for the purpose of selling it or administering it or causing it to be administered to one or more human beings.

1.2 The term 'medical product' means any unbranded or branded pharmaceutical product intended for use in humans which is promoted to the medical profession rather than directly to the lay public.

1.3 The terms 'medical profession', 'practice of medicine', 'practitioner' and 'doctor' should be interpreted to extend to the dental profession and be construed accordingly.

1.4 The term 'medical representative' means a representative whose duties comprise or include calling upon members of the medical profession.

2 Methods of promotion

Methods of promotion must never be such as to bring discredit upon, or reduce confidence in, the pharmaceutical industry.

The issue of rubber stamps to doctors for use as aids to prescription writing is one of methods of promotion barred by this clause.

3 Nature and availability of information

3.1 Upon reasonable request, the company concerned shall promptly provide members of the medical profession with accurate and relevant information about the medical products which the company markets.

3.2 Information about medical products should accurately reflect current knowledge or responsible opinion.

3.3 Information about medical products must be accurate, balanced and must not mislead either directly or by implication.

Claims for superior potency per unit weight are meaningless and best avoided unless they can be linked with some practical advantage, e.g. reduction in side-effects or cost of effective dosage.

3.4 Information must be capable of substantiation, such substantiation being provided without delay at the request of members of the medical profession.

4 Claims and comparisons

4.1 Claims for a medical product must be based on an up-to-date evaluation of all the evidence and must reflect this evidence accurately and clearly.

4.2 Exaggerated claims should not be made and all-embracing claims and superlatives avoided. Claims should not imply that a medical product, or an active ingredient, has some special merit, quality or property unless this can be substantiated.

Claims such as 'agent of choice' should be avoided unless they can be clearly substantiated.

4.3 Any statement about side-effects should be specific and based on data submitted with the licence

application or notified to the licensing authority, or on published data to which references are given. It should not be stated that a product has no side-effects, toxic hazards or risks of addiction. The word 'safe' must not be used without qualification.

4.4 The word 'new' should not be used to describe any product or presentation which has been generally available, or any therapeutic indication which has been generally promoted, for more than twelve months in the United Kingdom.

4.5 Comparisons of products must be factual, fair, and capable of substantiation. In presenting a comparison, care must be taken to ensure that it does not mislead by distortion, by undue emphasis, or in any other way.

Hangings comparatives, which merely claim that a product is 'better' or 'stronger' etc., should not be used.

4.6 Brand names of products of other companies must not be used unless the prior consent of the proprietors has been obtained.

5 Disparaging references

5.1 The products or services of other companies should not be disparaged either directly or by implication.

Substantiated comparative claims inviting fair comparisons with a group of products or with other products in the same field are permissible, provided that such claims are not presented in a way which is likely to mislead, whether by distortion, undue emphasis or otherwise.

5.2 The clinical and scientific opinions of members of the medical and allied professions should not be disparaged either directly or by implication.

6 Printed promotional material

6.1 The Medicines Act 1968 requires a pharmaceutical company to provide a practitioner with a data sheet before promoting a product directly to him. The content of such data sheets is determined by Regulations made under the Medicines Act.

Data Sheets for many prescription products are published in the ABPI Data Sheet Compendium which is issued at regular intervals. Copies of the Compendium are supplied to members of the medical and pharmaceutical professions.

6.2 All other printed material (including journal advertising) which is issued for promotional purposes by the product licence holder or with his authority must include certain information specified in this Code.

The requirements of Clause 6.3 or 6.4, as appropriate, must be complied with in any advertising directed towards the medical profession even if it is of a general nature, e.g. prestige advertisements listing a company's products.

An advertisement which would not otherwise conform with the Code should not be regarded as doing so by reason only of the fact that the content of the data sheet is reproduced as part of the advertisement or because a data sheet is sent with the advertisement.

6.3(i) Except for 'abbreviated advertisements', as defined in Clause 6.4, the following information must be given clearly and concisely on printed promotional material:

a The number of the relevant product licence and the name and address of the holder of the licence, or the business name and address of the part of his business responsible for the sale of the product.

b A quantitative list of the active ingredients, using approved names where such exist, or other non-proprietary names; alternatively, the non-proprietary name of the product if it is the subject of an accepted monograph.

Attention is drawn to the fact that the Medicines (Advertising to Medical and Dental Practitioners) Regulations 1978 (SI 1978 No. 1020) impose additional requirements which relate to the position and type size of this information.

c At least one authorised indication for use consistent with the data sheet.

d A succinct statement of the information in the data sheet relating to the dosage and method of use relevant to the indications quoted in the advertisement and, where not otherwise obvious, the route of administration.

e A succinct statement of the side-effects, precautions and contra-indications relevant to the indications in the advertisement, giving, in an abbreviated form, the substance of the relevant information in the data sheet.

f Any warning issued by the Medicines Commission, a committee appointed under Section 4 of the Medicines Act 1968 or the licensing authority, which is required to be included in advertisements.

g The cost of a product, except in the case of advertisements in journals which have an appreciable proportion of their circulation outside the United Kingdom.

The cost of a product is the cost (excluding value added tax) of either a specified package of the product, or a specified quantity or recommended daily dose, calculated by reference to any specified package of the product.

Attention is drawn to the fact that the Medicines (Advertising to Medical and Dental Practitioners) Regulations 1978 (SI 1978 No. 1020) impose a specific requirement to that proportion of the circulation of a journal which has to be outside the United Kingdom in order to qualify for the exception to this requirement.

6.3(ii) The information required by Clause 6.3 (d), (e) and (f) must be printed in such type and in such a position that its relationship to the claims and indications is readily appreciated by the reader.

6.4(i) The requirements of Clause 6.3 do not apply in the case of an 'abbreviated advertisement'. An 'abbreviated advertisement' is one, the text of which contains in relation to the product no more than:

a The brand name of the product.

b The approved names of the active ingredients where such names exist, or other non-proprietary names; alternatively, the non-proprietary name of the product if it is the subject of an accepted monograph.

Attention is drawn to the fact that the Medicines (Advertising to Medical and Dental Practitioners) Regulations 1978 (SI 1978 No. 1020) impose additional requirements which relate to the position and type of this information.

c The name and address of the product licence holder, or the business name and address of the part of his business responsible for the sale of the product.

d One indication for use, or more than one indication provided that these are related, consistent with the data sheet.

e A concise statement, consistent with the data sheet, giving the reason why the product is recommended for such indication or indications.

f A form of words which indicates clearly that further information is available on request to the licence holder or is to be found in the data sheet relating to the product.

6.4(ii) An 'abbreviated advertisement' must always contain the information required by Clause 6.4(i) (a), (b), (c) and (f). The information required by Clause 6.4(i) (d) and (e) is optional. An 'abbreviated advertisement' must not include any illustration which is likely to convey any information about the product or imply claims which are additional to those provided in accordance with Clause 6.4(i) (a) to (e) inclusive.

6.4(iii) An 'abbreviated advertisement' directed towards a doctor is permissible only when it constitutes an advertisement appearing in a publication sent or delivered wholly or mainly to doctors. A loose insert included in such a publication cannot be an 'abbreviated advertisement'.

Attention is drawn to the fact that the Medicines (Advertising to Medical and Dental Practitioners) Regulations 1978 (SI 1978 No. 1020) impose additional requirements which relate to the maximum permitted size of an 'abbreviated advertisement'.

6.4(iv) An 'abbreviated advertisement' is not permissible where the Medicines Commission, a committee appointed under Section 4 of the Medicines Act 1968 or the licensing authority, have required a warning to be included in any advertisement relating to the medical product, and the licensing authority have issued a direction that 'abbreviated advertisements' should not be issued.

6.5 Promotional material, such as mailings and journal advertisements, must not be designed to disguise its real nature.

Doctors rightly resent receiving promotional material in the guise of personal communications, as when advertisements are enclosed in a plain envelope or are addressed in real or facsimile handwriting on letters or postcards.

Envelopes should not be used for the dispatch of promotional material if they bear words implying that the contents are non-promotional, e.g. that the contents provide information relating to safety.

It is advisable to use first class mail only for important communications of a non-promotional nature such as notifications of warnings or cautions or the withdrawal or recall of a product.

Advertisements in journals should not be designed so as to resemble editorial matter.

6.6 Promotional material should conform, both in text and illustration to canons of good taste and should recognise the professional standing of the recipients.

Representations of the nude female form (even in silhouette) or partly clothed figures should not be used in promotional material in such a way as to arouse a visual or emotional response in order to attract attention to the text.

Displays of part of the naked body which are necessary to illustrate pictorially the message of the text are permissible provided that they conform to the dictates of decency and good taste.

6.7 Doctors' names or photographs must not be used

in a prominent manner in promotional material or in any other way that is contrary to the ethical code of the medical profession.

6.8 Promotional material should not imitate the devices, copy, slogans or general layout adopted by other companies in a way that is likely to mislead or confuse.

6.9 Where appropriate, for example, in technical and other informative material, the date of printing or the last review should be stated.

6.10 Extremes of format, size or cost of printed material should be avoided.

Large size mailings which cannot be put through letter boxes are a source of irritation to doctors and should be avoided as far as possible.

6.11 Postcards, other exposed mailings, envelopes or wrappers should not carry matter which might be regarded as advertising to the lay public or which could be considered unsuitable for public view.

Postcards and other exposed mailings should not contain copy or illustrations which ought not to be read or seen by lay persons.

6.12 Telegrams must not be used for promotional purposes.

6.13 In a multi-page press advertisement in which the pages follow consecutively, only one page need include the information required by Clause 6.3 of the Code, provided that each of the other pages (except the page on which, or facing which, the information is printed) includes a reference, on an outer edge, in at least 8 point type, indicating on which page that information appears. No initial recto or final verso must be false or misleading if read in isolation.

A loose insert included in a journal is not regarded as a 'multi-page press advertisement' for the purpose of this clause.

6.14 In a multi-page advertisement other than a press advertisement, the information required by Clause 6.3 of the Code must appear on one or more continuous pages and, where such an advertisement consists of more than four pages, the advertisement must include a clear indication as to where this information may be found.

7 References to official bodies

Promotional material should not include any reference to the Medicines Commissions, a committee appointed under Section 4 of the Medicines Act 1968 or the licensing authority, unless this is specifically required by the licensing authority.

8 References to the National Health Service

8.1 Where reference is made to the prescribing of a product under the National Health Service, the phrase 'freely prescribable' or similar phrases suggesting a lack of restriction or restraint must not be used.

This clause was inserted in the first edition of the Code in deference to the wishes of the then Ministry of Health. 'Freely' in this context means 'without restriction or restraint'.

Although NHS doctors are free to prescribe whatever medicines they consider necessary for the treatment of a patient, they are nevertheless required to exercise due economy.

8.2 Reproductions of official documents, such as prescription form FP 10, should not be used for promotional purposes unless the agreement of the appropriate Government department has been received.

The term 'reproduction' includes any depiction which simulates or might be taken to simulate the document in question.

9 Artwork, graphs, illustrations, etc

9.1 Illustrations must not mislead as to the nature of the claims or comparisons being made, nor as to the purposes for which the product is used; nor should illustrations detract from warnings or contra-indications.

9.2 Artwork and graphs must conform to the letter and the spirit of the Code. Graphs and tables should be presented in such way as to give a clear, fair, balanced view of the matters with which they deal, and should only be included if they are strictly relevant to the claims or comparisons being made.

9.3 Graphs and tables must not be used in any way which might mislead; for example, by their incompleteness or by the use of suppressed zeros or unusual scales.

10 Reprints, abstracts and quotations

This clause is included to accord with the views of the Ethical Committee of the British Medical Association; its object is to avoid the risk of contravention of the BMA Code of Ethics.

10.1 Reprints of articles by members of the medical profession must not be included in mailings but may be supplied to individual doctors on request. It is permissible to include in promotional material reasonably brief abstracts of, or quotations from, articles by members of the medical profession and to include in such material reference to doctors' names in a bibliography of published works. In no case, however, should doctors' names be used in a prominent manner in promotional material.

Quotations from public broadcasts, e.g. radio and television, may not be used in promotional material. It is permissible to use quotations from private occasions, e.g. medical conferences or symposia, with the written permission of the speaker.

10.2 Quotations from medical literature, or from personal communications received from doctors, must accurately reflect the meaning of the author and the significance of the study.

10.3 The utmost care must be taken to avoid ascribing claims or views to medical authors when such claims or views no longer represent, or may not represent, the current views of the author concerned.

11 Distribution of printed promotional material

11.1 Promotional material should only be sent or distributed to those categories of persons whose need for, or interest in, the particular information can reasonably be assumed.

11.2 Any information designed to encourage the use of medical products in clinics, industrial concerns, clubs or schools must be addressed to the medical adviser or medical officer or to medical auxiliary staff.

11.3 Restraint should be exercised on the frequency of distribution and on the volume of promotional material distributed.

The style of mailings is relevant to their acceptability to doctors and criticism of their frequency is most likely to arise where their informational content is limited or where they appear to be elaborate and expensive. A higher frequency rate will be accepted for mailings on 'new' products than for others.

11.4 Mailing lists must be kept up to date. Requests from doctors to be removed from promotional mailing lists must be complied with promptly and no name may be restored except at the doctor's request or with his permission.

12 Audio-visual material

12.1 Audio-visual material must comply with all relevant requirements of the Code, with the exception of Clause 6.3.

12.2 When audio-visual material is used to promote a product, copies of the relevant data sheet, or a document with the same content, should be made available to all persons present.

12.3 Audio-visual promotional material is subject to the certification requirements of Clause 13.

13 Certification of printed promotional material

13.1 No promotional material shall be issued unless the final text and layout have been certified by two persons on behalf of the member company in the manner provided by this Clause. One of the two persons shall be a doctor. The other shall be a pharmacist or some other appropriately qualified person or a senior official of the company. The doctor, pharmacist or other qualified person must be a senior employee of the company or an appropriately qualified person whose services are retained for that purpose.

13.2 The names of those nominated, together with their qualifications, shall be notified in advance to the licensing authority. The names and qualifications of designated alternative signatories must also be given. Changes in the names of nominees must be promptly notified.

13.3 The certificate shall certify that the signatories have examined the material in its final form and that in their belief it is in accordance with the requirements of the relevant advertising regulations and this Code of Practice, is consistent with the product licence and the data sheet, and is a fair and truthful presentation of the facts about the product.

13.4 Member companies shall preserve all certificates, together with the material in the form certified, for not less than three years and produce them upon request from the licensing authority or the Association at the instance of the Code of Practice Committee.

13.5 The foregoing procedure shall apply, with the necessary variations, to the certification of briefing material for representatives in accordance with Clause 15.12 and to audio-visual promotional material prepared by or on behalf of member companies.

14 Suspension of advertisements

In the event of the Code of Practice Committee requiring a member company to withdraw an advertisement

pending its decision on a complaint by the licensing authority relevant to the safe or proper use of the product, the member company shall at once make every possible endeavour to comply.

15 Medical representatives

15.1 Medical representatives must be adequately trained and possess sufficient medical and technical knowledge to present information on the company's products in an accurate and responsible manner.

15.2 Medical representatives should at all times maintain a high standard of ethical conduct in the discharge of their duties.

15.3 The requirements of the Code which aim at accuracy, fairness, balance, good taste apply to oral representations as well as printed material.

15.4 Unfair or misleading comparisons or comparisons implying a therapeutic advantage which is not in fact justified must be avoided by medical representatives.

15.5 Claims made for products by medical representatives must be limited to the indications permitted by the product licence.

15.6 Medical representatives must not employ any inducement or subterfuge to gain an interview. No payment of a fee should be made for the grant of an interview.

The practice of gaining or extending an interview on the pretext of carrying out a survey is to be avoided. This does not preclude the use of medical representatives to obtain bona fide survey information, but it is essential that the survey should be devised and conducted so as to leave no doubt in the doctor's mind that the survey will produce medically useful information.

15.7 Medical representatives must ensure that the frequency timing and duration of calls on doctors, or on hospitals, together with the manner in which they are made, do not cause inconvenience. The wishes of an individual doctor, or the arrangements in force at any particular establishment, must be observed by medical representatives.

The number of calls made on a medical practitioner and the intervals between successive visits are relevant to the determination of frequency.

Companies should arrange that intervals between visits do not cause inconvenience to practitioners and the number of calls made by a medical representative each year should not normally exceed, on average, three visits to each doctor.

Averages are to be calculated separately for general practitioners and other members of the medical profession to whom visits are made.

The calculation should exclude:

(i) Attendance by a medical representative at a scientific meeting or an audio-visual presentation given to a group of doctors.

(ii) A visit which is requested by a doctor or a call which is made in order to respond to a specific enquiry.

(iii) A visit to follow up a report of an adverse reaction.

A medical representative should not stay in a surgery in which another medical representative is already waiting, except with the doctor's or receptionist's approval.

Medical representatives must always endeavour to treat the doctor's time with the utmost respect and give him no cause to believe that his time might have been wasted. If, for any unavoidable reasons, an

appointment with a doctor cannot be kept, the longest possible notice must be given.

Calls on hospital medical staff should generally be limited to matters likely to be of specific interest to them. The majority are specialists and medical representatives should ensure that their specialised interests are borne in mind. It is preferable for most hospital staff to be seen only after making a prior appointment, at which time subjects for discussion should be identified.

15.8 Medical representatives must take adequate precautions to ensure the security of medical products in their possession.

15.9 Medical representatives must not use the telephone to promote products to the medical profession unless prior arrangement has been made with individual doctors.

15.10 Medical representatives should be paid on the basis of a fixed basic salary, and any addition proportional to sales of prescription medicines should not constitute an undue proportion of their remuneration.

15.11 When discussion about a product is initiated by a medical representative, he should place before the doctor for reference either a data sheet in respect of that product or another document with the same content. If, however, the doctor asks a question about a different product, then the medical representative will not be required to produce such data in respect of that other product.

15.12 Companies must prepare detailed briefing material for medical representatives on the technical aspects of any product which the medical representative is to promote. A copy of such material must be made available to the licensing authority on request. Briefing material must comply with the relevant requirements of the Code and, in particular, is subject to the certification requirements of Clause 13.

15.13 Medical representatives should not make a claim for a product based on the regulatory treatment of that product, or of competing products, or based on any warnings issued in relation to other products, unless in accordance with a specific requirement. However, a medical representative may refer to such matters in answer to a specific question.

15.14 A company may only employ as medical representatives persons who have passed the examination established by the Association except that:

(i) Persons with an acceptable professional qualification, e.g. in pharmacy, medicine or nursing will be exempt from this requirement.

(ii) Persons employed as medical representatives at the date upon which this edition of the Code comes into operation will be exempt from this requirement.

1 October 1979 (Clause 21.1 (iii)).

(iii) Trainee medical representatives may be employed for a period of up to two years from the date of commencing training as a medical representative.

16 Samples

16.1 Except when provided for identification or demonstration purposes, samples should only be supplied in response to a signed request from a doctor; such requests, except in respect of products controlled under the Misuse of Drugs Act, may not be accepted on a pre-printed card or form which incorporates more than the company name and address. The form must

be handed by a representative to the doctor who should then add all other details.

Wherever practicable, an individual sample should not represent more than four days treatment for a single patient. When samples are provided to assist doctors in the recognition or identification of a product, or to demonstrate the use of a particular apparatus or equipment, only the minimum quantity necessary for this purpose should be supplied.

16.2 Where samples of products restricted by law to supply on prescription are distributed by a representative, the sample must be handed direct to the doctor or given to a person authorised to receive the sample on his behalf. A similar practice must be adopted for products which it would be unsafe to use except under medical supervision.

16.3 Samples of products restricted by law to supply on prescription, which are made available to representatives for distribution, should be strictly limited in quantity and an adequate system of accountability should be established.

16.4 Samples sent by post must be packed so as to be reasonably secure against the package being opened by young children.

16.5 Distribution of samples in hospitals should comply with individual hospital regulations, if any.

17 Gifts and inducements

17.1 Subject to Clause 17.2 no gift or financial inducement shall be offered or given to members of the medical profession for purposes of sales promotion.

Schemes designed to test the extent to which mailings are opened and read and which involve a reward, e.g. a reward for the return of a voucher included in the mailing, are unacceptable if the gift is one which would not come within Clause 17.2.

17.2 Gifts in the form of articles designed as promotional aids, whether related to a particular product or of general utility, may be distributed to members of the medical and allied professions provided the gift is inexpensive and relevant to the practice or medicine or pharmacy.

Amongst other items, nail brushes, book matches and pens have been held to be reasonable gifts. Gifts of table mats have been held to be in contravention of the Code as being irrelevant to the practice of medicine or pharmacy.

17.3 The requirements of Clause 6.3 or Clause 6.4 do not apply if a promotional aid of the type mentioned in Clause 17.2 bears no more than one or more of the following particulars:

- (i) The name of the product.
- (ii) The name of the product licence holder or the name of that part of his business responsible for the sale of the product.
- (iii) The address of the product licence holder or the address of the part of his business responsible for the sale of the product.
- (iv) An indication that the product name is a trade mark.

If a promotional aid consists of a note pad in which the individual pages bear advertising material, there is no need for the individual pages to comply with Clause 6 provided that the information required by the clause is given elsewhere in the pad; for example, on the cover.

18 Hospitality

Entertainment or other hospitality offered to members of the medical and allied professions for purposes of sales promotion should always be secondary to the main purpose of the meeting. It should not extend beyond members of the professions. The level of hospitality should be appropriate and not out of proportion to the occasion; its cost should not exceed that level which the recipients might normally adopt when paying for themselves.

Medical and group meetings are desirable and are to be encouraged. Both the British Medical Association and the Association share the opinion that such meetings should only take place if the advertising content is supported by a clear educational content. If hospitality is offered at meetings attendance should be restricted to members of the medical and allied professions.

It follows, therefore, that invitations to such medical and group meetings should not be extended to wives or husbands unless they themselves are practising members of the medical or allied professions.

When organising a meeting at which hospitality will be offered, a factor to be taken into account is the impression which will be created in the minds of the recipients or those who hear about it. Hospitality which becomes little more than pure entertainment has limited value in terms of the provision of information and promotion; such hospitality can only be regarded, therefore, as irrelevant and wasteful.

19 Marketing research

Marketing research is the collection and analysis of information and must be unbiased and non-promotional. The use to which the statistics or information is put may well be promotional. The two phases should be kept distinct.

19.1 Methods used for marketing research must never be such as to bring discredit upon, or to reduce confidence in, the pharmaceutical industry. The following provisions apply whether the research is carried out directly by the company concerned or by an organisation acting on the company's behalf.

19.2 The following information must be made available to the informant at first approach:

- (i) The nature of the survey.
- (ii) The name and address of the organisation carrying out the work.
- (iii) The identity of the interviewer.
- (iv) The nature and length of the interview.

The requirement in Clause 19.2 (ii) does not mean that the organisation is also obliged to reveal the identity of its client. This must depend upon the contract between the client and the organisation.

19.3 Questions intended to solicit disparaging references to competing products or companies must be avoided.

19.4 Any written or oral statement given or made to an informant in order to obtain co-operation must be both factually correct and honoured.

19.5 Any incentives offered to the informants should be kept to a minimum and be commensurate with the work involved.

19.6 Marketing research must not in any circumstances be used as a disguised form of sales promotion

and the research *per se* must not have as a direct object the influencing of the opinions of the informant.

9.7 The identity of an informant must be treated as being confidential, unless he has specifically agreed otherwise.

In the absence of this agreement it follows that the information provided (as distinct from the overall results of the research) must not be used as the basis upon which a subsequent approach is made to that informant for the purpose of sales promotion.

19.8 Precautions should be taken to ensure that no embarrassment results for informants following on from an interview, or from any subsequent communication concerning the research project.

20 Relations with the general public and lay communication media

20.1 Requests from individual members of the public for information or advice on personal medical matters must always be refused and the enquirer recommended to consult his or her own doctor.

20.2 Medicines which cannot legally be sold or supplied to the public otherwise than in accordance with a prescription, or which are legally limited to promotion for sale or supply only on prescription, must not be advertised to the general public.

Posters or notices issued for display in doctor's surgeries, pharmacies or anywhere to which the public have access must not include any message likely to arouse a demand for any particular product.

20.3 Statements must never be designed or made for the purpose of encouraging members of the public to ask their doctor to prescribe a product.

20.4 Information about medical products or matters related thereto, including scientific discoveries or advances in treatment, should not in general be made available to the general public either directly or through any lay medium.

The intention is to ensure that arrangements made for a press conference, or the extent of a press release, are such as to confine the disclosure of information about medical products or matters relating thereto to persons who are capable of evaluating the information responsibly and not concerned to exaggerate or even sensationalise its significance.

20.5 The importance of such information and the existence of legitimate public interest in acquiring it may exceptionally justify holding a press conference or the issue of a press release.

Invitations to attend such a conference, or the distribution of such a press release, should be confined to persons who are either medically qualified or established as the representatives of the medical, pharmaceutical or scientific press, or as the medical correspondents of a responsible medium.

In the circumstances set out above as to the significance of the information, and in response to an unsolicited enquiry from a person of the standing described, information may also be released in an informal manner.

20.6 A further exception may arise when there exists a genuine mutual interest of a financial or commercial nature justifying the disclosure of information about medical products or related matters privately or to a restricted public. Examples are the interests of shareholders, financial advisers, employees and creditors.

When releasing information, it is essential to bear in mind the provisions of Clause 4.3 and, in particular, the extreme caution required in any reference to side-effects; it should also be emphasised that the treatment of a particular individual is solely a matter for decision by his medical practitioner.

20.7 On all occasions the information whether written, or communicated by other means, must be presented in a balanced way so as to avoid the risk of raising unfounded hopes of successful treatment or stimulating the demand for prescription of the particular product.

20.8 An announcement of the introduction of a new medical product must not be made by press conference or formal press release until the appropriate steps have been taken to inform the medical profession of its availability.

21 Transitional provisions

21.1 This Code shall not take effect:

(i) Until 1 March 1979, in relation to an advertisement contained in a publication sent or delivered wholly or mainly to doctors or dentists, except that in relation to any advertisement for a product which is the subject of a product licence granted on or after 1 December 1978, the Code shall take effect as from the date of grant.

(ii) Until 1 October 1982, in relation to any advertisement consisting of four or more pages or advertising on a promotional aid, printed before 1 December 1978 and sent through the post or otherwise delivered to a doctor or dentist.

(iii) Until 1 October 1979, in relation to any other advertisement and any other matter.

The other matters which take effect on 1 October 1979 are Clauses 13, 15, 16, 17, 18, 19 and 20.

Clause 14 takes effect on 1 March 1979 consequent upon the coming into operation on that date of the revised 'Constitution and Procedure' for the Code of Practice Committee.

21.2 Until such time as this Code takes effect in relation to any particular advertisement or matter, the requirements (if any) of the Fourth Edition of the Code shall continue to apply to that advertisement or matter.

Abbott Laboratories Limited
Queenborough
Kent ME11 5EL



ABBOCIN*

Presentation Each yellow, sugar-coated tablet contains 250 mg Oxytetracycline Dihydrate BP.

Uses Organisms sensitive to oxytetracycline include a large number of Gram-negative and Gram-positive pathogenic bacteria. Those organisms that are sensitive to tetracycline in the concentrations usually achieved in the body during treatment are *Bacillus anthracis*, *bordetella* spp., *brucella* spp., *Escherichia coli*, haemophilus spp., *klebsiella* spp., *Proteus vulgaris*, staphylococci, streptococci, mycoplasma, *Entamoeba histolytica*, *Trichomonas vaginalis*, certain rickettsias and larger viruses. *Pseudomonas aeruginosa*, salmonella spp. and *Mycobacterium tuberculosis* are less susceptible.

Dosage and administration For adults and older children the dose is 250 mg four times daily taken orally. In severe infections this dose may be doubled or trebled.

Contra-indications, warnings, etc

Contra-indications: Hypersensitivity to the tetracyclines.

Precautions and side-effects: As with other tetracyclines Abboicin should be administered with great care to individuals with renal or hepatic dysfunction. Because of the staining of teeth and effects on bone development, tetracyclines should not be given in pregnancy, or to children under 12 years of age. Tetracyclines should not be administered simultaneously with milk, antacids, or preparations containing iron, calcium or magnesium.

Side-effects include nausea, diarrhoea, and symptoms resulting from the overgrowth of non-susceptible organisms. Overgrowth of *Candida albicans* in the mouth may cause glossitis and stomatitis which may extend into the trachea and bronchi; overgrowth of *C. albicans* in the bowel results in pruritis ani; overgrowth of resistant coliform organisms such as *pseudomonas* and *proteus* may also cause diarrhoea. Occasionally resistant staphylococci may give rise to a fulminating enterocolitis. Allergic reactions and skin rashes are rare.

Treatment of overdose: Gastric lavage. Intensive supportive therapy. In cases of overdose, allergic reactions such as drug fever, anaphylactic shock and rash may occur. For treatment of anaphylaxis immediate administration of adrenaline, oxygen and artificial respiration is necessary.

Adrenaline is given subcutaneously as Adrenaline Injection BP 0.1% (equivalent to 0.1% adrenaline) at a rate of 0.05 ml/minute. For dyspnoea, aminophylline, calcium and antihistamines must be given. General measures, such as administration of plasma blood, vasopressor drugs or hydrocortisone (100 mg IV) may be necessary.

Incompatible with alkalis and chloramphenicol.

Pharmaceutical precautions Store below 25°C. Keep container tightly closed.

Legal category POM.

Package quantities Abboicin is supplied in Security-tainers of 1,000 sugar-coated tablets (List No. C945).

Further information Metabolisable carbohydrate content approx. 0.29 g per tablet.

Product licence number 0037/0095.

ABBOKINASE* ▼

Presentation Abbokinase is a highly purified sterile lyophilised formulation of urokinase obtained from cultures of human kidney cells. Urokinase is a plasminogen activator excreted in the urine of normal healthy individuals. Each vial of Abbokinase contains in excess of 250,000 iu so that, following reconstitution with 5.2 ml sterile water for injection, each ml of the 5 ml which can be withdrawn will contain 50,000 iu urokinase, 5 mg mannitol and 5 mg sodium chloride.

Uses Abbokinase *in-vivo* and *in-vitro* produces the release of plasmin by an enzymatic action on human plasminogen.

Abbokinase has only minimal activity in reducing fibrinogen levels but blood plasminogen levels are reduced, the effect being dose-dependent.

Abbokinase is virtually non-antigenic to humans and, in therapeutic doses, is thromboplastin-free.

Thrombolytic therapy is indicated in the treatment of vascular occlusions caused by forming or recently formed fibrin clots. Theoretically the best results will be obtained with thrombi less than 24 hours old.

Abbokinase is indicated as a thrombolytic agent in pulmonary embolism.

Dosage and administration Abbokinase is administered intravenously by continuous infusion, usually for a period of 12 hours.

It is recommended that Abbokinase be given in a solution of normal saline by constant infusion. An initial loading dose to be given during the first ten minutes of therapy is advocated.

This loading dose should be equal to the amount which it is planned to administer over each succeeding period of one hour. Ideally, an infusion pump should be used to maintain a constant rate of infusion.

Abbokinase is reconstituted with 5.2 ml sterile water for injection, without preservatives.

For administration the reconstituted solution should be further diluted with normal saline. It is strongly recommended that the total volume after dilution should be 195 ml, irrespective of the number of vials used, since this provides for a bolus dose of 15 ml followed by the infusion of 15 ml per hour over 12 hours. However, choice of another volume is possible, the physician being guided by considerations of possible effect on the patient of larger volumes and physical difficulties of measurement with smaller volumes. A chart is available detailing volumes of reconstitution and further dilution for use (on the basis of a final volume of 195 ml) in cases where the amount of Abbokinase immediately available is less than that required for the total treatment.

Armour Pharmaceutical Company Limited

Hampden Park
Eastbourne
East Sussex BN22 9AG

AAA* MOUTH AND THROAT SPRAY

Presentation Each can contains 7.5 g with a metered valve providing 60 x 100 mg doses.

Benzocaine PhEur 1.5% w/w
Cetalkonium chloride 0.0413% w/w

in an inert flavoured propellant.

Uses Treatment of sore throats caused by cold, post-nasal drip and other irritants, and minor infections of the mouth and throat.

Dosage and administration Shake can before use. **Adults:** 2 shots every two to three hours if required (not more than 16 shots in 24 hours or as directed by the physician).

Children aged 6-12: 1 shot every two to three hours if required (not more than 8 shots in 24 hours or as directed by the physician).

Contra-indications, warnings, etc

Side-effects: Hypersensitivity reactions to benzocaine have been reported.

Precautions: Avoid spraying into eyes.

Contents under pressure — do not puncture.

Keep away from heat and flames — do not throw finished container into fire.

Contra-indications: None known.

Pharmaceutical precautions Store in a cool place. Indefinite shelf-life. Shake can before use.

Legal category P.

Package quantities Each can contains 7.5 g with a metered valve providing 60 x 100 mg doses (shots).

Further information Published clinical studies have demonstrated antibacterial activity by the reduction in the population of pathogenic organisms of the buccal mucosa. Together with the spray's local anaesthetic activity, this has been found of value in the treatment of pain and infection following tonsillectomy.

Product licence number 0231/5026.

ACTHAR* GEL

ACTHAR*

Presentation Acthar Gel: Corticotrophin Gelatin Injection BP in vials containing 20, 40 and 80 i.u./ml for subcutaneous or intramuscular use only.

Acthar: Corticotrophin Injection BP in vials containing 40 i.u. as a lyophilised powder.

Uses Rheumatic and Collagen diseases. Asthma. Diseases of the GI tract (e.g. ulcerative colitis). Nephrotic syndrome. Diseases of the CNS (e.g. Bell's Palsy and Retrobulbar Neuritis). Adrenal function tests. Chronic skin and allergic conditions responsive to corticosteroids (e.g. psoriasis and certain eczemas and refractory hay fever unresponsive to conventional treatment).

Dosage and administration General information on dosage for therapeutic use. The aim of treatment with Acthar Gel is to obtain a satisfactory therapeutic effect with minimal dosage, the clinical response being the sole measure of adequate dosage. Therapeutic effects may appear within hours, although with some chronic diseases improvement may not show for several days.

Because patients' adrenal glands vary in their sensitivity to ACTH and because disease conditions vary in their response to corticosteroids, no specific uniform dose can be equally effective for all individuals. Some conditions, e.g. acute exacerbations of asthma and multiple sclerosis may require high doses initially to obtain a remission. Once the disease is under control the total daily dosage should be decreased as rapidly as possible. Dosage reduction should be consistent with maintaining clinical improvement. Some conditions, e.g. rheumatoid arthritis, nephrotic syndrome and chronic asthma may need long-term maintenance therapy. Again, the aim is to obtain satisfactory therapeutic effect with minimal dosage. If the treatment regimen is started on a daily basis when the smallest daily maintenance dose has been established (say 20 i.u.), attempts should be made to lengthen the dosage intervals. If at any step of dosage reduction symptoms reappear, a return to the previous effective schedule is necessary before a further attempt at dosage reduction is made. On occasions Acthar Gel can be completely withdrawn as the patient experiences a remission.

Instead of starting with daily injections, it may be more convenient to commence with an initial higher fixed unit dosage (say 40 i.u. per injection) twice or thrice weekly.

Suggested practical regimens for specific conditions are given below. These are guidelines only, the dosage should be titrated to the patient's response.

Conditions needing maintenance therapy

Rheumatoid arthritis: Initially a dose of 40 i.u. should be given daily. Review the dosage at intervals of three days and adjust according to the clinical response. The dosage should be increased or decreased bearing in mind that the ideal dosage is the minimum necessary to relieve symptoms.

Chronic asthma: Initially a dose of 40-80 i.u. should be given daily for a period of five days. Reduce by steps of 10 i.u. until symptoms are satisfactorily controlled. On remission of symptoms, treatment may be withdrawn completely. In some patients, however, continued therapy may be necessary.

Still's disease: 40 i.u. Acthar Gel daily for three days reducing to 20 i.u. on alternate days. Suppression of symptomatology without the appearance of 'cush-ingoid signs' is the aim of therapy.

The administration of ACTH to children should be confined to early morning (approximately 10 a.m.) to reduce the incidence of 'growth interference'.

Conditions requiring short - medium term therapy

Acute exacerbation of asthma: 200 i.u. Acthar Gel

Bayer UK Limited
Pharmaceutical Division
Burrell Road, Haywards Heath
West Sussex RH16 1TP



ADALAT* ▼

Presentation Orange, soft gelatin capsule containing a yellow viscous liquid. Each capsule contains 10 mg nifedipine.

Uses *Mode of action:* Adalat is a potent calcium antagonist. Its most important effect is to protect the heart against excessive oxygen utilisation during physical activity. There is a reduction in cardiac work and in myocardial oxygen demand. Adalat also causes peripheral vasodilatation and thus reduces peripheral resistance and heart work load. Adalat has no therapeutic antiarrhythmic effect. Since Adalat does not cause a rise in intraocular pressure, it can be used in patients with glaucoma.

Indications: For the treatment and prophylaxis of angina pectoris.

Dosage and administration For oral administration, the capsules should be taken with a little fluid during or after meals. The recommended dose is one 10 mg capsule three times daily. If necessary, up to two capsules three times daily may be taken.

Treatment may be continued indefinitely. If an immediate effect is required, the capsule should be bitten open and the liquid contents allowed to remain in the mouth.

Contra-indications, warnings, etc

Contra-indications: Must not be given to women capable of child-bearing.

Warnings and precautions: Adalat is not a beta-blocker and therefore gives no protection against the dangers of abrupt beta-blocker withdrawal; any such withdrawal should be by gradual reduction of the dose of beta-blocker, preferably over 8–10 days.

Adalat may be used in combination with beta-blocking drugs and other antihypertensive agents, but the possibility of an additive effect resulting in postural hypotension should be borne in mind. Adalat will not prevent possible rebound effects after cessation of antihypertensive therapy.

Adalat should be used with caution in patients whose cardiac reserve is poor.

Ischaemic pain has been reported in some patients, commonly within 30 minutes of the introduction of Adalat therapy. Patients experiencing this effect should discontinue Adalat.

The use of Adalat in diabetic patients may require adjustment of their control. There is no known drug incompatibility.

Side-effects: Adalat is well tolerated. Minor side-effects, usually associated with vasodilatation are mainly headache, flushing and lethargy. These are transient and invariably disappear with continued treatment.

Overdosage: Standard measures such as atropine and noradrenaline may be used for resultant bradycardia and hypotension. Intravenous calcium gluconate may be of benefit.

Pharmaceutical precautions The capsules should be protected from strong light and stored in the manufacturer's original container.

Legal category POM.

Package quantities Adalat is available in foil packs of 100 capsules.

Further information Nil.

Product licence number 0010/0021.

ALRHEUMAT*

Presentation Opaque 'off-white' hard gelatin capsules each containing 50 mg ketoprofen. Suppositories each containing 100 mg ketoprofen.

Uses Alrheumat is recommended for the management of the rheumatic diseases: rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, gout, other forms of non-infectious arthropathy; acute articular and peri-articular disorders—bursitis, tendinitis, synovitis, tenosynovitis, capsulitis of the shoulder; painful musculoskeletal conditions.

Dosage and administration Alrheumat is administered orally and should be taken with food. Dosage is usually 1 capsule (50 mg) three times daily. This dosage may be increased to 1 capsule four times daily or decreased to 1 capsule twice daily depending on the weight and clinical condition of the patient and the severity of the disease. As an alternative to oral therapy, one suppository should be inserted in the morning and before retiring. For the relief of night pain and morning stiffness, one suppository should be inserted before retiring. Combined oral and rectal therapy: one suppository should be inserted before retiring, supplemented during the day with Alrheumat capsules as needed, up to a maximum daily dosage of 200 mg ketoprofen. Paediatric usage has not been established.

Contra-indications, warnings, etc

Contra-indications: Ketoprofen should not be given to patients known to be sensitive to aspirin or to other non-steroidal anti-inflammatory agents which are prostaglandin inhibitors. In such patients, and in those with a history of bronchial asthma or allergic disease, severe broncho-spasm may be precipitated.

Ketoprofen should not be given to patients with active peptic ulceration.

Side-effects: Occasional gastro-intestinal disturbances occur and in some such cases a reduction in dosage has been helpful. In common with most other anti-inflammatory agents, there have been very rare reports of gastro-intestinal haemorrhage. Skin rashes have been rare.

Precautions: Patients with a history of peptic ulcer or chronic dyspepsia should be carefully monitored. Care should also be taken in patients with a history of impaired hepatic function. Alrheumat, in common

Immuno Ltd
 Arctic House, Rye Lane
 Dunton Green, Nr. Sevenoaks,
 Kent, TN14 5HB



HEPARIN-INJECT 5,000 BP 'IMMUNO'

Presentation Heparin-Inject BP is a sterile solution of 5,000 i.u. Heparin Sodium (mucous) dissolved in 0.3 ml Water for Injections BP. It is a clear liquid varying from colourless to straw coloured. Each pre-loaded syringe contains 2.7 mg of Sodium Chloride in 0.3 ml of injection.

Uses Prevention of thrombosis following surgery.

Dosage and administration Heparin-Inject 5,000 BP must be administered by the subcutaneous route preferably through the adipose tissue of the abdominal wall. The following dosage is recommended:

Pre-operative administration: 1 pre-loaded syringe containing Heparin-Inject 5,000 BP to be given two hours before surgery.

Post-operative administration: 1 pre-loaded syringe containing Heparin-Inject 5,000 BP to be given at intervals of 8-12 hours up to the 7th-12th day.

Contra-indications, warnings, etc Heparin should not be used in patients with the following conditions:

1. Heparin allergy.
2. Surgery carried out on the central nervous system or the eye.
3. Haemorrhagic diseases including haemophilia and thrombocytopenia and when linked with endocarditis.
4. Advanced stages of kidney, liver or pancreatic disease.
5. Post-operative seeping haemorrhage.

Precautions are necessary in patients with potential bleeding sites such as peptic ulcer, ulcerative colitis etc., also in pregnancy and in patients with persistent hypertension or cerebral thrombosis; also during simultaneous administration of Warfarin, Aspirin, other salicylates and medicaments having an impact on blood coagulation.

Experience indicates that Heparin can be used with very little risk in the prophylaxis of thrombosis. If, however, bleeding complications occur during or after an operation, the patient's thrombin time or partial thromboplastin time should be determined. If the results of these tests are within the normal range it is unlikely that heparinisation is the cause. It must, however, be borne in mind that on very rare occasions Heparin can cause thrombocytopenia and thus could be the cause of the haemorrhage. If neutralisation must be carried out, following injection of Heparin-Inject 5,000 Immuno BP, Protamine Sulphate Injection BP 10 mg in 1 ml must be given by slow (10 min.) intravenous injection. Ideally, the dose required should be accurately determined by titration. If there is insufficient time to titrate the dose, the following dosage scale is recommended:

Time interval following dose of 5000 i.u. of Heparin	Dose of Protamine Sulphate Injection 10 mg in 1 ml
Immediately after	5.0 ml
Half an hour after	2.5 ml
One hour after	1.25 ml

Pharmaceutical precautions It should be stored at a temperature not exceeding 25°C when it will have a shelf life of three years.

Legal category POM.

Package quantities Pre-loaded syringes containing 0.3 ml solution of 5,000 i.u. Heparin Sodium supplied in packs of 10 and 100 pre-loaded syringes.

Further information An increased tendency towards haemorrhage must be carefully avoided during the operation period and any error of dosage excluded. Heparin-Inject 5,000 BP is packed in a pre-loaded syringe which enables an accurate dose to be administered. The hazard of overdosage can therefore be avoided.

Product licence number 0215/0017.

HUMAN ALBUMIN FRACTION (SALINE) BP 4.3% 'IMMUNO' HUMAN PLASMA PROTEIN FRACTION BP 4.3% 'IMMUNO' (PPF)

Presentation Human Albumin Fraction (Saline) BP 4.3% Immuno is a clear amber liquid, presented as a solution for intravenous administration to human beings. It is prepared from the plasma of suitable human donors* whose transaminase levels are constantly checked and whose donations are shown by RIA to be free from HBsAg.

Human Albumin Fraction (Saline) BP 4.3% Immuno contains albumin and heat stable alpha - and beta - globulins prepared from human plasma. As stabilisers sodium caprylate and sodium acetyltryptophanate have been added, both at a concentration of 0.004M.

* Suitable human donors as described in the British Pharmacopoeia Addendum 1978 under Dried Antihæmophilic fraction.

Uses Human Albumin Fraction (Saline) BP 4.3% Immuno is indicated for volume replacement in hypovolaemic shock (e.g. following crush injury, severe trauma, surgery, burns or abdominal emergency) and for use whenever a predominant loss of plasma fluid has occurred.

Dosage and administration Adult dosage of Human Albumin Fraction (Saline) BP 4.3% Immuno for hypovolaemic shock is in the range of 250-500 ml. A flow rate of up to 16 ml/min (1 litre/hr) has been well tolerated in adults. The rate of infusion, which can be increased in emergency treatment, depends on response. In hypoproteinaemia the usual dosage range is 1,000-1,600 ml daily (equivalent to 43-70 g plasma protein), but larger amounts can be given in severe hypoproteinaemia with continuing loss. The flow rate should not exceed 5-8 ml/min.

Dosage for infants and young children in whom Human Albumin Fraction (Saline) BP 4.3% Immuno is indicated for shock due to dehydration or infection, should be in the range of 20-30 ml/kg body weight, infused at a rate of 10 ml/min. The infusion rate should be adjusted in accordance with the clinical

Package quantities Human Albumin 20% BP Immuno is supplied in rubber capped vials of 10 ml, 50 ml and 100 ml.

Further information Human Albumin 20% BP Immuno is processed in such a way that removal of all antibodies, particularly isoagglutinins, is achieved. It can therefore be given to patients regardless of their blood group or rhesus factor. It will not interfere with subsequent blood investigations.

Product licence number 0215/0009.

PROTHROMPLEX*

Presentation Prothromplex is a white, amorphous freeze-dried powder or friable solid without any characteristic odour. It is packed in rubber-capped vials containing 200 units or 500 units each of Factors II, IX and X.

It is prepared from the plasma of suitable human donors* whose transaminase levels are constantly checked and whose donations are shown by RIA to be free from HB_sAg. Pooled plasma and the final product are also tested by RIA for freedom from HB_sAg. Prothromplex is also tested to discount the likelihood of causing disseminated intravascular coagulation.

* Suitable human donors as described by the British Pharmacopoeia Addendum 1978 under Dried Antihæmophilic fraction.

Uses Treatment of cases of Factor IX deficiency (Haemophilia B).

By administering an appropriate dose of Prothromplex, it is possible to achieve a prompt and sufficient rise of Factor IX in the patient's plasma.

The effectiveness of treatment can be checked by simple laboratory tests. The activity of Factor IX is assayed through determination of the Partial Thromboplastin Time (PTT), however the most reliable results are obtained by quantitative activity assays of Factor IX.

Dosage and administration Immediately before use Prothromplex must be dissolved in 10 ml of the solvent provided.

After sterilising the cap of the solvent bottle remove 10 ml using the disposable syringe and one of the needles provided. Next sterilise the cap of the Prothromplex bottle and introduce the solvent using the second disposable needle. Reconstitute by gently shaking to and fro, thus avoiding frothing. Withdraw the reconstituted Prothromplex, then remove the syringe from the needle and attach the third disposable needle.

Prothromplex is now ready for slow intravenous injection taking about 10 minutes.

Only general directions can be given for the dosage of Prothromplex. It is dependent upon the severity of the coagulation defect and the degree of the traumatic and hæmorrhagic tissue damage. The suggested dosage for the treatment of Factor IX deficiency is given in the guide below.

Dosage guide for the treatment of severe and semi-severe cases of Factor IX deficiency: Formula for the calculation of the necessary quantity of Factor IX:

One unit of Factor IX/kg body weight = 1% increase of Factor IX in the patient's plasma.

It is suggested that a high initial dosage be chosen to ensure a rapid and sufficient increase of Factor IX thus achieving a reliable cessation of bleeding. Here, as well as with the subsequent maintenance therapy, the initial short half-life of the coagulation factors has to be considered. Depending on the *in vivo* half-life of Factor IX, which is approx. 12–30 hours, a successful result will be achieved by repeated administration of Prothromplex at intervals of 6–12 hours. To assure absolute control of treatment, determination of the PTT should be made and, where possible, quantitative assays of Factor IX activity. Treatment should be maintained up to the resorption of the tissue hæmor-

Prothromplex Dosage Table

Clinical manifestation	Therapeutically wanted minimum Factor IX level	Initial dose in units Factor IX per kg body weight	Maintenance dose at intervals of 6–12 (24) hours in units Factor IX per kg body weight
Surface bleedings of the skin and mucosae Superficial or deep hæmatoma Hæmarthroses Slight bleedings following injuries Uncomplicated dental extractions Severe muscle hæmatoma	5–10%	15 U	7–15 U
Moderate bleedings following injuries Gastric and intestinal hæmorrhages Bone fractures Cerebral bleedings Hæmatoma Complicated dental extractions Minor surgery	15–30%	20–30 U	15–30 U
Major surgery	more than 50%	75 U	50–75 U

rhage or until the wounds have healed completely, thus ensuring a complication-free post-operative course. The special advantage of Prothromplex lies in the fact that by application of small volumes of fluid and a slight amount of protein a high concentration of circulating coagulation Factor IX is achieved. The danger of volume or protein overloading of the patient is avoided even with the administration of high doses.

Contra-indications, warnings, etc With patients suffering from disseminated intravascular coagulation, (DIC), Prothromplex should not be given unless consumption of the coagulation factors has been previously interrupted by Heparin.

Side effects are rarely observed during treatment with Prothromplex though the following reactions may occur:

1. **Allergic reactions:** All forms of allergic reactions from mild and temporary urticarial rashes to severe anaphylactic shock are possible when human plasma derivatives are administered. If these occur, treatment with Prothromplex must be interrupted at once. Allergic reactions should be controlled with antihistamines and glucocorticoids and routine shock treatment given for anaphylactic shock. Careful and frequent recording of pulse rate and blood pressure is essential. If the pulse rate increases and/or the blood pressure falls a transfusion of 5% Dextrose should be started.

2. Despite the precautions taken in the checking of donors, donations and the final product, the transmission of hepatitis cannot be entirely excluded following the administration of coagulation factors. This should be taken into account before using Prothromplex to control haemorrhage in non life-threatening situations in liver disease patients and those undergoing anticoagulant therapy.

3. During every type of therapy involving blood or coagulation factor concentrates, the occurrence of a circulating coagulation factor inhibitor is a possibility. The time at which such an inhibitor is produced cannot be predicted and depends neither on the amount of the plasma preparation administered nor in the frequency of administration.

As far as is known neither corticosteroids nor immunosuppressive agents significantly influence the formation of inhibitors.

Pharmaceutical precautions Prothromplex has a shelf life of one and a half years when stored between +2°C and +6°C it should be protected from the light.

Legal category POM.

Package quantities 200 units or 500 units of Factors II, IX and X in each container.

1 rubber-capped vial containing lyophilised Prothromplex.

1 rubber-capped vial containing 10 ml Water for Injections BP.

1 10 ml disposable syringe.

3 disposable needles.

Further information Prothromplex can be stored in a domestic refrigerator, and can therefore be kept available for home treatment.

Prothromplex can be given in small volume injections, and is therefore suitable for home treatment.

Prothromplex can be moved in insulated containers to a refrigerator at some other location, giving a patient a greater degree of mobility.

Product licence numbers

200 units 0215/006

500 units 0215/007

**KRYOBULIN* DRIED HUMAN
ANTI-HAEMOPHILIC FRACTION BP**

Presentation Dried Human Antihaemophilic Fraction is a white to yellowish amorphous powder or a friable solid without any characteristic odour.

It is prepared from the plasma of suitable human donors* whose transaminase levels are constantly checked and whose donations are shown by RIA to be free from HB_sA_g. Pooled plasma and the final product are also tested for freedom from HB_sA_g.

It is packed in vials each containing approximately 250, 500 or 1,000 International Units of Factor VIII. Separate vials of solvent are also provided, these being Water for Injections BP.

One International Unit is the amount of Factor VIII activity contained in 12.745 mg of the 2nd International Standard for blood coagulation Factor VIII Human. It is approximately equivalent to the Factor VIII activity in 1 ml of average normal plasma.

* Suitable human donors as described by the British Pharmacopoeia Addendum 1978 under Dried Antihaemophilic fraction.

Uses Kryobulin corrects Factor VIII deficiency, and is used in the treatment of bleeding due to such deficiency in:

Haemophilia A

von Willebrand's disease

Haemophilia complicated by Factor VIII inhibitors

Dosage and administration Frequent tests of the patient's plasma level of Factor VIII must be made to allow correction of deficiency by Kryobulin administration, but for guidance an estimation of the required dosage can be made by the following calculation:

To achieve an increase of Factor VIII concentration of 1% it is necessary to administer 1 i.u. of Kryobulin per kg body weight, both for adults and children.

Initial treatment requires doses to be given at shorter intervals than in maintenance therapy, to provide an initial high level of activity and to replenish the extravascular compartment.

Bleeding from skin, nose and oral mucous membrane: Initial dose should be 10 i.u./kg at intervals of 6–12 hours.

Haemarthrosis: Initial dose should be approximately 10 i.u./kg and the maintenance dose 5–10 i.u. per kg at intervals of 6–12 hours. Combined with immobilisation of the affected joint for several days, the treatment should be sufficient to restore function.

Bruising: In most cases a single dose of 10 i.u./kg is sufficient. For widespread bruising, repeated administration of 5–10 i.u./kg at intervals of 6–12 hours may be required.

Heavy bleeding into muscles: Immediate treatment is required to prevent permanent deformity and loss of function, and initial immobilisation of the affected area is important. An initial dose of 15–20 i.u./kg should be given, the maintenance dose to be 10 i.u./kg at intervals of six hours from the first to the second day, and at intervals of 12 hours from the third to the fifth day.

Haematuria: Initial dose should be 15–20 i.u./kg, the maintenance dose to be 10 i.u./kg at intervals of 12 hours.

Major surgery on haemophilic patients: The initial dose should be at least 25–50 i.u./kg and the maintenance dose 20–40 i.u./kg at intervals of four hours from the first to the fourth day, of eight hours from the fifth to the eighth day, and of 12 hours until all wounds are healed.

The effect of treatment must be checked daily. Factor VIII activity should not be allowed to fall below 50%

of normal 100% average values. It is important that treatment be continued until all wounds have healed completely, as the risk of haemorrhage persists till then.

In addition to monitoring Factor VIII activity, tests for the development of Factor VIII inhibitors should also be made.

Dental extractions: The required dosage depends on the number and type of teeth to be extracted, and on the severity of the haemophilia. If *one or two* teeth are to be extracted from a patient with severe haemophilia an initial dose of 10–20 i.u./kg should be given. Maintenance treatment with this dosage at intervals of six hours from the first to the third day, and eight hours from the fourth to the eighth day after extraction, should be given. If *more than two teeth are to be extracted from patients with severe haemophilia* a minimum initial dose of 20–30 i.u./kg should be given, and a maintenance dose 10–20 i.u./kg at intervals of six hours from the first to the third day, and of eight hours for 12 more days. The plasma concentration of Factor VIII should not be allowed to fall below 10% of the normal 100% average value.

Factor VIII assay should be used to monitor the effectiveness of treatment, as partial thromboplastin time gives a less accurate value when large quantities of Kryobulin are being used.

Solutions of Kryobulin must be administered intravenously, at a rate not exceeding 10 ml in three minutes.

Contra-indications, warnings, etc Although the danger of volume overload is small with Kryobulin during major surgery, monitoring of the patient's central venous pressure and blood pressure, and serial chest X-rays, may be advisable.

In disseminated intravascular coagulation associated with low Factor VIII levels Heparin should be given to interrupt intravascular coagulation before therapy with Kryobulin is started.

A low incidence of adverse reactions is experienced with Kryobulin, but the following may occur:

1. **Allergic reactions:** All forms of allergic reaction from mild and transient urticaria to severe anaphylactic shock are possible when human plasma derivatives are administered. If such reactions occur, treatment with Kryobulin must be interrupted at once. Allergic reactions should be controlled with antihistamines and corticosteroids and routine treatment given for anaphylactic shock. Monitoring of pulse rate and blood pressure is essential. If the pulse rate increases and/or blood pressure falls transfusion of 5% Dextrose should be started.

2. **Hepatitis:** Despite the precautions taken in the selection and testing of donors and donations, the risk of transmitting hepatitis cannot be entirely excluded.

3. **Factor VIII Inhibitors:** The appearance of a circulating Factor VIII inhibitor is possible. Its appearance cannot be predicted as it does not relate to the amount of Kryobulin administered, nor to the frequency of administration. As far as is known neither corticosteroids nor immunosuppressive agents significantly influence the formation of inhibitors.

Pharmaceutical precautions Kryobulin must be stored between 2° and 6°C, and protected from light. It then has a shelf-life of two years. When stored between +20°C and +30°C it has a life of six months.

Legal category POM.

Package quantities **Kryobulin Home Treatment Pack:** Each pack contains 1 rubber-capped vial containing 250 or 500 i.u. Dried Human Antihaemophilic Fraction BP.

1 rubber-capped vial containing Water for Injections BP

This pack also contains a syringe I/V needles, winged adaptor needle and filter needle.

Kryobulin Hospital Pack: Each pack contains 1 rubber-capped vial containing 1,000 i.u. Dried Human Antihaemophilic Fraction BP.

1 rubber-capped vial containing Water for Injections BP.

The pack also contains a filter needle.

All three presentations of Kryobulin are available in red packs where the product is obtained from European plasma and blue packs where the product is obtained from American plasma.

Further information Kryobulin is especially suitable for Home Treatment. Packs contain all requirements and can be stored in a domestic refrigerator for two years and for up to six months at room temperature not exceeding 30°C.

Product licence number 0215/0003.

* Trade Mark