British Pharmacopœia 1988

Addendum 1992

British Pharmacopœia 1988 Addendum 1992

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Notices

The General Notices and Appendices included in the British Pharmacopœia 1988 apply to all matter contained in this Addendum unless the contrary is specifically stated.

The Addendum has the same authority as the British Pharmacopœia 1988. General Notices, Monographs and Appendices of the British Pharmacopœia 1988 that are amended by this Addendum supersede, in their amended forms, the original general notices, monographs and appendices.

Monographs of the European Pharmacopœia are distinguished by a five-pointed star against the title.

Patents

In this Addendum certain drugs and preparations have been included notwithstanding the existence of actual or pending patent rights. In so far as such substances are protected by Letters Patent their inclusion in this Addendum neither conveys, nor implies, licence to manufacture.

Effective Dates

Much of the material in this volume enters into force on 1 July 1992 but certain material that has been published earlier by Gazette Notices became effective on the date stated at the foot of the relevant entry.

Preface

This Addendum adds new material to and amends the British Pharmacopœia 1988. It is published by Her Majesty's Stationery Office for the Health Ministers on the recommendation of the Medicines Commission in accordance with sections 99(6) and 102 of the Medicines Act 1968.

The Medicines Commission expresses its gratitude to all who have helped to prepare this Addendum.

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* Term of office ends 31 December 1993.
† Term of office ends 31 December 1991.

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Introduction

In general, the effective date of this Addendum is 1 July 1992 but a number of items, particularly edited versions of European Pharmacopœia monographs, have already been, or will be, brought into effect at some other date. Where the effective date is not 1 July 1992, this is noted at the foot of the entry by means of an italicised statement of the month and the year. Where no such statement appears it is to be understood that the effective date is that of the Addendum as a whole. With the bringing into effect of this Addendum the British Pharmacopœia 1988 will comprise Volumes I and II and the Addenda 1989, 1990, 1991 and 1992. It should be noted that material in Amendments No 5 to the British Pharmacopœia 1988 has been incorporated into this Addendum.

Some Additions

Monographs introduced to the Pharmacopœia for the first time include the antiviral Acyclovir, the anti-emetic Buclizine Hydrochloride, Isometheptene Mucate which is used in the treatment of migraine, the hypnotic Loprazolam and Loprazolam Tablets, the beta-adrenoceptor antagonist Metoprolol Tartrate, the pharmaceutical aid Stearic Acid and the combination products Co-amilozide Oral Solution and Co-amilozide Tablets.

It is known that groups of experts of the European Pharmacopœia Commission are elaborating monographs for Acyclovir and Metoprolol Tartrate but it was decided not to delay publication of the monographs that had been prepared by the relevant committees of the British Pharmacopœia Commission. In parallel with the completion of these British Pharmacopœia monographs, the British experts and the Commission's staff are working with European colleagues to produce the European Pharmacopœia monographs that will, in due course, replace those published in this Addendum.

The monograph for Codeine Phosphate Oral Solution replaces the monograph for Codeine Phosphate Syrup in the British Pharmaceutical Codex 1973. This analgesic preparation contains 25 mg of Codeine Phosphate in 5 ml and it is not to be confused with the antitussive preparation Codeine Linctus which contains 15 mg of Codeine Phosphate in 5 ml.

Following the inclusion of a general monograph for Pressurised Inhalations, a monograph for Salbutamol Pressurised Inhalation has now been introduced.

Revision

The general revision of the Pharmacopœia continues. For example, tests for uniformity of content have been added to the monographs for Benzhexol Tablets and Calciferol Tablets.

Dissolution tests have been added to the monographs for Cortisone Tablets, Griseofulvin Tablets and Spironolactone Tablets in continuation of the Commission's policy to add requirements for dissolution to appropriate monographs for capsules and tablets on a selective basis. Because of the low solubility of the active ingredients in aqueous media, dissolution media containing sodium dodecyl sulphate or a relatively high concentration of isopropyl alcohol have been specified in these tests.

A dissolution technqiue based on a flow-through cell has been published in fascicule 15 of the second edition of the European Pharmacopœia and the text is added to Appendix XII D by means of this Addendum. It may be that use of such a technique will in the future reduce the need to place reliance on the use of modified dissolution media for materials with a low solubility.

European Pharmacopœia

This Addendum contains edited versions of material that has been published in fascicule 15 of the second edition of the European Pharmacopœia. With certain exceptions, monographs in that fascicule became effective on 1 Janauary 1992.

'Transparency'

Following requests by a number of users of the Pharmacopœia, the Commission has decided to add to appropriate new monographs for medicinal substances a statement giving the identities of impurities known to be limited by the specifications. It is to be emphasised that other, unnamed impurities may also be limited and the Commission would welcome information that would allow the lists to be extended in the future.

Use of Animals

Reference was made in the Introduction to the British Pharmacopœia 1988 to the deletion of the test for abnormal toxicity from a number of monographs. This came about as the result of a systematic review of all general safety tests. More recently the Commission has given further thought to the small number of monographs for biological materials and antibiotics in which the test has been retained. After careful consideration, the Commission has agreed that the test should no longer be included in the monographs for these materials. It is the opinion of the Commission that, in the current state of knowledge and widespread use of good pharmaceutical manufacturing practice, the test for abnormal toxicity contributes nothing to the monographs in question. With respect to a grossly contaminated product the Commission believes that the 'rational considerations' statement within the General Notice on Official Standards will provide an adquate basis for judging compliance. The test for abnormal toxicity has been deleted, therefore, from all monographs for biological materials, antibiotics and their preparations that are the direct responsibility of the British Pharmacopœia Commission. This action has been brought to the attention of the European Pharmacopœia Commission with a recommendation that a similar modification should be made to the relevant monographs of the European Pharmacopœia.

The European Pharmacopœia Commission also is pursuing a policy of reducing reliance on *in vivo* test methods wherever this is deemed to be compatible with providing satisfactory pharmacopœial standards. This is demonstrated by the new European Pharmacopœia monograph for Desmopressin which uses a liquid chromatographic method of assay. This is the final step in a phased transition from biological assay to chemical assay. A liquid chromatographic determination for the specific peptide, desmopressin, was included alongside the biological assay in the British Pharmacopœia 1988 monograph for Desmopressin and reliance was placed entirely on the chromatographic method for the assay of the dosage forms Desmopressin Injection and Desmopressin Intranasal Solution. This stepwise approach illustrates the caution that is an essential feature of pharmacopœial developments in this context. When a biological assay is currently retained as the pharmacopœial method, this

is the method to be used in case of doubt or dispute. It is emphasised, however, that this does not prevent a manufacturer from routinely using an alternative method, subject of course to the agreement of the appropriate licensing authority.

Index

The numbering of the pages in this addendum is consecutive with that of Volumes I and II of the British Pharmacopœia 1988 and the Addenda 1989, 1990 and 1991. The index, which is cumulative, contains references to all material published in the two main volumes and the four addenda.

Acknowledgements

The British Pharmacopœia Commission records its continued indebtedness to the members of its advisory committees and consultative groups. Without their dedicated enthusiasm and assistance its objectives could not be achieved.

Additions

The following monographs are added to the British Pharmacopœia 1988 by means of this Addendum.

Medicinal and Pharmaceutical Substances

Acyclovir
Buclizine Hydrochloride
Isometheptene Mucate
Loprazolam Mesylate
Metoprolol Tartrate
Stearic Acid

Formulated Preparations

EYE DROPS
Adrenaline Eye Drops
Betamethasone Eye Drops

EYE LOTIONS
Eye Lotions

IRRIGATION SOLUTIONS
Chlorhexidine Irrigation Solution
Sodium Citrate Irrigation Solution

ORAL LIQUIDS
Co-amilozide Oral Solution
Codeine Phosphate Oral Solution
Dihydrocodeine Oral Solution
Ferrous Fumarate Oral Suspension
Temazepam Oral Solution

PARENTERAL PREPARATIONS
Fortified Benethamine Penicillin Injection
Lorazepam Injection
Vitamins B and C Injection

PRESSURISED INHALATIONS
Salbutamol Pressurised Inhalation

SUPPOSITORIES
Morphine Suppositories

TABLETS
Co-amilozide Tablets
Loprazolam Tablets

Amendments

The following monographs of the British Pharmacopœia 1988 are amended by means of this Addendum.

Medicinal and Pharmaceutical Substances

Adrenaline
Benethamine Penicillin
Betamethasone Sodium Phosphate
Betamethasone Valerate
Calamine
Calcitonin (Pork)
Calcium Hydroxide
Calcium Sodium Lactate
Carbomer
Chlormethiazole
Chlormethiazole Edisylate
Clotrimazole
Clove Oil
Coriander Oil
Cyclopenthiazide
Cycloserine
Daunorubicin Hydrochloride
Dihydrocodeine Tartrate
Ethyl Hydroxybenzoate
Fenoprofen Calcium
Ferrous Fumarate
Fludrocortisone Acetate
Flurazepam Monohydrochloride
Hard Paraffin
Hydrotalcite
Labetalol Hydrochloride
Liquefied Phenol
Lorazepam
Mefenamic Acid
Metformin Hydrochloride
Mexiletine Hydrochloride
Mianserin Hydrochloride
Morphine Sulphate
Nicoumalone