DISCLAIMER

Every effort has been made to ensure the accuracy of this text, and that the best information available has been used. However, palliativedrugs.com Ltd neither represents nor guarantees that the practices described herein will, if followed, ensure safe and effective patient care. The recommendations contained in this book reflect the editors’ judgment regarding the state of general knowledge and practice in the field as of the date of publication. Recommendations such as those contained in this book can never be all-inclusive, and therefore will not be appropriate in all and every circumstance. Those who use this book should make their own determinations regarding specific safe and appropriate patient-care practices, taking into account the personnel, equipment, and practices available at the hospital or other facility at which they are located. Neither palliativedrugs.com Ltd nor the editors can be held responsible for any liability incurred as a consequence of the use or application of any of the contents of this book. Mention of specific product brands does not imply endorsement. As always, clinicians are advised to make themselves familiar with the manufacturer’s recommendations and precautions before prescribing what is, for them, a new drug.
EDITORIAL STAFF

Editors-in-Chief
Robert Twycross DM Oxon, FRCP London
Emeritus Clinical Reader in Palliative Medicine, Oxford University

Andrew Wilcock DM Nottm, FRCP London
Macmillan Clinical Reader in Palliative Medicine and Medical Oncology, Nottingham University
Consultant Physician, Hayward House, Nottingham University Hospitals NHS Trust, City Campus

Senior Editor
Julie Mortimer BPharm, MRPharmS
Malcolm Mortimer Media, Nottingham

Assistant Editors
Sarah Charlesworth BPharm, MRPharmS
Specialist Pharmacist, Palliative Care Information and Website Management, Hayward House, Nottingham University Hospitals NHS Trust, City Campus

Paul Howard BMedSci BMBS Nottm, MRCP London
Consultant in Palliative Medicine, Duchess of Kent House, Berkshire West Primary Care Trust

American editors
Joshua Cox PharmD, BCPS
Pain Management Consultant, Clinical Pharmacy Specialist Palliative Care, Good Samaritan Hospital, Dayton, Ohio
Clinical Pharmacy Specialist Palliative Care, ProCare HospiceCare, Steubenville, Ohio

Solomon Liao MD
Associate Professor of Medicine, Director of Palliative Care, University of California, Irvine, California
Director at Large, Board of Directors, American Academy of Hospice and Palliative Medicine

Mary Mihalyo BS, PharmD, RPh
Assistant Professor Clinical Pharmacy Practice, Duquesne University, Mylan School of Pharmacy, Pittsburgh, Pennsylvania
Founder and Palliative Care Consultant Pharmacist, Palliative Therapeutics, LLC, Steubenville, Ohio
Executive Vice President, ProCare HospiceCare, Steubenville, Ohio
Editorial Advisory Panel

Connie Beehler MS, MD
Associate Clinical Professor, Albany Medical College, Albany NY

Ann Berger MSN, MD
Chief Pain and Palliative Care, National Institutes of Health, Clinical Research Center, Bethesda MD

J Andrew Billings MD
Palliative Care Service, Massachusetts General Hospital, Boston MA

Susan Dale Block MD
Chief, Division of Psychosocial Oncology and Palliative Care, Dana-Farber Cancer Institute and Brigham and Women's Hospital. Co-Director, Harvard Medical School Center for Palliative Care. Professor of Psychiatry and Medicine, Harvard Medical School, Boston MA

Eduardo Bruera MD
Professor & Chair, Department of Palliative Care & Rehabilitation Medicine, MD Anderson Cancer Center, Houston TX

Ira Byock MD
Professor of Anesthesiology and Community & Family Medicine, Dartmouth Medical School. Director of Palliative Medicine, Dartmouth-Hitchcock Medical Center, Lebanon NH

Margaret Campbell PhD, RN, FAAN
Palliative Care Nurse Practitioner, Detroit Medical Center. Assistant Professor – Research, Center for Health Research, Wayne State University. Associate Director, Center to Advance Palliative-Care Excellence, Wayne State University, Detroit MI

James FCleary MD, FRACP, FAChPM
Associate Professor of Medicine (Medical Oncology), School of Medicine and Public Health, University of Wisconsin. Director, Palliative Care Service, University of Wisconsin Hospital and Clinics. Program Leader, Cancer Control Program, UW Paul P Carbone Comprehensive Cancer Center, Madison WI

Eardie Curry PharmD, BCOP, MBA
Director of Pharmacy, Seton Brackenridge Hospital, Austin TX

Constance Dahlin Adult NP, APRN, BC, ACHPN
Clinical Director, Palliative Care Service, Massachusetts General Hospital, Boston MA

Mellar Davis MD
Director of Research, Harry R Horvitz Center for Palliative Medicine, Taussig Cancer Center, Cleveland Clinic, Cleveland OH

Linda L Emanuel MD, PhD
Buehler Professor of Medicine. Director, Buehler Center on Aging, Health & Society, Feinberg School of Medicine. Adjunct Professor, Kellogg School of Management, Northwestern University, Chicago IL. Principal, The Education in Palliative and End-of-life Care (EPEC) Project. Principal, The Patient Safety Education Project (PSEP)

Betty Ferrell RN, PhD, FAAN
Research Scientist and Professor, City of Hope Medical Center, Duarte CA

Kathy Foley MD
Professor of Neurology, Neuroscience & Clinical Pharmacology, Memorial Sloan-Kettering Cancer Center, Weill Medical College of Cornell University, New York NY

Mike Frederich MD
Associate Professor, Department of Family Medicine, West Virginia University School of Medicine (Eastern Division), Martinsburg VA
Phyllis Grauer PharmD, RPh, CGP
Vice-President Clinical Services, Palliative Care Consulting Group, a division of HospiScript Services LLC, Dublin OH

Terry Gutgsell MD
Director of Education, Harry R Horvitz Center for Palliative Medicine, Taussig Cancer Center, Cleveland Clinic, Cleveland OH

Marcia Levetown MD
Principal, HealthCare Communication Associates, Houston TX

Arthur G Lipman PharmD, FASHP
Editor, Journal of Pain & Palliative Care Pharmacotherapy. University Professor, Department of Pharmacotherapy, College of Pharmacy. Adjunct Professor, Department of Anesthesiology, School of Medicine. Director of Clinical Pharmacology, Pain Management Center, University Health Care. University of Utah Health Sciences Center, Salt Lake City UT

Diane E Meier MD
Director, Center to Advance Palliative Care. Director, Hertzberg Palliative Care Institute. Professor, Departments of Geriatrics and Medicine. Gaisman Professor of Medical Ethics, Department of Geriatrics. Mount Sinai School of Medicine, New York NY

R Sean Morrison MD
Director, National Palliative Care Research Center, Hermann Merkin Professor of Palliative Care, Professor of Geriatrics and Medicine, Vice-Chair for Research, Brookdale Department of Geriatrics, Mount Sinai School of Medicine, New York NY

J Cameron Muir MD, FAAHPPM
Vice President, Medical Services, Capital Hospice, Falls Church, Virginia. Immediate Past-President, American Academy of Hospice and Palliative Medicine. Clinical Assistant and Professor of Medicine, Virginia Commonwealth University VA. Clinical Scholar, Georgetown Center for Bioethics, Washington DC

Don Piper MD
Medical Director, Hospice and Palliative Care, HealthEast Care System, St Paul MN

Russell Portenoy MD
Chairman and Gerald J and Dorothy R Friedman Chair in Pain Medicine and Palliative Care, Department of Pain Medicine and Palliative Care, Beth Israel Medical Center, New York NY

Maryjo Prince-Paul PhD
Master of Science in Nursing. Assistant Professor, Frances Payne Bolton School of Nursing, Case Western Reserve University, Cleveland OH

John Shuster MD
Director of Chronic Pain Clinic, Cooper Green Mercy Hospital, Birmingham AL

Martha Twaddle MD, FACP, FAAHPPM
Chief Medical Officer, Midwest Palliative and Hospice Care Center, Glenview IL

Charles F von Gunten MD, PhD
Editor-in-Chief Journal of Palliative Medicine. Provost and Vice President, Institute for Palliative Medicine, San Diego Hospice. Professor of Medicine, UCSD School of Medicine, San Diego CA

David Weissman MD
Director of Palliative Care Center. Professor, Medical College of Wisconsin, Milwaukee WI

www.palliativedrugs.com
## CONTENTS

- Preface xi
- Acknowledgements xii
- About www.palliativedrugs.com xiii
- Summary of main changes in 2nd edition of HPCFUSA xiv
- Getting the most out of HPCFUSA xv
- Using approved drugs for off-label purposes xix
- Pharmaco-economics in the USA xxiii
- Drug names xxvi
- List of abbreviations xxviii

### Part 1 Drug Monographs

1. **Gastro-intestinal system**
   - Antacids 1
   - Antimuscarinics (anticholinergics) 3
   - Prokinetics 11
   - H₂-receptor antagonists 13
   - Misoprostol 16
   - Proton pump inhibitors 17
   - Loperamide 21
   - Laxatives 22
   - Products for hemorrhoids 34
   - Pancreatin 34

2. **Cardiovascular system**
   - Cardiac failure 37
   - Furosemide 37
   - Spironolactone 40
   - Systemic local anesthetics 43
   - *Clonidine 49
   - Nitroglycerin (glyceryl trinitrate) 52
   - Nifedipine 55
   - Low molecular weight heparin (LMWH) 56
   - Antifibrinolytic drugs 73

3. **Respiratory system**
   - Bronchodilators 77
<table>
<thead>
<tr>
<th>CONTENTS</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhaled corticosteroids</td>
<td>93</td>
</tr>
<tr>
<td>Oxygen</td>
<td>96</td>
</tr>
<tr>
<td>Drugs for cough</td>
<td>104</td>
</tr>
<tr>
<td><strong>4 Central nervous system</strong></td>
<td>111</td>
</tr>
<tr>
<td>Psychotropics</td>
<td>111</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>112</td>
</tr>
<tr>
<td>Chloral hydrate</td>
<td>124</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>127</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>148</td>
</tr>
<tr>
<td>Psychostimulants</td>
<td>177</td>
</tr>
<tr>
<td>Cannabinoids</td>
<td>180</td>
</tr>
<tr>
<td>Anti-emetics</td>
<td>185</td>
</tr>
<tr>
<td>Scopolamine (hyoscine) hydrobromide</td>
<td>199</td>
</tr>
<tr>
<td>Anti-epileptics</td>
<td>201</td>
</tr>
<tr>
<td>Orphenadrine</td>
<td>216</td>
</tr>
<tr>
<td><strong>5 Analgesics</strong></td>
<td>219</td>
</tr>
<tr>
<td>Principles of use of analgesics</td>
<td>219</td>
</tr>
<tr>
<td>Adjuvant analgesics</td>
<td>222</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>228</td>
</tr>
<tr>
<td>Non-steroidal anti-inflammatory drugs (NSAIDs)</td>
<td>231</td>
</tr>
<tr>
<td>Weak opioids</td>
<td>262</td>
</tr>
<tr>
<td>Strong opioids</td>
<td>275</td>
</tr>
<tr>
<td>Opioid antagonists</td>
<td>328</td>
</tr>
<tr>
<td><strong>6 Infections</strong></td>
<td>341</td>
</tr>
<tr>
<td>Antibacterials in palliative care</td>
<td>341</td>
</tr>
<tr>
<td>Oropharyngeal candidosis</td>
<td>343</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>347</td>
</tr>
<tr>
<td>Urinary tract infections</td>
<td>349</td>
</tr>
<tr>
<td>Acute inflammatory episodes in a lymphedematous limb</td>
<td>350</td>
</tr>
<tr>
<td>Guidelines: AIEs in lymphedema</td>
<td>354</td>
</tr>
<tr>
<td>Ascending cholangitis</td>
<td>356</td>
</tr>
<tr>
<td><strong>Clostridium difficile</strong> diarrhea</td>
<td>357</td>
</tr>
<tr>
<td><em>Helicobacter pylori</em> gastritis</td>
<td>359</td>
</tr>
<tr>
<td><strong>7 Endocrine system and immunomodulation</strong></td>
<td>363</td>
</tr>
<tr>
<td>Bisphosphonates</td>
<td>363</td>
</tr>
<tr>
<td>Systemic corticosteroids</td>
<td>373</td>
</tr>
<tr>
<td>Demeclocycline</td>
<td>379</td>
</tr>
<tr>
<td>Desmopressin</td>
<td>381</td>
</tr>
<tr>
<td>Drugs for diabetes mellitus</td>
<td>382</td>
</tr>
<tr>
<td>Chapter</td>
<td>Title</td>
</tr>
<tr>
<td>---------</td>
<td>------------------------------------------------------</td>
</tr>
<tr>
<td>17</td>
<td>Analgesic drugs and fitness to drive</td>
</tr>
<tr>
<td>18</td>
<td>Continuous subcutaneous infusions</td>
</tr>
<tr>
<td>19</td>
<td>Spinal analgesia</td>
</tr>
<tr>
<td>20</td>
<td>Administering drugs via enteral feeding tubes</td>
</tr>
<tr>
<td>21</td>
<td>Nebulized drugs</td>
</tr>
<tr>
<td>22</td>
<td>Prolongation of the QT interval in palliative care</td>
</tr>
<tr>
<td>23</td>
<td>Cytochrome P450</td>
</tr>
<tr>
<td>24</td>
<td>Drug-induced movement disorders</td>
</tr>
<tr>
<td>25</td>
<td>Anaphylaxis</td>
</tr>
</tbody>
</table>

**Appendices**

- A1   Synopsis of pharmacokinetic data 553
- A2   The use of emergency kits in hospice care 567
- A3   Taking controlled substances to other countries 569
- A4   Medicare and Medicaid programs: Hospice Conditions of Participation 2008 573
- A5   Compatibility charts 575

**Drug Index** 587

**Subject Index** 597
PREFACE

Trans-Atlantic co-operation in relation to hospice and palliative care began some 40 years ago. Subsequently, in the early 1970s, as a result of the friendship between Florence Wald, Dean of the Nursing School at Yale, and Cicely Saunders, founder of St Christopher’s Hospice in London, Sylvia Lack was invited from the UK to become the Medical Director of the newly established Connecticut Hospice. Much water has flowed under the bridge since then, leading to the recognition in the USA in 2006 of Palliative Medicine as a medical sub-specialty.

HPCFUSA is a more recent example of Trans-Atlantic collaboration in this field. HPCFUSA grew out of the British Palliative Care Formulary (PCF). In addition to its obvious benefit to prescribers and other clinicians working wholly or mainly in palliative and hospice care, HPCFUSA is a valuable resource for those in related specialties, notably oncology, geriatrics, and family medicine.

The provision of economically sustainable end-of-life care is a continuing global challenge. Health professionals involved must not only become competent practitioners but also propagandists for the cause. If for no other reason, this specifically American edition is important.

Editors-in-chief

September 2008
ACKNOWLEDGEMENTS

The production of a book of this nature depends partly on the help and advice of numerous colleagues, past and present. We acknowledge with gratitude the support of close colleagues, particularly Claudia Bausewein, Patrick Costello, Vincent Crosby, Mervyn Dean, Bisharat El Khoury, Cathy Goddard, Annabella Marks, Claud Regnard, Constanze Remi, and Claire Stark Toller, and those members of palliativedrugs.com who have provided feedback on one or more of the monographs or contributed to the Syringe Driver Survey Database.

Doctor of Pharmacy students from Duquesne University Mylan School of Pharmacy, Ohio Northern University Raabe College of Pharmacy, and West Virginia University helped in various ways, particularly in relation to drug availability and costs.

The principal advisors for this edition were: Sara Booth (oxygen), Keith Budd (buprenorphine), Tim Carter (analgesic drugs and fitness to drive), Jo Chambers (renal effects of opioids), Albert Dahan (buprenorphine), Andrew Davies (Chapter 11), Tony Dickenson (strong opioids), Ken Gillman (serotonin toxicity), Vaughan Keeley (AIEs), Russell Kilpatrick (Chapter 12), Henry McQuay (management of postoperative pain in opioid-dependent patients), Peter Mortimer (AIEs), Simon Noble (LMWH), Victor Pace (NSAIDs and nabumetone), John Shuster (antidepressants), Vanessa Siddall (oral nutritional supplements), Anne Tattersfield (asthma and COPD), Hywel Williams (Chapter 12).

Correspondents included: Claire Amass (glycopyrrolate oral solution formula), David Baldwin (asthma and COPD), Richard Burden (prescribing in renal impairment), Rachel Howard (drug concentration interpretation), Ian Johnston (asthma and COPD), Martin Lennard (cytochrome P450), Staffan Lundström (propofol), Roger Knaggs (management of postoperative pain in opioid-dependent patients), Wolfgang Koppert (buprenorphine), John MacKenzie (management of postoperative pain in opioid-dependent patients), Heather Major (analgesic drugs and fitness to drive), Jim Mason (management of postoperative pain in opioid-dependent patients), Willie McGhee (oxygen), John Moyle (propofol), Felicity Murtagh (renal effects of opioids), Mark Nelson (oxygen), Don Page (oxygen), Judith Palmer (prescribing in renal impairment), Lukas Radbruch (buprenorphine), Andrew Raikes (drugs for diabetes), Reinhard Sittl (buprenorphine), Richard Sloan (p.r.n. prescribing), Andrew Staniforth (QT interval), Jo Thomas (continuous subcutaneous infusions), Adrian Tookman (phenobarbital), Robert Wilcox, Cheryl Williams (QT interval), Zbigniew Zylicz (pruritus).

We are also most grateful to Karen Isaac, Susan Wright and Susan Brown for their contributions in relation to general secretarial assistance, the preparation of the typescript, and copy-editing respectively.
We encourage readers of HPCFUSA to register with the website, and to participate fully in this online community. The website provides additional on-line information for thousands of members world-wide:

- **Bulletin Board** enables members to seek help and offer advice
- **Latest additions** informs members about the latest changes to the Formulary and website
- **News** informs members about drug-related news including changes in drug availability and/or formulation
- **Document library** (previously Research, Audit and Guidelines (RAG) Panel) acts as a repository for guidelines, policies and other documents donated by members
- **Syringe Driver Survey Database** has >1,000 observational compatibility reports of drug combinations given by continuous subcutaneous infusion (CSCI)
- **Online bookshop** enables members to purchase copies of HPCFUSA online.

We are constantly striving to improve the site and its resources, and welcome feedback via hq@palliativedrugs.com. We would also encourage readers to participate in the website satisfaction surveys.

We are committed to keeping www.palliativedrugs.com a free-access resource. Please help us do this by completing market research surveys when invited to do so from time to time.
SUMMARY OF MAIN CHANGES IN 2ND EDITION OF HPCFUSA

Guidance about prescribing in palliative care
This has been moved from the preliminary pages to Chapter 14, at the beginning of Part 2. Much expanded, it includes more explicit information about p.r.n. prescribing, both at home and in hospital. There are also new sections addressing prescribing in children, in the elderly, and in the presence of significant hepatic or renal impairment.

New monographs
Eight new monographs added: systemic local anesthetics, inhaled long-acting β2-adrenergic receptor agonists (LABAs), prochlorperazine, chlorpromazine, quetiapine, phenobarbital, nabumetone, and nalbuphine. In addition, the formerly separate monographs on transdermal and transmucosal fentanyl have been combined, as have those on typical and atypical antipsychotics.

Removed monographs
- Diamorphine
- Diflunisal
- Dihydrocodeine
- Domperidone
- Flurbiprofen
- Levomepromazine (methotrimeprazine)
- Quinine
- Scopolamine (hyoscine) butylbromide
- Topical cleansing agents and disinfectants.

New chapters
Three completely new chapters:
- Management of postoperative pain in opioid-dependent patients
- Analgesic drugs and fitness to drive
- Spinal analgesia.

In addition, seven appendices have been reformatted as chapters in Part 2:
- Anaphylaxis
- Opioid dose conversion ratios
- Prolongation of the QT interval in palliative care
- Cytochrome P450
- Drug-induced movement disorders
- Nebulized drugs
- Administering drugs via enteral feeding tubes.

In addition, there are two new appendices:
- The use of emergency kits in hospice care
The literature on the pharmacology of pain and symptom management in end-stage disease is growing continually, and it is impossible for anyone to be totally familiar with it. This is where HPCFUSA comes into its own as a major accessible resource for prescribing clinicians involved in palliative care.

HPCFUSA is not an easy read, indeed it was never intended that it would be read from cover to cover. It is essentially a reference book – to study the monograph of an individual drug, or class of drugs, with fairly specific questions in mind.

HPCFUSA is not a comprehensive manual of pain and symptom management. For more comprehensive advice, the reader should consult one or more of the numerous books about palliative care or symptom management which are currently available. Symptom Management in Advanced Cancer (4th edition, available in 2009) by Robert Twycross, Andrew Wilcock and Claire Stark Toller, may be obtained from www.palliativedrugs.com (or via Amazon). Although written primarily for UK palliative care clinicians, the contents are generally applicable elsewhere.

Readers should also be aware of Opioids in Cancer Pain (OUP 2005) edited by Mellar Davis, Paul Glare and Janet Hardy. This provides a wealth of additional data, and will be particularly useful for clinical teachers and Palliative Medicine Fellows.

The medication prices listed in HPCFUSA are derived from a mathematical formula applied to the Average Wholesale Price (AWP) to calculate approximate retail pharmacy prices (see Pharmacoeconomics in the USA, p.xxiii). These reflect current retail pharmacy market conditions in the USA for both brand-name and generic medications.

‘Not USA’
Unlike the 1st edition of HPCFUSA, drugs not available in the USA, such as diamorphine (heroin), hyoscine (scopolamine) butylbromide and levomepromazine (methotrimeprazine) are not included. However, the monographs relating to these and several other ‘not USA’ drugs are available on www.palliativedrugs.com.

Contra-indications and cautions
Contra-indications and cautions listed in Package Inserts (PIs) sometimes vary between different manufacturers of the same drug, or within a class of drugs. We have generally not included a contra-indication from the PI if the use of the drug in the stated circumstance is accepted prescribing practice in palliative care.

Instead, we advise a more cautious approach in some patient groups, e.g. the frail elderly, patients with hepatic impairment, renal impairment, and respiratory insufficiency. The contra-indications listed in HPCFUSA are thus limited to the most relevant and specific for a particular drug. For a full list of the manufacturer’s contra-indications and cautions, readers should refer to a drug’s PI.

Undesirable effects of drugs
In HPCFUSA, the term ‘undesirable effect’ is used rather than side effect or adverse effect. Undesirable effects are categorized as:
• very common (≥ 10%)
• common (≥ 10%, > 1%)
• uncommon (≥ 1%, > 0.1%)
• rare (≥ 0.1%, > 0.01%)
• very rare (≥ 0.01%).

However, as yet, all PIs are not compiled in this way.
Generally, *HPCFUSA* includes information on the very common and common undesirable effects. Selected other undesirable effects are also included, e.g. uncommon or rare ones which may have serious consequences. The manufacturer’s PI should be consulted for a full list of undesirable effects.

**Reliable knowledge and levels of evidence**

Research is the pursuit of reliable knowledge. The randomized control trial (RCT) is not the only source of reliable knowledge (Box A). In fact, if your vision is limited to RCTs, a lot of important information and helpful clinical guidance will be overlooked – to the detriment of your clinical care.

<table>
<thead>
<tr>
<th>Level</th>
<th>Type of evidence</th>
<th>Grade</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Evidence obtained from a single randomized controlled trial or a meta-analysis of randomized controlled trials</td>
<td>A</td>
<td>At least one randomized controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation (evidence level I) without extrapolation</td>
</tr>
<tr>
<td>IIa</td>
<td>Evidence obtained from at least one well-designed controlled study without randomization</td>
<td>B</td>
<td>Well-conducted clinical studies but no randomized clinical trials on the topic of recommendation (evidence levels II or III); or extrapolated from level I evidence</td>
</tr>
<tr>
<td>IIb</td>
<td>Evidence obtained from at least one other well-designed quasi-experimental study</td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities</td>
<td>C</td>
<td>Expert committee reports or opinions and/or clinical experiences of respected authorities (evidence level IV). This grading indicates that directly applicable clinical studies of good quality are absent or not readily available</td>
</tr>
<tr>
<td></td>
<td>Good Practice Point (GPP)</td>
<td></td>
<td>Recommended good practice based on the clinical experience of the Guidelines Development Group (GDG)</td>
</tr>
<tr>
<td>NICE</td>
<td>Evidence from NICE guideline or technology appraisal</td>
<td>NICE</td>
<td>Evidence from NICE guideline or technology appraisal</td>
</tr>
</tbody>
</table>
practice, and to the comfort of your patients. There are several sources of knowledge, which can be conveniently grouped under three headings:

- instrumental, includes RCT data and data from other high-quality studies
- interactive, refers to anecdotal data (shared clinical experience), including retrospective and prospective surveys
- critical, data unique to the individual in question (e.g. personal choice) and societal/cultural factors (e.g. financial and logistic considerations).

Relying on one type of knowledge alone is not good practice. All three sources must be exploited in the process of therapeutic decision-making.

Pharmaceutical company information

Although the manufacturer’s Package Insert (PI) is an important source of information about a drug, it is important to remember that many published studies are sponsored by the drug company in question. This can lead to a conflict of interest between the desire for objective data and the need to make one’s own drug as attractive as possible. It is thus best to treat information from company representatives as inevitably biased.

We should also remember that it is often safer to stick with the ‘old favorite’ and not seek to be among the first to prescribe the most recently released drug. Most new drugs today are ‘me-too’ drugs rather than true innovations. The information provided by \textit{HPCFUSA} is commercially independent, and thus serves as a counterbalance to manufacturer bias.

Generic drugs

It is the policy of \textit{HPCFUSA} to use generic drug names, and to encourage generic prescribing. With few exceptions, e.g. SR diltiazem, nifedipine and theophylline, there is little reliable evidence that different brands of the same drug are significantly different in terms of bio-availability and efficacy. However, including the proprietary (brand) name of a strong opioid analgesic on the prescription and dispensing label, particularly in the case of morphine, helps to reduce the scope for confusion over the various available formulations.

The recommended International Non-proprietary Names (rINNs) are 95% identical with United States Adopted Names (USAN, see p.xxvi). Where the names differ, the USAN is given first with the rINN in brackets afterwards.

In relation to people who travel to other countries, the FDA has issued a warning about using proprietary drug names (www.fda.gov/oc/opacom/reports/confusingnames.html). It has identified 18 foreign drug products which have the same brand name as an FDA-approved drug but contains a different active ingredient, e.g. Dilacor (= diltiazem in the USA but digoxin in Serbia, verapamil in Brazil and barnidipine in Argentina), Norpramin (= desipramine in the USA but omeprazole in Spain), Urex (= methenamine in the USA but furosemide in Australia). The memorandum also lists numerous examples of proprietary names used in the USA which are closely similar to approved proprietary names in other countries, and which could be misinterpreted by pharmacists in other countries. Thus, the importance of using generic names when prescribing cannot be overemphasized.

Literature references

It is not feasible to reference every statement in \textit{HPCFUSA}. However, readers are invited to enter into dialog with the Editors, and with some 15,000 health professionals registered with www.palliativedrugs.com, many of whom make use of the website’s Bulletin Board.

In choosing references for inclusion, articles in hospice and palliative care journals have frequently been selected preferentially. Such journals are likely to be more readily available to our readers, often contain detailed discussion and an extensive bibliography.

Electronic sources of information

As far as possible, American sources have been given prominence in \textit{HPCFUSA}. However, some UK sources have inevitably been included. To facilitate access to the relevant documents, website details are given below.
Free access

Bandolier (evidence-based articles for health professionals): available at www.jr2.ox.ac.uk/bandolier/


MeReC Bulletin: available via National Prescribing Center website at www.npc.co.uk/merec_bulletins.htm

National Institute for Health and Clinical Excellence (NICE) guidelines: available at www.nice.org.uk/


UK manufacturers’ Summary of Product Characteristics (SPC), broadly equivalent to the American Package Insert (PI) are available at www.medicines.org.uk

Subscription required


The Cochrane Library: available at http://www3.interscience.wiley.com/cgi-bin/mrwhome/106568753/HOME

Collection of evidence-based systematic reviews.

USING APPROVED DRUGS FOR OFF-LABEL PURPOSES

In palliative care, up to a quarter of all prescriptions are written for indications, dosage forms, or dose regimens not mentioned in the product’s approved labeling, and this is reflected in the recommendations contained in HPCF USA. The symbol † is used to draw attention to such use. However, it is impossible to highlight every example of off-label use. Often it is simply a matter of the route or dose being different from the manufacturer’s labeling. For example, haloperidol is widely used PO as an anti-emetic, whereas the labeling for use as an anti-emetic is restricted to the IM route. It is important to understand that the approval process for drugs regulates the marketing activities of pharmaceutical companies and not a doctor’s prescribing practice. The FDA recognizes that off-label use of drugs by prescribers is often appropriate and may represent standard practice. Further, drugs prescribed outside the product labeling can be dispensed by pharmacists and administered by nurses or midwives.

The licensing process
Marketing approval is necessary in the USA for a product for which therapeutic claims are made. After receiving satisfactory evidence of quality, safety and efficacy, the FDA grants approval for product marketing. This allows a pharmaceutical company to market and supply a product for the specific indications listed in its product labeling. Restrictions may be imposed by the FDA if evidence of safety and efficacy is unavailable in particular patient groups, e.g. children. Once a product is marketed, further clinical trials and experience may reveal other indications. For these to become approved indications in the product labeling, additional evidence needs to be submitted. The considerable expense of this, perhaps coupled with a small market for the new indication, often means that a revised application is not made.

Prescribing outside the product labeling
In the USA, a physician or other qualified clinician may legally:
• prescribe medications in unapproved conditions, doses, and routes of administration
• use compounded drug products in identified individual patients
• override the warnings and precautions given in the labeling.
The responsibility for the consequences of these actions lies with the prescribing clinician. In addition to use in clinical trials, such prescriptions may be justified:
• when prescribing generic formulations (for which indications are not described)
• with established drugs for proven but unapproved indications
• with drugs for conditions for which there are no other treatments (even in the absence of strong evidence)
• when using drugs in individuals not covered by the labeling, e.g. children.
The prescription of a drug (whether approved use/route or not) requires the prescriber, in the light of published evidence, to balance both the potential good and the potential harm which might ensue. Clinicians have a duty to act with reasonable care and skill in a manner consistent with the practice of professional colleagues of similar standing. Thus, when prescribing outside the terms of the product labeling, prescribers must be fully informed about the actions and uses of the drug, and be assured of the quality of the particular product. It is possible to draw a hierarchy of degrees of reasonableness relating to the unapproved use of a drug (Figure 1). The more dangerous the medicine and the more flimsy the evidence the more difficult it is to justify its prescription.
It has been recommended that when prescribing a drug outside its approved use, a clinician should:  

- record in the patient’s notes the reasons for the decision to prescribe outside the approved indications  
- where possible, explain the position to the patient (and family as appropriate) in sufficient detail to allow them to give informed consent; the Package Insert (PI) obviously does not contain information about unapproved indications  
- inform other professionals, e.g. pharmacist, nurses, primary care physician, involved in the care of the patient to avoid misunderstandings.  

However, in palliative care, the use of drugs for off-label uses or by unapproved routes is so widespread that such an approach is impractical. Indeed, in the UK, a survey showed that few (<5%) palliative medicine consultants always obtain verbal or written consent, document in the notes or inform other professionals when using approved drugs for off-label purposes/routes.  

Concern was expressed that not only would it be impractical to do so, but it would be burdensome for the patient, increase anxiety and might result in refusal of beneficial treatment. Some half to two-thirds indicated that they would sometimes obtain verbal consent (53%), document in the notes (41%) and inform other professionals (68%), when using treatments which are not widely used within the specialty, e.g. ketamine, octreotide, ketorolac.  

This is a grey area and each clinician must decide how explicit to be. Some institutions have policies in place and have produced information cards or leaflets for patients and caregivers (Box B).
<table>
<thead>
<tr>
<th>Status</th>
<th>The drug</th>
<th>Published data</th>
<th>The illness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most reasonable</td>
<td>Approved for the intended indication</td>
<td>Well known; generally safe</td>
<td>Life-threatening</td>
</tr>
<tr>
<td></td>
<td>Approved for another indication; other related products approved for the intended indication</td>
<td>Well known but some clear undesirable effects</td>
<td></td>
</tr>
<tr>
<td></td>
<td>An approved product; not approved for the intended indication, nor are similar medicines</td>
<td>Well known; has serious undesirable effects or Little studied; no clear undesirable effects</td>
<td></td>
</tr>
<tr>
<td>Least reasonable</td>
<td>Drug/product not approved at all</td>
<td>Not studied</td>
<td>Severe</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Little studied; has serious undesirable effects</td>
<td>Only poor quality studies reported</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Little studied; has serious undesirable effects</td>
<td>Only anecdotal evidence published</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Not studied</td>
<td>Trivial</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>No published data available</td>
<td></td>
</tr>
</tbody>
</table>

**Figure 1** Factors influencing the reasonableness of prescribing decisions.⁶
**Box B**  Example of a patient information leaflet about the use of medicines outside product labeling

**Use of Medicines in Unapproved Ways**
This leaflet contains important information about your medicines, please read it carefully.

Before a medicine can be marketed, approval must be obtained from the Food and Drug Administration (FDA) by the manufacturer. The FDA approves the ways in which the medicine can be marketed: for which conditions, in what doses, and which age groups. Manufacturers are obliged to include with their medicines a Package Insert which, by law, must be limited to the details of the FDA approval.

In practice, medicines are often prescribed in ways which are not approved by the FDA. However, this will only be done when there is research and experience to support such ‘off-label’ use.

You will know if one of your medicines is being used in an unapproved way when you read the Package Insert supplied by the manufacturer. You will notice that the information in it is not fully relevant to how you are taking the medicine.

Medicines used commonly ‘off-label’ include some antidepressants and anti-epileptics (anti-seizure drugs) which are used to relieve some types of pain. Also, because it is generally more comfortable and convenient, some medicines are often injected subcutaneously (under the skin) instead of being injected into a vein or muscle.

If you have any questions or concerns about your medicines, particularly in relation to ‘off-label’ use, your doctor or pharmacist will be happy to address them.

---

PHARMACO-ECONOMICS IN THE USA

In the USA, the majority of hospice patients are funded via the Hospice Medicare Benefit established by the federal government in 1982. Re-imbursement varies throughout the country. The median re-imbursement is $146 per patient day, ranging from $129 to $169. This daily allowance is intended to cover all aspects of care, including drugs. Keeping costs within this limit (while maintaining a high standard of care) is a major ongoing challenge. However, drug costs are one factor over which a hospice can exercise considerable control.

Most preferred drugs used for symptom management are available generically. Consequently, some hospices are able to achieve a generic:brand prescription ratio of 80:20. However, this generally requires a Pharmacotherapeutic Support System consisting of:

- Pharmacy and Therapeutics Committee (PTC)
- Preferred Drug List (PDL)
- Clinical pharmacy services.

Pharmacy and Therapeutics Committee
This Committee has direct oversight of drug utilization by the hospice. It is generally an interdisciplinary team with representatives from medicine, nursing, pharmacy, and social work, together with the Chief Executive Officer (CEO). A key task is the production of a Preferred Drug List (PDL) for the hospice, which should be reviewed annually.

The targeting of physicians by pharmaceutical companies and direct consumer advertising are influential forces with respect to drug use. These need to be countered by an evidence-based educational program. The educational program should be overseen by the PTC. A key element will be learning to think generically because generic products reduce drug costs by 35–40%. The acquisition cost for retail pharmacists in the USA for drugs purchased from a wholesaler is generally the Average Wholesale Price (AWP) minus 15% for brand name products, but minus 60% for generic products.

However, the use of the AWP as the benchmark for drug payment has been superseded by the Average Sales Price (ASP). This new benchmark is included in the Medicare Modernization Act (MMA) and, since 2005, replaces AWP as the basis for payment for most drugs covered under the Medicare medical benefit, known as Medicare Part B. With any such change, there is potential for confusion among private payers. This will be minimized if the terms and definitions in Box C are clearly understood.

Medicare Part D began at the beginning of 2006. It is a US government program which deals with outpatient drug benefit administered by private-sector bodies, i.e. stand alone Prescription Drug Plans (PDPs) or Medicare Advantage-Prescription Drug Plans (MA-DPs). PDPs and MA-DPs are typically Pharmacy Benefit Managers (PBMs) and commercial health plans which compete for customers on the basis of annual premiums, benefit structures, formulary drug components, pharmacy networks and quality of services.

It is essential that hospices set up systems for hospice patients to prevent Medicare Part D from paying for drugs which are related to the hospice terminal diagnosis. If the dispensing pharmacist is a retail pharmacist or mail order pharmacist, he or she must be informed by the hospice whether or not the ordered drug is related to the hospice terminal diagnosis. This will allow the dispensing pharmacist to correctly bill either Medicare Part D or the hospice. Further guidance from Centers for Medicare and Medicaid Services (CMS) to hospices is expected.
Preferred Drug List (PDL)

This is a list of the drugs the hospice prefers to use for pain and symptom management. The PDL can be organized by either symptom or therapeutic category, or both. The drugs included in the PDL will be the main influence affecting the cost of drug therapy. It is important that, as far as possible, published evidence is used when deciding on the 'drugs of choice'.

Morphine is a good example: the inclusion of morphine is validated to a great extent because it is the strong opioid recommended by the World Health Organization for cancer pain management. Morphine sulfate is available as a solution, a normal ('immediate') release tablet, a sustained-release tablet, a rectal suppository, and as an injection. Most of these can be purchased either as generic or proprietary products. The cost of a generic SR morphine tablet is about 1/2–1/4 of the cost of proprietary SR products (see p.292). The inclusion of generic morphine products in the PDL precludes the use of the more expensive proprietary products. The outcome of this decision is an equal standard of patient comfort and substantial financial savings.

The PTC can also restrict the use of other opioids to specific circumstances such as morphine-induced neurotoxicity (see Box 5.G, p.277) or renal impairment (see p.281), and can set criteria for using expensive treatments such as bisphosphonates and epoetin.

---

**Box C Drug cost definitions**

<table>
<thead>
<tr>
<th><strong>Average Wholesale Price (AWP)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>The average price paid by the pharmacist when purchasing drugs from a drug wholesaler. This is now regarded as a ‘sticker price’ rather than the net price for the drug after all discounts extended to the pharmacy by the wholesaler have been subtracted.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Wholesale Acquisition Cost (WAC)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>The average price that the drug wholesaler pays the drug manufacturer when purchasing drugs for resale to pharmacies. Like AWP, WAC is regarded as a ‘sticker price’ in that it also does not truly reflect all the discounts extended to the drug wholesaler by the drug manufacturer.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Average Sales Price (ASP)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>A volume-weighted average derived from data about the actual selling price submitted by the manufacturer. This includes most rebates, volume discounts, and other price concessions offered to the purchaser, which may be a pharmacy or a physician. ASP values are available on the Centers for Medicare and Medicaid Services (CMS) website. Private payers such as hospices can now identify the ASP and use this as the drug payment benchmark. ASP is generally regarded as AWP minus 49%. Drugs covered by Medicare Part B are re-imbursed at the rate of 106% of ASP.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Average Manufacturers Price (AMP)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>The price available to the retail class of trade (pharmacy). It reflects all discounts and other price concessions afforded to the retail class of trade. This new benchmark was created by the US Congress in 1990 to facilitate the calculation of rebates paid by manufacturers to states for drugs dispensed by pharmacies to Medicaid beneficiaries. The Deficit Reduction Act of 2005 (DRA) mandated that AMP be used instead of AWP for calculation of the federal upper limit (FUL), i.e. the maximum amount of federal matching funds the US federal government will pay to state Medicaid programs for eligible generic and multiple-source brand drugs. Today, the FUL is 250% of a drug’s AMP per DRA. AMP prices are mandated to be reported monthly and are also available on the CMS website. Thus private payers such as hospices may elect to use AMP as the basis for payment to retail pharmacies.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Maximal Allowable Cost (MAC)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>The re-imbursement rate paid by state Medicaid programs for certain prescription drugs available from multiple sources as branded products or as generic medications. MAC is based on the FUL for multiple-source brand and generic drugs. This rate is paid per individual pharmaceutical and strength, e.g. $0.50 per morphine 15mg tablet. Pharmacy Benefit Managers (PBMs) often use a proprietary MAC that may or may not be equal to the state MAC because no standardized definition of MAC exists.</td>
</tr>
</tbody>
</table>
Compounded preparations
A compounded preparation is a prescription drug prepared locally by a 'compounding pharmacist', often for one particular patient. Formulations include troches (dispensable tablets), capsules, powders, solutions, elixirs, syrups, emulsions, suspensions, ointments, creams, suppositories, and gels (see p.471). In hospice care, compounded drugs are widely used when the oral route becomes difficult or impossible. However, caution is necessary because the use of compounded preparations may increase drug acquisition costs. On the other hand, compounded diazepam 5mg suppositories typically cost about $1 each. This is a fraction of the cost of commercially available diazepam rectal gel (which costs about $150 per dose!).

Clinical pharmacy services
A clinical pharmacist is ideally placed to take the lead in promoting safe and effective drug use. Without the involvement of a clinical pharmacist it is difficult for a hospice to have a cost-effective Pharmacotherapeutic Support System. A hospice must therefore be prepared to spend money in order to save much more money.

In addition, there is scope for a hospice to facilitate drug distribution to their patients in various ways, including through:
• an in-house pharmacy
• collaboration with community retail pharmacy providers
• a mail-order pharmacy program.

Thus, a hospice may decide to use the services of a pharmacy benefit management company to develop a local preferred pharmacy network, and to allow electronic adjudication of prescription claims. Such a program facilitates the economic oversight of drug use by the clinical pharmacist.

DRUG NAMES

United States Adopted Names (USANs) are used throughout *HPCF USA*. Proprietary names are generally not included. In contrast, all drugs marketed within the European Union are known by their recommended International Non-proprietary Names (rINNs). Differences between USANs and rINNs are listed in Table 1.

Formerly, drugs in the UK were known by their British Approved Names (BANs). Where a BAN differs from the rINN, the BAN has also been included in the Table to aid understanding of the older UK literature. With combination products such as codeine and acetaminophen (paracetamol) or diphenoxylate and atropine, the UK conventional name is shown in Table 2, e.g. co-codamol or co-phenotrope.

Drugs which are not available in the USA but which are mentioned in *HPCF USA* are listed in Table 3.

Table 1  Drug names relevant to palliative care for which the USAN and rINN differ

<table>
<thead>
<tr>
<th>USAN</th>
<th>rINN</th>
<th>Former BAN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen</td>
<td>Paracetamol</td>
<td>–</td>
</tr>
<tr>
<td>Albuterol</td>
<td>Salbutamol</td>
<td>–</td>
</tr>
<tr>
<td>Aluminum</td>
<td>Aluminium</td>
<td>–</td>
</tr>
<tr>
<td>Amobarbital</td>
<td>Amobarbital</td>
<td>Amylobarbitone</td>
</tr>
<tr>
<td>Amphetamine</td>
<td>Amfetamine</td>
<td>Amphetamine</td>
</tr>
<tr>
<td>Beclomethasone</td>
<td>Beclometasone</td>
<td>Beclomethasone</td>
</tr>
<tr>
<td>Bendroflumethiazide</td>
<td>Bendroflumethiazide</td>
<td>Bendrofluazide</td>
</tr>
<tr>
<td>Benzathine penicillin</td>
<td>Benzathine benzylpenicillin</td>
<td>Benzathine penicillin</td>
</tr>
<tr>
<td>Benztrapine</td>
<td>Benztrapine</td>
<td>Benztrapine</td>
</tr>
<tr>
<td>Calcitonin</td>
<td>Calcitonin (salmon)</td>
<td>Salcatonin</td>
</tr>
<tr>
<td>Carboxymethylcellulose</td>
<td>Carmellose</td>
<td>–</td>
</tr>
<tr>
<td>Cephalexin (etc.)</td>
<td>Cefalexin (etc.)</td>
<td>Cephalexin (etc.)</td>
</tr>
<tr>
<td>Chlorpheniramine</td>
<td>Chlorphenamine</td>
<td>Chlorpheniramine</td>
</tr>
<tr>
<td>Cromolyn sodium</td>
<td>Sodium cromoglicate</td>
<td>Sodium cromoglycate</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>Ciclosporin</td>
<td>Cyclosporin</td>
</tr>
<tr>
<td>Dextroamphatetamine</td>
<td>Dexamfetamine</td>
<td>Dexamfetamine</td>
</tr>
<tr>
<td>Dicyclomine</td>
<td>Dicycloverine</td>
<td>Dicyclomine</td>
</tr>
<tr>
<td>Diestrol</td>
<td>Diestrol</td>
<td>Dienoestrol</td>
</tr>
<tr>
<td>Diethylstilbestrol</td>
<td>Diethylstilbestrol</td>
<td>Stilboestrol</td>
</tr>
<tr>
<td>Dimethicone</td>
<td>Dimeticone</td>
<td>Dimethicone</td>
</tr>
<tr>
<td>Dothiepin</td>
<td>Dosulepin</td>
<td>Dothiepin</td>
</tr>
<tr>
<td>Estradiol</td>
<td>Estradiol</td>
<td>Oestradiol</td>
</tr>
<tr>
<td>Furosemide</td>
<td>Furosemide</td>
<td>Frusemid</td>
</tr>
<tr>
<td>Glyburide</td>
<td>Glibenclamide</td>
<td>–</td>
</tr>
<tr>
<td>Glycopyrrolate</td>
<td>Glycypyrromion</td>
<td>–</td>
</tr>
<tr>
<td>Guafenesis</td>
<td>Guafenesis</td>
<td>Guafenesis</td>
</tr>
<tr>
<td>Indometacin</td>
<td>Indometacin</td>
<td>Indometacin</td>
</tr>
<tr>
<td>Isoproterenol</td>
<td>Isoprenaline</td>
<td>–</td>
</tr>
<tr>
<td>Levothyroxine</td>
<td>Levothyroxine</td>
<td>Thyroxine</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>Lidocaine</td>
<td>Lignocaine</td>
</tr>
<tr>
<td>Meperidine</td>
<td>Pethidine</td>
<td>–</td>
</tr>
<tr>
<td>Methenamine hippurate</td>
<td>Methenamine hippurate</td>
<td>Hexamine hippurate</td>
</tr>
<tr>
<td>Mineral oil</td>
<td>Liquid paraffin</td>
<td>–</td>
</tr>
<tr>
<td>Mitoxantrone</td>
<td>Mitoxantrone</td>
<td>Mitoxantrone</td>
</tr>
<tr>
<td>Nitroglycerin</td>
<td>Glyceryl trinitrate</td>
<td>–</td>
</tr>
</tbody>
</table>

continued
### Table 1 Continued

<table>
<thead>
<tr>
<th>USAN</th>
<th>rINN</th>
<th>Former BAN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxethazine</td>
<td>Oxetacaine</td>
<td>Oxethazine</td>
</tr>
<tr>
<td>Penicillin G</td>
<td>Benzylpenicillin</td>
<td>–</td>
</tr>
<tr>
<td>Penicillin V</td>
<td>Phenoxybenzylpenicillin</td>
<td>–</td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>Phenobarbital</td>
<td>Phenobarbitone</td>
</tr>
<tr>
<td>Phytomenadione</td>
<td>Phytomenadione</td>
<td>–</td>
</tr>
<tr>
<td>Procaine penicillin</td>
<td>Procaine benzylpenicillin</td>
<td>Procaine penicillin</td>
</tr>
<tr>
<td>Propoxyphene</td>
<td>Dextropropoxyphene</td>
<td>–</td>
</tr>
<tr>
<td>Psyllium</td>
<td>–</td>
<td>Ispaghula</td>
</tr>
<tr>
<td>Rifampin</td>
<td>Rifampicin</td>
<td>–</td>
</tr>
<tr>
<td>Simethicone</td>
<td>Simeticone</td>
<td>Simethicone</td>
</tr>
<tr>
<td>Sulfasalazine</td>
<td>Sulfasalazine</td>
<td>Sulphasalazine</td>
</tr>
<tr>
<td>Scopolamine</td>
<td>Hyoscine</td>
<td>–</td>
</tr>
<tr>
<td>Sulfathiazole</td>
<td>Sulfathiazole</td>
<td>Sulphathiazole</td>
</tr>
<tr>
<td>Sulfonamides</td>
<td>Sulfonamides</td>
<td>Sulphonamides</td>
</tr>
<tr>
<td>Tetracaine</td>
<td>Tetracaine</td>
<td>Amethocaine</td>
</tr>
<tr>
<td>Trihexyphenidyl</td>
<td>Trihexyphenidyl</td>
<td>Benzhexol</td>
</tr>
<tr>
<td>Trimeprazine</td>
<td>Alimemazine</td>
<td>Trimeprazine</td>
</tr>
<tr>
<td>Vitamin A</td>
<td>Retinol</td>
<td>Vitamin A</td>
</tr>
</tbody>
</table>

*a.* Silica-activated dimethicone; known in some countries as (di)methylpolysiloxane.

### Table 2 UK names for combination products

<table>
<thead>
<tr>
<th>Contents</th>
<th>US brand name</th>
<th>UK name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen-codeine phosphate</td>
<td>Tylenol with Codeine</td>
<td>Co-codamol</td>
</tr>
<tr>
<td>Acetaminophen-dihydrocodeine</td>
<td>Not available in the USA</td>
<td>Co-dydramol</td>
</tr>
<tr>
<td>Acetaminophen-propyophene</td>
<td>Darvocet</td>
<td>Co-proxamol</td>
</tr>
<tr>
<td>Amoxicillin-clavulanate</td>
<td>Augmentin</td>
<td>Co-amoxiclav</td>
</tr>
<tr>
<td>Diphenoxylate-atropine</td>
<td>Lomotil</td>
<td>Co-phenotrope</td>
</tr>
<tr>
<td>Magnesium hydroxide-aluminum hydroxide</td>
<td>Maalox</td>
<td>Co-magaldrox</td>
</tr>
<tr>
<td>Sulfamethoxazole-trimethoprim</td>
<td>Bactrim</td>
<td>Co-trimoxazole</td>
</tr>
</tbody>
</table>

### Table 3 Drugs not available in the USA

<table>
<thead>
<tr>
<th>rINN</th>
<th>Former BAN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alimemazine</td>
<td>Trimeprazine</td>
</tr>
<tr>
<td>Benorilate</td>
<td>Benorylate</td>
</tr>
<tr>
<td>Clomethiazole</td>
<td>Clormethiazole</td>
</tr>
<tr>
<td>Dantron</td>
<td>Dantrol</td>
</tr>
<tr>
<td>Diamorphine</td>
<td>Diamorphine</td>
</tr>
<tr>
<td>Domperidone</td>
<td>Domperidone</td>
</tr>
<tr>
<td>Dosulepin</td>
<td>Dothiepin</td>
</tr>
<tr>
<td>Etamsylate</td>
<td>Ethamsylate</td>
</tr>
<tr>
<td>Levomepromazine</td>
<td>Methotrimprazine</td>
</tr>
<tr>
<td>Oxetacaine</td>
<td>Oxethazine</td>
</tr>
<tr>
<td>Sodium cromoglicate</td>
<td>Sodium cromoglycate</td>
</tr>
</tbody>
</table>

*a.* cromolyn sodium (USAN).
LIST OF ABBREVIATIONS

Drug administration
In 2007, the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) published National Patient Safety Goals. These include a series of recommendations about ways in which confusion (and thus errors) can be reduced by avoiding the use of certain abbreviations when writing prescriptions. The full set of recommendations is available at www.jointcommission.org/PatientSafety/NationalPatientSafetyGoals/npsg_rfr.htm. In consequence, several time-honored abbreviations (e.g. h.s. for ‘at bedtime’) are no longer used in HPCF USA. Instead, the time of administration is written in full:

* at bedtime
* once daily
* each morning
* every other day.

Table 4 Acceptable abbreviations for the times of drug administration

<table>
<thead>
<tr>
<th>Times</th>
<th>USA</th>
<th>Latin</th>
<th>UK</th>
<th>Latin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Twice daily</td>
<td>b.i.d.</td>
<td>bis in die</td>
<td>b.d.</td>
<td>bis die</td>
</tr>
<tr>
<td>Three times daily</td>
<td>t.i.d.</td>
<td>ter in die</td>
<td>t.d.s.</td>
<td>ter die sumendus</td>
</tr>
<tr>
<td>Four times daily</td>
<td>q.i.d.</td>
<td>quarta in die</td>
<td>q.d.s.</td>
<td>quarta die sumendus</td>
</tr>
<tr>
<td>Every 4 hours etc.</td>
<td>q4h</td>
<td>quaque quarta hora</td>
<td>q4h</td>
<td>quaque quarta hora</td>
</tr>
<tr>
<td>Rescue medication (as needed/required)</td>
<td>p.r.n.</td>
<td>pro re nata</td>
<td>p.r.n.</td>
<td>pro re nata</td>
</tr>
<tr>
<td>Give immediately</td>
<td>stat</td>
<td>stat</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a.c. ante cibum (before food)
amp ampule containing a single dose (cf. vial)
CIVI continuous intravenous infusion
CR controlled-release (used for proprietary SR products only when it is part of the brand name)
CSCI continuous subcutaneous infusion
EC enteric-coated
ED epidural
ER extended-release (used for proprietary SR products only when it is part of the brand name)
IM intramuscular
IT intrathecal
IV intravenous
IVI intravenous infusion
OTC over the counter (i.e. can be obtained without a prescription)
p.c. post cibum (after food)
PO per os, by mouth
POM prescription only medicine
PR per rectum
PV per vaginum
SC subcutaneous
SL sublingual
SR sustained-release (preferred generic term for all slow-release products)
### Transdermal (TD) Vial
- Sterile container with a rubber bung containing either a single or multiple doses (cf. amp)
- Water for injections (WFI)

### List of Abbreviations

#### General
- ***:** Specialist use only
- **†:** Off-label use
- **AHFS:** American Hospital Formulary Service
- **ARP:** Average Retail Price (USA)
- **AWP:** Average Wholesale Price (USA)
- **BNF:** British National Formulary
- **BP:** British Pharmacopoeia
- **CHM:** Commission on Human Medicines (UK)
- **CSM:** Committee on Safety of Medicines (UK; now part of CHM)
- **DEA:** Drug Enforcement Agency (USA)
- **EMEA:** European Medicines Agency
- **EORTC:** European Organisation for Research and Treatment of Cancer
- **FDA:** Food and Drug Administration (USA)
- **IASP:** International Association for the Study of Pain
- **IDIS:** International Drug Information Service
- **MCAM:** Medicines Control Agency (UK; now MHRA)
- **MHRA:** Medicines and Healthcare products Regulatory Agency (UK; formerly MCA)
- **NICE:** National Institute for Health and Clinical Excellence (UK)
- **NPF:** Nurse Prescribers’ Formulary
- **PCS:** Palliative care service
- **PI:** Package Insert (USA)
- **PIL:** Patient Information Leaflet
- **rINN:** Recommended International Non-proprietary Name
- **SPC:** Summary of Product Characteristics (UK)
- **UK:** United Kingdom
- **USA:** United States of America
- **USP:** United States Pharmacopoeia
- **VAS:** Visual analog scale, 0–100 mm
- **WHO:** World Health Organization

#### Medical
- **ACD:** Anemia of chronic disease
- **ACE:** Angiotensin-converting enzyme
- **ADH:** Antidiuretic hormone (vasopressin)
- **AUC:** Area under the plasma concentration–time curve
- **β₂:** Beta 2 adrenergic (receptor)
- **BUN:** Blood urea nitrogen
- **CHF:** Congestive heart failure
- **CNS:** Central nervous system
- **COX:** Cyclo-oxygenase; alternative, prostaglandin synthase
- **COPD:** Chronic obstructive pulmonary disease
- **CRP:** C-reactive protein
- **CSF:** Cerebrospinal fluid
- **CT:** Computed tomography
- **δ:** Delta-opioid (receptor)
- **D₂:** Dopamine type 2 (receptor)
- **DIC:** Disseminated intravascular coagulation
- **DVT:** Deep vein thrombosis
- **ECG:** Electrocardiogram
- **ECT:** Electroconvulsive therapy
- **FEV₁:** Forced expiratory volume in 1 second
LIST OF ABBREVIATIONS

FRC functional residual capacity
FSH follicle-stimulating hormone
FVC forced vital capacity of lungs
GABA gamma-aminobutyric acid
Gl gastro-intestinal
Hb hemoglobin
H₁, H₂ histamine type 1, type 2 (receptor)
Ig immunoglobulin
INR international normalized ratio
κ kappa-opioid (receptor)
LABA long-acting β₂-adrenergic receptor agonist
LFTs liver function tests
LH luteinising hormone
LMWH low molecular weight heparin
MAOI mono-amine oxidase inhibitor
MARI mono-amine re-uptake inhibitor
MRI magnetic resonance imaging
MSU mid-stream specimen of urine
μ mu-opioid (receptor)
NaSSA noradrenergic and specific serotonergic antidepressant
NDRI norepinephrine (noradrenaline) and dopamine re-uptake inhibitor
NG nasogastric
NJ nasojejunal
NMDA N-methyl D-aspartate
NNH number needed to harm, i.e. the number of patients needed to be treated in order to harm one patient sufficiently to cause withdrawal from a drug trial
NNT number needed to treat, i.e. the number of patients needed to be treated in order to achieve 50% improvement in one patient compared with placebo
NRI norepinephrine (noradrenaline) re-uptake inhibitor
NSAID non-steroidal anti-inflammatory drug
PaCO₂ arterial partial pressure of carbon dioxide
PaO₂ arterial partial pressure of oxygen
PCA patient-controlled analgesia
PE pulmonary embolus/embolism
PEF peak expiratory flow
PG prostaglandin
PPI proton pump inhibitor
PUB gastro-intestinal perforation, ulceration or bleeding (in relation to serious GI events caused by NSAIDs)
RCT randomized controlled trial
RIMA reversible inhibitor of mono-amine oxidase type A
RTI respiratory tract infection
SNRI serotonin and norepinephrine (noradrenaline) re-uptake inhibitor
SSRI selective serotonin re-uptake inhibitor
TCA tricyclic antidepressant
TIBC total iron-binding capacity; alternative, plasma transferrin concentration
TlCO transfer factor of the lung for carbon monoxide
UTI urinary tract infection
VEGF vascular endothelial growth factor
VIP vaso-active intestinal polypeptide
WBC white blood cell

Units

cm centimeter(s)
cps cycles per sec
dL deciliter(s)
g gram(s)
Gy Gray(s), a measure of radiation
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>h</td>
<td>hour(s)</td>
</tr>
<tr>
<td>Hg</td>
<td>mercury</td>
</tr>
<tr>
<td>kg</td>
<td>kilogram(s)</td>
</tr>
<tr>
<td>L</td>
<td>liter(s)</td>
</tr>
<tr>
<td>mEq</td>
<td>milliequivalent(s)</td>
</tr>
<tr>
<td>mg</td>
<td>milligram(s)</td>
</tr>
<tr>
<td>micromol</td>
<td>micromole(s)</td>
</tr>
<tr>
<td>mL</td>
<td>milliliter(s)</td>
</tr>
<tr>
<td>mm</td>
<td>millimeter(s)</td>
</tr>
<tr>
<td>mmol</td>
<td>millimole(s)</td>
</tr>
<tr>
<td>min</td>
<td>minute(s)</td>
</tr>
<tr>
<td>mosmol</td>
<td>milli-osmole(s)</td>
</tr>
<tr>
<td>msec</td>
<td>millisecond</td>
</tr>
<tr>
<td>nm</td>
<td>nanometer(s)</td>
</tr>
<tr>
<td>nmol</td>
<td>nanomole(s); alternative, nM</td>
</tr>
<tr>
<td>sec</td>
<td>second(s)</td>
</tr>
</tbody>
</table>