PCF3

PALLIATIVE CARE FORMULARY

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PREFACE

We are pleased to introduce the third edition of the Palliative Care Formulary (PCF3) to our readers. Since the publication of PCF2 in 2002, every drug monograph has been reviewed, and most have been significantly revised and updated. Ten monographs have been removed and 17 new ones added (see p. xi). The formulary is now divided into two parts: Part 1 comprises the drug monographs, and Part 2 the more general topics, including continuous subcutaneous infusions and five new chapters (see p. xi). Altogether, PCF3 is about 50% bigger than PCF2.

PCF3 contains material relating to various general medical topics. We regard this as an important part of PCF because many patients referred for palliative care do not have cancer, or have one or more common co-morbidities. For example, COPD, congestive heart failure, and diabetes mellitus. Further, because of the overall perspective of the book, the information is presented in a more accessible form for those involved in palliative care.

PCF3 includes a number of clinical Guidelines. To enhance their usefulness in practice, each set of Guidelines is limited to no more than two pages, and references are not included. We welcome feedback on these. We also encourage donation of other people's guidelines for posting on our website (e-mail copies to hq@palliativedrugs.com).

PCF3 is also more focused on the UK. This is because it no longer stands alone. It is mirrored in the USA by its cousin, the Hospice and Palliative Care Formulary (HPCFusa), and by German and Italian versions. However, the target audience remains the same, namely doctors and other health professionals caring for patients for whom palliative care is appropriate. Although written primarily with cancer patients in mind, the contents of PCF3 are generally applicable to any form of end-stage progressive disease.

We are pleased to note that PCF is used in some localities to fulfil the NHS National Cancer Standards requirement for specialist palliative care services within a Cancer Centre and Network to have a core palliative care drug formulary. PCF3 also supplements Changing Gear: Guidelines for managing the days of life in adults, re-issued by the UK National Council for Palliative Care in 2006.

As always, readers should satisfy themselves as to the appropriateness of any information in PCF3 before applying it in practice. PCF3 often refers to uses of drugs which are outside the scope of their marketing authorization (product licence); the use of drugs in this way has implications for the prescriber (see p. xvii).

Editors-in-chief
August 2007
ACKNOWLEDGEMENTS

The production of a book of this nature depends partly on the help and advice of numerous colleagues, both past and present. We acknowledge with gratitude the support of close colleagues, particularly Patrick Costello, Vincent Crosby, Bisharat El Khoury, Annabella Marks 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. Figures 18.1 and 18.2 were kindly provided by Clinical Services Support, P.A. Smiths Medical International Ltd. We acknowledge with thanks the contributions from the following advisors and correspondents.

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), 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 (glycopyrronium oral solution formula), David Baldwin (asthma and COPD), Kathryn Blount (oral nutritional supplements), Richard Burden (prescribing in renal impairment), Rachel Howard (drug concentration interpretation), Ian Johnston (asthma and COPD), Judy Lawrence (oral nutritional supplements), 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), Reinhard Sittl (buprenorphine), Richard Sloan (p.r.n. prescribing), Mike Stroud (oral nutritional supplements), Jo Thomas (continuous subcutaneous infusions), Adrian Tookman (phenobarbital).

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.
**SUMMARY OF MAIN CHANGES IN PCF3**

**New monographs**
Seventeen new monographs added: systemic local anaesthetics, low molecular weight heparin (LMWH), enoxaparin, tiotropium, inhaled long-acting $\beta_2$-adrenergic receptor agonists (LABAs), drugs for cough, duloxetine, trazodone, pregabalin, phenobarbital, nefopam, nabumetone, antibiotics in palliative care, *Helicobacter pylori* gastritis, ibandronic acid, danazol and tamsulosin.

In addition, three monographs have been expanded: tranexamic acid now appears within antifibrinolytic drugs, carbocisteine in mucolytics and cyclizine in antihistaminic antimuscarinic anti-emetics.

**Removed monographs**
Ten monographs removed: oxetacaine, cisapride, aromatic inhalations, thioridazine, diflunisal, rofecoxib, stanozolol, indoramin, multivitamins and hyaluronidase.

In addition, the formerly separate monographs on transdermal and transmucosal fentanyl have been combined.

**New chapters**
Five completely new chapters:
- Opioid dose conversion ratios
- Management of postoperative pain in opioid-dependent patients
- Analgesic drugs and fitness to drive
- Spinal analgesia
- Oral nutritional supplements.

Six appendices have been reformatted as chapters in Part 2: anaphylaxis, prolongation of the QT interval in palliative care, cytochrome P450, drug-induced movement disorders, nebulized drugs and administering drugs via enteral feeding tubes.

**Guidance about prescribing in palliative care**
This has been moved from the preliminary pages to 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 the elderly, and in the presence of significant hepatic or renal impairment.

**Reprint July 2008**
In this reprint of PCF3, we have taken the opportunity to make several minor corrections, and include eight significant changes. The latter are:
- Furosemide (p.42), expansion of text about nebulized furosemide
- Choice of NSAID (p.236), ibuprofen and naproxen are now given equal ‘good choice’ status
- Tramadol (p.261), we have taken note of the extensive German clinical experience over many years, and changed the potency ratio of oral tramadol to oral morphine from about 1:5 to about 1:10. This has a knock-on effect later in the book, namely in Table 5.15 (p.269) and Table 15.1 (p.466)
- Opioids in end-stage renal failure (p.271) refers to new UK guidelines
- Diamorphine supply (p.283) confirms that all ampoule sizes are now readily available
- Opioid antagonists (p.319) features newly marketed *methylnaltrexone* (p.322)
- Chapter 25 Anaphylaxis (p.549), revised in the light of the publication of revised Guidelines by the Resuscitation Council (UK)
- Appendix 3 Taking controlled and prescription drugs to other countries (p.579), revised in the light of changes in the Home Office (UK) regulations.
We encourage readers of PCF3 to register with the website, and to participate fully in this online community. The website provides additional on-line information and support to >25 000 members world-wide, of whom 50% are from the UK:

- **Bulletin Board**: enables members to seek help and offer advice (reading and exchanging messages counts towards internal Continuing Medical Education)
- **Newsletter**: informs members about changes in drug availability and/or formulation, includes new or revised monographs, and reports the results of various membership surveys
- **Research, Audit and Guidelines (RAG) Panel**: acts as a repository for guidelines, policies and other documents donated by members
- **Syringe Driver Survey Database**: has over 750 observational compatibility reports of drug combinations used in continuous subcutaneous infusions (CSCI)
- **Online Store**: several palliative care books can be purchased by members online (for a wider selection, go to www.palliativebooks.com).

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.
GETTING THE MOST OUT OF PCF3

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 familiar with all of it. This is where a book like PCF3 comes into its own as a major accessible resource for prescribing clinicians involved in palliative care. On the other hand, PCF3 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.

The main sections in Part 1 of PCF3 generally follow the systematic order of the British National Formulary (BNF). Part 2 and the appendices deal with themes that transcend the drug monographs, e.g. important drug interactions, the use of nebulized drugs, named patient suppliers. Drugs marked with an asterisk (*) should generally be used only by, or after consultation with, a specialist palliative care service. Drug prices are net prices based on those in the BNF No. 52 (September 2006).

PCF3 does not replace the BNF or books on pain and symptom management; it is for use alongside them. Symptom Management in Advanced Cancer (Twycross, Wilcock and Toller, 4th edition 2009, palliativedrugs.com Ltd, Nottingham) should be seen as the companion book to PCF3.

Contra-indications and cautions
Contra-indications and cautions listed in Summaries of Product Characteristics (SPCs) can vary between different manufacturers of the same drug, or within a class of drugs. We have generally not included a contra-indication from the SPC 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 PCF3 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 SPC.

Undesirable effects of drugs
In PCF3, the term ‘undesirable effect’ is used rather than side effect or adverse drug reaction, as recommended by the European Commission. 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 SPCs are not compiled in this way.

Generally, PCF3 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 SPC 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 controlled trial (RCT) is not the only source of reliable knowledge, and various levels of evidence have been categorized. A modified system is used by NICE to indicate the level of evidence on which recommendations are based (Box A).

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

### Box A Hierarchy of evidence and recommendations grading scheme

<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></td>
<td>Good Practice Point (GPP)</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>
Pharmaceutical company information
The manufacturer’s SPC is an important source of information about a drug in specific formulations. However, many published studies are sponsored by industry. This can lead to a conflict between a desire to provide objective data and the desire for a company to make its own drug as attractive as possible. It is thus sensible to regard information from company representatives as inevitably biased. We would stress that the information provided by PCF3 is commercially independent, and should serve as a counterbalance to manufacturer bias.

Remember: it is often safer to stick with an ‘old favourite’ rather than seek to be one of the first to prescribe a newly marketed drug. Most new drugs today are ‘me-too’ drugs rather than true innovations.

Generic drugs
It is the policy of PCF3 to use generic drug names, and to encourage generic prescribing. With occasional exceptions, e.g. for m/r formulations of diltiazem, nifedipine and theophylline, there is little reliable evidence that different preparations of the same drug are significantly different in terms of bioavailability and efficacy. However, the Department of Health (London) recommends including the brand name of opioid analgesics on the prescription and dispensing label, particularly for oral morphine preparations, to avoid confusion over the various strengths and formulations available.

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

It is clearly not feasible to reference every statement in PCF3. However, readers are invited to enter into constructive dialogue with the Editorial Team via the Bulletin Board on www.palliative-drugs.com. This is currently accessed by > 25 000 health professionals.

Electronic sources of information
Several of the sources cited in PCF3 can be accessed free online by UK users. To facilitate access to the relevant documents, website details are given below.

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


Free registration required.


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


Site also gives access to Hospital Pharmacist (London).

UK manufacturers’ SPCs: available from www.medicines.org.uk

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

Collection of evidence-based systematic reviews.

A subscription is required in certain other countries.

Various other sources and full-text core journals (e.g. the British Medical Journal and the Lancet) are available free to UK NHS staff with an Athens password through the National Library for Health (NLH) at www.library.nhs.uk/Default.aspx
PALLIATIVE CARE FORMULARY

USING LICENSED DRUGS FOR UNLICENSED PURPOSES

In palliative care, up to a quarter of all prescriptions written are for licensed drugs given for unlicensed indications, and/or via an unlicensed route, and this is reflected in the recommendations contained in PCF3. The symbol † is used to draw attention to such use. However, it is impossible to highlight every example of unlicensed use. Often it is simply a matter of the route or dose being different from those in the manufacturer’s SPC. Thus, it is important to recognize that the licensing process for drugs regulates the marketing activities of pharmaceutical companies and not a doctor’s prescribing practice. Unlicensed use of drugs by prescribers is often appropriate and may represent standard practice, and a doctor’s clinical freedom to prescribe in this way is specifically safeguarded in the Medicines Act 1968. Further, drugs prescribed outside the licence can be dispensed by pharmacists and administered by nurses or midwives.

The licensing process
A marketing licence is necessary in the UK for a product for which therapeutic claims are made. New medicines for use in Europe are first evaluated by the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMEA). After receiving satisfactory evidence of quality, safety and efficacy, the CHMP issues a positive opinion recommending marketing. Subject to further scrutiny to satisfy its own criteria, the Licensing Authority of the Medicines and Healthcare products Regulatory Agency (MHRA) then grants a licence called the Marketing Authorization. This allows a pharmaceutical company to market and supply a product in the UK for the specific indications listed in its SPC. Restrictions are imposed by the MHRA 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 licensed, 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 licence
In the UK, a doctor may legally:
- prescribe unlicensed medicines
- use unlicensed products specially prepared, imported or supplied for a named patient
- use or advise using a licensed medicine for indications or in doses or by routes of administration outside the licensed recommendations
- supply another doctor with an unlicensed medicine
- override the warnings and precautions given in the licence
- use unlicensed drugs in clinical trials.

Further, nurses, pharmacists, chiropodists/podiatrists, physiotherapists and radiographers who are registered as supplementary prescribers can, in partnership with a doctor or dentist (the independent prescriber), prescribe:
- licensed medicines outside their licensed indications
- unlicensed medicines

provided this is done in the framework of an agreed clinical management plan for a specific patient.

Nurses or pharmacists who are registered as independent prescribers can prescribe licensed medicines outside their licence if this is accepted clinical practice, but cannot prescribe unlicensed medicines.
The responsibility for the consequences of these actions lies with the prescriber.\textsuperscript{5–7} In addition to clinical trials such prescriptions may be justified:

- when prescribing generic formulations for which indications are not described
- with established drugs for proven but unlicensed 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 licence, e.g. children.

Prescription of a drug (whether licensed 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. Prescribers 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 licence, 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 use of unlicensed drugs (Figure 1).\textsuperscript{8} 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 licence, a prescriber should:\textsuperscript{4,6–9}

- document in the patient’s records the reasons for the decision to prescribe outside the licensed indications
- where possible, explain the position to the patient (and family as appropriate) in sufficient detail to allow them to give informed consent; the Patient Information Leaflet obviously does not contain information about unlicensed indications
- inform other professionals, e.g. pharmacist, nurses, general practitioner, involved in the care of the patient to avoid misunderstandings.

However, in palliative care, the use of drugs for unlicensed uses or by unlicensed 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 licensed drugs for unlicensed purposes/routes.\textsuperscript{10} 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 NHS Trusts and other institutions have policies in place and have produced information cards or leaflets for patients and caregivers (Box B). A position statement has also been produced by the Association for Palliative Medicine and the Pain Society (Box C).
<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>Licensed for the intended indication</td>
<td>Well known; generally safe</td>
<td>Life-threatening</td>
</tr>
<tr>
<td></td>
<td>Licensed for another indication; other related products licensed for the intended indication</td>
<td>Well known; some clear undesirable effects</td>
<td></td>
</tr>
<tr>
<td></td>
<td>A licensed product; not licensed 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>Severe</td>
</tr>
<tr>
<td>Least reasonable</td>
<td>Drug/product not licensed at all</td>
<td>Little studied; has serious undesirable effects</td>
<td>Mild</td>
</tr>
<tr>
<td></td>
<td>Not studied</td>
<td>Only anecdotal evidence published</td>
<td>Trivial</td>
</tr>
</tbody>
</table>

**Figure 1** Factors influencing the reasonableness of prescribing decisions.8
**Box B**  Example of a patient information leaflet about the use of medicines outside their licence

<table>
<thead>
<tr>
<th><strong>Use of Medicines Outside their Licence</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>This leaflet contains important information about your medicines, so please read it carefully.</td>
</tr>
<tr>
<td>Medicines prescribed by your doctor or bought over-the-counter from a pharmacist are licensed for use by the Medicines and Healthcare products Regulatory Agency (MHRA).</td>
</tr>
<tr>
<td>The product licence (or 'marketing authorization') specifies the conditions for which the medicine should be used and how it should be given.</td>
</tr>
<tr>
<td>Patient Information Leaflets (PILs) which accompany the medicines reflect the product licence.</td>
</tr>
<tr>
<td>Medicines are often used for conditions or in ways that are not specified on the product licence. This is true for a lot of medicines used in palliative care.</td>
</tr>
<tr>
<td>Your doctor will use medicines outside the product licence only when there is research and experience to back up such use.</td>
</tr>
<tr>
<td>Medicines used very successfully outside the product licence include some antidepressants and anti-epileptics (anticonvulsants) which are used to relieve some types of pain.</td>
</tr>
<tr>
<td>Also, instead of being injected into a vein or muscle, medicines are often injected subcutaneously (under the skin) because this is more comfortable and convenient for you.</td>
</tr>
<tr>
<td>When a medicine is used outside the product licence, the information on the PIL may not be relevant to how you are taking the medicine.</td>
</tr>
<tr>
<td>If you find this confusing, your doctor or pharmacist will be happy to help.</td>
</tr>
<tr>
<td>Alternatively, contact:</td>
</tr>
<tr>
<td>Dr/Nurse ..........................................................</td>
</tr>
<tr>
<td>Hospital ..........................................................</td>
</tr>
<tr>
<td>..........................................................</td>
</tr>
<tr>
<td>Tel ..........................................................</td>
</tr>
</tbody>
</table>
The recommendations of the Association for Palliative Medicine and the Pain Society

The use of drugs beyond licence in palliative care and pain management

1 This statement should be seen as reflecting the views of a responsible body of opinion within the clinical specialties of palliative medicine and pain management.

2 The use of drugs beyond licence should be seen as a legitimate aspect of clinical practice.

3 The use of drugs beyond licence in palliative care and pain management practice is currently both necessary and common.

4 Choice of treatment requires partnership between patients and health professionals, and informed consent should be obtained, whenever possible, before prescribing any drug. Patients should be informed of any identifiable risks and details of any information given should be recorded. It is often unnecessary to take additional steps when recommending drugs beyond licence.

5 Patients, carers and health professionals need accurate, clear and specific information that meets their needs. The Association for Palliative Medicine and the Pain Society should work in conjunction with pharmaceutical companies to design accurate information for patients and their carers about the use of drugs beyond licence.

6 Health professionals involved in prescribing, dispensing and administering drugs beyond licence should select those drugs that offer the best balance of benefit against harm for any given patient.

7 Health professionals should inform, change and monitor their practice with regard to drugs beyond licence in the light of evidence from audit and published research.

8 The Department of Health should work with health professionals and the pharmaceutical industry to enable and encourage the extension of product licences where there is evidence of benefit in circumstances of defined clinical need.

9 Organizations providing palliative care and pain management services should support therapeutic practices that are underpinned by evidence and advocated by a responsible body of professional opinion.

10 There is urgent need for the Department of Health to assist healthcare professionals to formulate national frameworks, guidelines and standards for the use of drugs beyond licence. The Pain Society and the Association for Palliative Medicine should work with the Department of Health, NHS Trusts, voluntary organizations and the pharmaceutical industry to design accurate information for staff, patients and their carers in clinical areas where drugs are used beyond their licence (off-label). Practical support is necessary to facilitate and expedite surveillance and audit which are essential to develop this initiative.


Following a European Union directive, all drugs marketed in Europe are now known by their recommended International Non-proprietary Names (rINNs). Previously, in the UK, drugs were known by their British Approved Names (BANs). Differences between BANs and rINNs are listed in Table 1.

Where United States Adopted Names (USANs) differ from rINNs and BANs, the USANs have also been included to aid understanding of the US literature.

With compound preparations such as codeine and paracetamol (USAN acetaminophen) or diphenoxylate and atropine, the UK conventional name is shown in Table 2, e.g. co-codamol or co-phenotrope.

### Table 1 Drug names relevant to palliative care for which the rINN, BAN and/or USAN differ

<table>
<thead>
<tr>
<th>rINN</th>
<th>BAN</th>
<th>USAN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alimemazine</td>
<td>Trimeprazine</td>
<td>Trimeprazine</td>
</tr>
<tr>
<td>Aluminium</td>
<td></td>
<td>Aluminum</td>
</tr>
<tr>
<td>Amfetamine</td>
<td></td>
<td>Amphetamine</td>
</tr>
<tr>
<td>Amobarbital</td>
<td>Amylobarbitone</td>
<td></td>
</tr>
<tr>
<td>Beclometasone</td>
<td>Beclomethasone</td>
<td>Beclomethasone</td>
</tr>
<tr>
<td>Bendroflumethiazide</td>
<td>Bendrofluzide</td>
<td>Bendroflumethiazide</td>
</tr>
<tr>
<td>Benorilate</td>
<td>Benorylate</td>
<td></td>
</tr>
<tr>
<td>Benzathine benzylpenicillin</td>
<td>Benzathine penicillin</td>
<td>Benzathine penicillin</td>
</tr>
<tr>
<td>Benzatropine</td>
<td>Benztropine</td>
<td>Benztropine</td>
</tr>
<tr>
<td>Benzylnpenicillin</td>
<td></td>
<td>Penicillin G</td>
</tr>
<tr>
<td>Calcitonin (salmon)</td>
<td>Salcatonin</td>
<td>Calcitonin</td>
</tr>
<tr>
<td>Carmellose</td>
<td></td>
<td>Carboxymethylcellulose</td>
</tr>
<tr>
<td>Cefalexin (etc.)</td>
<td>Cephalexin (etc.)</td>
<td>Cephalexin (etc.)</td>
</tr>
<tr>
<td>Chlorphenamine</td>
<td>Chlorpheniramne</td>
<td>Chlorpheniramne</td>
</tr>
<tr>
<td>Ciclosporin</td>
<td>Cyclosporin</td>
<td>Cyclosporine</td>
</tr>
<tr>
<td>Clomethiazole</td>
<td>Chlormethiazole</td>
<td></td>
</tr>
<tr>
<td>Colestyramine</td>
<td>Cholestyramine</td>
<td></td>
</tr>
<tr>
<td>Dantron</td>
<td>Danthron</td>
<td></td>
</tr>
<tr>
<td>Dexamfetamine</td>
<td>Dexamphetamine</td>
<td>Dextroamphetamine</td>
</tr>
<tr>
<td>Dextropropoxyphene</td>
<td></td>
<td>Propoxyphene</td>
</tr>
<tr>
<td>Dicycloverine</td>
<td>Dicyclomine</td>
<td></td>
</tr>
<tr>
<td>Dienestrol</td>
<td>Dienoestrol</td>
<td></td>
</tr>
<tr>
<td>Diethylstilbestrol</td>
<td>Stilboestrol</td>
<td>Diethylstilbestrol</td>
</tr>
<tr>
<td>Dimeticone</td>
<td>Dimethicone</td>
<td>Dimethicone</td>
</tr>
<tr>
<td>Dosulepin</td>
<td>Dothiepin</td>
<td>Dothiepin</td>
</tr>
<tr>
<td>Estradiol</td>
<td>Oestradiol</td>
<td></td>
</tr>
<tr>
<td>Etamsylate</td>
<td>Etmamsylate</td>
<td></td>
</tr>
<tr>
<td>Furosemide</td>
<td>Frusemide</td>
<td></td>
</tr>
<tr>
<td>Gilbenclamide</td>
<td></td>
<td>Glyburide</td>
</tr>
<tr>
<td>Glycerid trinitrate</td>
<td></td>
<td>Nitroglycerin</td>
</tr>
<tr>
<td>Glycopyronium</td>
<td>Glycopyrrolate</td>
<td></td>
</tr>
<tr>
<td>Hyoscine</td>
<td></td>
<td>Scopolamine</td>
</tr>
<tr>
<td>Indometacin</td>
<td>Indomethacin</td>
<td>Indomethacin</td>
</tr>
<tr>
<td>Isoprenaline</td>
<td>Ispaghula</td>
<td>Isoproterenol</td>
</tr>
<tr>
<td>Levomepromazine</td>
<td>Methotrimeprazine</td>
<td></td>
</tr>
<tr>
<td>Levothyroxine</td>
<td>Thyroxine</td>
<td></td>
</tr>
<tr>
<td>Lidocaine</td>
<td>Lignocaine</td>
<td></td>
</tr>
</tbody>
</table>
Table 1  Continued

<table>
<thead>
<tr>
<th>rINN</th>
<th>BAN</th>
<th>USAN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liquid paraffin</td>
<td>Mineral oil</td>
<td></td>
</tr>
<tr>
<td>Meclozine</td>
<td>Meclizine</td>
<td></td>
</tr>
<tr>
<td>Methenamine hippurate</td>
<td>Hexamine hippurate</td>
<td></td>
</tr>
<tr>
<td>Mitoxantrone</td>
<td>Mitozantrone</td>
<td></td>
</tr>
<tr>
<td>Oxetacaine</td>
<td>Oxethazine</td>
<td></td>
</tr>
<tr>
<td>Paracetamol</td>
<td>Acetaminophen</td>
<td></td>
</tr>
<tr>
<td>Pethidine</td>
<td>Meperidine</td>
<td></td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>Phenobarbitone</td>
<td></td>
</tr>
<tr>
<td>Phenoxymethylpenicillin</td>
<td>Penicillin V</td>
<td></td>
</tr>
<tr>
<td>Phytomenadione</td>
<td>Phytanadione</td>
<td></td>
</tr>
<tr>
<td>Procaine benzylpenicillin</td>
<td>Procaine penicillin</td>
<td></td>
</tr>
<tr>
<td>Retinol</td>
<td>Vitamin A</td>
<td></td>
</tr>
<tr>
<td>Rifampicin</td>
<td>Rifampin</td>
<td></td>
</tr>
<tr>
<td>Salbutamol</td>
<td>Albuterol</td>
<td></td>
</tr>
<tr>
<td>Simeticone&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Simethicone</td>
<td></td>
</tr>
<tr>
<td>Sodium cromoglicate</td>
<td>Sodium cromoglycate</td>
<td>Cromolyn sodium</td>
</tr>
<tr>
<td>Sulfasalazine</td>
<td>Sulphasalazine</td>
<td></td>
</tr>
<tr>
<td>Sulfathiazole</td>
<td>Sulphathiazole</td>
<td></td>
</tr>
<tr>
<td>Sulfonamides</td>
<td>Sulphonamides</td>
<td></td>
</tr>
<tr>
<td>Tetracaine</td>
<td>Amethocaine</td>
<td></td>
</tr>
<tr>
<td>Trihexyphenidyl</td>
<td>Trihexyphenidyl</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> silica-activated dimeticone; known in some countries as activated dimethylpolysiloxane.

Table 2  UK names for compound preparations

<table>
<thead>
<tr>
<th>Contents</th>
<th>UK name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin-clavulanate</td>
<td>Co-amoxiclav</td>
</tr>
<tr>
<td>Diphenoxylate-atropine</td>
<td>Co-phenotrope</td>
</tr>
<tr>
<td>Magnesium hydroxide-aluminium&lt;sup&gt;a&lt;/sup&gt; hydroxide</td>
<td>Co-magaldrox</td>
</tr>
<tr>
<td>Paracetamol&lt;sup&gt;b&lt;/sup&gt;-codeine phosphate</td>
<td>Co-codamol</td>
</tr>
<tr>
<td>Paracetamol-dextropropoxyphene&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Co-proxamol</td>
</tr>
<tr>
<td>Paracetamol-dihydrocodeine</td>
<td>Co-dydramol</td>
</tr>
<tr>
<td>Sulfamethoxazole-trimethoprim</td>
<td>Co-trimoxazole</td>
</tr>
</tbody>
</table>

<sup>a</sup> aluminum (USAN)
<sup>b</sup> acetaminophen (USAN)
<sup>c</sup> propoxyphene (USAN).
LIST OF ABBREVIATIONS

Drug administration

Table 3  Drug administration times

<table>
<thead>
<tr>
<th>Times</th>
<th>UK</th>
<th>Latin</th>
<th>USA</th>
<th>Latin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Once daily</td>
<td>o.d.</td>
<td>omni die</td>
<td>q.d.</td>
<td>quaque die</td>
</tr>
<tr>
<td>Every morning</td>
<td>o.m.</td>
<td>omni mane</td>
<td>q.a.m.</td>
<td>quaque ante meridiem</td>
</tr>
<tr>
<td>At bedtime</td>
<td>o.n.</td>
<td>omni nocte</td>
<td>h.s.</td>
<td>hora somni</td>
</tr>
<tr>
<td>Twice daily</td>
<td>b.d.</td>
<td>bis die</td>
<td>b.i.d.</td>
<td>bis in die</td>
</tr>
<tr>
<td>Three times daily</td>
<td>t.d.s.</td>
<td>ter die sumendus</td>
<td>t.i.d.</td>
<td>ter in die</td>
</tr>
<tr>
<td>Four times daily</td>
<td>q.d.s.</td>
<td>quarta die sumendus</td>
<td>q.i.d.</td>
<td>quarta in die</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</td>
<td>p.r.n.</td>
<td>pro re nata</td>
<td>p.r.n.</td>
<td>pro re nata</td>
</tr>
<tr>
<td>(as needed/required)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Give immediately</td>
<td>stat</td>
<td></td>
<td></td>
<td>stat</td>
</tr>
</tbody>
</table>

a.c. ante cibum (before food)
amp ampoule containing a single dose (cf. vial)
CD preparation subject to prescription requirements under the Misuse of Drugs Act (UK); for regulations see BNF
CIVI continuous intravenous infusion
CSCI continuous subcutaneous infusion
e/c enteric-coated
ED epidural
IM intramuscular
IT intrathecal
IV intravenous
IVI intravenous infusion
m/r modified-release; alternatives, slow-release, sustained-release, controlled-release, extended-release
NHS not prescribable on NHS prescriptions
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
TD transdermal
vial sterile container with a rubber bung containing either a single or multiple doses (cf. amp)
WFI water for injections
General

* specialist use only
† unlicensed use
BNF British National Formulary
BP British Pharmacopoeia
CHM Commission on Human Medicines
CSM Committee on Safety of Medicines (now part of CHM)
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
MCA Medicines Control Agency (now MHRA)
MHRA Medicines and Healthcare products Regulatory Agency (formerly MCA)
NICE National Institute for Health and Clinical Excellence
NPF Nurse Prescribers’ Formulary
PCS/PCU Palliative care service/unit
PIL Patient Information Leaflet
rINN recommended International Non-proprietary Name
SPC Summary of Product Characteristics
UK United Kingdom
USA United States of America
VAS visual analogue scale, 0–100mm
WHO World Health Organization

Medical

ACD anaemia 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
FRC functional residual capacity
FSH follicle-stimulating hormone
FVC forced vital capacity of lungs
GABA gamma-aminobutyric acid
GI gastro-intestinal
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
\( \mu \) mu-opioid (receptor)
NaSSA noradrenergic and specific serotonergic antidepressant
NDRI noradrenaline (norepinephrine) 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 noradrenaline (norepinephrine) re-uptake inhibitor
NSAID non-steroidal anti-inflammatory drug
PaCO\(_2\) arterial partial pressure of carbon dioxide
PaO\(_2\) arterial partial pressure of oxygen
PCA patient-controlled analgesia
PE pulmonary embolus/embolism
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 noradrenaline (norepinephrine) re-uptake inhibitor
SSRI selective serotonin re-uptake inhibitor
TCA tricyclic antidepressant
TIBC total iron-binding capacity; alternative, plasma transferrin concentration
TiCO transfer factor of the lung for carbon monoxide
UTI urinary tract infection
VIP vaso-active intestinal polypeptide

**Units**

- cm centimetre(s)
- cps cycles per sec
- dL decilitre(s)
- g gram(s)
- Gy Gray(s), a measure of radiation
- h hour(s)
- Hg mercury
- kcal kilocalories
- kg kilogram(s)
- L litre(s)
- mg milligram(s)
- micromol micromole(s)
- ml millilitre(s)
- mm millimetre(s)
- mmol millimole(s)
- min minute(s)
- mosmol milli-osmole(s)
- msec millisecond
- nm nanometre(s)
- nmol nanomole(s); alternative, nM
- sec second(s)