

# PCF3

# PALLIATIVE CARE FORMULARY

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PCF1 1998

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# CONTENTS

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Preface	ix
Acknowledgements	x
Summary of main changes in PCF3	xi
www.palliativedrugs.com	xii
Getting the most out of PCF3	xiii
Using licensed drugs for unlicensed purposes	xvii
Drug names	xxii
List of abbreviations	xxiv
<b>Part I Drug Monographs</b>	
<b>1 Gastro-intestinal system</b>	<b>1</b>
Antacids	1
Antimuscarinics (anticholinergics)	4
Prokinetics	13
H <sub>2</sub> -receptor antagonists	15
Misoprostol	18
Proton pump inhibitors	19
Loperamide	23
Laxatives	24
Products for haemorrhoids	39
Pancreatin	40
<b>2 Cardiovascular system</b>	<b>41</b>
Furosemide	41
Spironolactone	44
Systemic local anaesthetics	46
*Clonidine	52
Glyceryl trinitrate	55
Nifedipine	57
Low molecular weight heparin (LMWH)	59
Etamsylate	75
Antifibrinolytic drugs	77
<b>3 Respiratory system</b>	<b>81</b>
Bronchodilators	81
Inhaled corticosteroids	97

	Oxygen	100
	Drugs for cough	108
4	Central nervous system	115
	Psychotropics	115
	Benzodiazepines	116
	Typical antipsychotics	128
	Atypical antipsychotics	135
	Antidepressants	142
	Psychostimulants	167
	Cannabinoids	171
	Anti-emetics	175
	Hyoscine hydrobromide	190
	Anti-epileptics	192
	Orphenadrine	207
5	Analgesics	209
	Principles of use of analgesics	209
	Adjuvant analgesics	212
	Paracetamol	218
	Nefopam	221
	Non-steroidal anti-inflammatory drugs (NSAIDs)	223
	Weak opioids	252
	Strong opioids	263
	Opioid antagonists	319
6	Infections	329
	Antibiotics in palliative care	329
	Oropharyngeal candidosis	331
	Metronidazole	334
	Urinary tract infections	336
	Acute inflammatory episodes in a lymphoedematous limb	338
	Ascending cholangitis	343
	<i>Clostridium difficile</i> diarrhoea	343
	<i>Helicobacter pylori</i> gastritis	345
7	Endocrine system and immunomodulation	349
	Bisphosphonates	349
	Systemic corticosteroids	362
	Demeclocycline	368
	Desmopressin	370
	Drugs for diabetes mellitus	371
	*Octreotide	375
	Progestogens	379

	Danazol	383
	*Thalidomide	385
8	Urinary tract disorders	389
	Tamsulosin	389
	Oxybutynin	390
	Methenamine hippurate and nitrofurantoin	392
	Cranberry juice	393
	Catheter patency solutions	394
	Discoloured urine	395
9	Nutrition and blood	397
	Anaemia	397
	Ascorbic acid (vitamin C)	403
	Phytomenadione (vitamin K <sub>1</sub> )	404
	Potassium	405
	Magnesium	407
10	Musculoskeletal and joint diseases	411
	Depot corticosteroid injections	411
	Rubefaciants and other topical preparations	412
	Skeletal muscle relaxants	414
11	Ear, nose and oropharynx	421
	Mouthwashes	421
	Artificial saliva and topical saliva stimulants	422
	Pilocarpine	424
	Drugs for oral inflammation and ulceration	425
	Cerumenolytics	430
12	Skin	431
	Emollients	431
	Topical antipruritics	436
	Barrier preparations	438
	Topical cleansing agents and disinfectants	439
13	Anaesthesia	441
	Glycopyrronium	441
	*Ketamine	443
	*Propofol	449
Part 2 General Topics		
14	Guidance about prescribing in palliative care	453
15	Opioid dose conversion ratios	465
16	Management of postoperative pain in opioid-dependent patients	473
17	Analgesic drugs and fitness to drive	475

18	Continuous subcutaneous infusions	479
19	Spinal analgesia	493
20	Administering drugs via enteral feeding tubes	503
21	Nebulized drugs	525
22	Prolongation of the QT interval in palliative care	531
23	Cytochrome P450	535
24	Drug-induced movement disorders	545
25	Anaphylaxis	549
26	Oral nutritional supplements	551
Appendices		
A1	Synopsis of pharmacokinetic data	563
A2	Special orders and named patient supplies	577
A3	Taking controlled and prescription drugs to other countries	579
A4	Compatibility charts	583
	Index	599

# PREFACE

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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@palliatedrugs.com](mailto:hq@palliatedrugs.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

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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 post-operative 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.

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# SUMMARY OF MAIN CHANGES IN PCF3

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## 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.

# www.palliativedrugs.com

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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](http://www.palliativebooks.com)).

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

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# GETTING THE MOST OUT OF PCF3

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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, 4<sup>th</sup> edition 2009, palliatedrugs.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.<sup>1</sup> A modified system is used by NICE to indicate the level of evidence on which recommendations are based (Box A).<sup>2</sup>

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

- *critical*, data unique to the individual in question (e.g. personal choice) and societal/cultural factors (e.g. financial and logistic considerations).<sup>3</sup>
- 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<sup>2,4,5</sup>

Level	Type of evidence	Grade	Evidence
I	Evidence obtained from a single randomized controlled trial or a meta-analysis of randomized controlled trials	A	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
IIa	Evidence obtained from at least one well-designed controlled study without randomization	B	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
IIb	Evidence obtained from at least one other well-designed quasi-experimental study		
III	Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies		
IV	Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities	C	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
		Good Practice Point (GPP)	Recommended good practice based on the clinical experience of the Guidelines Development Group (GDG)
NICE	Evidence from NICE guideline or technology appraisal	NICE	Evidence from NICE guideline or technology appraisal

### 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.<sup>6</sup> 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.<sup>6</sup>

### 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 bio-availability and efficacy.<sup>7</sup> 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.<sup>8</sup>

### 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](http://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/](http://www.jr2.ox.ac.uk/bandolier/)

*British National Formulary*: two editions/year, March and September. Latest edition available from [www.bnf.org.uk/bnf/](http://www.bnf.org.uk/bnf/)  
Free registration required.

Current Problems in Pharmacovigilance: available via MHRA website at [www.mhra.gov.uk/home/idcplg?ldcService=SS\\_GET\\_PAGE&nodId=368](http://www.mhra.gov.uk/home/idcplg?ldcService=SS_GET_PAGE&nodId=368)

MeReC Bulletin: available via National Prescribing Centre website at [www.npc.co.uk/merec\\_bulletins.htm](http://www.npc.co.uk/merec_bulletins.htm)

*Pharmaceutical Journal* (official weekly journal of the Royal Pharmaceutical Society of Great Britain): available from [www.pjonline.com](http://www.pjonline.com)

Site also gives access to Hospital Pharmacist (London).

UK manufacturers' SPCs: available from [www.medicines.org.uk](http://www.medicines.org.uk)

The Cochrane Library: available from [www3.interscience.wiley.com/cgi-bin/mrwhome/106568753/HOME](http://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](http://www.library.nhs.uk/Default.aspx)

- 1 Agency for Health Care Policy and Research (1992) Acute pain management, operative or medical procedures and trauma 92-0032. In: *Clinical Practice Guideline Quick Reference Guide for Clinicians*. AHCPH Publications, Rockville, Maryland, USA, pp. 1–22.
- 2 NICE (2004) *Depression: Management of depression in primary and secondary care*. In: National Clinical Practice Guideline Number 23. National Institute for Clinical Excellence. Available from: [www.nice.org.uk/page.aspx?o=236667](http://www.nice.org.uk/page.aspx?o=236667)
- 3 Aoun SM and Kristjanson LJ (2005) Challenging the framework for evidence in palliative care research. *Palliative Medicine*. **19**: 461–465.
- 4 DoH (1996) *Clinical Guidelines: Using Clinical Guidelines to Improve Patient Care Within the NHS*. Department of Health: NHS Executive, Leeds.
- 5 Eccles M and Mason J (2001) How to develop cost-conscious guidelines. *Health Technology Assessment*. **5** (16).
- 6 Angell M (2004) *The Truth About the Drug Companies: how they deceive us and what to do about it*. Random House, New York.
- 7 National Prescribing Centre (2000) Modified-release preparations. *MeReC Bulletin*. **11**: 13–16.
- 8 Smith J (2004) *Building a Safer NHS for Patients – Improving Medication Safety*. Department of Health, London, pp. 105–111. Available from: [www.dh.gov.uk/assetRoot/04/08/49/61/04084961.pdf](http://www.dh.gov.uk/assetRoot/04/08/49/61/04084961.pdf)

# USING LICENSED DRUGS FOR UNLICENSED PURPOSES

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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,<sup>1,2</sup> 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<sup>3</sup> and administered by nurses or midwives.<sup>4</sup>

## 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 (EMA). 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.<sup>5</sup>

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.<sup>6</sup>

The responsibility for the consequences of these actions lies with the prescriber.<sup>5-7</sup> 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.

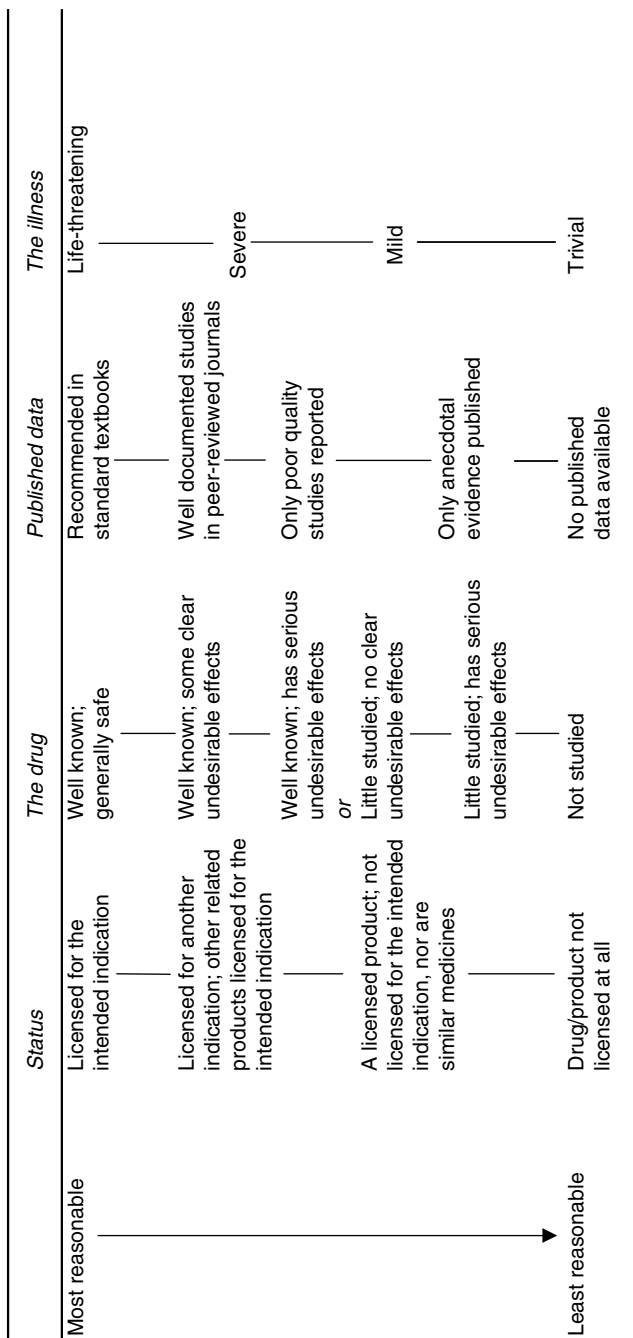
Prescription of a drug (whether licensed use/route or not) requires the prescriber, in the light of published evidence, to balance both the potential good and the potential harm which might ensue. Prescribers have a duty to act with reasonable care and skill in a manner consistent with the practice of 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).<sup>8</sup> 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:<sup>4,6-9</sup>

- 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.<sup>10</sup> 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).



**Figure 1** Factors influencing the reasonableness of prescribing decisions.<sup>8</sup>

**Box B** Example of a patient information leaflet about the use of medicines outside their licence

**Use of Medicines Outside their Licence**

This leaflet contains important information about your medicines, so please read it carefully.

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).

The product licence (or 'marketing authorization') specifies the conditions for which the medicine should be used and how it should be given.

Patient Information Leaflets (PILs) which accompany the medicines reflect the product licence.

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.

Your doctor will use medicines outside the product licence only when there is research and experience to back up such use.

Medicines used very successfully outside the product licence include some antidepressants and anti-epileptics (anticonvulsants) which are used to relieve some types of pain.

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.

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.

If you find this confusing, your doctor or pharmacist will be happy to help.  
Alternatively, contact:

Dr/Nurse .....  
Hospital .....  
.....  
.....  
Tel .....

**Box C** 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.

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- 3 Royal Pharmaceutical Society of Great Britain (2007) *Fitness to practise and legal affairs directorate fact sheet: five. The use of unlicensed medicines in pharmacy*. Pharmaceutical Society of Great Britain. Available from: [www.rpsgb.org/pdfs/factsheet5.pdf](http://www.rpsgb.org/pdfs/factsheet5.pdf)
- 4 DTB (1992) Prescribing unlicensed drugs or using drugs for unlicensed indications. *Drug and Therapeutics Bulletin*. **30**: 97–99.
- 5 DoH (2005) *Supplementary prescribing by nurses, pharmacists, chiropodists/podiatrists, physiotherapists and radiographers within the NHS in England: a guide for implementation*. HMSO, London. Available from: [www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH\\_4110032](http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4110032)
- 6 DoH (2006) *Improving patients' access to medicines: a guide to implementing nurse and pharmacist independent prescribing within the NHS in England*. HMSO, London. Available from: [www.dh.gov.uk/assetRoot/04/13/37/47/04133747.pdf](http://www.dh.gov.uk/assetRoot/04/13/37/47/04133747.pdf)
- 7 Tomkins C (1988) Drugs without a product licence. *Journal of the Medical Defence Union*. **Spring**: 7.
- 8 Ferner R (1996) Prescribing licensed medicines for unlicensed indications. *Prescribers' Journal*. **36**: 73–79.
- 9 Cohen P (1997) Off-label use of prescription drugs: legal, clinical and policy considerations. *European Journal of Anaesthesiology*. **14**: 231–235.
- 10 Pavis H and Wilcock A (2001) Prescribing of drugs for use outside their licence in palliative care: survey of specialists in the United Kingdom. *British Medical Journal*. **323**: 484–485.

# DRUG NAMES

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

rINN	BAN	USAN
Alimemazine	Trimeprazine	Trimeprazine
Aluminium		Aluminium
Amfetamine		Amphetamine
Amobarbital	Amylobarbitone	
Beclometasone	Beclomethasone	Beclomethasone
Bendroflumethiazide	Bendrofluazide	Bendroflumethiazide
Benorilate	Benorylate	
Benzathine benzylpenicillin	Benzathine penicillin	Benzathine penicillin
Benzatropine	Benztropine	Benztropine
Benzylpenicillin		Penicillin G
Calcitonin (salmon)	Salcatonin	Calcitonin
Carmellose		Carboxymethylcellulose
Cefalexin (etc.)	Cephalexin (etc.)	Cephalexin (etc.)
Chlorphenamine	Chlorpheniramine	Chlorpheniramine
Ciclosporin	Cyclosporin	Cyclosporine
Clomethiazole	Chlormethiazole	
Colestyramine	Cholestyramine	Cholestyramine
Dantron	Danthron	
Dexamfetamine	Dexamphetamine	Dextroamphetamine
Dextropropoxyphene		Propoxyphene
Dicycloverine	Dicyclomine	Dicyclomine
Dienestrol	Dienoestrol	
Diethylstilbestrol	Stilboestrol	Diethylstilbestrol
Dimeticone	Dimethicone	Dimethicone
Dosulepin	Dothiepin	Dothiepin
Estradiol	Oestradiol	
Etamsylate	Ethamsylate	
Furosemide	Frusemide	
Glibenclamide		Glyburide
Glyceril trinitrate		Nitroglycerin
Glycopyrronium		Glycopyrrolate
Hyoscine		Scopolamine
Indometacin	Indomethacin	Indomethacin
Isoprenaline		Isoproterenol
	Ispaghula	Psyllium
Levomepromazine	Methotrimeprazine	
Levothyroxine	Thyroxine	
Lidocaine	Lignocaine	

**Table 1** Continued

<i>r</i> INN	BAN	USAN
Liquid paraffin		Mineral oil
Meclozine		Meclizine
Methenamine hippurate	Hexamine hippurate	
Mitoxantrone	Mitozantrone	
Oxetacaine	Oxethazine	Oxethazine
Paracetamol		Acetaminophen
Pethidine		Meperidine
Phenobarbital	Phenobarbitone	
Phenoxymethylpenicillin		Penicillin V
Phytomenadione		Phytonadione
Procaine benzylpenicillin	Procaine penicillin	Procaine penicillin
Retinol	Vitamin A	Vitamin A
Rifampicin		Rifampin
Salbutamol		Albuterol
Simeticone <sup>a</sup>	Simethicone	Simethicone
Sodium cromoglicate	Sodium cromoglycate	Cromolyn sodium
Sulfasalazine	Sulphasalazine	
Sulfathiazole	Sulphathiazole	
Sulfonamides	Sulphonamides	
Tetracaine	Amethocaine	
Trihexyphenidyl	Benzhexol	Trihexyphenidyl

a. silica-activated dimeticone; known in some countries as activated dimethylpolysiloxane.

**Table 2** UK names for compound preparations

Contents	UK name
Amoxicillin-clavulanate	Co-amoxiclav
Diphenoxylate-atropine	Co-phenotrope
Magnesium hydroxide-aluminium <sup>a</sup> hydroxide	Co-magaldrox
Paracetamol <sup>b</sup> -codeine phosphate	Co-codamol
Paracetamol-dextropropoxyphene <sup>c</sup>	Co-proxamol
Paracetamol-dihydrocodeine	Co-dydramol
Sulfamethoxazole-trimethoprim	Co-trimoxazole

a. aluminum (USAN)

b. acetaminophen (USAN)

c. propoxyphene (USAN).

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# LIST OF ABBREVIATIONS

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## Drug administration

**Table 3** Drug administration times

<i>Times</i>	<i>UK</i>	<i>Latin</i>	<i>USA</i>	<i>Latin</i>
Once daily	o.d.	<i>omni die</i>	q.d.	<i>quaque die</i>
Every morning	o.m.	<i>omni mane</i>	q.a.m.	<i>quaque ante meridiem</i>
At bedtime	o.n.	<i>omni nocte</i>	h.s.	<i>hora somni</i>
Twice daily	b.d.	<i>bis die</i>	b.i.d.	<i>bis in die</i>
Three times daily	t.d.s.	<i>ter die sumendus</i>	t.i.d.	<i>ter in die</i>
Four times daily	q.d.s.	<i>quarta die sumendus</i>	q.i.d.	<i>quarta in die</i>
Every 4 hours etc.	q4h	<i>quaque quarta hora</i>	q4h	<i>quaque quarta hora</i>
Rescue medication (as needed/required)	p.r.n.	<i>pro re nata</i>	p.r.n.	<i>pro re nata</i>
Give immediately	stat		stat	

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 <i>BNF</i>
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)
EMA	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
$\beta_2$	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
$\delta$	delta-opioid (receptor)
D <sub>2</sub>	dopamine type 2 (receptor)
DIC	disseminated intravascular coagulation
DVT	deep vein thrombosis
ECG	electrocardiogram
ECT	electroconvulsive therapy
FEV <sub>1</sub>	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
H <sub>1</sub> , H <sub>2</sub>	histamine type 1, type 2 (receptor)
Ig	immunoglobulin
INR	international normalized ratio
$\kappa$	kappa-opioid (receptor)
LABA	long-acting $\beta_2$ -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	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
NTT	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 <sub>2</sub>	arterial partial pressure of carbon dioxide
PaO <sub>2</sub>	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
Tl <sub>CO</sub>	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)