# PCF

# PALLIATIVE CARE FORMULARY

Canadian edition

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# EDITORIAL STAFF

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# PREFACE

We are pleased to introduce the Canadian edition of the *Palliative Care Formulary* (*PCF*) to our readers. Although written primarily with cancer patients in mind, the contents of *PCF* are more widely applicable to any form of end-stage progressive disease. Thus, sections relating to general medical topics, e.g. COPD, diabetes mellitus, are important parts of the book.

*PCF* 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).

The Canadian edition of *PCF* is one of a growing family of country-specific editions. The parent *PCF* is produced in the UK, and is mirrored in the United States of America by the *Hospice and Palliative Care Formulary* (*HPCF*$_{USA}$). There are also German, Italian, and Polish editions. In each country, the target audience remains the same, namely doctors, pharmacists, and other health professionals caring for patients receiving palliative care.

As always, readers should satisfy themselves as to the appropriateness of any information in *PCF* before applying it in practice. *PCF* often refers to uses of drugs which are outside the scope of their marketing licence. The use of drugs in this way has implications for the prescriber, and is discussed on p.xvii.

Editors-in-chief
*March 2010*

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Chapter 4, Ken Gillman (serotonin toxicity);
Chapter 5, Jo Chambers, Felicity Murtagh (renal effects of opioids);
Chapter 6, Andrew Davies (candidosis); Vaughan Keeley (AIEs); Tony Tavenor (*Helicobacter pylori* gastritis);
Chapter 12, Joe Coffey, Russell Kilpatrick;
Chapter 14, Lynda Brook, Susie Lapwood (prescribing for children); Richard Burden, Judith Palmer (prescribing in renal impairment), Rachel Howard (drug concentration interpretation);
Chapter 16, Roger Knaggs, John MacKenzie, Jim Mason;
Chapter 17, Judith Bedford-Jones, Alison Gardner;
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# ABOUT www.palliativedrugs.com

We encourage readers of *PCF* 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 *PCF* 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.

# MONOGRAPHS AVAILABLE ELSEWHERE

The contents of this edition of the *Palliative Care Formulary* are mostly restricted to drugs currently available and used in palliative care in Canada. Monographs of other drugs used in palliative care in the UK and/or the USA are listed below.

**www.palliativedrugs.com and *Palliative Care Formulary* 3rd edition (PCF)**

Chapter 1 GI: propantheline
Chapter 2 Cardiovascular: etamsylate
Chapter 3 Respiratory: chemical mucolytics (carbocisteine, mecysteine)
Chapter 4 CNS: duloxetine
orphenadrine
Chapter 5 Analgesics: nefopam
flurbiprofen
dihydrocodeine
diamorphine
buprenorphine (with guidelines for TD patches)
Chapter 7 Endocrine: ibandronic acid
demeclocycline
Chapter 9 Nutrition and blood: epoetin
Chapter 26 Oral nutritional supplements (products are UK-specific).

***Hospice and Palliative Care Formulary* 2nd edition (HPCFUSA)**

Pharmaco-economics in the USA
Chapter 1 GI: propantheline
Chapter 4 CNS: chloral hydrate
chlorpromazine
quetiapine
duloxetine
orphenadrine
Chapter 5 Analgesics: choline magnesium salicylate
hydrocodone
buprenorphine
nalbuphine
Chapter 7 Endocrine: demeclocycline
Chapter 9 Nutrition and blood: epoetin
Appendix: Medicare/Medicaid conditions of hospice participation.

# GETTING THE MOST OUT OF PCF

The literature on the pharmacology of pain and other symptom management in end-stage disease is growing continually, and it is impossible for anyone to be totally familiar with it. This is where *PCF* comes into its own as a major accessible resource for prescribing clinicians involved in palliative care.

*PCF* 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.

Drugs marked with an asterisk (*) should generally be used only by, or after consultation with, a specialist palliative care service.

*PCF* 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. In Canada, *Symptom Relief in Palliative Care* (Dean et al 2006, Radcliffe Publishing, Oxford; ISBN 1 85775 6290) should be seen as the companion book to *PCF*.

Readers should also be aware of *Opioids in Cancer Pain* 2nd edition (Davis *et al.* 2009, OUP). This provides a wealth of additional data, and will be particularly useful for clinical teachers and Palliative Medicine Fellows.

## Drugs costs

The prices listed in *PCF* for both prescription drugs and OTC products are derived from current wholesale prices from a national wholesaler, and are given in Canadian dollars unless stated otherwise. A common mark-up percentage was applied to the wholesale pricing for OTC products to provide an anticipated market price. Variation will occur, dependent upon local retail market conditions. Further, drugs bought on contract are generally much cheaper.

Prices under $5 have been rounded up to a half dollar; prices over $5 are rounded up to a full dollar. Prices change over time, and the prices given in this edition of *PCF* should be regarded as a rough guide rather than currently exact.

Drugs included in provincial and territorial government prescription drug programmes vary across the country. It may be necessary to prescribe an alternative if a drug recommended in *PCF* is not available through the local programme. However, both third party insurers and government programmes may cover the cost of a particular drug if the prescribing physician requests a special authorization for a named patient.

## Indications, cautions, and contra-indications

Indications, cautions and contra-indications listed in Product Monographs sometimes vary between different manufacturers of the same drug, and between the same manufacturer in different countries. In an international work of this kind, there inevitably is a degree of 'syncretism' and selection. Thus, when using a drug for the first time, the prescriber should familiarize themselves with the indications, cautions, and contra-indications as listed in their national Product Monograph. Be aware that a caution in some countries becomes a contra-indication in another, and *vice versa*.

In this edition of *PCF*, we have *not* included universal contra-indications (e.g. history of hypersensitivity to the drug), and have generally *not* included a contra-indication from the Product Monograph if the use of the drug in the stated circumstance is accepted prescribing practice in palliative care.

As always, a cautious approach is generally necessary when prescribing for the frail elderly, patients with hepatic impairment, renal impairment, and respiratory insufficiency (see p.486).

The use of drugs for unlicensed (off-label) indications is common in palliative care (and indeed in all areas of medical practice) and is discussed on p.xvii.

## Undesirable effects of drugs

In *PCF*, the term 'undesirable effect' is used rather than side effect or adverse effect. Wherever possible, undesirable effects are categorized as:

- very common (>10%)
- common (<10%, >1%)
- uncommon (<1%, >0.1%)
- rare (<0.1%, >0.01%)
- very rare (<0.01%).

*PCF* 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 Product Monograph should be consulted for a full list of undesirable effects.

## Reliable knowledge and levels of evidence

Research is the pursuit of reliable knowledge. The gold standard for drug treatment is the randomized controlled trial (RCT) or, better, a systematic review of homogeneous RCTs.

Over the last 25 years, numerous systems have been published for categorizing levels of evidence and the strength of the derived recommendations. Box A reproduces the system used by the *British Medical Journal*. This checklist is based on material published by three main sources, namely the US Agency for Health Care Policy and Research, the NHS Management Executive, and the North of England Guidelines Group.[1,2,3]

**Box A** A scheme for categorizing evidence and grading recommendations[4]

| Category | Level of evidence | Grade | Strength of recommendations |
|---|---|---|---|
| Ia | Evidence obtained from a meta-analysis of RCTs | A | Directly based on Category I evidence without extrapolation |
| Ib | Evidence from at least one RCT | | |
| IIa | Evidence obtained from at least one well-designed controlled study without randomization | B | Directly based on Category II evidence or by extrapolation from Category 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 | C | Directly based on Category III evidence or by extrapolation from Category I or II evidence |
| IV | Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities | D | Directly based on Category IV evidence or by extrapolation from Category I, II, or III evidence. This grading indicates that directly applicable clinical studies of good quality are absent or not readily available |

However, it is important to recognize that the RCT is *not* the only source of reliable knowledge. Broadly speaking, sources of knowledge 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).[5]

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 Product Monograph 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.[6] It is thus best to treat information from company representatives as inevitably biased. The information provided by *PCF* is commercially independent, and should serve as a counterbalance to manufacturer bias.

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 a newly released product – which may simply be a 'me-too' drug rather than a true innovation.[6]

## Generic drugs

It is the policy of *PCF* to use generic drug names, and to encourage generic prescribing. With occasional exceptions, e.g. SR 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.[7] However, including the proprietary (brand) name of a strong opioid analgesic on the prescription and dispensing label, particularly in the case of oral morphine, is good practice because it helps to reduce the scope for confusion over the various available formulations.

## 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 not feasible to reference every statement in *PCF*. However, readers are invited to enter into constructive dialogue with the Editorial Team via the *Bulletin Board* on www.palliativedrugs.com.

## Electronic sources of information

As far as possible, Canadian sources have been given prominence in *PCF*. However, some UK sources have inevitably been included. To facilitate access to the relevant documents, website details are given below.

### *Canadian free access resources*

Canadian Agency for Drugs and Technology in Health (CADTH, formerly CCOHTA) Database: available from www.cadth.ca/index.php/en/hta/reports-publications/search
Gives access to free, full-text systematic reviews, health technology assessments (HTAs) and economic assessments from a Canadian perspective. A free email alert service is available.

Drug Product Database, Health Canada: available from
www.hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php
Contains product-specific information on human pharmaceutical and biological drugs, veterinary drugs and disinfectant products approved for use in Canada. Also allows access to some product monographs.

***Canadian resources, subscription required***

Electronic Compendium of Pharmaceuticals and Specialties (e-CPS): available from http://www.pharmacists.ca/content/products/ecps_english.cfm

***UK free access resources***

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

Current Problems in Pharmacovigilance: available via MHRA website at www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=368

Drug Safety Update: available via MHRA website at www.mhra.gov.uk/Publications/Safetyguidance/DrugSafetyUpdate/index.htm

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

National Institute for Health and Clinical Excellence (NICE) guidelines: available from www.nice.org.uk/
Evidence-based cost-effectiveness guidelines for health professionals, with simplified versions for the general public.

UK manufacturers' Summary of Product Characteristics (SPCs), broadly equivalent to the Canadian Product Monographs, available from www.medicines.org.uk

***UK and international resources, subscription required***

*British National Formulary*: two editions/year, March and September. Latest edition available from www.bnf.org

The Cochrane Library: available at http://www3.interscience.wiley.com/cgi-bin/mrwhome/106568753/AccessCochraneLibrary.html#canada. Collection of evidence-based systematic reviews. Access temporarily free in Canada

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


1 Agency for Health Care Policy and Research (1992) Acute pain management, operative or medical procedures and trauma 92-0032. In: *Clin Pract Guidel Quick Ref Guide Clin*. AHCPR Publications, Rockville, Maryland, USA, pp. 1–22.

2 DoH (1996) *Clinical Guidelines: Using Clinical Guidelines to Improve Patient Care Within the NHS*. Department of Health: NHS Executive, Leeds.

3 Eccles M *et al*. (1996) North of England evidence based guidelines development project: methods of guideline development. *British Medical Journal*. **312**: 760–762.

4 BMJ Publishing Group (2009) Resources for authors. Checklists and forms: clinical management guidelines. Available from: http://resources.bmj.com/bmj/authors/checklists-forms/clinical-management-guidelines

5 Aoun SM and Kristjanson LJ (2005) Challenging the framework for evidence in palliative care research. *Palliative Medicine*. **19**: 461–465.

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.

# USING LICENSED DRUGS FOR OFF-LABEL PURPOSES

In palliative care, up to 1/4 of all prescriptions are for licensed drugs given for an off-label indication or in doses, formulations or a route not covered by the licence,[1,2] and this is reflected in the recommendations contained in *PCF*. 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 those in the manufacturer's Product Monograph. Thus, it is important to recognize that the approval and licensing process for drugs regulates the marketing activities of pharmaceutical companies and not a practitioner's prescribing practice. Off-label use of drugs is often appropriate and may represent standard practice.[3]

## The approval and licensing process

All new therapeutic products intended for sale in Canada must undergo an extensive clinical trial, approval and licensing process.[4] New drugs are evaluated by the Health Products and Food Branch (HPFB) of Health Canada. After receiving satisfactory evidence of quality, safety and efficacy via the pharmaceutical company's New Drug Submission, the HPFB issues a marketing authorization (licence), known as a Notice of Compliance (NOC), and a Drug Identification Number (DIN). This allows the pharmaceutical company to market and supply the product in Canada for specific indications and at specified doses in a defined patient population. These are all listed in its Product Monograph and other labelling information. Restrictions are imposed by the HPFB if evidence of safety and efficacy is unavailable in particular patient groups, e.g. children. Once a NOC is received, the manufacturer can apply for listing on provincial and territorial drug formularies, which means that the drug will be covered for reimbursement, either in full or in part, by the healthcare plan which manages that formulary.[4,5] 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 via a Supplemental New Drug Submission.[4,5] 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 Canada, there is no law or formal advice from professional bodies governing the off-label prescribing of licensed drugs. However, it is accepted that a physician may legally prescribe and use, or advise using:

- unlicensed medicines which are:
  - specially prepared (compounded) products *or*
  - imported or supplied for a named patient through Health Canada's Special Access Programme (SAP)
- licensed drugs for indications or in doses, formulations or routes outside the licensed recommendations, i.e. off-label
- drugs for conditions for which there are no other treatments (even in the absence of strong evidence)
- for individuals not covered by the licence, e.g. children
- unlicensed drugs in clinical trials, providing the trial has been approved by the HPFB.[6]

In addition, a physician may override the warnings and precautions given in the licence. The responsibility for the consequences of these actions lies with the prescriber.[3,6] Further, although drugs prescribed outside the licence can be dispensed by pharmacists and administered by nurses or midwives, it is good professional practice for them to inform themselves about the use of the drug in the proposed off-label indication, and of any potential safety issues, before doing so.[7]

In some provinces and territories, some nurses, midwives and pharmacists have limited prescribing powers. Depending on the province/territory, they may either act as independent prescribers or prescribe under the direction of a physician. Providing they meet the SAP's required criteria for practitioner status, they are eligible to request unlicensed drugs under the SAP (see p.xx).

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 and other health professionals 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, administering or dispensing drugs outside the terms of the licence, they must:

- inform themselves fully about the published evidence supporting the intended off-label use[7–9]
- assure themselves 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).[10] The more dangerous the medicine and the more flimsy the evidence the more difficult it is to justify its prescription. Further, it is good practice to report any undesirable effects of off-label drugs to the Canadian MedEffect programme (www.hc-sc.gc.ca/dhp-mps/medeff/index-eng.php).[3]

It has also been recommended that when prescribing a drug outside its licence, a prescriber should:

- record in the patient's records the reasons for the decision to prescribe outside the licensed indications
- ensure that the patient (and family as appropriate) is as fully informed as possible about the expected benefits and potential risks (undesirable effects, drug interactions, etc.) of the treatment, ideally in sufficient detail to allow them to give informed consent; the Patient Package Insert obviously does not contain information about unlicensed indications
- inform other professionals, e.g. pharmacist, nurses, family practitioner, involved in the care of the patient to avoid misunderstandings and to ensure appropriate monitoring.[3,6,7,10,11]

However, in palliative care, the use of drugs for off-label indications or by unapproved routes is so widespread that such an approach is impractical. Indeed, a survey in the UK showed that $<5\%$ of palliative medicine specialists *always* obtain verbal or written consent, document in the notes or inform other professionals when using licensed drugs for unlicensed purposes/routes.[12] 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 1/2 to 2/3 indicated that they would *sometime*s 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; an appropriate level of counselling and a sensitive approach is essential. Some institutions have policies in place and have produced information cards or leaflets for patients and caregivers (Box B). In the UK, a position statement has also been produced by the Association for Palliative Medicine and the Pain Society (Box C).

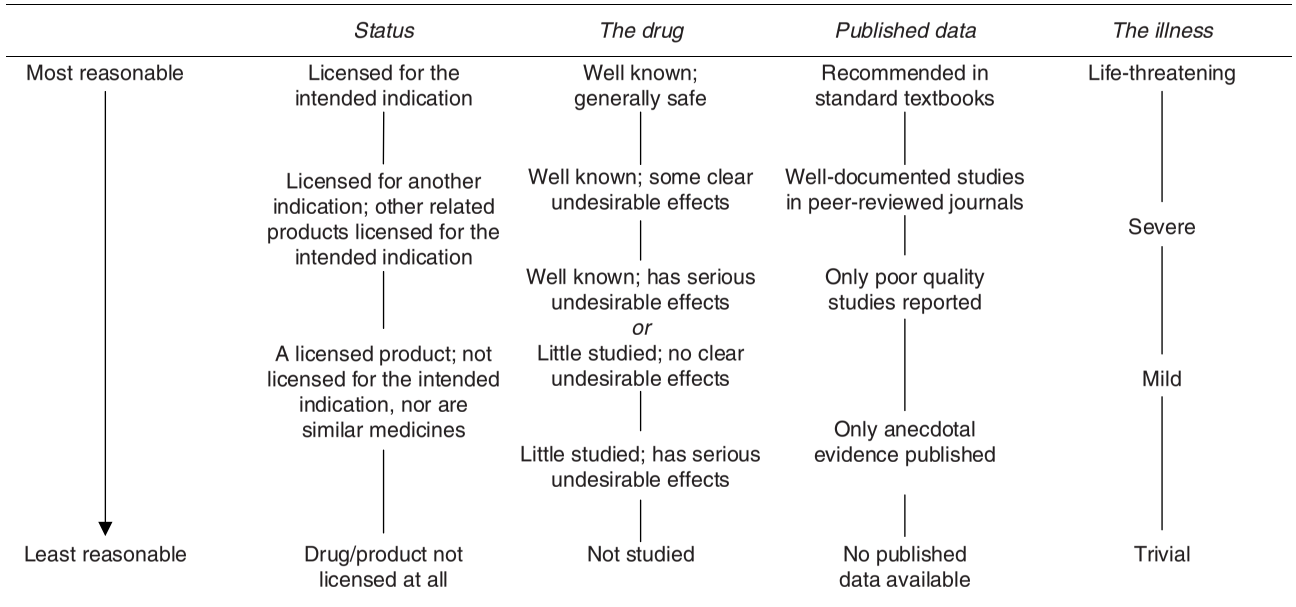


**Figure 1** Factors influencing the reasonableness of prescribing decisions.[10]

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

**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 Health Canada by the manufacturer. Health Canada 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 all their medicines a Patient Package Insert which, by law, must be limited to the details of the Health Canada approval.

In practice, medicines are often prescribed in ways which are not approved by Health Canada. 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 Patient 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.

## The Special Access Programme (SAP)

Practitioners who are authorized to treat patients with drugs listed in Schedule F of the Food and Drug Regulations can gain access to limited supplies of drugs which are not licensed for sale in Canada through the SAP. In some provinces and territories, health professionals other than physicians, e.g. nurses, midwives and pharmacists, are allowed to prescribe and may thus qualify as practitioners for purposes of requesting SAP drugs. Individuals should consult their provincial or territorial professional regulatory body to ascertain their Schedule F prescriber status, and submit any relevant documentation to the SAP with their request for consideration as a practitioner.[13] Lists of professional bodies are available from: www.cna-aiic.ca/CNA/nursing/regulation/regbodies/default_e.aspx (nurses), http://cmrc-ccosf.ca/node/2 (midwives) and www.napra.org/pages/Licensing_Registration/Authorities.aspx?id=1971 (pharmacists).

SAP drugs can be requested for patients with serious or life-threatening conditions when conventional treatments have failed, are unavailable or are unsuitable. Access is considered on a case-by-case basis, taking into account the nature of the emergency and/or any compassionate grounds.[4,14]

Full guidance on applying for the SAP and an application form can be downloaded from: www.hc-sc.gc.ca/dhp-mps/acces/index-eng.php


1 Atkinson C and Kirkham S (1999) Unlicensed uses for medication in a palliative care unit. *Palliative Medicine*. **13**: 145–152.
2 Todd J and Davies A (1999) Use of unlicensed medication in palliative medicine. *Palliative Medicine*. **13**: 466.
3 de Paulsen N (2005) The regulatory gap: off-label drug use in Canada. *University of Toronto Faculty of Law Review*. **63**: 183–211.
4 Health Products and Food Branch (2006) Access to Therapeutic Products. The Regulatory Process in Canada. Health Canada, Ottawa. Available from: www.hc-sc.gc.ca/ahc-asc/alt_formats/hpfb-dgpsa/pdf/pubs/access-therapeutic_acces-therapeutique-eng.pdf
5 Health Canada (2007) Drug licensing process. Introduction to the current system. Available from: www.hc-sc.gc.ca/dhp-mps/homologation-licensing/system/intro-eng.php
6 Canadian Medical Association legal department (2009) Personal communication.
7 Friesen M (2008) Off-label prescribing. Veering off the beaten path. *Pharmacy Practice*. **February**: 26–29.
8 Palacioz K (2003) Off-label uses of Neurontin (gabapentin). Detail document 190812. *Pharmacist'sLetter/Prescriber's Letter.* **19 (August)**: 1–4.
9 Gazarian M et *al*. (2006) Off-label use of medicines: consensus recommendations for evaluating appropriateness. *Medical Journal of Australia*. **185**: 544–548.

**Box C** The recommendations of the Association for Palliative Medicine and the Pain Society (UK)

**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 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.

10 Ferner R (1996) Prescribing licensed medicines for unlicensed indications. *Prescribers' Journal.* **36**: 73–79.
11 Cohen P (1997) Off-label use of prescription drugs: legal, clinical and policy considerations. *European Journal of Anaesthesiology.* **14**: 231–235.
12 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.
13 Health Canada (2009) Personal communication SAP drugs department.
14 Health Canada (2008) Release of final Special Access Programme (SAP) for drugs guidance document. Available from: www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/acces/sapg3_pasg3-eng.pdf

# DRUG NAMES

Canadian approved names are used throughout *PCF*. These are generally the same as United States Adopted Names (USANs). Proprietary (brand) 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 Canadian approved names, 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 Table 1 to aid understanding of the older UK literature. As a further aid to understanding UK literature, the UK conventional names for combination products, such as codeine and acetaminophen (paracetamol) or diphenoxylate and atropine, are shown in Table 2, e.g. co-codamol or co-phenotrope.

**Table 1** Drug names relevant to palliative care for which the Canadian approved name, USAN, rINN and/or BAN differ

| *Canadian approved name* | *USAN* | *rINN* | *Former BAN* |
|---|---|---|---|
| Acetaminophen | Acetaminophen | Paracetamol | – |
| Aluminum | Aluminum | Aluminium | – |
| Amphetamine | Amphetamine | Amfetamine | Amphetamine |
| Beclomethasone | Beclomethasone | Beclometasone | Beclomethasone |
| Benzathine penicillin | Benzathine penicillin | Benzathine benzylpenicillin | Benzathine penicillin |
| Benztropine | Benztropine | Benzatropine | Benztropine |
| Calcitonin | Calcitonin | Calcitonin (salmon) | Salcatonin |
| Carboxymethylcellulose | Carboxymethycellulose | Carmellose | – |
| Cephalexin (etc.) | Cephalexin (etc.) | Cefalexin (etc.) | Cephalexin (etc.) |
| Chlorpheniramine | Chlorpheniramine | Chlorphenamine | Chlorpheniramine |
| Cholestyramine | Cholestyramine | Colestyramine | Cholestyramine |
| Cyclosporine | Cyclosporine | Ciclosporin | Cyclosporin |
| Dextroamphetamine | Dextroamphetamine | Dexamfetamine | Dexamphetamine |
| Dicyclomine | Dicyclomine | Dicycloverine | Dicyclomine |
| Diethylstilbestrol | Diethylstilbestrol | Diethylstilbestrol | Stilboestrol |
| Dimethicone | Dimethicone | Dimeticone | Dimethicone |
| Epinephrine | Epinephrine | Epinephrine | Adrenaline |
| Estradiol | Estradiol | Estradiol | Oestradiol |
| Furosemide | Furosemide | Furosemide | Frusemide |
| Glyburide | Glyburide | Glibenclamide | – |
| Glycerin | Glycerin | Glycerol | Glycerine |
| Glycopyrrolate | Glycopyrrolate | Glycopyrronium | – |
| Guaifenesin | Guaifenesin | Guaifenesin | Guaiphenesin |
| Hyoscine (used in relation to the *butylbromide* salt; scopolamine is used for the *hydrobromide* salt) | Scopolamine | Hyoscine | – |
| Indomethacin | Indomethacin | Indometacin | Indomethacin |
| Isoproterenol | Isoproterenol | Isoprenaline | – |
| Levothyroxine | Levothyroxine | Levothyroxine | Thyroxine |
| Lidocaine | Lidocaine | Lidocaine | Lignocaine |
| Meclizine | Meclizine | Meclozine | – |

*continued*

**Table 1** Continued

| *Canadian approved name* | *USAN* | *rINN* | *Former BAN* |
|---|---|---|---|
| Meperidine | Meperidine | Pethidine | – |
| Methenamine | Methenamine | Methenamine | Hexamine |
| Methotrimeprazine | Methotrimeprazine | Levomepromazine | Methotrimeprazine |
| Mineral oil | Mineral oil | Liquid paraffin | – |
| Mitoxantrone | Mitoxantrone | Mitoxantrone | Mitozantrone |
| Nitroglycerin | Nitroglycerin | Glyceryl trinitrate | – |
| Oxethazine | Oxethazine | Oxetacaine | Oxethazine |
| Penicillin G | Penicillin G | Benzylpenicillin | – |
| Penicillin V | Penicillin V | Phenoxymethylpenicillin | – |
| Phenobarbital | Phenobarbital | Phenobarbital | Phenobarbitone |
| Phytonadione | Phytonadione | Phytomenadione | – |
| Procaine penicillin | Procaine penicillin | Procaine benzylpenicillin | Procaine penicillin |
| Propoxyphene | Propoxyphene | Dextropropoxyphene | – |
| Psyllium | Psyllium | – | Ispaghula |
| Rifampin | Rifampin | Rifampicin | – |
| Salbutamol | Albuterol | Salbutamol | – |
| Scopolamine (used in relation to the *hydrobromide* salt; hyoscine is used for the *butylbromide* salt) | Scopolamine | Hyoscine | – |
| Simethicone[a] | Simethicone | Simeticone | Simethicone |
| Sodium cromoglycate | Cromolyn sodium | Sodium cromoglicate | Sodium cromoglycate |
| Sulfasalazine | Sulfasalazine | Sulfasalazine | Sulphasalazine |
| Sulfonamides | Sulfonamides | Sulfonamides | Sulphonamides |
| Tetracaine | Tetracaine | Tetracaine | Amethocaine |
| Trihexyphenidyl | Trihexyphenidyl | Trihexyphenidyl | Benzhexol |
| Trimeprazine | Trimeprazine | Alimemazine | Trimeprazine |
| Vitamin A | Vitamin A | Retinol | Vitamin A |

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

**Table 2** UK names for combination products

| *Contents* | *UK name* |
|---|---|
| Acetaminophen-codeine phosphate | Co-codamol |
| Acetaminophen-dihydrocodeine[a] | Co-dydramol |
| Acetaminophen-propoxyphene[a] | Co-proxamol |
| Aluminum hydroxide-magnesium hydroxide | Co-magaldrox |
| Amoxicillin-clavulanate | Co-amoxiclav |
| Atropine-diphenoxylate | Co-phenotrope |
| Sulfamethoxazole-trimethoprim[b] | Co-trimoxazole |

a. not available in Canada
b. also known as cotrimoxazole in Canada.

# LIST OF ABBREVIATIONS

## Drug administration

In 2005, the US 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 on prescriptions. The full set of recommendations is available at www.jointcommission.org/PatientSafety/DoNotUseList/. These recommendations have been adopted by the Institute for Safe Medication Practices Canada (ISMP Canada).[1] Although some traditional abbreviations remain acceptable (e.g. Table 3), other commonly used abbreviations are not. Thus, ISMP now recommends that the following are written in full:

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

These four recommendations have also been adopted in *PCF*. However, several other abbreviations which are now unacceptable on prescriptions are still used in *PCF*.

Although the following conventions have *not* been adopted in *PCF*, readers should be aware of the following recommendations for handwritten and printed prescriptions, and other printed medical matter, e.g. packaging, patient records:

- include a space between the drug dose and the unit of measure, e.g. 25 mg, not 25mg
- write 'per' instead of an oblique (mistaken for a figure 1), e.g. 200 mg per day, not 200mg/day
- use 'subcut' or 'subcutaneous' instead of SC (mistaken for SL)
- write 'less than' or 'greater than' instead of < and > (mistaken for a letter L or figure 7; or written the wrong way round and thus signifying the opposite of the intended meaning).

**Table 3** Abbreviations used in *PCF* for the times of drug administration

| *Times* | *Canada and USA* | *Latin* | *UK* | *Latin* |
|---|---|---|---|---|
| Twice daily | b.i.d. | *bis in die* | b.d. | *bis die* |
| Three times daily | t.i.d. | *ter in die* | t.d.s. | *ter die sumendus* |
| Four times daily | q.i.d. | *quarta in die* | q.d.s. | *quarta die sumendus* |
| Every 4 hours etc. | q4h | *quaque quarta hora* | q4h | *quaque quarta hora* |
| Rescue medication (as needed/required) | p.r.n. | *pro re nata* | p.r.n. | *pro re nata* |
| Give immediately | stat | | stat | |

| | |
|---|---|
| a.c. | ante cibum (before food) |
| amp | ampoule containing a single dose (compare with vial) |
| CIVI | continuous intravenous infusion |
| CR | controlled-release (used for proprietary SR products only when it is part of the brand name); see SR |
| 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); see SR |

| | |
|---|---|
| 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) |
| TD | transdermal |
| vial | sterile container with a rubber bung containing either a single or multiple doses (compare with amp) |
| WFI | water for injections |

**General**

| | |
|---|---|
| * | specialist use only |
| † | off-label use |
| BNF | British National Formulary |
| BP | British Pharmacopoeia |
| CADTH | Canadian Agency for Drugs and Technologies in Health |
| CDSA | Controlled Drugs and Substances Act |
| CHM | Commission on Human Medicines (UK) |
| CPS | Compendium of Pharmaceuticals and Specialities |
| CSM | Committee on Safety of Medicines (UK; now part of CHM) |
| EMEA | European Medicines Agency |
| EORTC | European Organisation for Research and Treatment of Cancer |
| FDA | Food and Drug Administration (USA) |
| HPFB | Health Products and Food Branch (of Health Canada) |
| IASP | International Association for the Study of Pain |
| MCA | Medicines Control Agency (UK; now MHRA) |
| MHRA | Medicines and Healthcare products Regulatory Agency (UK; formerly MCA) |
| NYHA | New York Heart Association |
| NICE | National Institute for Health and Clinical Excellence (UK) |
| NOC | Notice of Compliance |
| PCS | Palliative care service |
| PEG | percutaneous endoscopic gastrostomy |
| rINN | recommended International Non-proprietary Name |
| SAP | Special Access Programme |
| SPC | Summary of Product Characteristics (UK; broadly equivalent to the Canadian Product Monograph) |
| UK | United Kingdom |
| USA | United States of America |
| USP | United States Pharmacopoeia |
| VAS | visual analogue scale, 0–100mm |
| 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 |
| $\beta_2$ | 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) |
| $D_2$ | dopamine type 2 (receptor) |
| DIC | disseminated intravascular coagulation |
| DVT | deep vein thrombosis |
| ECG | electrocardiogram (also known as EKG) |
| ECT | electroconvulsive therapy |
| $FEV_1$ | 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 |
| Hgb | hemoglobin |
| HIV | human immunodeficiency virus |
| $H_1$, $H_2$ | 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 | luteinizing 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 serotoninergic 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 |
| $PaCO_2$ | arterial partial pressure of carbon dioxide |
| $PaO_2$ | 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 |
| $TI_{CO}$ | 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 | centimetre(s) |
| cps | cycles per sec |
| dL | decilitre(s) |
| g | gram(s) |
| Gy | Gray(s), a measure of radiation |
| h | hour(s) |
| Hg | mercury |
| kg | kilogram(s) |
| L | litre(s) |
| mg | milligram(s) |
| microL | microlitre(s) |
| micromol | micromole(s) |
| mL | millilitre(s) |
| mm | millimetre(s) |
| mmol | millimole(s) |
| min | minute(s) |
| mosmol | milli-osmole(s) |
| msec | millisecond(s) |
| nm | nanometre(s) |
| nmol | nanomole(s); alternative, nM |
| sec | second(s) |

1 Institute for Safe Medication Practices Canada (2006) Eliminate use of dangerous abbreviations, symbols, and dose designations. *ISMP Canada Safety Bulletin.* **6(4)**: 1–2.