QUALITY USE OF MEDICINES FOR PALLIATIVE CARE

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Abstract

Many of the drugs commonly used in palliative care are not listed on the Pharmaceutical Benefits Scheme in Australia and are therefore not freely available to patients outside the acute hospital system. In an attempt to address the inequity faced by patients being cared for in the community or hospices, the Palliative Care Medicines Working Group was established by the Australian Government. This has resulted in a separate palliative section within the Schedule of Pharmaceutical Benefits Scheme which allows for authority prescribing of a number of medications that may be required by a palliative care patient. This paper discusses the medications currently on this listing, the processes by which they were selected and the ongoing efforts to broaden access to required medications.

In 2000, members of the Australian and New Zealand Society of Palliative Medicine were surveyed to compile a list of the medications they considered essential in the practice of palliative care and the indications for which they were prescribed.[1] A number of the drugs that respondents highlighted were available on the nationally subsidised Pharmaceutical Benefits Scheme (PBS), such as morphine in its indication for the management of cancer-related pain and haloperidol for control of delirium. However, many other medications commonly used in palliative care were not listed on the PBS (see tables 1 and 2) and were therefore not freely available to patients outside hospitals ie. those patients in hospices, residential aged care facilities and in the community. Midazolam, used for terminal restlessness and hyoscine hydrobromide to control end-stage respiratory secretions, were two such agents used frequently and effectively, but not available on the PBS.

One of the *Standards for Providing Quality Palliative Care for all Australians* published by Palliative Care Australia is that the needs and wishes of patients, their caregivers and families are acknowledged and used to guide decision-making and care planning.[2] The fact that those patients choosing to remain at home are obliged to buy many of their essential medications at full cost profoundly disadvantages patients who wish to die in the community – potentially restricting any real choices they may have in deciding about some aspects of their care. Moreover, many of these medications being prescribed in the palliative care setting are being used 'off-licence' for indications, routes of delivery and doses not yet approved by the Therapeutics Goods Administration (TGA).

These difficulties have been recognised and acknowledged by the Department of Health and Ageing and the Australian Government.

Table 1. *Top 25 drugs identified as being most useful in the management of a number of symptoms*[1]

Medication	Indication	PBS availability+
Morphine	pain	Y
	dypsnoea	N
Haloperidol	delirium	Y
Dexamethasone	anorexia/cachexia	Y
Midazolam	terminal restlessness	N
Metoclopramide	nausea/vomiting	Y
Clonazepam	insomnia	Y
Paracetamol	pain	Y
Amitriptyline	neuropathic pain	Y
Pamidronate	hypercalcaemia	Y
Cyclizine	nausea/vomiting	N
Hyoscine hydrobromide	retained resp secretions	N
Diazepam	insomnia	Y
Lorazepam	insomnia	N
Omeprazole	dyspepsia	Y
Chlorpromazine	delirium	Y
Fentanyl		
– transdermal	pain	Y
– parenteral	pain	N
Spironolactone	ascites	Y
Ranitidine	dyspepsia	Y
Promethazine	pruritis	N
Frusemide	fluid retention	Y
Ondansetron	nausea/vomiting*	Y
Docusate/senna	constipation	N
Temazepam	insomnia	Y
Prednisolone	anorexia	Y
Methadone	pain	
– tablet		Y
– liquid		N

+ PBS listing for many of these drugs is general and not specific to the indication noted.

** approved only for chemotherapy and radiotherapy induced nausea/vomiting.*

Table 2. *Top 10 non-PBS listed drugs for the management of common symptoms*[3]

Medication	Indication
Midazolam	terminal restlessness
Cyclizine	nausea/vomiting
Hyoscine hydrobromide	respiratory secretions
Lorazepam	insomnia
Fentanyl (injection)	pain
Ondansetron	non-chemo, RT nausea/vomiting
Docusate/senna	constipation
Methadone (liquid)	pain
Gabapentin	neuropathic pain
Ketamine	pain
Phenobarbitone	terminal restlessness

Hence, a key area of the National Palliative Care Program is to improve access to affordable medicines through the PBS.

Improving access to medications

The Palliative Care Medicines Working Group (PCMWG) was established by the Australian Government in an attempt to remedy this situation. This expert group comprises invited clinicians, pharmacists and pharmaceutical industry representatives, along with government and drug regulatory officers. Its aim is to provide advice to the Australian Government on how to improve access to and quality use of medicines in the community. A communication sub-group has been established to raise awareness within the primary health care workforce of palliative care medicines already listed on the PBS and ways to improve access to essential medicines used in palliative care through a new PBS framework.

The first successful initiative has been the inclusion of a palliative care section within the PBS. This is the first section ever created in the PBS for a specific patient population. It allows for authority prescribing for those people meeting the definition of a palliative care patient and includes all patients with life-limiting disease (eg. those with end-stage heart or renal failure or motor neuron disease) (see box 1). It does not limit prescribing to those felt to have a specified prognosis, but rather focuses on maximising quality of life as the primary intent of care. This section is intended to complement and be used with the general listings, but the indications cited are often broader than those indications listed in the general section. For example, while non steroidal anti-inflammatory drugs (NSAIDs) are authorised only for patients with pain secondary to osteoarthritis in the general PBS section, they can be prescribed for severe pain of any aetiology to palliative care patients. Similarly, a prescription of a prolonged course of benzodiazepines is not restricted to residents of an aged care facility who have failed a trial of drug withdrawal. The restriction on opioid prescribing for patients with non-malignant disease has also been lessened. While previously, opioids could only be initiated in hospital, under a palliative care authority they can also be started in the community. All palliative care listings are "authority required". Continuing treatment beyond four months requires a consultation with a specialist palliative care service, but this can be in the form of a telephone call between the general practitioner and a specialist or specialist service and does not require a face-to-face patient visit.

Box 1. *Definition of a palliative care patient for PBS purposes*

"A patient with an active, progressive, far-advanced disease for whom the prognosis is limited and the focus of care is on quality of life."

It is important to note that the change sought is often not only for any particular drug to be available, but also for the specific indication, formulation and/or route of delivery. A good example of this is clonazepam. The drug previously had approval only for the treatment of established epilepsy. The PCMWG has subsequently gained approval so that the indication for clonazepam is extended to include the prevention of epilepsy (including myoclonus).

One criticism of the content of the palliative care section as it currently stands is that it lists a relatively small number of drugs (see table 3) and the 'wish-list' of those practising palliative care remains substantially longer. However, the process of listing a drug on the PBS is rigorous and is dependent on the approval of a number of committees, including the TGA and the Pharmaceutical Benefits Advisory Committee. The quality, safety and efficacy of any drug must be judged satisfactory prior to any product registration and any application for PBS listing. The comparative safety, efficacy and cost-effectiveness of the new agent must then be assessed against existing products and the list price negotiated. Furthermore,

Table 3. *Drugs listed in the palliative care section to date*

Benzydamine hydrochloride
Carmellose sodium
Hyoscine butylbromide (injection)
Promethazine hydrochloride (tablets, oral liquid)
Laxatives (bisacodyl, docusate, stercula, lactulose, macrogol, glycerol, sorbitol)
Non-steroidal anti-inflammatories (extended indication)
Morphine (extended supply)
Methadone (extended supply)
Paracetamol (suppositories and modified release formulations)
Clonazepam (extended indication)
Benzodiazepam derivatives (extended supply)

the whole process is dependent on there being a sponsor willing to meet the time, effort and costs required to take the drug through the various stages. Only the sponsor (usually a pharmaceutical company) can apply to list a medicine or change a listed indication on the Australian Register of Therapeutic Goods.

To commence the process of improved access to palliative care medications, one of the first tasks the PCMWG undertook was to identify those drugs that already met the requirements necessary for PBS listing or those which could be listed with only minor changes in indication required. This led to drugs such as promethazine, hyoscine butylbromide, long-acting paracetamol and various laxatives quickly coming into the PBS within the palliative care section. The more slow and difficult task has been in getting the necessary approval for a whole range of other medications that have been identified by the Australian palliative care community as being of a high priority.

The Australian Government is supporting this next step in a number of ways. Significantly, funding has been made available to set up the infrastructure necessary to help gather scientific evidence necessary for the approval process and to support a national clinical trials network – the Palliative Care Clinical Studies Collaborative (PaCCSC). The collaborative is comprised of a number of centres across the country that have a proven ability to undertake clinical studies. The primary aim of PaCCSC is to complete a series of multi-site, well designed controlled clinical trials in order to substantiate the efficacy (or otherwise) of the palliative care community's priority drugs and from there further the argument for improved access to medications through the PBS. The current trials in design phase are centred on ketamine, risperidone, octreotide, ketorolac and megestrol acetate.

Conclusion

The palliative care section within the Schedule of Pharmaceutical Benefits reflects a commitment by the Australian Government to provide affordable and equitable access to palliative care medicines that have an established efficacy and proven pharmaco-economic base. Our responsibility as palliative care physicians is to improve awareness within the primary healthcare workforce of existing palliative care medicines listed on the PBS, encourage our colleagues to use the palliative care section and to promote quality use of medicines and best practice prescribing within palliative care. We must encourage sponsors to consider palliative indications as part of the registration process on the Australian Register of Therapeutic Goods and assist with the gathering of evidence to demonstrate the quality, efficacy and safety of the medicines we have prioritised.

References

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2. Palliative Care Australia. Standards for Providing Quality Palliative Care for all Australians May 2005. Palliative Care Australia; 2005.
3. Good P. Unpublished data from Australia and New Zealand Society of Palliative Medicine survey. 2000.