

Pain Relief Connection

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Journal Watch

- Tran QNH, Fancher T. [Achieving Analgesia for Painful Ulcers Using Topically Applied Morphine Gel](http://www.supportiveoncology.net/journal/articles/0506289.pdf). *Journal of Supportive Oncology* 2007 June;5(6):289-293.
<http://www.supportiveoncology.net/journal/articles/0506289.pdf>
- Reisfield, G. & Wilson, G. (2007) Rational use of sublingual opioids in palliative medicine. *The Journal of Palliative Medicine* April 10(2) 465-475.
- The Intersection of Pain Management and Addictive Illness
http://www.massgeneral.org/painrelief/Addictive_illness.htm
- Foley, K.M. (2006). Appraising the WHO Analgesic Ladder on its 20th anniversary. http://www.whocancerpain.wisc.edu/eng/19_1/Interview.html

In the News

Sativex® receives Qualifying Notice for approval in Canada for the relief of Cancer Pain

Porton Down, UK; Toronto, Canada; 19 June 2007: GW Pharmaceuticals plc (AIM: GWP) and Bayer HealthCare Pharmaceuticals announce that Health Canada, the Canadian regulatory agency, has issued a Qualifying Notice for the approval of Sativex® in the relief of cancer pain. Sativex is already approved and marketed in Canada as adjunctive treatment for the symptomatic relief of neuropathic pain in Multiple Sclerosis (“MS”) in adults. This approval was granted under the NOC/c policy.

GW filed the application in October 2006 with Health Canada under the Notice of Compliance with conditions (NOC/c) policy. The approved indication will be “adjunctive analgesic treatment in adult patients with advanced cancer who experience moderate to severe pain during the highest tolerated dose of strong opioid therapy for persistent background pain”. Health Canada has completed its regulatory review in line with its 200 day review target.

Sativex has been developed by UK-based GW Pharmaceuticals and is exclusively marketed in Canada by Bayer.

Under the NOC/c process, the issue of a Qualifying Notice confirms that Sativex qualifies to be considered for approval in cancer pain and sets out the conditions and post-approval undertakings upon which the marketing authorization for Sativex in this indication can be granted. The conditions for the approval of Sativex in cancer pain are in accordance with standard guidance provided by the regulator for NOC/c approvals and include a commitment to ongoing clinical research. This process is identical to that under which Sativex is already approved in the MS neuropathic pain indication.

GW is required to respond and accept the conditions within 30 days. Following this, Health Canada will review this response, subject to a 30 day review target. Should the response be acceptable, Health Canada can then be expected to proceed to finalise the marketing authorisation.

Dr Geoffrey Guy, GW’s Chairman, said, “We are delighted to receive this Qualifying Notice from Health Canada and look forward to receiving regulatory approval for Sativex in the relief of cancer pain in the next few months. This additional regulatory approval represents a further step in our broad-based regulatory strategy for Sativex, which is designed to secure approvals for this important new medicine across a range of separate therapeutic indications in countries across the world over the coming years.”

**Preventing
pain
is easier than
treating pain**

Pain ... The 5th Vital Sign

Philip Blake, President and CEO of Bayer Inc., said, "Pain is one of the most debilitating and feared symptoms of advanced cancer. The approval of Sativex for the treatment of these high need patients is further recognition of the value of this important medicine and we shall now actively commence our launch plans for this indication."

Sativex in Cancer Pain

GW has completed a positive Phase III study in Europe in 177 patients with cancer pain. The trial was a multi-center double-blind, randomized, placebo-controlled parallel group study. Patients in the study had advanced cancer and were experiencing pain that was not responding adequately to strong opioid medication (e.g. morphine). In addition to study medication, all patients remained on their existing opioid and other analgesic medication during the trial. In this study, Sativex achieved a statistically significant improvement in comparison with placebo in pain as measured on a numerical rating scale ($p=0.014$), a primary endpoint of the study. A responder analysis showed that 43 per cent of patients on Sativex showed a greater than 30 per cent improvement in their pain ($p=0.024$).

Cancer-related pain can be defined as pain caused by cancer, by cancer treatment such as surgery, radiation therapy or chemotherapy, or by the side effects of treatment. Severe pain is experienced by at least two thirds of patients with advanced disease. It is estimated that between 14 per cent and 47 per cent of these patients will achieve inadequate pain relief from opioid based approaches and will continue to suffer pain.

Dr Paul Daeninck, Director, Symptom Management Group for Cancer Care Manitoba and Assistant Professor, Depts of Internal Medicine and Family Medicine, University of Manitoba, said, "Pain remains a significant unmet medical need for many patients with cancer, who may be unable to gain adequate pain relief from even the best use of existing strong opioid medicines. Furthermore, a proportion of patients are simply unable to tolerate opioids in doses that may be required to relieve their pain. In short, there is a clear need for effective new analgesics. The results with Sativex show that it can provide additional pain relief to this group of patients and may represent an important new option in the treatment of cancer pain."

Clinical Focus: Ten Guidelines for assessing and Treating Pain

This is the 8th and final instalment in a series on principles and guidelines for pain management.

10. Use available resources to update clinical knowledge and to improve utilization of specialty care.

The vast majority of patients can have their pain adequately managed by clinicians for whom pain is not a specialty practice. Information on the management of most pain is readily available and has been for decades. CCHSA (Canadian Council on Health Services Accreditation) have suggested that clinicians adequately assess and appropriately treat pain, using a multidisciplinary approach involving the patient and family as well as professionals.

Unlearning obsolete practices and assumptions can improve pain management. Examples include:

- Meperidine (Demerol) is restricted for use at BRHC. It should be used only for a short-term indication such as post-op shivering and rigors associated with the use of Amphotericin and only if other opioids are inappropriate due to allergic reaction, for example. If it is used, it should be for maximum 48 hours only. Neurotoxicity (toxic to the brain) occurs with high doses or repeated dosing of Meperidine due to the active metabolite normeperidine.
- Codeine and mixed antagonist/agonist agents (Talwin for example) should be avoided for chronic use or for severe pain because of ceiling effects (the dose above which there is no further analgesia but increased side effects occur) and/or toxicity.
- "Drug-seeking" is more likely to be a symptom of inadequate pain control than of addiction. Using this phrase has been shown to have different meanings and connotations depending on the person who uses this phrase: drug-seeking behaviour is often used by health care providers in reference to the behaviours of some patients with pain who request opioids for pain relief. Often the phrase is used to describe a "difficult" patient. It is useful to know that describing a patient as difficult is considered a stigmatizing act (McDonald 2003). Instead of stigmatizing a patient with the label "drug-seeking", the behaviour should be described and discussed with the patient in a respectful manner to determine meanings and causes of the behaviour, seeking to work with the patient for solutions. Portenoy (1996) emphasizes that "the diagnosis of an addiction disorder should be made only if the criteria for this diagnosis are met and there is no credible alternative diagnosis". The first step to be taken with

such behaviours if to rule out pseudoaddiction by thoroughly examining the pain management plan and escalating opioids and other pain-relief methods to determine whether the behaviours are driven by undertreatment of pain.

- Patients with a history of substance abuse can be treated for pain with opioid analgesics.
- Providing analgesia for patients with acute abdomen does not prevent accurate diagnosis of the underlying condition.
- Neonates and infants experience pain in all situations in which older children and adults experience pain.

It is inevitable that some patients will not respond as expected to standard interventions for pain. When this occurs, the patient's pain should be reassessed, neuropathic pain should be considered, and psychosocial factors should be explored. Consultation with a multidisciplinary pain team or specialist should be considered when:

- The patient's pain persists beyond the expected time for healing
- Symptoms of neuropathic pain are present
- There are concerns about addiction (addiction is a disease that should be diagnosed and managed by a specialist in addiction medicine)
- The patient has a current or prior history of substance abuse, including alcohol and prescription drugs
- The patient or family psychological issues complicate the inherent complexity of patient care.

Specialty pain consultation: The Pain Clinic

Health Sciences Centre
GG539A
820 Sherbrook Street
Winnipeg, Mb R3A 1R9
(204) 787-3018
fax (204) 787-3127

Due to the long waiting list, the Pain Management Resource Nurse is available to professionals for pain assessments by calling 578-4202 or sending a request via Orders Communication at BRHC.

References used for the Pain Relief Connection Newsletter include among others, the following:

Care Beyond Cure A Pharmacotherapeutic Guide to Palliative Care 2000
McCaffery M., Pasero C., *Pain Clinical Manual* 2nd Edition 1999 Mosby
Professional's Handbook of Drug Therapy for Pain Springhouse 2001
Ballantyne Jane C., *The Massachusetts General Hospital Handbook of Pain Management* 3rd Edition
Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain 5th Edition American Pain Society 2005
Pereira, J., Bruera e., *Alberta Palliative Care Resource Guide* Alberta Cancer Board 2001 2nd Edition
Roman D. Jovey, MD editor *Managing Pain the Canadian Healthcare Professional's Reference* 2002

End-of-Life Physician Education Resource Center www.eperc.mcw.edu

EDUCATION:

Managing Pain Before It Manages You This once-a-week for 9 weeks program is for individuals who are living with persistent (chronic) pain and who are interested in learning how to learn to manage their pain. The classes are one-hour long and are limited to 10 participants. For more information, please contact Bev More, Pain Management Resource Nurse at 578-4202 or to register, contact Pat Shaw, Clinics Clerk 578-4200. The next classes start September 13, 2007 from 1030-1130 and continue until November 8, 2007.



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Regional Anaesthesia & Pain Medicine 2007

If you have a question that you would like answered or a case study that you would like to see profiled here, please send the information to Bev More, Pain Management Resource Nurse, CS1-200 BRHC or email to: moreb@brandonrha.mb.ca

Feedback about this newsletter is welcome. Please send comments to moreb@brandonrha.mb.ca