Reference Material

Disclaimer: The "Palliative Pain and Symptom Management Pocket Reference Guide" provides pain and symptom management information; this information is not medical advice. This guide was developed as general information for physicians and registered nurses with palliative care expertise only; physicians and nurses should exercise their own independent clinical judgment. To the best of our ability, we have provided references for the information contained within this reference guide. Where references are not available, the information reflects local practice by Palliative Care Expert Physicians in the Erie St. Clair and South West Local Health Integration Networks (LHINs). Health care providers must be fully informed before prescribing any products and while we endeavour to keep the information up to date and correct, we make no representation or warranties of any kind, express or implied about the completeness, accuracy, reliability or suitability with respect to the information or products.

In no event will we be liable for any loss or damages including without limitation, indirect or consequential loss or damage or any loss or damage whatsoever arising from or out of the use of this reference guide.

Note: many references for the **PALLIATIVE PAIN & SYMPTOM MANAGEMENT POCKET REFERENCE GUIDE** originate with The Pallium Palliative Pocket Book 2008. To purchase this manual visit http://www.market-marche.chpca.net/

PALLIATIVE CARE: PAIN MANAGEMENT

PAIN MANAGEMENT STEPS

√ **ESAS**

Link – www.palliative.org

Reference(s):

Chang, V.T., Hwang, S.S., Feuerman, M. Validation of the Edmonton Symptom Assessment Scale. 2000; 88(9): 2164-7.

Heedman, P.A., Strang, P. Symptom assessment in advanced palliative home care for cancer patients using the ESAS: Clinical Aspects. Anticancer Research 2001; 21(6A): 4077-82.

Smith, P.J., Craft, P., Lickiss, N. Concurrent validity of the modified Edmonton Symptom Assessment System with the Rotterdam Symptom Checklist and the Brief Pain Inventory. Support Care Cancer 1998; 6(6): 539-41.

Watanabe, S., et al. Palliative care nurses' perceptions of the Edmonton Symptom Assessment Scale: a pilot survey. International Journal of Palliative Nursing 2006; 12(3):111-4.

Developed by Palliative Care Experts, chaired by: Dr. Ingrid Harle, M.D., FRSCS, CCFP, FCFP, ABHPM (2007-October 2009); Dr. Glen Maddison, M.D. (Nov. 2009-present)
Palliative Pain & Symptom Management Consultation Program. Southwestern Ontario.
St. Joseph's Health Care, London, Ontario. November 2009.
Web Sites: www.palliativecareswo.ca; www.thehealthline.ca

√ Assess to determine the etiology of the pain

Reference(s):

Gordon, D.B., Pellino, T.A., Miaskowski, C., et al. A 10-year review of quality improvement monitoring in pain management: recommendations for standardized outcome measures. Pain Management Nursing 2002; 3:116-130.

Morrison, R., et al. Improving the Management of Pain in Hospitalized Adults. Archives of Internal Medicine 2006; 166:1033-1039.

√ PPS

Link – www.victoriahospice.org/health-care-professionals/clinical-tools

√ Consult with a palliative care expert when comfort goals are not being met

Pain Crisis:

- When all the patient can concentrate on is pain
- If pain has a sudden onset, acute, severe and is persistent
- Pain score 10/10 for or greater than 48 hours despite maximum use of prescribed breakthrough analgesia

OR

- Pain scores 10/10 for or greater than 24 hours with maximum use of prescribed breakthrough analgesia and or signs/symptoms of opioid toxicity

Management Strategy:

- Focus on pain diagnosis, differentiating reversible from intractable causes of pain
- Select opioid and monitor and treat adverse effects
- Titrate and rotate opioid and co-analgesics
- Consult experts to treat a pain crisis as quickly as possible to prevent unnecessary suffering
- Co-op the available institutional resources

Palliative Care Physicians:

London/Middlesex/Elgin/Huron/Perth: 519-685-8588
Dr. Megan Miller: pager #18838
Dr. Gil Schreier: pager #17221
Dr. Niven Shetty: pager #15848

Oxford:
Dr. Karen Fryer: pager 519 536-4635

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Palliative Pain & Symptom Management Consultation Program. Southwestern Ontario.
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Web Sites: www.palliativecareswo.ca; www.thehealthline.ca

Sarnia-Lambton:
Dr. Glen Maddison: pager 519-464-3056

Grey-Bruce:
Dr. Hilli Huff: page through switchboard 519-372-3920

Windsor-Essex:
Palliative Medicine Program- Hospice Windsor and Essex County- 519-974-7100

OPIOID DOSAGE

√ **There is no ceiling dose unless using a mixed analgesic such as Tylenol with codeine or oxycocet, which contain acetaminophen as well as an opioid; acetaminophen has a total daily intake limit of 2.6 gm (in the elderly or those with organ impairment) to 4.0 gm (healthy patient)**

Reference(s):

Compendium of Pharmaceuticals and Specialties, Canadian Pharmacists' Association. Thirty-sixth edition, 2001.

Jovey, R. (2008). Managing Pain: The Canadian Healthcare Professional's Reference, Baker Edwards Consulting Inc., Stittsville, Ontario K2S 0A5: 91

Additional References for Opioid Dosage:

Cleeland, C. S. (1998). Undertreatment of Cancer Pain in Elderly Patients. *JAMA* 279: 1914-1915.

Davis, M.P. Acute pain in advanced cancer: an opioid dosing strategy and illustration. American Journal of Hospice Palliative Care. 2004 Jan-Feb; 21 (1):47-50.

Klepstad, P., Kaasa, S., Jystad, A., et al. Immediate or sustained release morphine for dose finding during start of morphine to cancer patients: a randomized double blind trial. Pain 2003 Jan; 101 (1-2): 193-8.

Zeppetella, G., Ribeiro, M.D. Opioids for the management of breakthrough (episodic) pain in cancer patients. Cochrane Database System Rev. 2006; Jan. 25; (1): CD004311.

TITRATION OF OPIOIDS

√ **If pain is not managed, increase BT doses, using IR opioids (e.g., morphine, hydromorphone) until it is safe to titrate the patch.**

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Web Sites: www.palliativecareswo.ca; www.thehealthline.ca

Reference(s):

Jovey, R. (2008). Managing Pain: The Canadian Healthcare Professional's Reference, Baker Edwards Consulting Inc., Stittsville, Ontario K2S 0A5: 91

Wells,, N., Murphy, B., Douglas, S., Yelton, N. Establishing the safety and efficacy of an opioid titration protocol. American Journal of Hospice Palliative Care. 2004 Sep-Oct;21(5):373-80.

Morita, T., et al. Opioid Rotation from Morphine to Fentanyl in Delirious Cancer Patients: An open-label trial. Journal of Pain and Symptom Management. 2005; 30(1): 96-103.

OPIOID ROTATION

√ **When rotating opioids, determine the equianalgesic dose and then decrease the dose of new drug by 30% to account for incomplete cross-tolerance.**

Reference(s):

Emmanuel L.L., Librach L.S. (2007) Palliative Care: Core Skills and Clinical Competencies, Saunders Elsevier, Philadelphia PA: 108.

Gallagher R., (2005). Managing Cancer Pain: The Canadian Healthcare Professional's Reference, Healthcare & Financial Publishing, Rogers Media, Toronto ON: 39-40.

EQUIANALGESIC DOSE

√ **Remember incomplete cross-tolerance**

Reference(s):

Brant, J.M. Opioid equianalgesic conversion: the right dose. Clinical Journal of Oncology Nursing 2001 5 (4) :163-5.

Gammaitoni, A.R., Fine, P., Alvarez, N, McPherson, M.L., Bergmark, S. Clinical application of opioid equianalgesic data. Clinical Journal of Pain. 2003 Sep-Oct;19(5):286-97.

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Web Sites: www.palliativecareswo.ca; www.thehealthline.ca

Pereira, J., Lawlor, P., Vigano, A., Dorgan, M., Bruera, E. Equianalgesic dose ratios for opioids. a critical review and proposals for long-term dosing. Journal of Pain and Symptom Management. 2001 Aug;22(2):672-87. Review.

Weinstein, S.M., Shi, M., Buckley, B.J., Kwarcinski, M.A. Multicenter, open-label, prospective evaluation of the conversion from previous opioid analgesics to extended-release hydromorphone hydrochloride administered every 24 hours to patients with persistent moderate to severe pain. Clinical Therapies 2006 Jan; 28 (1): 86-98.

√ **Methadone is used for analgesia. It has unusual pharmacodynamics and pharmacokinetics and multiple interactions with other drugs. Physicians require an exemption license to prescribe methadone for pain**

Reference(s):

Bruera, E., Sweeney, C. Methadone Use in Cancer Patients with Pain: A Review. Journal of Palliative Medicine. 2002; 5(1): 127-139.

Moryl, N., Santiago-Palma, J., Kornick, C., et al. Pitfalls of opioid rotation: substituting another opioid for methadone in patients with cancer pain. Pain 2002 Apr; 96 (3):325-8.

Link- www.eperc.mcw.edu/ff_index.htm

FENTANYL PATCH

√ **… opioid naïve**

Link- www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/duragesic_hpc-cps-eng.pdf

Link - www.ismp-canada.org/download/safetyBulletins/ISMPCSB2006-05Fentanyl.pdf

√ **Fentanyl does not have a short acting oral equivalent for BT pain.**

Reference(s):

Skaer, T.L. Practice guidelines for transdermal opioids in malignant pain. Drugs 2004; 64(23):2629-38.

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Web Sites: www.palliativecareswo.ca; www.thehealthline.ca

Breitbart, W., Chandler, S., Eagle, B., Ellison, N., Enck, R.E., Lefkowits, M., Payne, R. An alternative algorithm for dosing transdermal fentanyl for cancer-related pain. Oncology (Williston Park). 2000 May; 14(5): 695-705; discussion 705, 709-17.

Starting fentanyl:

√ **Starting dose: Starting dose: 60 - 134 mg oral morphine per day is approximately equal to fentanyl 25 mcg patch q 72h**

Reference(s):

Skaer, T.L. Practice guidelines for transdermal opioids in malignant pain. Drugs 2004; 64(23):2629-38.

Breitbart, W. Chandler, S., Eagle, B., Ellison, N., Enck, R.E., Lefkowitz, M., Payne, R. An alternative algorithm for dosing transdermal fentanyl for cancer-related pain. Oncology (Williston Park). 2000 May; 14(5):695-705; discussion 705, 709-17.

ANALGESICS TO AVOID

Reference(s):

University of Wisconsin Hospitals and Clinic Guidelines for Use of Meperidine ISMP Canada Safety Bulletin. Volume 4, Issue 8. August 2004.

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OPIOID OVERDOSE

√ **Use sedation scale to determine level of sedation.**

Tool:

SEDATION SCALE

S= Normal Sleep: easy to arouse
(arouses from sleep to verbal stimuli or gentle touch)

0=Awake and Alert

1= Mild: occasionally drowsy, easily aroused
(arouses to **verbal stimuli** or gentle touch,
may drift off ***after*** conversation, obeys commands**)**

2= Moderate: frequently drowsy, easily aroused
(arouses to **physical stimuli/gentle shaking**,
drifts off ***during*** conversation, slow to follow commands)

3= Severe: somnolent, difficult to arouse
(**minimal verbal response** to **vigorous shaking/noxious stimuli**,
does not obey commands)

√ **Starting IV dosing: dilute 0.4 mg/ml of naloxone… sedation level 3.**

Link- http://palliative.info/resource_material/FlowchartExcessiveOpioids.pdf

Reference(s):

Mercadante, S., Villari, P., Ferrera, P. Naloxone in treating central adverse effects during opioid titration for cancer pain. Journal of Pain and Symptom Management 2003 Aug; 26 (2) 691-3.

Developed by Palliative Care Experts, chaired by: Dr. Ingrid Harle, M.D., FRSCS, CCFP, FCFP, ABHPM (2007-October 2009); Dr. Glen Maddison, M.D. (Nov. 2009-present)
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Web Sites: www.palliativecareswo.ca; www.thehealthline.ca

COMMON OPIOID SIDE EFFECTS

√ **Sedation**

Reference(s):

Rozans, M., et al. Palliative Uses of Methylphenidate in Patients with Cancer: A Review. Journal of Clinical Oncology 2001; 20:335-339.

MUST KNOW

√ **Most patients over time do become physically dependent on opioids.**

√ **Opioid tolerance and physical dependence are physiological and do NOT equate with addiction.**

Reference(s):

Jovey, R. (2008). Managing Pain: The Canadian Healthcare Professional's Reference, Baker Edwards Consulting Inc., Stittsville, Ontario K2S 0A5: 105-107.

Opioid Addiction, Physical Dependence and Tolerance

- **Addiction** is a primary, chronic, neurobiological disease, with genetic, psychological, and environmental factors influencing its development and manifestations. It is characterized by behaviours that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving (American Psychiatric Association, 2001). True addictions need to be distinguished from pseudo-addiction caused by under-treatment of pain, behavioural/family/psychological dysfunction, and drug diversion with criminal intent.
- **Physical dependence** is a state of adaptation that often includes tolerance and is manifested by a drug class specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing drug level of the drug, and or administration of an antagonist (Jovey, 2008). This normal response often occurs with the persistent use of certain medications including beta blockers, corticosteroids, antidepressants and other medications not associated with addictive disorders. When no longer needed, drugs that induce physical dependence should be carefully tapered. Abruptly discontinuing an opioid may result in withdrawal

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symptoms such as tachycardia, hypertension, diaphoresis, piloerection, nausea and vomiting, diarrhea, body aches, abdominal pain, psychosis, and/or hallucinations. If the dose is lowered too quickly and withdrawal symptoms occur, a transient increase in the opioid dose, treatment with clonidine, or a small dose of a benzodiazepine (for example lorazepam) may be necessary to settle distressing symptoms.

- **Pharmacological tolerance** is a state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more of the drug's effects over time. The region of the CNS where tolerance is thought to occur is anatomically and functionally separate from the brain pathways related to addiction (Jovey, 2008). When increasing doses of analgesic are required, suspect a worsening disease rather than pharmacologic tolerance. Tolerance to the side effects of opioid drugs varies. Tolerance to sedation and nausea usually develops within days or weeks but tolerance to constipation rarely develops (Gallagher, 2005).

  People with histories of substance abuse can also develop significant pain; they deserve compassionate treatment of their pain when it occurs. Most will need to adhere to strict dosing protocols, and a contract between physician and person may become necessary. Physicians/health care providers who are unfamiliar with these situations may need the help of specialists in pain management and/or addiction medicine.

Narcotic Addiction. Weissman, D.E. Is it Pain or Addiction. Journal of Palliative Medicine 2005; 8(6):1282.

Weissman, D.E. Pseudoaddiction. Journal of Palliative Medicine 2005 8(6): 1283.

Link- www.eperc.mcw.edu/ff_index.htm

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Web Sites: www.palliativecareswo.ca; www.thehealthline.ca

WOUNDS

√ Morphine in intrasite gel for local analgesia

Reference(s):

Pereira JL, Associates. The Pallium palliative pocketbook: a peer-reviewed, referenced resource. 1st Cdn ed. Edmonton, Canada: The Pallium Project 2008: 16:18.

INCIDENT PAIN/PROCEDURAL PAIN

√ **Fentanyl Injectable can be used sublingually for incident or procedural pain.**

Link- http://palliative.info/IncidentPain.htm

Reference(s):

Cleary, J. Incident Pain. Palliative Medicine. 2005 Jan;19(1):1-2.

Gardner-Nix, J. Oral transmucosal fentanyl and sufentanil for incident pain. Journal of Pain and Symptom Management. 2001 Aug;22(2):627-30.

Lennernas, B., Hedner, T., Holmberg, M, Bredenberg, S., et al. Pharmacokinetics and tolerability of different doses of fentanyl following sublingual administration of a rapidly dissolving tablet to cancer patients: a new approach to treatment of incident pain. British Journal of Clinical Pharmacology. 2005 Feb;59(2):249-53.

Rhiner, M., Palos, G., Termini, M. Managing breakthrough pain: a clinical review with three case studies using oral transmucosal fentanyl citrate. Clinical Journal of Oncology Nursing. 2004 Oct;8(5):507-12. Review.

ADJUVANT INTERVENTIONS FOR

Neuropathic Pain:

√ **Gabapentin: for starting dose and titration guidelines**

Starting dose of Gabapentin:
100 mg. orally tid; titrate to effective dose (usually 2400 – 3600 mg. daily)

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Web Sites: www.palliativecareswo.ca; www.thehealthline.ca

Reference(s):

Daeninck, P., Shadd, J.; Chapter 7, page 60 in Managing Cancer Pain, Toronto: Healthcare & Financial Publishing, Rogers Media; 2005.

Pereira JL, Associates. The Pallium palliative pocketbook: a peer-reviewed, referenced resource. 1st Cdn ed. Edmonton, Canada: The Pallium Project 2008: 5:64.

√ **Pregabalin: indicated for diabetic peripheral neuropathy and postherpetic neuralgia**

Reference(s):

Freynhagen, R., et al. Efficacy of pregabalin in neuropathic pain evaluated in a 12-week, randomized, double-blind, multicentre, placebo-controlled trial of flexible and fixed dose regimes. Pain 2005; 115:254-263.

√ **Methadone is used for analgesia. It has unusual pharmacokinetics and multiple interactions with other drugs.**

Reference(s):

Bruera, E., Sweeney, C. Methadone Use in Cancer Patients with Pain: A Review. Journal of Palliative Medicine. 2002; 5(1): 127-139.

Moryl, N., Santiago-Palma, J., Kornick, C., et al. Pitfalls of opioid rotation: substituting another opioid for methadone in patients with cancer pain. Pain 2002 Apr; 96 (3):325-8.

Link- www.eperc.mcw.edu/ff_index.htm

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PALLIATIVE CARE: SYMPTOM MANAGEMENT

√ G.I. PROTECTION

Reference(s):

Pereira JL, Associates. The Pallium palliative pocketbook: a peer-reviewed, referenced resource. 1st Cdn ed. Edmonton, Canada: The Pallium Project 2008: 5:80-81.

Emmanuel L.L., Librach L.S. (2007) Palliative Care: Core Skills and Clinical Competencies, Saunders Elsevier, Philadelphia PA: 103.

NAUSEA (CONSIDER ETIOLOGY)

5HT3 antagonist:
√ ondansetron * 4 – 8 mg po/subcut/ IV BID – TID (main indication for use in early radiation/chemo induced nausea & vomiting)

Reference(s):

Pereira JL, Associates. The Pallium palliative pocketbook: a peer-reviewed, referenced resource. 1st Cdn ed. Edmonton, Canada: The Pallium Project 2008: 8-11.

√ MOUTH CARE

Regional Palliative Care Program, Capital Health, Edmonton Alberta (2006). 99 common Questions About Hospice Palliative Care, A Nurses handbook, 3rd Edition: 80-82.

Link - http://www.emedicine.com/derm/topic682.htm
Woo, S. Chemotherapy-induced oral mucositis. EMedicine. Feb 10, 2005. Accessed May 13, 2006.

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BOWEL ROUTINE (daily dosing and prn)

√ Consider etiology of Constipation

Reference(s):

Pereira JL, Associates. The Pallium palliative pocketbook: a peer-reviewed, referenced resource. 1st Cdn ed. Edmonton, Canada: The Pallium Project 2008: 8:13-17.

Link -www.palliativedrugs.com – search constipation

√ methylnaltrexone (MNTX)

Methylnaltrexone (MNTX) is a selective peripheral mu opioid antagonist.

- Does not cross blood brain barriers
- No change in pain levels
- No opioid withdrawal symptoms

Contraindications to use:
Bowel obstruction
Studies on MNTX excluded patients with ostomies

For further information: 1-800-461-8844 or www.wyeth.ca

COMPLETE BOWEL OBSTRUCTION

√ venting Gastronomy Tubes

Reference(s):

Pereira JL, Associates. The Pallium palliative pocketbook: a peer-reviewed, referenced resource. 1st Cdn ed. Edmonton, Canada: The Pallium Project 2008: 8:22-23.

√ **HICCUPS** (note - chlorpromazine causes orthostatic hypotension)

Reference(s):

Sanchack, K. Hiccups: When the Diaphragm Attacks. Journal of Palliative Medicine. 2004; 7(6): 870-874.

Viera, A.J., Sullivan, S.A.: Remedies for prolonged hiccups. American Family Physician 2001; 163:1684.

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Web Sites: www.palliativecareswo.ca; www.thehealthline.ca

Link - http://www.emedicine.com/emerg/topic252.htm. Wilkes G: Hiccups on eMedicine. Last updated May 24, 2005. Accessed May 14, 2006.

DYSPNEA

First Line:

√ **Oxygen for ODB criteria**

Reference(s):

http://www.health.gov.on.ca/english/providers/pub/adp/hop_manual05.pdf

Renewal requires qualifying oximetry strip (≤88% for ≥2 minutes), may also require supporting letter from physician, renewal for 90 days again. If person is still requiring oxygen, renewal is required again after 9 months.

Second Line:

√ **Recent studies have indicated**

Reference(s):

Pereira JL, Associates. The Pallium palliative pocketbook: a peer-reviewed, referenced resource. 1st Cdn ed. Edmonton, Canada: The Pallium Project 2008: 6:13.

√ **Titration of opioid using pain management principles**

Reference(s):

RNAO Nursing Best Practice Guidelines, Assessment and Management of Pain, www.rnao.org/Storage/29/2351_BPG_Pain_and_Supp.pdf%20.%20 By right clicking on the left side of the page, you may choose "pages" - this will provide thumbnail pages for the entire document. Highlight the thumbnail of the desired page to view or print it.

Recommendation 30

Ensure that the timing of analgesics is appropriate according to personal characteristics of the individual, pharmacology (i.e. Duration of action, peak-effect and half-life) and route of the drug. *(Grade of Recommendation=B)*

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Recommendation 31

Recognize that opioids should be administered on a regular time schedule according to the duration of action and depending on the expectation regarding the duration of severe pain. (*Grade of Recommendation = A*)

- If severe pain is expected for 48 hours post-operatively, routine administration may be needed for that period of time. Late in the post-operative course, analgesics may be effective given on an "as needed" basis.
- In chronic cancer pain, opioids are administered on an "around-the-clock" basis, according to their duration of action.
- Long-acting opioids are more appropriate when dose requirements are stable.

Recommendation 32

Use principles of dose titration specific to the type of pain to reach the analgesic dose that relieves pain with a minimum of side effects, according to: (*Grade of Recommendation=B*)

- cause of the pain;
- individual's response to therapy;
- clinical condition;
- concomitant drug use;
- onset and peak effect;
- duration of the analgesic effect;
- age; and
- known pharmacokinetics and pharmacodynamics of the drugs administered. Doses are usually increased every 24 hours for persons with chronic pain on immediate release preparations, and every 48 hours for persons on controlled release opioids. The exception to this is transdermal fentanyl, which can be adjusted every 3 days.

Recommendation 33

Promptly treat pain that occurs between regular doses of analgesic (breakthrough pain) using the following principles:
(*Grade of Recommendation =C*)

- Breakthrough doses of analgesic in the post-operative situation are dependent on the routine dose of analgesic, the individual's respiratory rate, and the type surgery and are usually administered as bolus medications through PCA pumps.

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- Breakthrough doses of analgesic should be administered to the person on an "as needed" basis according to the peak effect of the drug (po/pr = q1hr; SC/IM-q30 min; IV – q 10-15 min).
- It is most effective to use the same opioid for breakthrough pain as that being given for "around-the-clock" dosing.
- Individuals with chronic pain should have:
    - An immediate release opioid available for pain (breakthrough pain) that occurs between the regular administration times of the "around-the-clock" medication.
    - Breakthrough doses of analgesic for continuous cancer pain should be calculated as 10-15 per cent of the total 24-hour dose of the routine "around-the-clock" analgesic.
    - Breakthrough analgesic doses should be adjusted when the regular "around-the-clock" medication is increased.
    - Adjustment to the "around-the-clock" dose is necessary if more than 2-3 doses of breakthrough analgesic are required in a 24-hour period, and pain is not controlled.

√ SEVERE PROGRESSIVE DYSPNEA

Reference(s):

Fronenac, Lennox & Addington (KFL&A) Palliative Care Integration Project: Dyspnea management guidleines for Palliative Care. In Symptom Management Guidelines. Kingston, Ontario, Canada: KFL&A Palliative Care Integration Project, 2003, pp 41-44. Copyright by KFL&A Palliative Care Integration Project.

√ Protocol for sedation for intractable symptoms at the end of life may have to be enacted

Reference(s):

Pereira JL, Associates. The Pallium palliative pocketbook: a peer-reviewed, referenced resource. 1st Cdn ed. Edmonton, Canada: The Pallium Project 2008: 18:1-10.

Sedation for intractable symptoms:

This process involves pharmacological interventions aimed to induce/maintain sedation, in order to palliate refractory symptoms in the terminally ill.

Developed by Palliative Care Experts, chaired by: Dr. Ingrid Harle, M.D., FRSCS, CCFP, FCFP, ABHPM (2007-October 2009); Dr. Glen Maddison, M.D. (Nov. 2009-present)
Palliative Pain & Symptom Management Consultation Program. Southwestern Ontario.
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The purpose of sedation is to reduce patient awareness of distressing symptom(s).
Inducing sedation could conceivably shorten life by reducing airway protective mechanisms.
For the physician therefore, the ethical principle of **"double-effect"** operates in this situation. Here the ***primary intent*** (relief of distress from refractory symptoms) outweighs a foreseen potentially ***negative outcome*** (potential shortening of life).
Despite the emotive debate concerning the underlying ethical principles, most situations where the need arises in clinical practice present relatively straightforward indications.

Types of pharmacological sedation and clinical indications:

Maintenance
Agitated delirium uncontrolled on less sedating neuroleptics, e.g., haloperidol
Dyspnea uncontrolled on maximal standard therapy.
Any refractory symptom that is uncontrolled using best standard care.

Specific Emergencies
Seizure/acute stridor/massive bleeding. Sedation order written as prn.
Use a rapid onset, short-acting benzodiazepine, e.g., midazolam or lorazepam

Questions that need to be answered prior to initiating sedation:

Q: Has a ***thorough assessment*** been conducted to identify and ***treat reversible problems***?
Q: Have appropriate ***consultations*** been made with ***palliative care and other specialists***?
Q: Have ***non-pharmacological approaches been maximized***, e.g., distraction or relaxation techniques in the case of anxiety/dyspnea?
Q: Have ***other pharmacological treatments been maximized***, e.g., appropriate titration of opioids in the case of dyspnea or appropriate dosing of neuroleptics for delirium?
Q: Have the ***goals of sedation*** been ***explained*** to and discussed with the patient and/or family?
Q: Has a ***consensus*** been reached as a result of the discussions? ***(Conference)***
Q: Has ***temporary sedation*** been considered? Consider, if necessary, in the event of potentially reversible delirium, and while awaiting the outcome of interventions aimed at reversal.

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Suggested agents for inducing/maintaining pharmacological sedation:

Methotrimeprazine(can be tried prior to midazolam)
6.25mg sc q8 hourly (h) and q 1h prn for breakthrough (BT) agitation.
If necessary, increase dose to 12.5 or 25mg sc q8h and q1h prn for BT
If ineffective, or **deeper sedation needed**, proceed to **midazolam**

Midazolam
(short-acting, hence given as **infusion** except for seizures, stridor or bleeding)
In **some situations** (severe agitation) a **loading dose** of 2.5mg sc is given
Start **infusion at 1mg/hour sc, titrate** to keep patient **sleepy/sedated**
The infusion can be titrated up/down every 5-10 minutes as needed.
For **seizure** activity, a massive **bleed**, or acute **stridor** give 5mg im stat (im route -faster absorption) Preloaded syringes last 30 days approx.

Less commonly used agents include chlorpromazine (iv or pr) and propofol (iv). Midazolam has rapid onset of effect, ease of titration, and reversal (short half-life), if indicated.

Please consult palliative care physicians as needed, especially if indications are not straightforward.

Palliative Care Tips - Edited by Doreen Oneschuk MD. Tertiary Palliative Care Unit, Grey Nuns Community Hospital. Original Contributor: Peter Lawlor, MD - Issue #21 June2002.

Ellershaw, J.E., et al. Care of the dying: setting standards for symptom control in the last 48 hours of life. Journal of Pain and Symptom Management 2001; 21:12-17.

Krakauer, E.L., et al. Sedation for Intractable Distress of a Dying Patient: Acute Palliative Care and the Principle of Double Effect. The Oncologist 2000; 5:53-62.

Link - www.palliative.org

√ **HYPERCALCEMIA** (corrected value over 2.65 mmol)

Reference(s):

Roemer-Becuwe, C., et al. Safety of subcutaneous clodronate and efficacy in hypercalcemia in malignancy: a novel route of administration. Journal of Pain and Symptom Management 2003; 26(3):843-8

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Shustik, C. Tumour-induced hypercalcemia. Current Oncology 2001; 7:173-9.

Stewart, A.F. Hypercalcemia associated with cancer. New England Journal of Medicine 2005; 352:373-9.

Link - www.palliativedrugs.com – search bisphosphonates

DELIRIUM

√ **Hyperactive and hypoactive (may masquerade as depression; look for disordered thinking)**

Reference(s):

Fabbro, E., et al. Symptom control in Palliative Care – Part 111. Dyspnea and delirium. 2006 9(2); 422-437.

Lawlor, P.G., et al. Occurrence, causes and outcome of delirium in patients with advanced cancer. A prospective study. Archives of Internal Medicine 2000; 160:786-794.

Morita, T., et al. Underlying pathologies and their associations with clinical features in terminal delirium of cancer patients. Journal of Pain and Symptom Management 2001; 22:997-1006.

Von Gunten, C. Interventions to Manage Symptoms at End of Life. Journal of Palliative Medicine 2005: S:88-94.

√ **ACUTE SEIZURE CONTROL** - if patient is actively seizuring

Reference(s):

Krouwer, H.G.J., et al. Management of Seizures in Brain Tumor Patients at End of Life. Journal of Palliative Medicine 2000; 3 (4): 465-475.

Pereira JL, Associates. The Pallium palliative pocketbook: a peer-reviewed, referenced resource. 1st Cdn ed. Edmonton, Canada: The Pallium Project 2008: 14:7.

Link - www.palliativedrugs.com - search for midazolam, phenobarbitol, anticonvulsants

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√ **MYOCLONIC JERKING** (can be due to opioid toxicity)

Reference(s):

Pereira JL, Associates. The Pallium palliative pocketbook: a peer-reviewed, referenced resource. 1st Cdn ed. Edmonton, Canada: The Pallium Project 2008: 5:30-32.

INTRACTABLE SYMPTOMS AT END OF LIFE

√ **Criteria for sedation for intractable symptoms**

* See Severe Progressive Dyspnea

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√ Developed by: Palliative Care Expert Committee

Windsor and Essex County

Sharon Allen, NP, M.Sc.N., CHPCN(C)

Angie Deneweth, NP

Janet Elder, Reg.N, CHPCN(c)

Jim Gall, MD

Carole Gill, Reg.N., CHPCN(C)

Karen Riley, BScPhm, Pharm D, BCPS, RPh

Kent and Lambton Counties

Ann Brignell, Reg.N., CHPCN(C)

Glen Maddison, MD

Elgin and Oxford Counties

Brian Fathers, BSc Pharm, R Pharmacist

Ida Tigchelaar, Reg.N., CHPCN(C)

London and Middlesex County

Sharon Baker, MD

Ingrid Harle, MD, FRCSC, CCFP, FCFP, ABHPM

Nancy Keat, Reg.N., B.Sc.N., M.Sc., CHPCN(C)

Huron and Perth Counties

Judy White, Reg.N., CHPCN(C)

Grey and Bruce Counties

Hilli Huff, MD, CCFP

Liz Laird, Reg.N., BScN, CHPCN(C)

Marie Palmer, Reg.N., B.A., CHPCN(C)

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