MANUAL ON

THE USE OF ESSENTIAL PALLIATIVE CARE MEDICINES FOR ADULTS

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IAHPC INTERNATIONAL ASSOCIATION for Hospice & Palliative Care

IAHPC Manual on the Use of Essential Palliative Care Medicines for Adults

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Disclaimer

The Information included in this Manual is presented as is, and should not be relied upon as complete or accurate, nor should it be relied on to suggest a course of treatment for a particular individual. This Manual reflects the opinion of palliative care workers and experts from around the globe.

The treatment of the underlying cause should be considered, if possible. Non-pharmacological interventions are not included in this Manual but should always be implemented when appropriate.

Physicians and pharmacists are encouraged to review the cited guidelines, as well as any others applicable in their own settings, and consult with experts as needed. Patients with health care related questions or concerns are advised to contact their physician and their pharmacist.

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Cover photo by Karen Gschwend, in Knysna, South Africa, depicting a staff member of Knysna Sedgefield Hospice visiting a patient at her home. Photo submitted to the 2023 IAHPC Photo Contest. Used with permission.

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Foreword

In the late 1970's the World Health Organization (WHO) developed the concept of Essential Medicines, accompanied by a Model List of Essential Medicines (EML), to identify medicines that are widely available for common health conditions and accepted by health professionals as safe, efficacious, and cost-effective. This list, which is updated biennially, has informed the development of national essential medicines programs.

A section on Medicines for Pain and Palliative Care in the WHO EML includes 24 medications[1]. It is used by policymakers — particularly those in resource-limited countries — to inform decisions about the procurement and tracking of medicines that are essential when providing palliative care.

In 2018, the Lancet Commission on Pain and Palliative Care described the worldwide prevalence of serious health-related suffering due to severe illness and recommended the integration of palliative care into global health systems[2]. The Commission introduced the Lancet Essential Package (LEP) of palliative care components, including medicines, basic equipment, and human resources. With limited exceptions, the list of medicines in the LEP was based on the EML. The Commission proposed that governments ensure the availability of the LEP, including the recommended medicines, to address the immense global need for care, particularly in resource-limited countries. Although some countries have made progress in providing ready access to these medicines, availability in low-income settings remains poor.

IAHPC recognizes the efforts of governments and agencies to ensure the availability of the medications included in the WHO EML and in the Lancet Commission Report. However, improved access to medicines cannot ensure that they are optimally used. Health professionals require information based on the best available evidence to effectively manage these medications in patients with palliative care needs.

This Manual provides practical recommendations for the safe and effective use of the medications for palliative care included in the WHO EML and in the Lancet Commission Report. Tramadol is also included due to its widespread use in low-and-middle-income countries (LMICs). The Manual is intended to support health professionals who are not specialists in palliative care — physicians and others providing generalist or primary palliative care. It is organized by symptom, and for each recommended medicine, offers consensus-based recommendations, including starting dose, maximum daily dose, and frequency of dosing, as well as additional recommendations proposed by individual experts.

Recognizing the limited availability of evidence in palliative care, this Manual consolidates insights and experiences from palliative care experts around the world. Its goal is to empower providers to confidently and competently deliver symptom management and alleviate suffering of adults with palliative care needs, ensuring patients and their families receive compassionate care close to home from trusted primary care teams.

The Manual also emphasizes the importance of leveraging palliative consultation services for advice, coaching, and mentorship. Many health authorities offer courses, workshops, and other resources to help clinicians strengthen skills and enhance the care provided. While these guidelines are primarily tailored

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1 Web Annex A. World Health Organization Model List of Essential Medicines – 23rd List, 2023. In: The selection and use of essential medicines 2023: Executive summary of the report of the 24th WHO Expert Committee on the Selection and Use of Essential Medicines, 24 – 28 April 2023. Geneva: World Health Organization; 2023 (WHO/MHP/HPS/EML/2023.02). Licence: CC BY-NC-SA 3.0 IGO.

2 Knaul FM et al. Alleviating the access abyss in palliative care and pain relief-an imperative of universal health coverage: the Lancet Commission report. Lancet. 2018;391(10128):1391-1454. doi: 10.1016/S0140-6736(17)32513-8.

for physicians and nurses, allied health professionals will also find them valuable for improving palliative care delivery.[3]

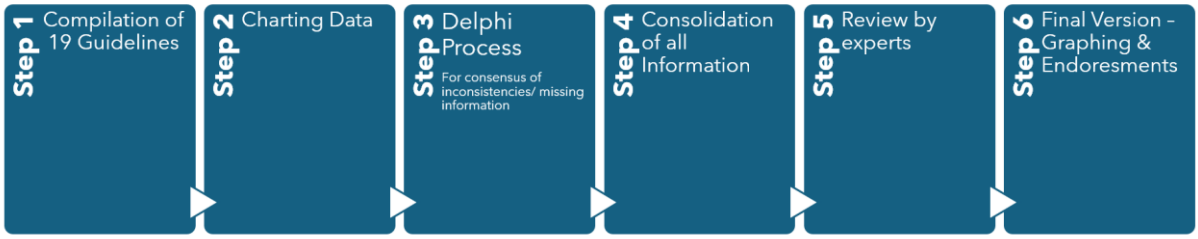
This Manual is intended to support health professionals providing generalist or primary palliative care. These photos, submitted by IAHPC members for the 2021 and 2023 photo contest, depict different moments of palliative care provision in primary care around the globe.

Photo credits and descriptions at the end of the document. Photos used with permission.

[3] For more information about the method used, refer to the open access publication:
Pastrana T, De Lima L, Dudgeon D, Voeuk A, Ahmed E, Radbruch L. Use of Essential Medicines for Pain Relief and Palliative Care: A Global Consensus Process. J Pain Symptom Manage. 2025;69(1):53-64. doi: 10.1016/j.jpainsymman.2024.10.024

Methodology

The process used to develop this Manual including the following steps[4]:



1. An initial core group of five IAHPC expert advisers and board members was convened in December 2022 to identify the current and existing guidelines on the therapeutic use of EMs for pain relief and palliative care. A request for submission of existing guidelines on the use of essential medicines was sent to the IAHPC membership.
2. The core group reviewed the guidelines and developed recommendations for the starting dose, the frequency of dosing, and the maximum dose for each medication included in the WHO EML and/or the Lancet Commission's Essential Package (EP). The core group also included tramadol, despite its exclusion from these lists, because of its widespread use for pain management.
3. The core group then recruited a group of IAHPC members — physicians, nurses, or pharmacists specializing in palliative care — to participate in a Delphi process designed to build consensus about the use of the EMs. Those who agreed to participate (N=57) represented varied regions around the world and countries with varied income levels. Each participant independently reviewed the work of the core group, either concurring with the recommendations or offering their own recommendations on the initial or maximum dose, and/or the dosing frequency.
4. The Delphi process had two rounds. After round 1, recommendations with ≥70% endorsement were retained and others were modified based on the input of the participants. The modified recommendations were presented to the group in round 2, and those recommendations with ≥70% endorsement by the participants were retained.
5. The consensus-derived recommendations that emerged from the Delphi process were then reviewed by a group of 23 palliative care experts (physicians or pharmacists) from 21 countries, some of whom participated in the Delphi process. This review led to some wording changes to ensure that the recommendations are consistent and prioritize patient safety; additional comments about those recommendations that did not achieve consensus also were elicited and were included as comments.

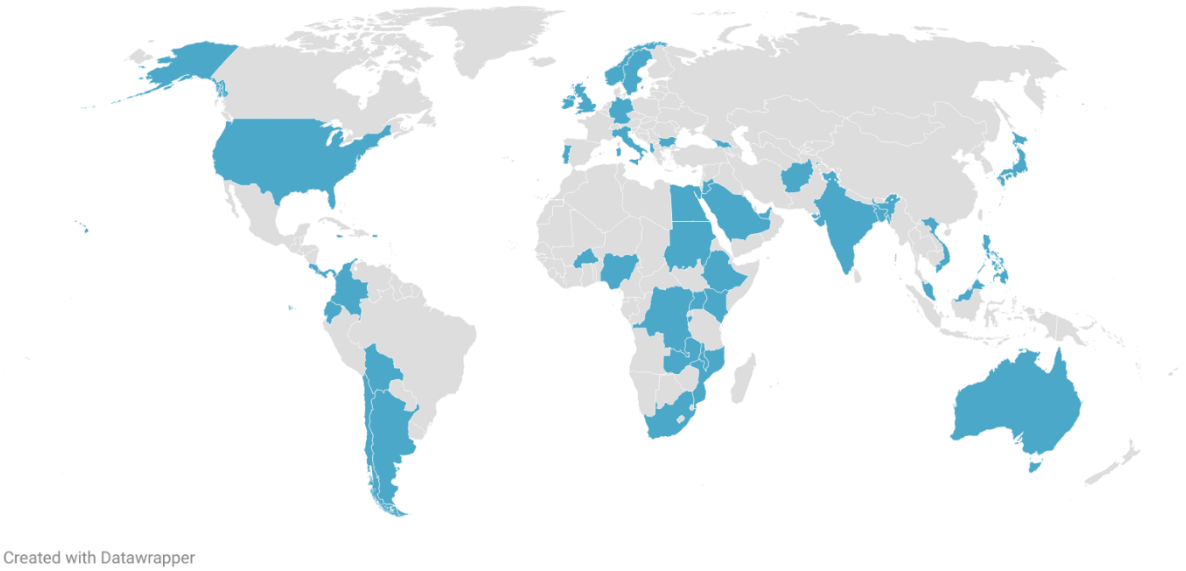
[4] Pastrana T et al. Use of Essential Medicines for Pain Relief and Palliative Care: A Global Consensus Process. J Pain Symptom Manage. 2025;69(1):53-64. doi: 10.1016/j.jpainsymman.2024.10.024

Acknowledgments

Delphi Rounds

We are grateful to the IAHPC members who participated in the two Delphi rounds (in alphabetical order by first name): Alejandra Palma (Chile), Ali Xhixha (Albania), Ancu Feng (Costa Rica), Andrew Amata (Zambia), Arnold Nzale Nzali (DR Congo), Carla Ripamonti (Italy), Chitra Venkateswaran (India), Christine Banda (Malawi), Claudia Bausewein (Germany), Dagny Faksvåg Haugen (Norway), David Currow (Australia), Diego Ezequiel Candelmi, Dingle Spence (Jamaica), Aleesha Adatia (Uganda), Duncan Kwaitana (Malawi), Duong Le (Vietnam), Emilia Pinto (Mozambique), Esther Cege-Munyoro (Kenya), Eve Namisango (Uganda), Fadi Abu-Farsakh (Jordan), Fazle Biswas (Bangladesh), Felicia Loh (Malaysia), Folaju Oyebola (Nigeria), GV Chamath Fernando (Philippines), Jane Bates (UK), Jaishree Sharmini (Malaysia), James Cleary (USA), Juhliad Lebenu Woldegiorgs (Ethiopia), Julia Ambler (South Africa), Lankoandé Martin (Burkina Faso), Lukas Radbruch (Germany), Lyubima Despotova-Toleva (Bulgaria), Maria Cristina Cervantes (Ecuador), Maria Mercedes Fajardo (Colombia), Mary Lynn McPherson (USA), Matthias Brian (Sweden), Michelle Mikus (USA), Scott Mitchell (South Africa), Mitsuru Sakitani (Japan), Mohamad Hamade (Saudi Arabia), Mohammad Al-Shahri (Saudi Arabia), Mukelabai Mukelabai (Zambia), Nahla Gafer (Sudan), Natalia Carafizi, Neil Nijhawan (UAE), Noreen Chan (Singapore), Nshimirimana Mwadjuma (Burindi), Pati Dzotsenidze (Georgia), Regina Mc Quillan (Ireland), Rosa Buitrago (Panama), Rui Carneiro (Portugal), Rumana Dowla (Bangladesh), Samy Alsirafy (Egypt), Sefanit Gebreab (Ethiopia), Sofia Bunge (Argentina), Vanesa Rocio Orellana Caro (Bolivia), Victoria Hewitt (UK).

Figure 1: Geographic distribution of participants in Delphi rounds



Review by Palliative Care Experts

We are also grateful to the palliative care experts in palliative medicine or pharmacology for their review of the results (in alphabetical order by first name):

Alberto Alonso-Babarro (Spain)
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Michelle Mikus (United States)
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Mohammad Al-Shahri (Saudi Arabia)
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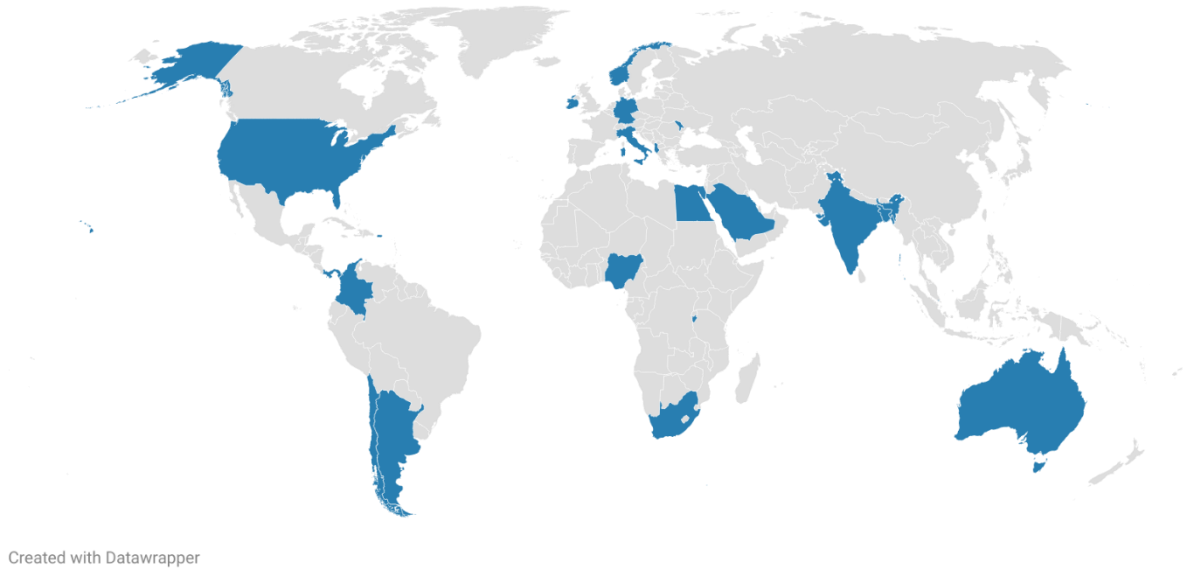
Noreen Chan (Singapore)
Nshimirimana Mwadjuma (Burundi)
Regina Mc Quillan (Ireland)
Russell Portenoy (United States)
Samy Alsirafy (Egypt)
Sofía Bunge (Argentina)

Figure 2: Geographic distribution of experts



Guidelines Consulted

The guidelines provided the basis for the initial information which was then presented to the participants of the Delphi rounds. These guidelines are available for free. Other guidelines which were suggested to the members of the task force were behind paywalls and thus were not included.

1. BC Centre for Palliative Care. BC Interprofessional Palliative Symptom Management Guidelines; 2019. Available from: https://bc-cpc.ca/wp-content/uploads/2019/10/SMG-Interactive-Oct-16-2019.pdf. Last accessed: August 28, 2024.
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12. NENC Palliative and End of Life Care Symptom Control Guidelines for cancer and non-cancer patients – 5th Edition; 2021. Available from: https://northerncanceralliance.nhs.uk/wp-content/uploads/2022/06/20220615-Palliative-and-End-of-Life-Care-Guidelines-2021-DOWNLOAD.pdf. Last accessed: August 28, 2024.

13. University of California SFU. Palliative Care; ND. Available from: https://hospitalhandbook.ucsf.edu/content/07-symptom-management-palliative-care-0. Last accessed: August 28, 2024.
14. Suliman I, Phantumvanit, Victor , Rostamnjad L, Blouin G, Scullion B. Adult Guidelines for Assessment and Management of Nausea and Vomiting (Green Book); Dana-Farber Cancer Institute; 2023. Available from: https://pinkbook.dfci.org/assets/docs/Adult%20Guidelines%20for%20Assessment%20and%20Management%20of%20Nausea%20and%20Vomiting_2023.pdf. Last accessed: August 28, 2024.
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17. Yorkshire and Humber Palliative and End of Life Care Groups. A guide to symptom management in palliative care Version 6; NHS; 2016 (rev. 2019). Available from: https://www.lindseylodgehospice.org.uk/LindseyLodge/media/Lindsey-Lodge-Media/Downloads/YH-Palliative-care-symptom-guide-2016-v6.pdf. Last accessed: August 28, 2024.

To Use this Manual

- The Manual is organized by symptoms. Each symptom is followed by the medications recommended in the WHO EML or Lancet Commission's LEP. Each medication is described in terms of a starting dose; dosing frequency, increases, and reductions; maximum daily dose; and precautions. These recommendations are intended for primary care practice for adults in a community setting; they prioritize safety.

  Note: The consensus development process produced the recommendations that are described in the boxes after each medication. Variation in expert practices is reflected in the bullet points that follow each box.

- Clinical decisions, including medicine selection, dosing, and monitoring, may be informed by this information but depend on a careful patient assessment and individualized determination of anticipated benefits balanced against the risks and burdens associated with treatment.

- Symptoms may be manageable with medications not included in the Manual. The information in the Manual is not intended to provide a comprehensive list of all potential side effects and precautions. Physicians and pharmacists are encouraged to review the cited guidelines, as well as any others applicable in their own settings, and consult with experts as needed.

- The Manual does not include information about the role of primary therapies. When symptoms can be ameliorated by treatment of their underlying causes, this approach should be considered. It also does not discuss non-pharmacological interventions and these therapies also should be considered and implemented when appropriate.

Acronyms and abbreviations:

g = gram

mg = milligram

ms = millisecond

mL = millilitres

sec = second

secs = seconds

min = minute

mins = minutes

hr= hour

hrs = hours

EKG = electrocardiogram

Anorexia

- Anorexia is prevalent in many chronic illnesses. Symptoms may include distressing loss of appetite, unwanted weight loss, or gastrointestinal symptoms such as nausea, early satiety, or constipation. Treatment for anorexia or an associated symptom is considered if the potential for benefit exists and outweighs the potential risks.
- Several medications are used to manage anorexia, particularly when accompanied by weight loss. The evidence base is limited, with mixed results, and most studies have been conducted in the cancer population.[5]
- Despite a paucity of evidence, dexamethasone is used based on clinical experience.

Dexamethasone

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral SC IV	2 mg/day	Daily	4 mg/day	▪ Dose in the morning. ▪ Titrate dose by 2 mg weekly if needed. ▪ Add proton pump inhibitor if concurrent NSAID therapy. ▪ Monitor for agitation/delirium, hyperglycemia, hypertension, proximal weakness, as appropriate. ▪ Before stopping therapy, taper dose if treatment has continued for more than a week. ▪ Use cautiously in patients with diabetes, hypertension, psychosis, anxiety, or confusion.

Comments

- Some experts:
  - limit use to 2 - 3 weeks.
  - start with a higher dose (4mg) for a week and then lower the dose and tapering to the lowest effective dose after period of dose titration identifies a benefit.
  - recognize that higher doses (e.g., up to 16 mg/day) are used for other indications and recommend titration to these doses if therapy is well tolerated but ineffective at the lower dose.

[5] Saeteaw M, et al., Efficacy and safety of pharmacological cachexia interventions: systematic review and network meta-analysis. BMJ Support Palliat Care. 2021;11(1):75-85. doi: 10.1136/bmjspcare-2020-002601.

Anxiety

- Anxiety may be acute and self-limited or persistent. Persistent anxiety may represent an exacerbation of a premorbid disorder or a new diagnosis. Anxiety may occur in isolation or accompany other conditions, such as delirium or depression.
- Anxiety often fluctuates, with exacerbations related to emotional or medical factors, or both. Exacerbations may be spontaneous or triggered by events. As patients approach the end of life, anxiety may worsen and feature specific fears of symptoms such as pain or breathlessness, of dependency or abandonment, or of death itself.
- Regular assessment of anxiety is a best practice and should characterize the symptom and clarify both somatic (e.g., early delirium) and psychological (e.g., depression) causes.
- Non-pharmacological psychological and psychosocial interventions are recommended for the treatment of anxiety and may be sufficient if the symptoms are not severe.[6] Benzodiazepines are preferred for the management of severe anxiety, despite limited evidence; other medications also used when appropriate, e.g., neuroleptics to manage anxiety in delirium and selective serotonin reuptake inhibitors (SSRI) or another type of antidepressant to manage generalized anxiety or anxiety with depressed mood.[7]
- Despite the lack of evidence of effectiveness, benzodiazepines have been identified as Essential Medications for Palliative Care. Diazepam is widely available; while other shorter-acting benzodiazepines are recommended by experts.

Diazepam

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral SC IV	2 mg/day	Daily, often at night; after titration, dose may be given 2 - 3 times daily	20 mg/day	▪ Use the lowest effective dose for the shortest time necessary. ▪ Titrate dose by 2 - 5 mg as necessary to achieve symptom control. ▪ Monitor for sedation, use cautiously if the patient has respiratory compromise or is subject to falls. ▪ To avoid serious withdrawal symptoms, it is best to perform a slow taper of the benzodiazepine after a few days of treatment; dose reduction requires monitoring of symptoms (e.g., agitation, insomnia, nausea, tachycardia, hypotension, or sweating).

Comments

- Some experts:
  - use a higher initial dose for panic, e.g. up to 10 mg.
  - recommend a lower (10 mg) or higher (30 mg) maximum dose.
  - suggest using a lower dose and use cautiously when using the IV route.
  - recommend dosing at daily or twice daily due to a long half – life.
  - recommend against SC administration.
  - recommend rectal administration, if a formulation is available.

[6] Carlson LE et al. Integrative oncology care of symptoms of anxiety and depression in adults with cancer: Society for Integrative Oncology-ASCO Guideline. J Clin Oncol. 2023;41(28):4562-4591. doi: 10.1200/JCO.23.00857.

[7] Salt S et al. Drug therapy for symptoms associated with anxiety in adult palliative care patients. Cochrane Database Syst Rev. 2017;5(5):CD004596. doi: 10.1002/14651858.CD004596.pub3.

Midazolam

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
SC IV	1 mg - 2.5 mg	Single dose or repeated doses.	Varies	▪ Initial dose to manage panic is higher (5 mg); use a lower initial dose (2.5 mg) in older and frail adults. ▪ Dosing frequency can be every 4 hrs as needed, or if given around-the-clock, every 8 - 12 hrs. ▪ For patients with severe anxiety, repeat the starting dose as often as every 10 - 15 mins for up to several doses. ▪ To avoid withdrawal symptoms, slowly taper the daily dose after a few days of treatment. Monitor symptoms (e.g., agitation, insomnia, nausea, tachycardia, hypotension, or sweating) during dose reduction.

Comments

- Some experts:
  - recommend using midazolam only for urgent needs or the dying patient; others use it more regularly to manage severe anxiety.
  - recommend using oral midazolam and other experts recommend against this route. If used, it is administered either as a single dose for severe anxiety or as repeated doses. The initial or single dose is 1 - 2.5 mg; multiple doses may be titrated, given 2 - 3 times daily, and have a maximum of 4 - 30 mg daily.
  - recommend a maximum dose, which varies among experts between 2 - 150 mg/day; some suggest that upward titration continue until effectiveness or toxicity, noting that occasional patients require doses of 150 - 400 mg/day.

Constipation

- Among populations with serious chronic illness, constipation is highly prevalent and multifactorial in etiology. Common causes include adverse effects of opioids or other medications, malnourishment or dehydration, bedbound status, electrolyte disturbances (e.g., hypercalcemia), autonomic neuropathy related to the primary disease or comorbid conditions (e.g., diabetes), and comorbid conditions (e.g., hypothyroidism, functional bowel disease). Severe constipation may be highly distressing and can contribute to other symptoms, including nausea, anorexia, and depression.
- Regular assessment of gastrointestinal symptoms, including constipation, is a best practice in palliative care. When the risk of constipation is high, such as occurs with the initiation of opioid therapy, preventative laxative therapy, and non-pharmacological interventions (e.g., increased fluid management, dietary changes, and psychoeducation) should be considered.
- Constipation treatment should employ non-pharmacological approaches if possible, and in most cases, daily pharmacological therapy.[8] There is little evidence to guide treatment with common non-prescription therapies, but they are considered first-line based on extensive experience. They include stimulants (e.g., bisacodyl, senna) and osmotics (e.g., lactulose). Some experts recommend a combination of different types of laxatives when constipation is difficult to manage, as may occur during opioid therapy. When conventional therapies are ineffective, newer prescription therapies are considered, if these are available; they include the peripherally-acting mu opioid receptor antagonists (e.g., methylnaltrexone), linaclotide, plecanatide, and lubiprostone.

Bisacodyl

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral	5 mg/day	Daily, often at night; twice daily dosing may be used after titration	20 mg/day	▪ Increase starting dose using daily titration; consider switching to twice daily dosing. ▪ Continue titration to effect or maximum dose. ▪ If maximum dose is reached without benefit, switch to an alternative therapy. ▪ If maximum dose is reached and partial benefit occurs, continue treatment and add another type of laxative. ▪ Patients with irritable bowel syndrome may experience painful cramps. ▪ Avoid using if patient has bowel obstruction.

Comments

- Some experts:
  - initiate therapy with twice daily doses or use 2 - 3 doses per day.
  - initiate therapy with a higher dose (e.g., 10 mg) when constipation is opioid-related.
  - use a higher maximum dose, up to 30 mg/day, in select cases.

[8] Larkin PJ et al. Diagnosis, assessment and management of constipation in advanced cancer: ESMO Clinical Practice Guidelines. Ann Oncol. 2018;29(Suppl 4):iv111-iv125. doi: 10.1093/annonc/mdy148.

Senna

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral	8.6 mg/day (if liquid is used (check concentration to determine dose in mL)	Daily, often at night; twice daily dosing may be used after titration	36 mg/day	▪ Increase starting dose using daily titration; consider switch to twice daily dosing. ▪ Continue titration to effect or maximum dose. ▪ If maximum dose is reached without benefit, switch to an alternative therapy. ▪ If maximum dose is reached and partial benefit occurs, continue treatment and add another type of laxative. ▪ Patients with irritable bowel syndrome may experience painful cramps. ▪ Avoid using if patient has bowel obstruction.

Comments

- Some experts:
  - recommend initiating therapy with 17.2 mg.
  - recommend a higher maximum dose, up to 72 mg/day.

Docusate Sodium

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral	100 mg/day	2 - 3 times daily after dose titration	300 - 400 mg/day	▪ May require several days to work.

Comments

- Some experts:
  - initiate therapy with higher doses, either 100 mg three times daily or 100 - 200 mg twice daily.
  - recommend dosing no more frequently than twice daily to reduce treatment burden.
  - suggest that docusate is a surfactant and not a stimulant at typical doses, and therefore, may be used in the presence of partial bowel obstruction.
  - consider the efficacy of docusate to be limited.

Lactulose

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral	10 g/day (check concentration to determine dose in mL)	Up to 4 doses daily after titration.	40 g/day	▪ Effectiveness requires normal fluid intake. ▪ May cause bloating and flatus. ▪ Will not affect diabetes management. ▪ Avoid using if patient has bowel obstruction or if patient is lactose intolerant or galactosemic.

Comments

- Some experts:
  - initiate therapy with twice daily doses.
  - may titrate using divided doses but then initiate maintenance therapy using once daily or twice daily dosing.
  - recommend titration using 50% increase in dose every 1 - 2 days, as needed.
  - recommend dosing between meals due to sweet taste.

Delirium

- Delirium is a neuropsychiatric syndrome characterized by acute onset; fluctuating course; disturbance in consciousness; and variable impairment in cognition, attention, concentration, memory, and perception. The syndrome is highly prevalent in populations with serious illnesses and there are numerous risk factors and etiologies. Reversibility usually depends on treatment of the etiology, if this is possible; at the end of life, terminal delirium may precede active dying.
- Delirium can cause high levels of distress for the patients affected and their families. Management of symptoms, such as fear and anxiety, confusion, and agitation, is therefore a best practice.
- Management should include non-pharmacological therapies to ensure safety and reduce distress, and pharmacological therapies when symptoms are moderate or severe.[9] [10]
- Conventional practice employs neuroleptics and sometimes benzodiazepines when agitation is severe; other therapies, such as dexmedetomidine, are sometimes employed in inpatient settings.
- Neuroleptics, such as haloperidol, are widely used to manage the symptoms of delirium, but evidence of efficacy is mixed. Although some studies suggest the possibility of serious adverse effects, including worsening of symptoms, cardiovascular and extrapyramidal effects, and increased mortality among patients with dementia,[11] extensive experience suggests that some patients benefit from reduction in distressing symptoms. Treatment should be undertaken cautiously, particularly in older adults.

Haloperidol

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral SC IV	0.5 mg Older adults: 0.25 mg	Hourly dosing can be used at the start of treatment until agitation lessens; dosing at 4 - 6 times per day may be used for ongoing treatment of moderate or severe delirium.	20 mg/day	▪ Given evidence that haloperidol may cause harms that exceed benefits in populations with advanced illness, the decision to treat should be based on a careful evaluation of clinical need and risks, and careful ongoing assessment of harms is needed when the medication is used. ▪ Use cautiously when treating older adults with delirium; the potential for serious adverse effects in this population, including increased mortality, warrants consideration of other treatments, if any are available. ▪ The IV route may increase the potential for cardiovascular toxicity and should be avoided, if possible. ▪ Can prolong the QTc interval. Avoid using if ECG shows QTc >500 ms; if ECG is unavailable, use cautiously if significant risk factors for QTc are present. ▪ Avoid using in patients with Parkinsonism.

Comments

- Some experts:
  - recommend a starting dose of 1 mg for adults and 0.5 mg for older adults.
  - use a higher initial dose if delirium is accompanied by severe agitation; some recommend a dose up to 5 mg and others recommend a dose of 1 mg or 2 mg.

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[9] Jackson GP et al. Improving the Detection, Assessment, Management and Prevention of Delirium in Hospices (the DAMPen-D study): Feasibility study of a flexible and scalable implementation strategy to deliver guideline-adherent delirium care. Palliat Med. 2024;38(4):447-456. doi: 10.1177/02692163241236325.

[10] Bush SH et al. Adaptation, implementation, and mixed methods evaluation of an interprofessional modular clinical practice guideline for delirium management on an inpatient palliative care unit. BMC Palliat Care. 2022;21(1):128. doi: 10.1186/s12904-022-01010-6.

[11] Agar MR et al. Efficacy of Oral Risperidone, Haloperidol, or Placebo for Symptoms of Delirium Among Patients in Palliative Care: A Randomized Clinical Trial. JAMA Intern Med. 2017 ;177(1):34-42. doi: 10.1001/jamainternmed.2016.7491. Erratum in: JAMA Intern Med. 2017 ;177(2):293. doi: 10.1001/jamainternmed.2016.9336.

- recommend a maximum dose no higher than 10 mg or 15 mg.
- suggest caution when prescribing along with other medications with potential extrapyramidal effects, e.g., antidepressants.

Depression

- Depression, one of the most prevalent symptoms in populations with serious chronic illness, undermines quality of life and can lead to a desire for a hastened death. It is often underdiagnosed and inadequately treated.
- There is evidence favoring both non-pharmacological and pharmacological treatments for depression.[12] [13] Evidence supports the efficacy of numerous antidepressant therapies. Studies indicate that the effectiveness of tricyclic antidepressants (such as amitriptyline) is comparable to the selective serotonin reuptake inhibitors (SSRIs, such as fluoxetine) and other newer classes, although the latter have a more favorable safety profile.[14]

Amitriptyline

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral	25 mg/day Older adults: 10 mg/day	Daily	150 mg/day	▪ Increase initially by 10 - 25 mg weekly (depending on starting dose), and then by 25 - 50 mg weekly (after 50 mg is reached). ▪ Anticipate a delay of weeks to observe antidepressant effects. ▪ Use cautiously in older adults and patients with cardiovascular disease, dementia, seizure disorder, fall risk or decreased mobility, urinary retention, or history of prostatism, glaucoma, or history of mania/hypomania.

Comments

- Some experts recommend:
  - nighttime dosing.
  - titrate the dose more frequently, e.g., every 5 days.
  - a maximum daily dose of 75 - 100 mg.
  - always starting with a SSRI, if available due to concerns about the toxicity of tricyclic antidepressants.

[12] Perusinghe M et al. Evidence-Based Management of Depression in Palliative Care: A Systematic Review. J Palliat Med. 2021;24(5):767-781. doi: 10.1089/jpm.2020.0659.

[13] Apóstolo J et al. The effectiveness of nonpharmacological interventions in older adults with depressive disorders: a systematic review. JBI Database System Rev Implement Rep. 2015;13(6):220-78. doi: 10.11124/jbisrir-2015-1718.

[14] Cipriani A et al. Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis. Lancet. 2018;391(10128):1357-1366. doi: 10.1016/S0140-6736(17)32802-7.

Fluoxetine

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral	20 mg/day Older adults: 10 mg/day	Daily	80 mg/day	▪ Titrate the dose by 20 mg weekly if no beneficial effects are observed and no treatment-limiting side effects occur. ▪ Titration can continue to the maximum dose, but if any positive effect occurs after a dose is initiated, continue this dose given the possibility of weeks-long delay in achieving the full antidepressant effect.

Comments

- Some experts suggest:
  - that the maximum dose is the same as the starting dose, whereas others suggest slow titration to a higher maximum dose, which varies among experts between 40 and 80 mg/day.
  - caution in patients with cardiovascular disease due to a low risk of QTc prolongation.
  - if possible, tapering the dose when stopping therapy, due to a low risk of discontinuation syndrome from fluoxetine.

Diarrhea

- Diarrhea may be acute and self-limited; it is considered chronic if it recurs or persists for more than a month. When severe, it may be associated with distress and complications such as skin breakdown and dehydration.
- Patients with serious chronic illness may develop persistent diarrhea because of the chronic illness or its treatment, or as a comorbid condition. The potential etiologies are numerous and may involve infection, medicine toxicity, food intolerance, or systemic diseases such as inflammatory or functional bowel disease. The assessment of the patient with severe or persistent diarrhea may reveal a treatable etiology.[15]
- Symptomatic treatment of diarrhea includes fluid replacement, skin care if needed, and various pharmacological therapies to reduce the number and severity of episodes. The opioid loperamide is a first-line approach, despite limited evidence; other medications, such as anticholinergics and somatostatin analogues, also lack evidence of efficacy but are considered, when available, in refractory cases.[16]

Loperamide

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral	2 mg	For acute management, starting dose may be repeated after each subsequent episode of diarrhea until symptom relief or maximum dose; for chronic diarrhea, dosing frequency is 2 - 4 times daily.	16 mg/day	▪ For acute diarrhea, 48 hrs of therapy may be sufficient, and stop to determine whether further treatment is needed; if further treatment is required, the usual dose is 2 - 4 mg, 2 - 4 times per day. ▪ Higher than recommended doses have been associated with cardiotoxicity. ▪ Avoid using if clostridium difficile infection is suspected, or diarrhea is bloody or accompanied by fever. ▪ Can prolong the QTc interval. Avoid using if ECG shows QTc >500 ms; if ECG is unavailable, use cautiously if significant risk factors for QTc are present.

[15] Ihara E et al. Evidence-Based Clinical Guidelines for Chronic Diarrhea 2023. Digestion. 2024;105(6):480-497. doi: 10.1159/000541121.

[16] Ihara E et al. Evidence-Based Clinical Guidelines for Chronic Diarrhea 2023. Digestion. 2024;105(6):480-497. doi: 10.1159/000541121.

Breathlessness

- Breathlessness (also referred to as dyspnea), a prevalent and highly distressing symptom, may be a direct consequence of progressive pulmonary or cardiac disease or result from comorbid complications such as pneumonia or pleural effusion. All patients should undergo an assessment to identify the contributing factors and determine whether etiologic treatments are possible and appropriate.
- Symptomatic treatment of breathlessness may be attempted using both pharmacological[17] and non-pharmacological interventions.[18] There is limited evidence supporting the efficacy of pharmacological therapy. Opioids, particularly morphine, have been widely used and clinical observations suggest that some patients have substantial benefit; studies have not confirmed this benefit, however,[19] and there is no evidence for other medications that are sometimes used empirically, such as benzodiazepines.

Morphine Immediate Release

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral	Opioid-naïve patients: 2.5 mg. Opioid- treated patients: 10% of the total daily dose (average dose during the past few days).	Every 4 hrs	Maximum is determined by the development of treatment-limiting side effects.	▪ Titrate the dose based on an assessment of benefit and adverse effects associated with the current dose; increase the dose only if symptom control is inadequate and there are no treatment-limiting adverse effects. ▪ Titrate the dose in increments equal to the amount of the starting dose; after several increases, increase to approximately 25% to 50% of the starting dose. ▪ Titrate the dose as often as several times daily if breathlessness is severe; once symptoms are improved, titrate every several days. ▪ Carefully monitor for opioid side effects, including somnolence, confusion, nausea, and constipation, especially during dose titration and early in treatment. ▪ Due to risks associated with diminished respiratory reserve and respiratory depression, consider severity of cardiopulmonary disease when selecting doses. ▪ Due to the accumulation of active metabolites, use cautiously (lower doses and increased monitoring) in patients with renal insufficiency.

[17] Holland AE Lewis A. Evidence-based management of symptoms in serious respiratory illness: what is in our toolbox? Eur Respir Rev. 2024;33(174):240205. doi: 10.1183/16000617.0205-2024.

[18] Spathis A et al. Multicomponent services for symptoms in serious respiratory illness: a systematic review and meta-analysis. Eur Respir Rev. 2024 Oct 30;33(174):240054. doi: 10.1183/16000617.0054-2024.

[19] Smallwood NE et al. Opioids for the palliation of symptoms in people with serious respiratory illness: a systematic review and meta-analysis. Eur Respir Rev. 2024;33(174):230265. doi: 10.1183/16000617.0265-2023.

Morphine Immediate Release (contd.)

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
SC IV	Opioid-naïve patients: 1–2.5 mg. Opioid- treated patients: 10% of the total daily dose (average dose during the past few days).	Every 4 hrs but use a shorter interval (as brief as 30 min) if the symptom is severe; once the symptom has improved, dosing can be 4 - 6 times daily.	Maximum is determined by the development of treatment-limiting side effects.	▪ The decision to titrate the dose should be based on an assessment of benefit and adverse effects associated with the current dose; the dose should be increased only if symptom control is inadequate and there are no treatment-limiting adverse effects. ▪ Titrate the dose in increments equal to the amount of the starting dose; after several increases, increase to approximately 25% to 50% of the starting dose. ▪ By bypassing the gastrointestinal track, titration can be done more quickly (as often as every 30 min) to achieve initial symptom improvement; once symptoms are improved, titrate every several days. ▪ Consider respiratory risk and risk due to renal insufficiency, as above. ▪ Carefully monitor for opioid side effects, including somnolence, confusion, nausea, and constipation, especially during dose titration and early in treatment.

Comments

Oral:

- Some experts:
  - initiate therapy with 1 mg in older adults with COPD or heart failure
  - initiate therapy in opioid-treated patients using whatever dose is currently taken for breakthrough pain.
  - initiate therapy in opioid-naïve patients using a long-acting morphine formulation at 10 mg/day.
  - reduce the frequency of dosing to 4 times daily when patients are stable if immediate release morphine is used.
  - recommend using “as needed” dosing rather than fixed schedule dosing to reduce risk.
  - do not recommend the use of “as needed” dosing for chronic breathlessness
  - use a dosing frequency of every 2 hrs if needed.
  - consider a lack of response at 30 - 60 mg per day in an opioid-naïve patient an indicator of non-responsiveness and stop titration.

SC/IV

- Some experts:
  - initiate therapy in the opioid-naïve patient with 0.25 - 0.5 mg dose
  - recommend against starting therapy in the opioid-naïve patient with a dose above 1 mg.
  - initiate therapy in opioid-treated patients using whatever dose is currently taken for breakthrough pain.
  - recommend using “as needed” dosing rather than fixed schedule dosing to reduce risk, at least during the first few days of treatment.
  - recommend using a fixed scheduled dose plus an “as needed” dose for symptom flares after the symptom is improved.

Fatigue

- Persistent fatigue is extremely common among patients with serious illnesses and its causes are numerous and often multifactorial. Fatigue may be a direct effect of the illness or a consequence of one or more complications or comorbidities, such as anemia, hypoxemia, electrolyte disturbances, sleep disorder, depression, or treatment with a centrally-acting medication.
- The management of fatigue includes treatment of its etiologies, if possible; non-pharmacological interventions, including both regular physical activity and cognitive-behavioral therapies; and pharmacological therapy.
- There is little evidence about the effectiveness of pharmacological therapies for fatigue associated with serious illness. Studies in populations with advanced cancer have yielded mixed results for dexamethasone[20,21] and limited support for the use of methylphenidate, modafinil, and paroxetine.[22]

Dexamethasone

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral	2 mg	Daily	4 - 20 mg/day	▪ Dose in the morning. ▪ Titrate dose by 2 mg weekly. ▪ Add proton pump inhibitor if concurrent NSAID therapy. ▪ Monitor for agitation/delirium, hyperglycemia, hypertension, proximal muscle weakness, as appropriate ▪ After titration to the maximum or maximumly tolerated dose, stop therapy after a week if there is no benefit. ▪ Before stopping therapy, taper dose if treatment has continued for more than a week. ▪ Use cautiously in patients with diabetes, hypertension, psychosis, anxiety, or confusion.

Comments

- Some experts:
  - initiate therapy with 4 mg and stop treatment if there is no benefit after 5 - 7 days.
  - suggest tapering the dose to the lowest effective dose after a period of dose titration identifies a benefit.
  - recommend a maximum dose of 4 mg/day, while other experts recommend a maximum dose of 8 mg/day, 12 mg/day, 16 mg/day, or 20 mg/day.

Gastroprotection

- Gastroprotection refers to a therapy intended to reduce the risk of potentially hemorrhagic upper gastrointestinal ulcers or erosions. It is an indication for a medication that reduces gastric acid

[20] Sandford A et al. Corticosteroids for the management of cancer-related fatigue in adults with advanced cancer. Cochrane Database Syst Rev. 2023;1(1): CD013782. doi: 10.1002/14651858.CD013782.pub2.

[21] Yennurajalingam S et al. Physical Activity and Dexamethasone for Cancer-Related Fatigue: A Preliminary Placebo-Controlled, Randomized, Double-Blind Trial. J Natl Compr Canc Netw. 2025;23(1):e247071. doi: 10.6004/jnccn.2024.7071.

[22] Chow R et al. Cancer-related fatigue-pharmacological interventions: systematic review and network meta-analysis. BMJ Support Palliat Care. 2023;13(3):274-280. doi: 10.1136/bmjspcare-2021-003244.

production; other uses for these medications include the treatment of peptic ulcer disease and the treatment of symptoms associated with acid production or gastroesophageal reflux.

- The medications usually used for gastroprotection are proton pump inhibitors (PPIs), such as omeprazole; H2 blockers and misoprostol also are used.

Omeprazole

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral	20 mg/day	Daily	40 mg/day	▪ In populations with serious chronic illness, consider prescribing to: o patients receiving long-term NSAID therapy; and o patients receiving long-term anti-platelet therapy who have other risk factors, including age >60, concurrent anticoagulant, or corticosteroid use, or known *Helicobacter pylori* infection.

Comments

- Some experts:
  - prescribe gastroprotection to critically ill patients at risk for stress ulcers, particularly patients admitted to a critical care unit.
  - use 20 mg/day unless there are upper gastrointestinal symptoms that do not respond satisfactorily; in this situation, a higher dose is tried.
  - advise periodically evaluating whether treatment can be discontinued; although the medication is generally safe, long-term therapy has been associated with varied harms, including increased risk of pneumonia, bone fracture, enteric infections, cardiovascular events, chronic kidney disease, and dementia.

Nausea and Vomiting

- In populations with serious chronic illnesses, nausea is a common and heterogeneous condition. It may be acute, recurrent, or chronic; the etiology may be directly related to the primary illness or related instead to disease or treatment complications or comorbid conditions.
- Whether acute and self-limited or a persistent symptom, the management of nausea and vomiting may include etiologic treatment, non-pharmacological approaches (e.g., cognitive-behavioral therapy, acupuncture, and others), and anti-emetic medications.
- Numerous therapies are used for nausea and vomiting. Apart from substantial evidence base related to the management of post-chemotherapy symptoms,[23] evidence to guide selection and dosing is limited.[24] Conventional practices and an assessment of individual risk and benefit therefore inform clinical practice.

Cyclizine

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral	25 mg	Every 8 hrs	150 mg/day	▪ Avoid in patients with known heart disease or history of cardiac arrhythmia.
SC	100 mg/day continuous infusion. Older adults: 50 mg/day continuous infusion.	In 24 hrs	200 mg/day	▪ Avoid in patients with known heart disease or history of cardiac arrhythmia.

Comments

Oral

- Some experts:
  - initiate therapy at the starting dose given up to three times daily as needed.
  - initiate therapy with 50 mg single dose, repeated as needed up to three times daily.

SC

- Some experts use intermittent SC administration using the orally recommended dosing schedule.

[23] Bosnjak S et al. MASCC antiemetic consensus recommendations: resource-limited settings. Support Care Cancer. 2025 Feb 12;33(3):181. doi: 10.1007/s00520-025-09211-4.

[24] Hardy J, Davis MP. The management of nausea and vomiting not related to anticancer therapy in patients with cancer. Curr Treat Options Oncol. 2021;22(2):17. doi: 10.1007/s11864-020-00813-0.

Dexamethasone

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral SC IV	Low-to-high regimen: 4 mg. High-to-low regimen: 8 - 10 mg.	Daily or twice daily	16 mg/day	▪ The "low-to-high" regimen starts with low dose and up-titrates the dose on a daily or twice daily basis. ▪ The "high-to-low" regimen starts with a loading dose and then down-titrates the dose beginning the second day. ▪ Consider using only a morning dose to reduce risk of insomnia. ▪ Add proton pump inhibitor if concurrent NSAID therapy. ▪ Monitor for agitation/delirium, hyperglycemia, hypertension, proximal muscle weakness, as appropriate. ▪ Consider stopping therapy after a week if there is no benefit. ▪ Before stopping therapy, taper dose if treatment has continued for more than a week. ▪ Use cautiously in patients with diabetes, hypertension, psychosis, anxiety, or confusion.

Comments

- Some experts:
  - initiate therapy with 2 mg.
  - recommend a maximum dose of 8 - 12 mg/day.
  - recommend the high-to-low regimen when starting therapy to accelerate improvement, especially if the symptom is severe.
  - recommend a twice daily dose (instead of just a morning dose) only if no sleep impairment; twice daily dosing, if desired, could be morning and midday.
  - suggest tapering the dose to the lowest effective dose after dose titration (starting with either the low-to-high or high-to-low regimen) identifies a benefit, e.g., after several days.
  - recommend using this first-line option for symptomatic bowel obstruction or intracerebral mass lesions and second-line (after other anti-emetics are ineffective) in other conditions.

Diphenhydramine

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral IV	25 mg	Every 4 - 6 hrs	150 - 300 mg/day	▪ Avoid using as first-line therapy for nausea in patients with serious chronic illnesses.

Comments

- Some experts:
  - stop the treatment after several days if no clear benefits are observed, even if the dose is not the maximum.
  - recommend stopping the medication if uncomfortable somnolence or confusion occur.

Haloperidol

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral SC IV	0.5 mg Older adults: 0.25 mg	Every 4 - 8 hrs	5 mg/day	▪ Avoid use in individuals with Parkinsonism. ▪ Can prolong the QTc interval. Avoid using if ECG shows QTc >500 ms; if ECG is unavailable, use cautiously if significant risk factors for QTc are present. ▪ Given the potential for increased cardiovascular toxicity, avoid the IV route if possible.

Comments

- Some experts:
  - recommend a higher starting dose, up to 2 - 2.5 mg.
  - recommend higher doses up to 15 - 20 mg/day.
  - suggest a dosing frequency of 6 - 8 hrs.
  - suggest extending to every 12 hours after titration to an effective dose.
  - advise caution when prescribing along with other medications with potential extrapyramidal effects, e.g., antidepressants.

Metoclopramide

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral SC IV	5 mg	Every 4 - 6 hrs	60 mg/day	▪ Use cautiously and in lower doses in patients with renal dysfunction. ▪ Avoid treatment in patients with complete bowel obstruction. ▪ Avoid in patients with Parkinsonism and patients taking other medications with extrapyramidal effects, e.g., antidepressants.

Comments

- Some experts:
  - recommend a starting dose of 10 mg every 8 hrs.
  - recommend a dosing frequency of 6 - 8 hrs.
  - recommend a maximum dose of 40 mg/day.
  - recommend a higher maximum dose, up to 120 mg/day.

Ondansetron

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral SC IV	4 mg	Every 8 - 24 hrs	24 mg/day End-stage liver disease: 8 mg/day	▪ If nausea is severe, a higher starting dose can be used, e.g. 8 mg. ▪ Be aware of headache and constipation as potential side effects. ▪ Can prolong the QTc interval. Avoid using if ECG shows QTc >500 ms; if ECG is unavailable, use cautiously if significant risk factors for QTc are present.

Comments

- Some experts:
  - recommend using a starting regimen of 4 mg every 4 - 6 hrs as needed or 8 mg every 8 hrs as needed.
  - recommend a maximum dose of 32 mg/day.
  - do not recommend it as a first-line option in primary palliative care.

Candidiasis

- Oropharyngeal or esophageal candidiasis is a common complication in populations with advanced illness, particularly patients characterized by severe immunocompromise. In addition to the risk of systemic dissemination, these infections are associated with loss of taste, pain, and dysphagia - all potentially contributing to reduced oral intake.
- Oropharyngeal candidiasis may be treated using a topical anti-fungal therapy, such as nystatin; esophageal candidiasis and severe oral disease often can be managed using oral fluconazole.

Fluconazole

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral	50 mg	Daily	400 mg/day	▪ If nausea is severe, use a higher starting dose, e.g., 8 mg. ▪ If oropharyngeal candidiasis, treat for a minimum of 2 weeks; If esophageal candidiasis, treat for a minimum of 3 weeks. ▪ Use cautiously due to potential interaction with other therapies.

Comments

- Some experts:
  - recommend a one-time loading dose of 100 mg, 200 mg, or 400 mg, then continuing therapy with a daily dose of 100 mg or 200 mg.
  - recommend 150 mg daily for 3 days and then 150 mg every other day to every week for a period of 4 weeks, depending on the patient's response.
  - recommend that the patient be periodically re-evaluated to determine response; if the response is unsatisfactory, the dose should be increased up to the maximum.

Pain

- Pain is a highly prevalent symptom in populations with serious illnesses. Progression of disease is associated with increased prevalence and severity. Evidence informing treatment has largely originated in studies of cancer pain. Although guidelines based on these studies and clinical experience focus on cancer pain,[25] they are extrapolated to other seriously-ill populations.
- Guidelines emphasize the need for a detailed pain assessment followed by a tailored pain management plan. This plan may include disease-targeted treatments, such as radiotherapy for focal tumor-related pain, specific therapy for malignant bone pain and several other cancer syndromes such as bowel obstruction, and the systematic use of non-pharmacological and pharmacological therapies.
- Non-pharmacological approaches are typically co-administered with analgesic therapies. These approaches include a variety of psychological, integrative, and rehabilitative approaches. In some settings, other interventions, such as neuromodulation or neural blockade are available.
- Analgesics are usually effective in mitigating the distress associated with pain. Moderate or severe pain should be treated with an opioid analgesic, prescribed in accordance with guidelines, and sometimes with co-administered nonopioid and adjuvant analgesics.[26] Guidelines for analgesic management are applicable to resource-limited settings.[27]

Acetylsalicylic acid (ASA)

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral	300 mg	Every 4 - 6 hrs	4000 mg/day	▪ For mild pain, use alone; For severe pain, may use as a co-analgesic combined with an opioid. ▪ Use cautiously when prescribing to patients with a history of peptic ulcer disease, any bleeding disorder, and renal insufficiency.

Comments

- Some experts:
  - recommend a starting dose of 500 mg every 6 - 8 hrs.
  - recommend using 2000 mg/day or 2400 mg/day as the maximum dose.
  - suggest that acetylsalicylic acid (ASA) should not be used as a first-line option due to adverse effect profile.

[25] Chapman EJ et al. Practice review: Evidence-based and effective management of pain in patients with advanced cancer. Palliat Med. 2020;34(4):444-453. doi: 10.1177/0269216319896955.

[26] Swarm RA et al. NCCN clinical practice guidelines in oncology: Adult cancer pain. Version 1, 2020.

[27] Ahmedzai SH, et al. Cancer Pain management in Resource-limited settings (CAPER) Working Group. Optimizing cancer pain management in resource-limited settings. Support Care Cancer. 2019;27(6):2113-2124. doi: 10.1007/s00520-018-4471-z.

Ibuprofen

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral	400 mg	Every 6 - 8 hrs	2400 mg/day	▪ For mild pain, use alone; for severe pain, may use as a co-analgesic combined with an opioid. ▪ Based on response, titrate to 600 mg, and then 800 mg, every 6 - 8 hrs. ▪ Use cautiously and in lower doses when prescribing to older adults or to patients with a history of peptic ulcer disease, cardiac disease, any bleeding disorder, and renal or hepatic insufficiency.

Comments

- Some experts:
  - recommend a starting dose of 600 mg every 6 - 8 hrs for most patients and a lower dose of 400 mg every 6 - 8 hrs for high-risk patients.
  - recommend using 1200 mg/day or 1800 mg/day as the maximum dose.
  - recommend considering a higher maximum dose, 3200 mg/day or 3600 mg/day, for patients who have a partial response at 2400 mg/day and are tolerating treatment.
  - Note the need for caution in patients with dysproteinemias, such as multiple myeloma.

Paracetamol/Acetaminophen

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral	500 mg	Every 4 - 6 hrs	4000 mg/day	▪ For mild pain, use alone; for severe pain, may use as a co-analgesic combined with an opioid. ▪ Consider a longer dosing interval, such as 8 hrs, in older adults and patients with liver disease.

Comments

- Some experts:
  - recommend a starting dose of 500 mg to 1000 mg every 6 - 8 hrs.
  - recommend using 3000 mg/day as the maximum dose.

Codeine

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral	30 mg	Every 6 hrs	240 mg/day	▪ Anticipate variation in response because codeine is a pro-drug of morphine and its analgesic effect is dependent on a genetically determined rate of conversion to morphine. A small proportion of the population has very little to no response to codeine. ▪ Because dosages >60 mg have not shown to improve pain relief and are associated with an increased incidence of adverse effects, titrate from the starting dose and stop if treatment-limiting adverse effects occur or when the maximum dose is reached.

Comments

- Some experts:
  - recommend a dosing frequency of every 4 hrs.
  - recommend a maximum dose of 120 mg/day and some recommend a maximum dose of 360 mg/day.
  - recommend that codeine not be used to treat young patients because of reported toxicity that may occur in children who convert codeine to morphine at a high rate.
  - recommend assessing the risks associated with codeine like those occurring with other opioids, including those associated with diminished respiratory reserve in patients with cardiopulmonary diseases and those related to common side effects, such as somnolence, confusion, nausea, and constipation.

Tramadol Immediate Release

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral	50 mg	Every 6-8 hrs.	400 mg/day	▪ Use lower doses and slower titration when prescribing to older adults, patients with renal insufficiency, and patients taking a selective serotonin, or selective serotonin norepinephrine reuptake inhibitor. ▪ Titrate from the starting dose. Stop if treatment-limiting adverse effects occur or when the maximum dose is reached. ▪ As a medication with an active metabolite and two modes of action — opioid agonist and monoaminergic reuptake inhibitor — its risks include both opioid-related and those associated with selective serotonin reuptake inhibitors. Use cautiously in patients with renal insufficiency; consider reducing the dose by 50% and lengthening the dosing interval to reduce risk.

Comments

- Some experts:
  - recommend starting with 25 mg every 12 hrs when treating older and frail adults.
  - recommend a maximum dose of 300 mg/day when using the extended-release formulations.
  - recommend using “as needed” to reduce the risk of side effects instead of fixed scheduled doses.
  - consider dosing frequency of every 4 hrs.

- recommend a maximum dose of 120 mg/day and some recommend a maximum dose of 360 mg/day.
- recommend assessing the risks like those occurring with other opioids, including those associated with diminished respiratory reserve in patients with cardiopulmonary diseases and those related to common side effects, such as somnolence, confusion, nausea, and constipation.

Morphine Immediate Release

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral	Opioid-naïve adults: 5 mg Older adults: 2.5 mg	Every 4 hrs, with more frequent dosing during dose titration, if needed, and when using an "as needed" dose for breakthrough pain.	There is no fixed maximum daily dose for morphine. Maximum dose is determined by the presence of treatment-limiting side effects.	▪ If scheduled doses are generally controlling the pain but the patient has moderate or severe breakthrough pain, add an "as needed" dose to the scheduled dose, initially providing 10% of the total daily dose every 2-3 hrs "as needed" for breakthrough pain. ▪ Titrate dose as often as every hr for severe pain; if pain is not severe, titration frequency is reduced, e.g., to 1 - 2 times per day. ▪ Due to risks associated with accumulation of morphine's active metabolites, use cautiously in patients with renal insufficiency; reduce doses by 50% and lengthen the dosing interval to reduce risk.
SC IV	Opioid-naïve adults: 2 mg Older adults: 1 mg	Every 4 hrs, with additional dosing during titration, if necessary, and when using an "as needed" (rescue) dose for breakthrough pain.	There is no fixed maximum daily dose for morphine. Maximum dose is determined by the presence of treatment-limiting side effects.	▪ By bypassing the gastrointestinal track, titrate more quickly (as often as every 30 min) to achieve initial symptom improvement; if pain is not severe, titrate less frequent e.g., to 1 - 2 times per day. ▪ If scheduled doses are helpful but the patient has moderate or severe breakthrough pain, add an "as needed" dose to the scheduled dose, initially providing 10% of the total daily dose every 2 - 3 hrs "as needed" for the breakthrough pain.

Comments
Oral

- Some experts:
  - recommend initially titrating the dose by the amount of the starting dose; after several increases, the increment can be increased to approximately 25% to 50% of the dose.
  - suggest that, during dose titration, the daily dose can be incremented by the amount of "as needed" (rescue) medication taken during the past day.
  - emphasize that the decision to titrate should be based on assessed benefit and adverse effects; the dose is increased only if pain control is inadequate and there are no treatment-limiting adverse effects.
  - recommend changing to dosing every 6 hours or using a long-acting formulation after titration.
  - recommend using "as needed" to reduce the risk of side effects instead of fixed scheduled doses.
  - recommend caution (smaller dose increments and longer intervals for observation) when treating those with diminished respiratory reserve due to cardiopulmonary disease and patients with renal insufficiency.

- recommend carefully monitoring for opioid side effects, including somnolence, confusion, nausea, and constipation, especially during dose titration and early in treatment.

SC / IV

- Some experts:
  - initiate therapy in the opioid-naïve patient with 1 mg and other experts initiating with 2.5 mg.
  - recommend dosing every 3 - 4 hrs.
  - recommend using "as needed" to reduce the risk of side effects instead of fixed scheduled doses.
  - recommend for initial titration to increase the dose by the amount of the starting dose; after several increases, the increment can be increased to approximately 25% to 50% of the dose.
  - recommend cautions, monitoring, and careful assessment of benefits and adverse effects prior to dose change, similar to oral therapy.

Fentanyl Transdermal Patch

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Transdermal	Opioid-naïve adults: 12 mcg/hr. For patients already receiving an opioid, dose of transdermal fentanyl is selected using a dose conversion table.	Every 72 hrs.	There is no fixed maximum daily dose for fentanyl. Maximum dose is determined by the presence of treatment-limiting side effects.	▪ Apply the patch to flat, non-hairy skin, e.g., the back; a new skin area is selected when changing doses. ▪ Although dose titration can be 1 - 2 days after a patch is applied (12 to 24 hrs usually required to achieve therapeutic blood levels), usual titration is every 3 days, by which time the blood levels have usually approached steady state. ▪ Avoid exposing the patch to external heat, which can increase drug release. ▪ Avoid using as first-line therapy for patients with widely fluctuating pain, recurrent fever, frequent or excessive sweating, or cachexia. ▪ Avoid using as the first-line in opioid-naïve patients and in patients with acute pain.

Comments

- Some experts:
  - recommend being aware of shorter duration of effects in some patients, necessitating patch changes after 48 hrs or between 48 and 72 hrs.
  - support the use of the 12 mcg/hr patch for opioid-naïve patients.
  - recommend co-prescribing an "as needed" (rescue) short-acting opioid, such as oral morphine, for moderate or severe breakthrough pain; safe dosing of this medication begins with a low dose (e.g., starting dose for opioid-naïve patients) and quickly up-titrates to find an effective dose.
  - recommend monitoring and careful assessment of benefits and adverse effects prior to dose change, in a manner similar to morphine therapy (and additional caution in patients with renal insufficiency).

Hydromorphone Immediate Release

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral	Opioid-naïve adults: 1 mg Older adults: 0.5 mg	Every 4 hrs	There is no fixed maximum daily dose for hydromorphone. Maximum dose is determined by the presence of treatment-limiting side effects.	▪ Similar to oral morphine.

Comments

- Some experts:
  - observe that hydromorphone is similar to morphine but there are large intra-individual and inter-individual differences in the responses to the two medications, both in terms of analgesia and side effects; some patients have better outcomes with morphine and some with hydromorphone.
  - recommend using "as needed" to reduce the risk of side effects instead of fixed scheduled doses.
  - recommend that cautions, monitoring, and careful assessment of benefits and adverse effects prior to dose change be similar to oral morphine therapy

Methadone

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral	Opioid-naïve adults: 2.5 mg Older adults: 1 mg	Every 8 hrs	There is no fixed maximum daily dose for methadone. Maximum dose is determined by the presence of treatment-limiting side effects.	▪ Titrate from the starting dose; after several increases, increase to 5 mg/dose and then higher. ▪ Given methadone's half-life (average about 24 hrs), titrate the dose no more frequently than every 5 days; if faster titration is desired, consider consulting a specialist. ▪ Use cautiously when prescribing to patients with significant liver disease. ▪ Can prolong the QTc interval. Avoid using if ECG shows QTc >500 ms; if ECG is unavailable, use cautiously if significant risk factors for QTc are present. ▪ Not usually preferred as the first-line in opioid-naïve patients and in patients with acute pain; when switching to methadone from treatment with another opioid, be aware of the need to adjust the equianalgesic dose in accordance with guidelines and consider consulting a specialist.

Comments

- Some experts:
  - note methadone's unique pharmacology and emphasize the difference between starting methadone in opioid-naïve and opioid treated patients; a starting dose in opioid-naïve patients of 1 - 2.5 mg every 8 - 12 hrs should be safe, but selecting a starting dose in opioid-treated patients requires caution and the use of published guidelines for dose conversion and titration.
  - suggest, given the risks associated with methadone, that it should only be used by clinicians who have knowledge and experience with the medication, or access to a specialist for guidance.
  - recommend that cautions, monitoring, and careful assessment of benefits and adverse effects prior to dose change be similar to oral morphine therapy.

Oxycodone Immediate Release

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral	Opioid-naïve adults: 2.5 mg	Every 4 hrs	There is no fixed maximum daily dose for oxycodone. Maximum dose is determined by the presence of treatment-limiting side effects.	▪ Similar to oral morphine; use cautiously (lower doses and longer dosing interval) in patients with renal or hepatic insufficiency.

Comments

- Some experts:
  - recommend a starting dose of 2.5 mg – 5 mg, noting that the lower dose should be used in older or frail adults.
  - observe that oxycodone is similar to morphine but there are large intra-individual and inter-individual differences in the responses to the two medications, both in terms of analgesia and side effects; some patients have better outcomes with morphine and some with oxycodone.
  - recommend using "as needed" to reduce the risk of side effects instead of fixed scheduled doses.
  - recommend that cautions, monitoring, and careful assessment of benefits and adverse effects prior to dose change be similar to oral morphine therapy.

Naloxone for opioid overdose emergency

Used to reverse opioid-induced respiratory depression; should not be given for other side effects, such as somnolence or confusion. The goal of treatment is to improve respiration, not somnolence.

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
IV	0.08 mg	Every 30 - 60 secs until improvement in symptoms.	Maximum dose is determined by patient's response.	▪ Repeat initial doses until respiratory rate improves, e.g., >10 per min. ▪ Given the short half-life of naloxone, repeated doses are likely to be needed, usually every 20 - 30 min after the initial doses; these subsequent doses may be larger than the starting dose, as suggested by the total amount required to obtain the initial benefit. ▪ Monitoring, with repeated naloxone dosing as necessary, continues until the opioid effect wears off; longer periods of monitoring, e.g. 1 - 2 days, are needed when reversing the effects of transdermal fentanyl or methadone.

Comments

- Some experts:
  - recommend a higher starting dose, e.g., 0.4 mg.
  - recommend a lower starting dose, e.g., 0.02 mg – 0.04 mg.
  - recommend selecting a starting dose in the range of 0.02 mg – 2 mg, and giving this dose every few minutes until the desired effect on respiration is obtained.
  - recommend administering an initial dose intramuscularly.
  - suggest that the need for more than 10 mg – 15 mg in total to manage an episode of respiratory depression suggests that the opioid is not the only cause and necessitates further assessment.
  - note that pain may recur when the opioid effect is reversed by naloxone and a plan for pain management during naloxone treatment should be considered.

Edema (pulmonary or peripheral)

- Fluid overload is very heterogeneous in populations with serious chronic illness. Excessive fluid may be generalized or regional and related to major organ dysfunction, such as heart failure, or to local disease impeding vascular or lymphatic drainage. The associated syndromes may be acute and life-threatening, such as pulmonary edema, or insidious and mostly impacting physical functioning and quality of life, such as peripheral leg edema or localized lymphedema. Patients with edema should be evaluated to determine the etiology, physiologic impact, and urgency of treatment.
- Patients with pulmonary edema are usually treated with a systemic diuretic; patients with peripheral edema may or may not be candidates for this approach, depending on an assessment of likely benefits and risks. The use of a loop diuretic, such as furosemide, is a first-line therapy for heart failure and often used for all types of edema; other loop diuretics and diuretics with other modes of action are available in some settings.[28]

Furosemide

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral	20 mg	Every 6 - 8 hrs	--	--
IV	10 mg	Every 6 hrs	--	--

Comments

Oral

- Some experts:
  - initiate therapy with a 40 mg dose.
  - titrate the dose every 8 - 48 hrs while monitoring symptoms, urinary output, vital signs, and if appropriate laboratory tests of renal function, electrolytes, and magnesium; if tolerated, the dose is titrated up until symptoms improve or maximum dose is reached.
  - recommend 1 - 2 doses/day when the patient is stable.
  - suggest a maximum dose of 120 - 240 mg/day.
  - advise caution (use of lower dose and slower titration) if a patient is oliguric, there is concern about hypotension, or there is renal insufficiency or electrolyte disturbances
  - advise monitoring for ototoxicity at higher doses (e.g., 240 mg/day) and routinely monitoring renal function, electrolytes, and magnesium level.

IV

- Some experts:
  - recommend more rapid titration than is done with oral dosing; initial titration at a 2 hr interval may be necessary if effects do not occur.
  - recommend the same cautions and monitoring applied during oral administration.
  - suggest that the medication can be administered subcutaneously if preferred.

[28] Eid PS et al. Comparative effects of furosemide and other diuretics in the treatment of heart failure: a systematic review and combined meta-analysis of randomized controlled trials. Heart Fail Rev. 2021;26(1):127-136. doi: 10.1007/s10741-020-10003-7.

Respiratory secretions

- Difficulty in managing respiratory secretions is a common symptom in some conditions, such as Parkinsonism; it also may manifest as the end-of-life approaches, sometimes resulting in the audible sounds known as "death rattle."
- Although there is very little evidence demonstrating the effectiveness of anticholinergic medications for secretions at the end of life,[29] this treatment is widely used to improve comfort and lessen noisy respiration as death approaches. Several agents and formulations are available.

Hyoscine butylbromide

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral SC Slow IV	20 mg Older adults: 10 mg	Every 4 - 6 hrs	120 mg/day	▪ Can also cause somnolence and confusion but may have lower risk of these effects than hyoscine hydrobromide. ▪ Use cautiously in patients with dryness or urinary hesitancy because these symptoms may worsen.

Comments

- Some experts:
  - avoid use in patients with abundant, thick, and symptomatic secretions because of the potential to hinder clearance and thereby worsen symptoms.
  - recommend a maximum dose of 80 mg/day.

Hyoscine hydrobromide

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Transdermal patch	1 mg	Every 72 hrs	--	▪ May cause dryness, urinary retention, somnolence, and confusion.

Comments

- Some experts recommend a maximum dose of 2 mg (2 patches)

Hyoscine hydrobromide

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
SC	400 mcg	Every 4 - 6 hrs.	2.4 mg/day	▪ May cause dryness, urinary retention, somnolence, and confusion. ▪ Maximum frequency of administration is 6 doses per day.

[29] Taburee W et al. Effects of Anticholinergics on Death Rattle: A Systematic Review and Network Meta-Analysis. J Palliat Med. 2023;26(3):431-440. doi: 10.1089/jpm. 2022.0386.

Wound care

- Wounds are highly prevalent in populations with advanced illness, especially when patients are bedbound or cognitively impaired. Wounds may be painful and malodorous, negatively impacting the patient's ability to move, sit, or engage in social interactions.
- Among the many interventions used in the management of wounds is the topical or systemic administration of the antibiotic metronidazole to reduce odor and the topical application of petroleum jelly to provide local skin hydration and protection.

Metronidazole tablets

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Oral IV Topical (crushed oral tablets)	200 - 250 mg	1-2 times per day, as needed.	--	▪ Oral or IV dose is 250 mg every 6 - 8 hrs. ▪ Topical dose involves crushing 2 - 4 tablets into a fine powder and sprinkling on a malodorous wound with each dressing change.

Comments

- Some experts:
  - use the IV solution topically by spraying on the malodorous wound
  - recommend a topical approach if the main goal is reduction of odor

Petroleum jelly

Route	Starting Dose	Frequency	Maximum Dose	Dosing Recommendations/ Precautions
Topical	--	As needed	As needed	▪ Apply to clean and dry areas as necessary; apply to gauze with dressing changes.

Comments

- Some experts do not use petroleum jelly in the clinical setting.

Photo credits and description (from collage on pg. 5)

Clockwise, from top left:

1. Photo by Christina Vazou from Athens, Greece, of a home visit with a patient in hospice care.
2. Photo by Dr. Lankoandé Martin, of Hospice Burkina in Burkina Faso, offering home-based palliative care to a patient with advanced cancer, explaining the oral morphine intake to manage her pain.
3. Photo by Wisdom Muleya Munkombwe of Livingston, Zambia. The photo depicts the hospice nurse visiting a patient and distributing his medicines.
4. Photo by Daniela Dahlien Neumanova for Cesta Domu in Prague, Czech Republic, of a doctor visiting a hospice patient at her home.
5. Photo by Germanus Natuhwera of Hoima, Uganda. Students (physicians' assistants) on clinical placement at Little Hospice Hoima participating in care of an 89-year elderly male patient with chronic ulcer on a home visit.
6. Photo by Farah Anil Joseph from Hyderabad, in Sindh, Pakistan of the home-based palliative care team of St. Elizabeth hospital on the motor bike ambulance providing a home care service to terminally ill cancer patients.
7. Photo by Reena Sharma from Punjab, India. The photo depicts a CanSupport doctor with home care patient in Bhatinda, India.

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