A Textbook of

Clinical Pharmacy

for Pharmacy Students

Lesson 9:

Clinical Pharmacy for Patients in Palliative Care

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9.1 Pharmacotherapy in Palliative Care

Palliative pharmacotherapy is grounded in the broader concept of palliative care as an approach that **seeks to improve quality of life for patients with life-limiting illness and for their families by preventing and relieving suffering through early identification, careful assessment and treatment of physical, psychological, and social problems**. In contrast to curative or disease-modifying strategies, which aim primarily at prolonging survival or eradicating disease, palliative pharmacotherapy focuses on alleviating the symptom burden and supporting function within the constraints of advanced illness, even when underlying pathology is no longer reversible. This implies that **the success of treatment is measured less by laboratory or imaging surrogates and more by the patient's own experience of relief, comfort and ability to engage in valued activities**.[1]

From a pharmacotherapeutic perspective, this shift in goals has several practical consequences. Medicines that were once prescribed to modify long-term prognosis, such as lipid-lowering agents, strict glycemic control regimens or intensive antihypertensive strategies, often become less relevant as the expected time to benefit exceeds the remaining life expectancy, whereas symptomatic treatments for pain, dyspnea, nausea, anxiety, insomnia or delirium move to the foreground. **Dose selection is guided not only by organ function and pharmacokinetics but also by the balance between rapid symptom relief and the acceptability of adverse effects** such as sedation or constipation, which may be tolerated to a greater extent when distress from symptoms is severe.

Palliative care applies across a range of disease trajectories rather than being confined to advanced cancer. In patients with metastatic malignancies, symptom burden often arises from tumor progression, treatment-related toxicities and complications such as bone metastases, neuropathic pain or malignant bowel obstruction. In advanced organ failure (heart failure, chronic obstructive pulmonary disease, end-stage liver or kidney disease), the course is frequently characterized by recurrent exacerbations, progressive functional decline and complex decisions about continuing or withdrawing disease-modifying drugs (e.g., high-dose diuretics, disease-modifying heart failure therapies or immunosuppression), while managing breathlessness, fatigue, oedema and other disabling symptoms. Neurodegenerative diseases

[1] Li S, Wang Q, Qi B, et al. Role of clinical pharmacists in palliative care team: A scoping review. Palliat Support Care. 2026;24:e33.

such as amyotrophic lateral sclerosis, advanced Parkinson's disease or dementia bring additional challenges of communication difficulties, swallowing impairment and cognitive decline, which profoundly influence route of administration, treatment priorities and the feasibility of complex regimens.

Examples of Palliative Care Scenarios

1. Advanced metastatic cancer with high symptom burden

A 68-year-old woman with metastatic lung cancer receiving palliative chemotherapy experiences severe bone pain from vertebral metastases, opioid-responsive dyspnea and recurrent chemotherapy-induced nausea. Disease-modifying treatment continues, but palliative pharmacotherapy focuses on multimodal analgesia (paracetamol, strong opioids, adjuvant agents), low-dose opioids for breathlessness and optimized antiemetic regimens, while de-emphasizing long-term preventive medicines whose benefit will not be realized within her expected lifespan.

2. End-stage heart failure with repeated hospitalizations

A 75-year-old man with advanced heart failure, severe dyspnea at rest and multiple admissions for decompensation is receiving maximal guideline-directed medical therapy. Despite this, his prognosis remains poor and functional capacity is severely limited. Palliative care is introduced to prioritize relief of breathlessness and fatigue, rationalize diuretic and vasodilator use, and reconsider preventive drugs such as high-intensity statins or tight glycemic control, which no longer confer meaningful benefit. Pharmacotherapy is adjusted to balance symptom control, electrolyte disturbances and hypotension.

3. Advanced chronic obstructive pulmonary disease (COPD) with chronic breathlessness

A 72-year-old woman with severe COPD on maximal inhaled therapy has chronic breathlessness that persists despite optimized bronchodilators and pulmonary rehabilitation. Palliative pharmacotherapy adds low-dose oral or subcutaneous opioids targeted specifically at dyspnea rather than pain, along with as-needed short-acting bronchodilators and anxiolytics when appropriate, while monitoring for sedation and carbon dioxide retention. Here, the goal is not to reverse the underlying lung damage but to reduce the intensity and distress associated with each breath.

4. End-stage kidney or liver disease not eligible for transplantation

A 63-year-old patient with cirrhosis and refractory ascites, or a 70-year-old with advanced chronic kidney disease who declines dialysis, may have multiple distressing symptoms including pruritus, muscle cramps, insomnia, nausea and pain. Palliative care shifts the focus from strict metabolic targets to symptom-driven use of diuretics, anti-pruritic agents, carefully selected analgesics and sleep-promoting strategies, taking into account altered drug handling and increased susceptibility to adverse effects.

(continues in next page)

Examples of Palliative Care Scenarios (continue)

5. Progressive neurodegenerative disease with cognitive and functional decline

A 60-year-old man with amyotrophic lateral sclerosis, gradually loses mobility, swallowing ability and capacity to communicate. In this context, palliative pharmacotherapy includes treatment of pain (often under-recognized in dementia), management of spasticity or muscle cramps, control of drooling or respiratory secretions, and careful use of psychotropic medicines for agitation or depression.

6. Early palliative integration alongside curative-intent therapy

A 54-year-old with locally advanced head and neck cancer receiving chemoradiotherapy develops mucositis, severe odynophagia and weight loss. Although oncological treatment has curative intent, early palliative care is essential to provide aggressive symptom management (topical anesthetics, systemic analgesics, antiemetics, saliva substitutes) and nutritional support, aiming to maintain treatment intensity and quality of life. This illustrates that palliative pharmacotherapy is compatible with curative goals when it addresses treatment-related suffering.

7. The last days of life

In the terminal phase (characterized by profound weakness, minimal oral intake, progressive decrease in consciousness and hours-to-days prognosis), the focus of pharmacotherapy narrows to a small set of parenteral or sublingual medicines for pain, dyspnea, agitation, delirium and respiratory secretions. Long-term preventive medicines and most chronic disease therapies are withdrawn, and the clinical pharmacist can help simplify to a "comfort-only" regimen that is feasible for nurses and family caregivers to administer.

- Krumm L, Bausewein C, Rémi C. Drug Therapy Safety in Palliative Care-Pharmaceutical Analysis of Medication Processes in Palliative Care. Pharmacy (Basel). 2023;11(5):160.

Within this context, palliative pharmacotherapy is inherently multidisciplinary. Optimal symptom control rarely depends on medication alone and must be integrated with psychological support, social care, spiritual or existential counselling and rehabilitative interventions, a concept sometimes summarized as attention to "**total suffering**". Physicians, nurses, psychologists, and social workers each contribute to understanding the sources of distress and to tailoring interventions, but the **clinical pharmacist has a specific mandate to ensure that the medicine-related component of care is rational, evidence-based and aligned with patient goals**. This includes reviewing and simplifying complex regimens, anticipating and managing adverse effects, selecting appropriate formulations and routes (e.g., subcutaneous administration when oral intake is no longer possible), and supporting the safe use of high-risk

medicines such as strong opioids, antipsychotics and sedatives in home, hospice and hospital settings.[2]

The scope of palliative pharmacotherapy therefore extends from early integration to the final days of life, when the focus narrows to a small number of drugs aimed at controlling a limited set of common terminal symptoms. Throughout this trajectory, therapeutic decisions should be made through shared deliberation with patients and families, explicitly weighing the expected symptomatic benefits of each medicine against its burdens, and revisited as the disease and the person's priorities evolve.

9.1.1 Principles of pharmacotherapy optimization in palliative care

Pharmacotherapy optimization in palliative care rests on a set of main principles that differ in emphasis from those guiding treatment earlier in the disease trajectory. The central starting point is **individualization: each regimen should be tailored to the person's prognosis, current symptom burden, comorbidities and explicitly stated goals of care**. When life expectancy becomes limited and the likelihood of meaningful long-term benefit from preventive interventions diminishes, **drugs are evaluated primarily for their capacity to relieve symptoms, maintain function and support the patient's priorities rather than for their impact on distant outcomes**. This reorientation requires explicit conversations with patients and families about what they hope pharmacotherapy will achieve and what level of adverse effects or treatment burden they are willing to accept.

Prioritization of symptom-relieving over preventive drugs follows logically from this individualized approach. As patients approach the terminal phase, the relative value of drugs such as statins, bisphosphonates, certain antihypertensives or tight glycemic control regimens decreases, while drugs for pain, dyspnea, agitation, nausea, delirium or insomnia become central to care. Observational studies in hospice and home-based palliative care consistently show a reduction in the average number of systemic medicines from admission to the final days of life, driven largely by systematic discontinuation of long-term preventive treatments and concomitant simplification of cardiovascular, metabolic and supplementation therapies. In parallel, there is often an increased use of opioids, anxiolytics, antipsychotics and antiemetics, as pharmacotherapy is refocused on controlling a limited set of distressing symptoms that dominate the last phase of illness. The clinical task is not merely to "add" symptom-relieving drugs on top of existing regimens, but to rebalance the entire treatment plan so that each remaining medicine has a clear and near-term purpose.[3]

Cautious use of polypharmacy is therefore a core principle of palliative pharmacotherapy. Many patients enter palliative programs with multiple chronic diagnoses and a long list of medicines initiated over years in different settings, leading to high baseline rates of complex regimens, interactions and treatment-related harm. As life expectancy shortens, the risk–benefit ratio of continuing such combinations often shifts unfavorably: the incremental value of strict blood pressure or lipid control diminishes, while the potential for dizziness, falls, confusion or gastrointestinal adverse effects increases. Optimization in this context involves deliberately limiting the number of concurrent agents, simplifying dosing schedules, and choosing drugs with

[2] Krumm L, Bausewein C, Rémi C. Drug Therapy Safety in Palliative Care-Pharmaceutical Analysis of Medication Processes in Palliative Care. Pharmacy (Basel). 2023;11(5):160.
[3] Novosadová M, Filip S, Molnárová V, et al. Adjustment of pharmacotherapy during the final days of life in home hospice care: a pilot retrospective study. Ann Palliat Med. 2025;14(2):136-145.

the broadest symptomatic benefit and the most favorable tolerability profiles. Subcutaneous or transdermal administration and the use of continuous infusions may further reduce the complexity of administration for patients and caregivers who can no longer manage intricate oral schedules.

Dynamic reassessment is another defining principle. Palliative needs evolve rapidly as disease progresses, acute events occur, and functional status changes. A regimen that was appropriate weeks earlier may become burdensome or ineffective as oral intake fails, organ function declines or new symptoms emerge. Regular, structured reviews of all prescribed and actually taken medicines is essential, with explicit attention to whether each drug still has a realistic chance of achieving its intended goal within the patient's remaining lifespan. In home hospice cohorts, repeated medication review has been associated with substantial stepwise reductions in the number of systemic medicines and a shift from oral to predominantly subcutaneous administration as death approaches, illustrating how pharmacotherapy must adapt to new clinical realities, including impaired swallowing and reduced renal or hepatic clearance. This iterative process also ensures that new or worsening symptoms are recognized and treated promptly, rather than being attributed solely to disease progression.

Within this framework, **deprescribing emerges as a structured and proactive process rather than an ad hoc reaction to perceived overmedication**. Contemporary literature defines deprescribing as the planned, supervised reduction or discontinuation of medicines that may no longer be beneficial or may be causing harm, with the explicit aim of improving outcomes and aligning treatment with patient goals. In palliative cancer care, systematic deprescribing programs have demonstrated reductions in polypharmacy and exposure to potentially inappropriate medications, without evidence of worsened symptom control, and sometimes with improvements in quality of life and treatment burden. Tools and guidelines developed specifically for patients with advanced disease can support clinicians in identifying candidates for tapering or discontinuation manly of drugs with long time-to-benefit, limited symptomatic value, or high risk of adverse effects in the context of frailty and organ dysfunction. Importantly, **deprescribing in palliative care is not synonymous with abandoning care; instead, it represents an active therapeutic choice to focus pharmacotherapy on what matters most to the patient in the time that remains**.[4]

Clinical pharmacists are particularly well positioned to support safe simplification of regimens and to embed these principles in routine practice. Pharmacist-led medication reconciliation and medication review in palliative settings can identify inappropriate continuation of preventive drugs, suboptimal doses in the presence of renal or hepatic impairment, burdensome administration schedules, and untreated or undertreated symptoms. medication reconciliation and medication review will be further explored in Pharmaceutical Care course (5th year).

9.1.2 Route of administration and formulation strategies in palliative care

Loss of reliable oral intake is one of the defining transitions in advanced illness and obliges a shift from complex oral regimens towards routes and formulations that remain feasible, effective and safe in frail patients under palliative care. Route selection should follow the phase of illness, symptom pattern and care setting, **balancing pharmacokinetic advantages against the**

[4] de Andrade FK, Nunes RPI, Zanetti MOB, et al. Validated medication deprescribing instruments for patients with palliative care needs: a systematic review. Farm Hosp. 2024;48(2):83-89. doi:10.1016/j.farma.2023.08.004

practical skills of nurses, patients and caregivers. In early palliative stages, oral therapy is usually preferred for its familiarity and convenience, but as dysphagia, nausea, reduced consciousness or delirium emerge, sublingual, transdermal, subcutaneous and occasionally rectal or parenteral routes become more appropriate, often with a deliberate reduction in the number of different medicines and administration times.

The **oral route** remains central for as long as patients can swallow safely and tolerate gastrointestinal absorption, particularly for long-term background treatments and adjuvant agents such as antidepressants, anticonvulsants or laxatives. However, even before oral intake is lost, once-daily or twice-daily modified-release formulations may need to be replaced by immediate-release preparations to allow more flexible titration and to reduce the risk of accumulation in organ dysfunction or when doses are skipped. In cancer, severe mucositis[5] and odynophagia[6] may render oral opioids and other analgesics intolerable despite preserved swallowing, prompting early transition to transdermal or parenteral routes while maintaining other oral medicines that are well tolerated and still contribute meaningfully to comfort.

Sublingual administration offers a useful intermediate option when swallowing is impaired but small volumes can still be managed, particularly for short-acting opioids, benzodiazepines and certain antiemetics. Its advantages include relatively rapid absorption without the need for swallowing and the possibility of using small, infrequent doses for breakthrough symptoms, but absorption can be inconsistent in patients with dry mouth, poor cooperation or reduced consciousness. Buccal and sublingual routes also require that caregivers are comfortable placing tablets or drops in the mouth and monitoring for choking, which may limit their practicality in some home settings.

Transdermal formulations are especially valuable when stable, long-acting systemic exposure is desired and swallowing is no longer reliable, as with fentanyl or buprenorphine patches for background pain control. They provide continuous drug delivery over several days, simplify administration for caregivers and can reduce peaks and troughs compared with intermittent dosing, but onset and offset are slow and dose titration is relatively inflexible. In cachectic patients with little subcutaneous fat, altered skin perfusion, fever or profuse sweating, transdermal absorption may become unpredictable, so transdermal therapy is best reserved for relatively stable clinical situations and supplemented by short-acting subcutaneous or sublingual rescue doses when symptoms fluctuate.

The **subcutaneous route**, including continuous subcutaneous infusion (CSCI) via a syringe driver, is the keystone of pharmacotherapy in the last days of life, when oral intake is minimal and repeated intravenous access is neither feasible nor desirable. Subcutaneous bolus injections allow flexible, as-needed dosing of opioids, antiemetics, antipsychotics and anticholinergics, while CSCI provides a steady background level of one or more drugs over 24 hours, reducing the need for frequent injections and night-time dosing. When using CSCI, compatibility and stability of drug mixtures must be checked carefully, as not all combinations of opioids, antiemetics and sedatives can be safely mixed in the same syringe. Pharmacists should play a key role in advising on suitable diluents, maximum concentrations, and alternatives when incompatibilities are

[5] Mucositis is a painful inflammation and ulceration of the mucous membranes, most often affecting the oral cavity as a complication of chemo- or radiotherapy.
[6] Odynophagia is the term for pain on swallowing, typically felt in the throat or chest when eating or drinking.

identified. Conversion between oral, subcutaneous and transdermal formulations requires use of equianalgesic ratios and an appropriate dose reduction to account for incomplete cross-tolerance, with close clinical monitoring during the first 24–48 hours after switching.

Rectal administration can be a pragmatic alternative for selected medicines when oral and subcutaneous routes are unavailable or unacceptable and intravenous access is not indicated, particularly for analgesics, antipyretics and some anticonvulsants. Its limitations include variable absorption, potential discomfort or embarrassment, and cultural or personal reluctance, so it is generally reserved for specific indications and used in agreement with the patient or family. Intravenous administration is usually confined to hospital or specialist units and is most appropriate when rapid onset is critical, as in uncontrolled pain, refractory dyspnea or status epilepticus.

Intrathecal or epidural routes are highly specialized options for refractory pain and require experienced teams and careful selection of candidates, with pharmacists involved in ensuring correct preparation, concentration and stability of solutions for implantable pumps or epidural infusions.

9.1.3 Optimization of pain pharmacotherapy in palliative care

Pain pharmacotherapy in palliative care follows the same general pharmacological principles that are discussed in detail in the dedicated Lesson 12 on pain and opioid management, but its application is strongly shaped by limited prognosis, advanced organ dysfunction and evolving goals of care. The central aim is not only to reduce pain intensity but to maintain function and comfort with the smallest feasible treatment burden, recognizing that the balance between analgesia and adverse effects often shifts as disease progresses and as patients and families reassess their priorities.

Assessment of pain in advanced disease must account for communication barriers due to delirium, dementia, severe fatigue or reduced consciousness, and relies more heavily on behavioral cues, collateral history and repeated observation over time. Standard numerical rating scales may be unusable, so clinicians often combine simple self-report tools with proxy assessments and structured observational scales, especially in advanced dementia or in the last days of life. In this context, clinical pharmacists can help interpret apparently poor responses to analgesics by distinguishing inadequate dosing or inappropriate mechanism-targeting from non-pain sources of distress such as anxiety or dyspnea.

Non-opioid analgesics and adjuvant agents remain important, but their role is adapted to organ dysfunction and limited life expectancy. **Paracetamol** is often retained for mild musculoskeletal or background pain because of its favorable safety profile, **while non-steroidal anti-inflammatory drugs (NSAIDs)** are used cautiously or avoided in advanced renal, cardiac or gastrointestinal disease. **Adjuvant drugs for neuropathic pain** (such as certain antidepressants or anticonvulsants) may still provide benefit, but long titration periods and risks of sedation, falls and interactions often limit their use when prognosis is short, so decisions focus on agents that can achieve meaningful relief within weeks rather than months.

Opioid therapy is frequently central to pain management in palliative care, yet even here the emphasis is on optimization rather than automatic dose escalation. Choice of opioid is influenced by renal and hepatic function, prior exposure, route feasibility and the coexistence of other symptoms such as dyspnea that may also respond to opioids. Titration focuses on achieving stable background control with around-the-clock dosing (oral, transdermal or

subcutaneous) supplemented by predictable rescue doses for breakthrough pain, with attention to equianalgesic ratios and the need for dose reduction when rotating between opioids to account for incomplete cross-tolerance. Common adverse effects, like constipation, nausea, sedation, delirium and opioid-induced neurotoxicity, should be anticipated and actively managed, for example by routine laxative co-prescription, antiemetic use where needed and consideration of dose reduction or opioid rotation when neurotoxic features emerge.

Safe use of strong opioids in home and hospice care raises additional, palliative-specific considerations. Regimens must be simple enough for family caregivers or non-specialist staff to administer correctly, with clear written instructions about regular and rescue dosing, maximum daily quantities and when to seek help. Storage and documentation of opioid supplies should minimize the risk of accidental ingestion by children, errors in dosing, or diversion, particularly in settings with multiple visitors or complex family dynamics.

9.1.4 Optimization of pharmacotherapy for other prevalent symptoms in palliative care

Pharmacotherapy for non-pain symptoms in palliative care aims to relieve distress with the smallest feasible regimen, tailoring drug choice and dosing to advanced organ dysfunction, limited prognosis and the care setting. Within this framework, symptom-focused strategies for dyspnea, gastrointestinal disturbances, neuropsychiatric symptoms, and terminal secretions should be embraced.

Dyspnea and cough

Opioids are the pharmacological cornerstone for refractory breathlessness in advanced disease, typically **using low-dose oral or parenteral morphine** (or an equianalgesic opioid) titrated against relief and sedation, with attention to prior opioid exposure and to overlapping analgesic regimens. In patients whose dyspnea remains distressing despite optimized opioids and non-pharmacological measures, **short-acting benzodiazepines** may be added, particularly when anxiety is prominent, but evidence for benzodiazepines as specific anti-dyspneic agents is weak and oversedation or delirium can occur. **Bronchodilators** (e.g. inhaled β agonists and antimuscarinics) are reserved for patients with reversible airflow obstruction, while **systemic corticosteroids, diuretics or antibiotics** are used only when an underlying exacerbating pathology is present and their expected benefit is compatible with prognosis. For intractable dyspnea in the last days of life, continuous subcutaneous infusions of an opioid, sometimes combined with a benzodiazepine such as midazolam, may be appropriate as part of proportionate palliative sedation in collaboration with experienced teams.

Gastrointestinal symptoms

Nausea and vomiting are managed according to the likely mechanism: **dopamine antagonists** such as metoclopramide or haloperidol for drug- or metabolic-related nausea, **5-HT_3 antagonists** for chemotherapy-induced symptoms, and **antihistaminic or anticholinergic** agents when vestibular or motion-related components are suspected. Constipation should be anticipated in almost all patients receiving strong opioids and reduced mobility, with routine prescription of **stimulant or osmotic laxatives** and adjustment to renal function. Dyspepsia and reflux symptoms may respond to short courses of proton pump inhibitors or H_2 receptor antagonists, but prolonged acid suppression near the end of life is rarely necessary unless it contributes meaningfully to comfort or prevents bleeding in high-risk patients.

Delirium, agitation and insomnia

Delirium is common in advanced illness, and management starts with addressing reversible precipitants (e.g. infections, psychoactive drugs, uncontrolled pain), orienting communication, sleep–wake normalization and environmental measures. When pharmacological treatment is needed for distressing agitation or risk to self or others, **low-dose antipsychotics** such as haloperidol remain first-line, titrated carefully and used for the shortest possible duration, while **benzodiazepines** are reserved for refractory cases, terminal agitation or specific indications such as alcohol withdrawal, due to their potential to worsen confusion. For insomnia, simple sleep hygiene strategies, reassurance and optimization of symptom control are preferred.

Anxiety, depression and existential distress

Psychological and existential distress are integral to symptom burden in palliative care, and non-pharmacological interventions (supportive communication, psychotherapy, spiritual care) should accompany or precede medicines. When pharmacotherapy is indicated, **selective serotonin reuptake inhibitors** or other **modern antidepressants** may be used for major depressive episodes in patients with an expected survival long enough to benefit, with dose adjustments in hepatic or renal impairment and careful monitoring for drug–drug interactions. **Short-acting benzodiazepines** can alleviate acute anxiety or panic, but in advanced disease their use should be intermittent, at the lowest effective dose, and regularly reviewed because of additive sedation, falls, and potential worsening of cognitive symptoms.

Respiratory secretions and terminal phase symptoms

Noisy respiratory secretions ("death rattle")[7] in the last hours to days of life are often more distressing to families than to patients, who are usually unconscious or minimally aware. Simple measures such as repositioning, avoiding routine deep suctioning and reducing or discontinuing non-essential parenteral fluids are first-line, since excessive hydration can worsen secretions. When pharmacological treatment is desired, subcutaneous or transdermal **anticholinergics** (e.g. hyoscine butylbromide, glycopyrronium, or scopolamine) may reduce new secretion production but do not clear existing fluid. They should be started early when the pattern is recognized, with awareness of possible adverse effects such as dry mouth, urinary retention and, less commonly, delirium.

[7] **Death rattle** is a colloquial term for noisy breathing caused by pooled secretions in the upper airways of a person who is very close to death and no longer able to swallow or cough effectively.