UPMC PALLIATIVE AND SUPPORTIVE INSTITUTE

THE TABLET: PALLIATIVE CARE PHARMACY TIPS

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If you have a topic you would like the pharmacy team to answer, please send your suggestions to: lowrymf@upmc.edu

TODAY'S TOPIC:

New Guideline Highlight: Opioid Conversion in Adults with Cancer

Background:

Patients with cancer often take opioids to manage cancer-related pain. It is not uncommon for opioid switching to occur in practice either between routes of administration or between opioid agents for certain clinical reasons. Opioid conversions are a debated topic in the literature as well as clinical practice; variability exists nationally and internationally for opioid conversion ratios across doses and routes used in practice. The new guidelines are summarized below. I highly encourage you to check out the full guidelines and appendix below for more details!

Importance:

Until now, no guideline existed for opioid conversions in adults with cancer. A recent guideline was published this year detailing opioid conversions in adults with cancer. The goal of this guideline is to "establish an international best practice baseline than can be built upon by new research and better-designed trials."

The Guideline:

Support Care Cancer. 2025 Mar 3;33(3):243.

Opioid conversion in adults with cancer: MASCC-ASCO-AAHPM-HPNA-NICSO Guideline

Objective: to standardize and improve the safety and efficacy of opioid conversion in people with cancer

Methods: Expert panel developed recommendations based on systematic review of the literature[1] and formal consensus process (2 rounds of consensus at 75% agreement)

Results: systematic review identified 208 eligible studies

- 58 of 84 statements met expert panel consensus
- Appendix (online) details statements that did not reach consensus

Pre-conversion Assessment Recommendation
Multidimensional pain assessment (initial and follow up)
Thorough review of pain pathology and other management options
Review of comorbidities, drug-drug interactions, adverse effects
History of opioid usage (dose, efficacy, route, tolerability, adherence)
Opioid risk assessment
Evaluation for organ (renal/hepatic) dysfunction
Availability of caregivers to monitor patient after adjustment made
Discussion with patient re: acceptability of different regimens

Situations in which opioid conversion may be offered:

- Pain uncontrolled despite titration of current regimen or intolerability of dose increase of current opioid, intolerable side effects, opioid-induced neurotoxicity, if pharmacokinetic factors affect absorption/metabolism/excretion of current regimen, social determinants of health constraints

Opioid Conversion Recommendations
Opioids should be adjusted individually based on patient-specific characteristics
Conversion ratios are not synonymous with equianalgesic doses; doses are adjusted based on analgesic response for individual patient needs
Can convert by calculating the morphine equivalent daily dose (MEDD) of first opioid to transition to alternate opioid
For breakthrough pain, 10-15% of MEDD should be used initially to manage breakthrough pain using an immediately release opioid
Reduction for incomplete cross tolerance when switching between opioids *did not reach consensus*, as adjusted doses do not represent published conversion ratios where there is clinical experience
It is important to remember that most clinical trials of opioid conversions excluded patients with substance use disorder, psychiatric illness, renal and hepatic impairment and reflect the experiences of a healthier population
Fentanyl conversions did not reach consensus as these conversions become even more difficult in those with cancer and cancer-related cachexia and variable conversions between fentanyl and morphine exist in existing literature
Methadone did not reach consensus, although experts agreed that only clinicians with experience in converting to methadone should prescribe it noting that multiple conversion strategies are typically used depending on the clinical situation
Bidirectional differences did not reach consensus as studies investigating bidirectional conversion strategies involve a small number of patients and were underpowered
Pharmacogenetics can influence opioid responses and conversion ratios although not routinely done in clinical practice; this is an area for future research

Table 3. Opioid conversion ratios that reached consensus

Converting from	Converting to	Recommended conversion ratios*	*n* agreed/*n* voted, % agreement
Oral morphine	Oral oxycodone	1.5:1	34/38, 89.4%
Oral morphine	Oral hydromorphone	5:1	33/37, 89.1%
Oral morphine	Oral oxymorphone	3:1	16/20, 80%
Parenteral morphine	Parenteral alfentanil	10:1	15/18, 83.3%
Oral oxycodone	Oral morphine	Between 1:1 and 1:2*	32/38, 84.2%
Oral oxycodone	Oral oxymorphone	2:1	17/19, 89.4%
Oral oxycodone	Oral tapentadol	1:5	20/24, 83.3%
Oral oxycodone	Intravenous oxycodone	2:1	22/25, 88%
Oral hydrocodone	Oral morphine	1:1	23/26, 88.4%
Oral hydrocodone	Oral oxycodone	1.5:1	21/26, 80.7%
Oral tramadol	Oral morphine	10:1	29/36, 80.5%
Oral codeine	Oral hydrocodone	8:1	18/22, 81.8%
Oral tapentadol	Oral morphine	3:1	21/25, 84%
Subcutaneous administration (any opioid)	Intravenous administration (any opioid)	1:1	33/36, 91.6%

*A range was provided because of variability between the study conversion ratios

CLINICAL PEARL: This is the first guideline detailing opioid conversions in adults with cancer. Variability in clinical trial data and expert opinion still exist, noting the importance for continued research surrounding opioid conversions.

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Post-Conversion Assessment Recommendations
Assess efficacy through pain severity during different levels of activity and best/worst throughout the day; can use nonverbal pain behaviors if cannot complete numeric rating scale
Assess pain-related functional impacts on daily living activities
Ask about utilization of breakthrough opioid regimen
Monitor for opioid adverse effects (new) including: sedation, nausea/vomiting, confusion/delirium, constipation, itching, sleep and mood
Adjust dose based on pain severity, functionality, and side effects
Continue to evaluate for aberrant behavior surrounding opioids
Check QTc if on methadone, depending on clinical circumstance. likely unnecessary for patients with limited life expectancy or enrolled in hospice
Reinforce expectations, instructions, medication administration schedule and monitoring with patient/caregivers

Discussion:

- This document can serve as best practice baseline that can be built upon by new research and better-designed clinical trials
- 26 statements did not reach consensus among the expert panel highlighting that this topic remains “gray”
- Areas that did not reach consensus
    - Reducing for incomplete cross-tolerance
    - Bidirectional differences in opioid conversion ratios
    - Methadone conversions
    - Fentanyl conversions
    - Buprenorphine conversions
    - Some hydromorphone conversions
- Conversions that did reach consensus (above) are generally in-line with our internal conversion ratios: UPMC Reference Guide 2024
    - Highlighting differences here:
        - Tramadol : morphine is 4:1 internally versus 10:1 in guideline
        - Oral morphine : Oral hydromorphone 4:1 internally versus 5:1 in guideline
- Does this warrant a change in our practice?
    - I am less worried about tramadol : morphine conversion, even though a larger difference cited between our internal document and guideline as I rarely recommend tramadol in clinical practice or do a “conversion,” when switching to or from tramadol. I still remained concerned to use tramadol as we have to worry about opioid side effects, serotonin syndrome, drug interactions at CYP2D6, and lowering seizure threshold
    - I do wonder about oral morphine to oral hydromorphone consensus of 5:1 as we have generally accepted 4:1… how clinically relevant is this?
        - This would be a difference of 30mg oral morphine to 6mg oral hydromorphone rather than 8mg (rounding up from 7.5mg) hydromorphone
        - Given that we typically still reduce by 25-50% (I usually do 33%) for cross tolerance, we would still get to 6mg (4:1) conversion
- I was surprised that the panel did not reach consensus surrounding the practice to reduce for incomplete cross (“non-cross analgesic”) tolerance
    - Admittedly, my clinical practice varies on this depending on patient scenario so maybe the verdict is still out on when this practice is appropriate depending on the clinical scenario?
    - If pain controlled and switching opioids for another clinical or logistical reason: I reduce by 33%
    - If pain uncontrolled, I skip the step to reduce for incomplete cross tolerance to account for my “dose increase” when rotating between opioids
- I am looking forward to the research that is completed as a result of this guideline!

Abbreviations:
MASCC: Multinational Association of Supportive Care in Cancer
ASCO: American Society of Clinical Oncology
AAHPM: American Academy of Hospice and Palliative Medicine
HPNA: Hospice and Palliative Nurses Association
NICSO: Network Italiano Cure di Supporto in Oncologia

References:

1. Davis MP, Davies A, McPherson ML et al (2024) Opioid analgesic dose and route conversion ratio studies: a scoping review to inform an eDelphi guideline. Support Care Cancer 32:542

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