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EXCELLENCE.

CIVA
PHARMACY SERVICES

UNDERSTANDING AND IMPLEMENTING DOSE BANDING

The National Association of Pharmacy Regulatory Authorities (NAPRA) Model Standards for Pharmacy Compounding are being implemented in various provinces across Canada.[1] Cancer Care Ontario (CCO) projected drug waste of $13–$26 million in Ontario when establishing a beyond-use date of six hours for single-dose vials.[2]

CCO recommends dose banding to minimize drug waste, ensure accuracy during drug preparation, and reduce healthcare expenditures.[3] Dose banding in place of patient-specific dosing resulted in **no significant difference in treatment efficacy**.[2] Cost analyses estimate savings ranging from tens of thousands to millions of dollars, depending on the drug and the number of doses dispensed per patient per year.[4–11]

Baxter CIVA can compound patient-specific and dose-banded chemotherapy at the highest quality in a NAPRA-compliant facility. Our goal is to reduce healthcare expenditures; improve productivity, efficiency, and accuracy with compounding; and ensure patients can receive their chemotherapy closer to home in a timely manner.

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DOSE BANDING

Drug doses are grouped and rounded to a set of predefined standard doses.[2] Dose rounding up or down to the nearest vial size should be **within 5%–10% of the prescribed dose**.[3]

CLINICAL RATIONALE

- Dose adjustment for toxicity commonly results in a 20%–30% dose reduction, so a dose modification of 5%–10% would **not result in a meaningful clinical change**.[11]
- Relative dose intensity for optimal therapeutic efficacy for cytotoxic chemotherapy is >85%, so doses of up to 15% or lower than intended dose **achieve equal efficacy**.[11]
- United States Pharmacopeia (USP) standard for actual concentration of active ingredient per product label is +/- 10%, so a variance of 10% is **not expected to produce meaningful physiologic impact**.[11]

BENEFITS

PHARMACY

Improved efficiency and safety[3]
- Streamlines pharmacy preparation workflow
- Facilitates outsourcing
- Reduces patient wait times
- Reduces phone calls to the prescriber to alter the dose

Cost avoidance and savings[3]
- Ability to re-dispense product when treatment is cancelled
- Direct savings from rounding down the dose
- Reduced wastage by rounding up or down to the nearest vial size

PHYSICIAN

Reduces patient wait times

Provides administration of chemotherapy on the chosen facilitated day

Supports the treatment of patients closer to home[3]

LIMITATIONS

- Pediatric population: dosing difficult up to 30 kg or 8–10 years, as there are smaller numbers of patients[12]
- Clinical trials: banding may not be approved in protocols and methods of drug administration have not been consistent between trials[12]
- Obese population: risk of overdosing and underdosing[12]

THE ALTERNATIVE: PATIENT-SPECIFIC DOSING

- Doses traditionally individualized for patients using body surface area (BSA) or weight.
- Limitations include[12]:
  - Complex prescribing since BSA is estimated, not measured
  - Variation in results between formulae used
  - Study on which most common BSA formula is based is not robust
  - Imprecise correlation between drug clearance and BSA
  - Labour-intensive pharmacy practice as each dose is individually prepared

EVIDENCE

- CCO recommends dose banding for select drugs to help with system efficiencies, to reduce wait times, and to minimize drug wastage.[2]
- The Hematology Oncology Pharmacy Association (HOPA) position statement on dose rounding recommends mAbs and other biologic agents be dose rounded to the nearest vial size within 10% of the prescribed dose, unless exempt per the institution's dose-rounding policy.[3] This position statement is endorsed by the National Comprehensive Cancer Network (NCCN) and the International Society of Oncology Pharmacy Practitioners (ISOPP).[3]
- Each cytotoxic drug should be considered independently in the context of product- and regimen-based toxicity potential to determine the appropriateness of the dose-rounding parameters.[3]

EFFICACY

- Dose banding in place of individualized dosing resulted in no significant difference in drug exposure.[13]
- Dose banding reduces patient wait times, drug waste, and medication errors while also improving pharmacy efficacy in the preparation of chemotherapy.[14]

WASTE AND COST

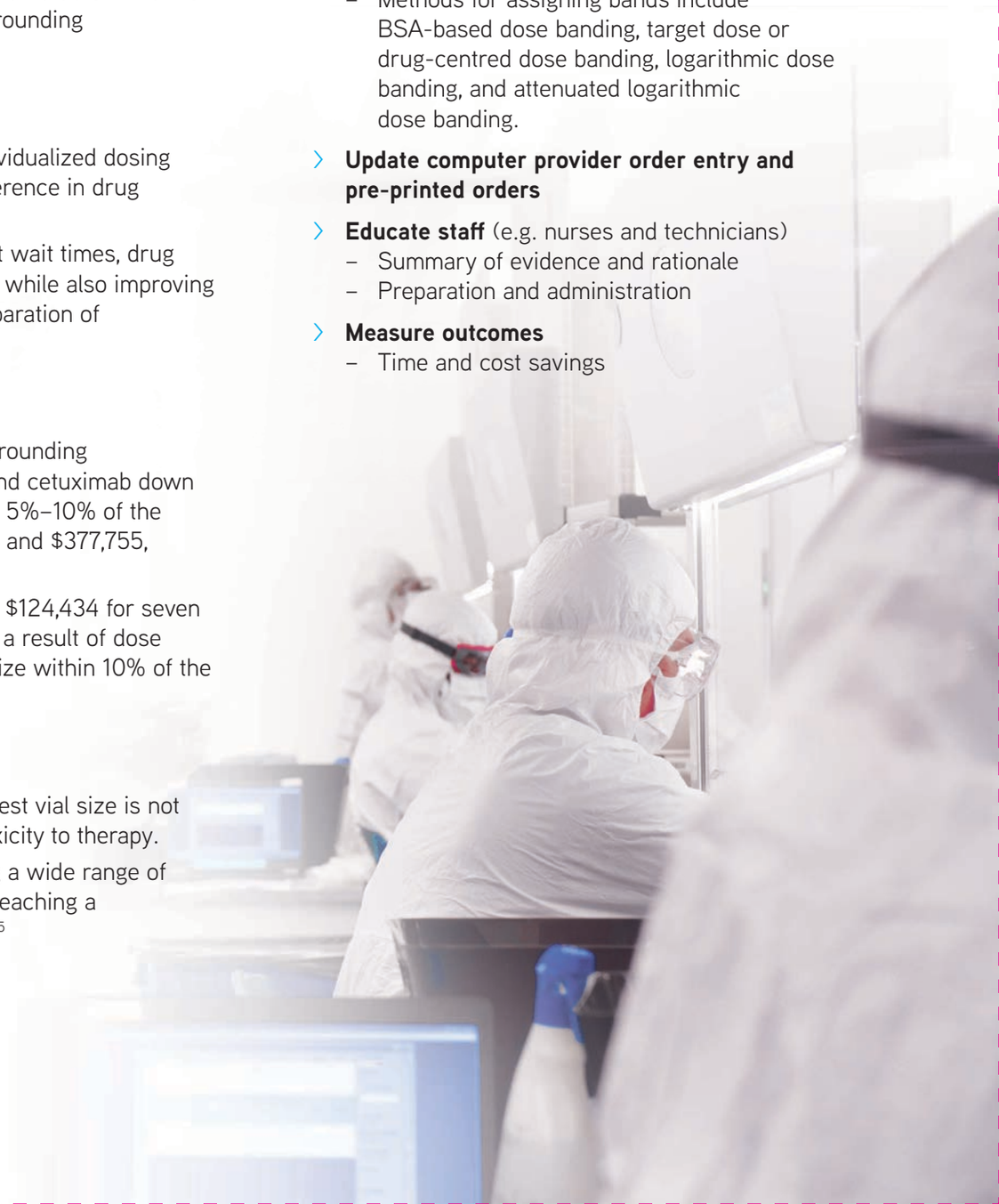
- Projected annual savings for rounding bevacizumab, trastuzumab, and cetuximab down to the nearest vial size within 5%–10% of the prescribed dose are $181,944 and $377,755, respectively.[5]
- Annualized cost avoidance of $124,434 for seven biologic anticancer agents as a result of dose rounding to the nearest vial size within 10% of the prescribed dose.[8]

TOXICITY

- Dose rounding up to the nearest vial size is not expected to add excessive toxicity to therapy.
- mAbs have been tested using a wide range of doses, with some drugs not reaching a maximum-tolerated dose.[5–12,15]

IMPLEMENTATION

- **Collaboration initiative (e.g. physicians)**
  - Tangible benefits (e.g. efficiency, savings, opportunities for re-investment)
  - Efficacy and safety
  - Input on drug selection, maximum acceptable variance (e.g. 5%–10%), exclusions
- **Selection of drugs**
  - Efficiency and savings (e.g. high-cost agents)
  - Frequently used and/or labour-intensive agents
  - Adequate stability (e.g. beyond-use date)
- **Define dose bands**
  - Main determinants include dose/m^2, maximum acceptable variance (+/- 5%–10%), strength of formulation (mg/mL), and maximum fill volume per delivery device.
  - Methods for assigning bands include BSA-based dose banding, target dose or drug-centred dose banding, logarithmic dose banding, and attenuated logarithmic dose banding.
- **Update computer provider order entry and pre-printed orders**
- **Educate staff** (e.g. nurses and technicians)
  - Summary of evidence and rationale
  - Preparation and administration
- **Measure outcomes**
  - Time and cost savings



CIVA
PHARMACY SERVICES

BAXTER CIVA QUALITY COMPOUNDING AND STABILITY METHODOLOGY

For the past three decades, Baxter CIVA Centre has been the pioneer in essential admixing services for healthcare providers across Canada. Our goal is to be your trusted leader in pharmacy admixing services by collaborating with your healthcare community.

Baxter CIVA has significant internal capabilities for performing stability studies, as well as established relationships with external laboratories that are qualified and routinely audited via Baxter's Supplier Quality Management team.

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References:

1. National Association of Pharmacy Regulatory Authorities (NAPRA) Model Standards for Pharmacy Compounding.
2. Cancer Care Ontario. Beyond Use Date Mitigation Strategy Working Group. Waste Mitigation Strategies Report. 2018.
3. Bott AM, Fahrenbruch R, Gilmore S, et al. Dose Rounding of Biologic and Cytotoxic Anticancer Agents: A position statement of the Hematology/Oncology Pharmacy Association (HOPA). 2017.
4. Patel S, Le A. Rounding rituximab dose to nearest vial size. *J Oncol Pharm Pract*. 2013;19(3):218–222.
5. Francis SM, Heyliger A, Miyares MA, et al. Potential cost savings associated with dose rounding antineoplastic monoclonal agents. *J Oncol Pharm Pract*. 2015;21(4):280–284.
6. Winger BJ, Clements EA, DeYoung JL, et al. Cost savings from dose rounding of biologic anticancer agents in adults. *J Oncol Pharm Pract*. 2011;17(3):246–251.
7. Jarkowski A, 3rd, Nestico JS, Vona KL, et al. Dose rounding of ipilimumab in adult metastatic melanoma patients results in significant cost savings. *J Oncol Pharm Pract*. 2014;20(1):47–50.
8. Dooley MJ, Singh S, Michael M. Implications of dose rounding of chemotherapy to the nearest vial size. *Support Care Cancer*. 2004;12(9):653–656.
9. Fasola G, Aprile G, Marini L, et al: Drug waste minimization as an effective strategy of cost-containment in oncology. *BMC Health Serv Res*. 2014;14:57.
10. Field K, Zelenko A, Kosmider S, et al. Dose rounding of chemotherapy in colorectal cancer: An analysis of clinician attitudes and the potential impact on treatment costs. *Asia Pac J Clin Oncol*. 2010;6(3):203–209.
11. Vandyke TH, Athmann PW, Ballmer CM, et al. Cost avoidance from dose rounding biologic and cytotoxic antineoplastics. *J Oncol Pharm Pract*. 2017;23(5):379–383.
12. Gillian A. Toolkit: How to Implement Dose Banding of Chemotherapy. Cancer Network Pharmacists Forum. 2010 Aug. 1–28.
13. Chatelut E, White-Koning ML, Mathijssen RHJ, et al. Dose banding as an alternative to body surface area-based dosing of chemotherapeutic agents. *Br J Cancer*. 2012;107(7):1100–1106.
14. Kaestner S, Sewell G. Pharmacoeconomic aspects of dose-banding. *Hosp Pharm Eur*. 2006;26:33–34.
15. Baxter Corporation: Data on File.

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