International Society of Oncology Pharmacy Practitioners

Reducing Drug Vial Wastage

International Perspective

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Reducing cancer drug expenditure

International survey - 2016

- 20 diverse countries

Product Information

- Parenteral cytotoxic agents, monoclonal antibodies (mAbs)
  - 45 cancer drugs

Range of vial sizes, overage, stability data, presentation forms

Results

- Vial sizes varied widely, often only one size
- Stability data inconsistent, usually only 24 hours
- Many expensive medications suitable for cost-reduction strategies

Gilbar PJ, Chambers CR, Gilbar EC. Opportunities to significantly reduce expenditure associated with cancer drugs. *Future Oncol* 2017; 13: 1311-1322

Strategies to avoid drug wastage

Guarantee availability of a range of vial sizes in all countries that drugs are marketed

- Same vial sizes should be available in all countries

Encourage vial sharing options

- Legislation, accreditation for manufacturing facilities

Explore dose rounding and dose banding options

Guarantee sufficient overage available in parenteral vials

- Including powder vials

Guarantee usable stability data on all manufactured products

- Stability research - part of pharmaceutical industry R&D

Ensure appropriate presentation forms available for cancer drugs

Gilbar PJ, Chambers CR. How can we ensure value for money from expenditure on injectable cancer drugs?
J Oncol Pharm Pract 2018; 24: 473-476

Optimising Vial Sizes

Method for analysis of optimum fill volumes of injectable pharmaceuticals to minimise wastage across a patient population

Determine vial sizes through modelling of the structure of the patient population

- Consider the distribution of patient characteristics, patient geographies and indications
  - e.g. many diseases appear more commonly in one gender, smaller body size in some races/countries
- Data from clinical trials or general population data

Consider combinations of vial sizes that are viable from a commercial or healthcare perspective

- e.g. ease or cost of manufacture, doses easily calculated by healthcare professionals

When the larger vial size is perfectly divisible by the smaller vial size (e.g. 50 mg/100 mg)

- Wastage is markedly higher

Hatswell AJ, Porter JK. Reduced drug wastage in pharmaceuticals dosed by weight or body surface areas by optimising vial sizes. *Appl Health Econ Health Policy* 2019; 17: 391-397

Vial sharing - Australia

Therapeutic Goods Administration (TGA)

- Provides guidelines for the use of “partial” vials

Pharmacy Board of Australia (PBA)

- Provides guidelines on assigning “beyond use dating” (BUD) on compounded sterile injectable products

Society of Hospital Pharmacists of Australia (SHPA)

- Supports the practice of vial sharing
  - In specialised aseptic pharmacy facilities and licensed compounding facilities
  - Following rigorous governance frameworks and professional standards of practice

TGA. Compounded medicines and good manufacturing practice. May 2017
PBA. Guidelines on compounding of medicines. August 2017.

Pharmaceutical Benefits Scheme (PBS)

Medications need to be registered by the TGA

Pharmaceutical Companies apply for drugs to be added to the PBS for government subsidy

- Based on evidence of efficacy and safety plus pharmacoeconomic evaluation
- Price negotiated

Same funding is provided to all patients

- Both Public and Private Hospitals
- Private Health Insurance may cover some non-PBS medication costs

Efficient Funding of Chemotherapy Program

- Goal to minimise wastage and reduce costs to patients and the Commonwealth of Australia by funding the lowest combination of vials for prescription chemotherapy medicines
- Reimbursed up to a defined quantity
  - Patient co-payment
- Depends on drug, diagnosis/indication and set clinical criteria

Vial sharing – International research

Australia

- Retrospective review - mAbs prepared in Hospital Pharmacy over 2 year period
- Vial sharing using CSTD (PhaSeal) – extending BUD to 7 days (only largest size vial)
- Compared with individual doses prepared using the minimum # of vials
- Yearly cost saving – US$ 352,500

Albania

- Retrospective review – Bortezomib. Drug costs reduced by 26%

India

- Prospective study measuring residue left in vials & retrospective analysis of drug wastage
- Predicted 9% reduction in drug costs (mAbs not included)

Siderov J. Utility of PhaSeal, a closed-system drug transfer device, in facilitating vial sharing to reduce waste and assist in medication cost savings. *J Pharm Pract Res* 2019; 49: 421-425

Rustemi J et al. Cost reduction as a result of bortezomib vial sharing in the University Hospital Center 'Mother Theresa' Tirana. *Eur J Hosp Pharm 2019*; 26: 237-238

Gopisankar MG et al. Cancer chemotherapy drug wastage in a tertiary care hospital in India – A 3-month prospective and 1-year retrospective study. *Br J Clin Pharmacol* 2019; 85; 2428-2435

Vial sharing - Applications

Dose rounding

- Rounding prescribed dose either up or down
  - Up to ± 5% for cytotoxic agents or ± 10% for mAbs
    - If rounded to vial size – doesn't necessarily reduce spending on leftover drug
  - Facilitates recycling of already prepared products

Drug days

- Patients treated with expensive, not commonly used drugs are treated on the same day
  - Allows vial sharing by increasing # of doses made on given day
- Ipilimumab
  - Drug days used in 3 of 21 Italian centres studied
  - Predicted savings of $US 8276 per patient per dose

Damuzzo V et al. Optimization of resources by drug management: a multicentred web-administered study on the use of ipilimumab in Italy. *J Oncol Pharm Pract* 2019; 25: 787-792

Closed System Transfer Devices (CSTDs)

CSTD Definition

- "A drug transfer device that mechanically prohibits the transfer of environmental contaminants into the system and the escape of hazardous drug or vapour concentrates outside the system"
  - Should not allow any bacteria or particulate matter into the system during compounding, thus maintaining sterility

CSTDs can facilitate vial sharing by allowing the extension of beyond use dating (BUD)

- Numerous published studies (PhaSeal®)
- Microbial Ingress testing for unpreserved drug vials
  - "Evaluation of the ability of a medical device to resist or inhibit the transfer of infectious microorganisms under repeated simulated use conditions"

Proven cost saving initiative

- In Australia, compounding companies charge customers on a per mg basis (rather than per vial) for commonly used drugs, for which vial sharing techniques can be employed

Gilbar PJ et al. How can the use of closed system transfer devices to facilitate sharing of drug vials be optimised to achieve maximum cost savings? *J Oncol Pharm Pract* 2019; 25: 205-209

Recommendations for manufacturing standards of practice for vial sharing - proposed

Legislation to allow vial sharing should be introduced in all countries

Formal testing procedures, to ensure Microbial Ingress should be performed on all CSTD brands

- Should be standardised and validated to allow compliant CSTDs to be accredited to extend BUD
- Length of time that vials can be classified as sterile following connection to a CSTD must be stipulated for all brands
- Preparation and storage conditions that must be met to guarantee stability and sterility of vials following connection to a CSTD must be stipulated for all drugs
  - e.g. temperature conditions, ISO 5 environment

Formal testing procedures should be performed on all CSTD brands to ensure

- Containment integrity, potential for coring, extractable and delivered volume (hold-up volume)

Gilbar PJ et al. How can the use of closed system transfer devices to facilitate sharing of drug vials be optimised to achieve maximum cost savings? *J Oncol Pharm Pract* 2019; 25: 205-209
Besheer A et al. Evaluation of different quality relevant aspects of closed system transfer devices (CSTDs). *Pharm Res* 2020; 37: 81

Stability

Compounded anticancer drugs

- Given very short expiry dates due to lack of reliable data

Stability studies

- Pharmaceutical Industry
  - Only designed for registration; largely restricted to 24 hours for bacteriological reasons
- Published research
  - Many drugs have much longer stability
- Compounding companies
  - Perform in-house studies

Solution

- Drug development programs include stability studies
  - Available to pharmacy; allows a more flexible clinical approach

Gilbar PJ, Chambers CR. How can we ensure value for money from expenditure on injectable cancer drugs?
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Recycling

Prospective study over 6 months – Regional Cancer Centre

- Drugs purchased from external compounding companies
  - Extended stability on prepared products

Unused cancer drugs – potentially discarded

- 12.2% of ordered drugs – orphaned

Reused for same patient or another patient

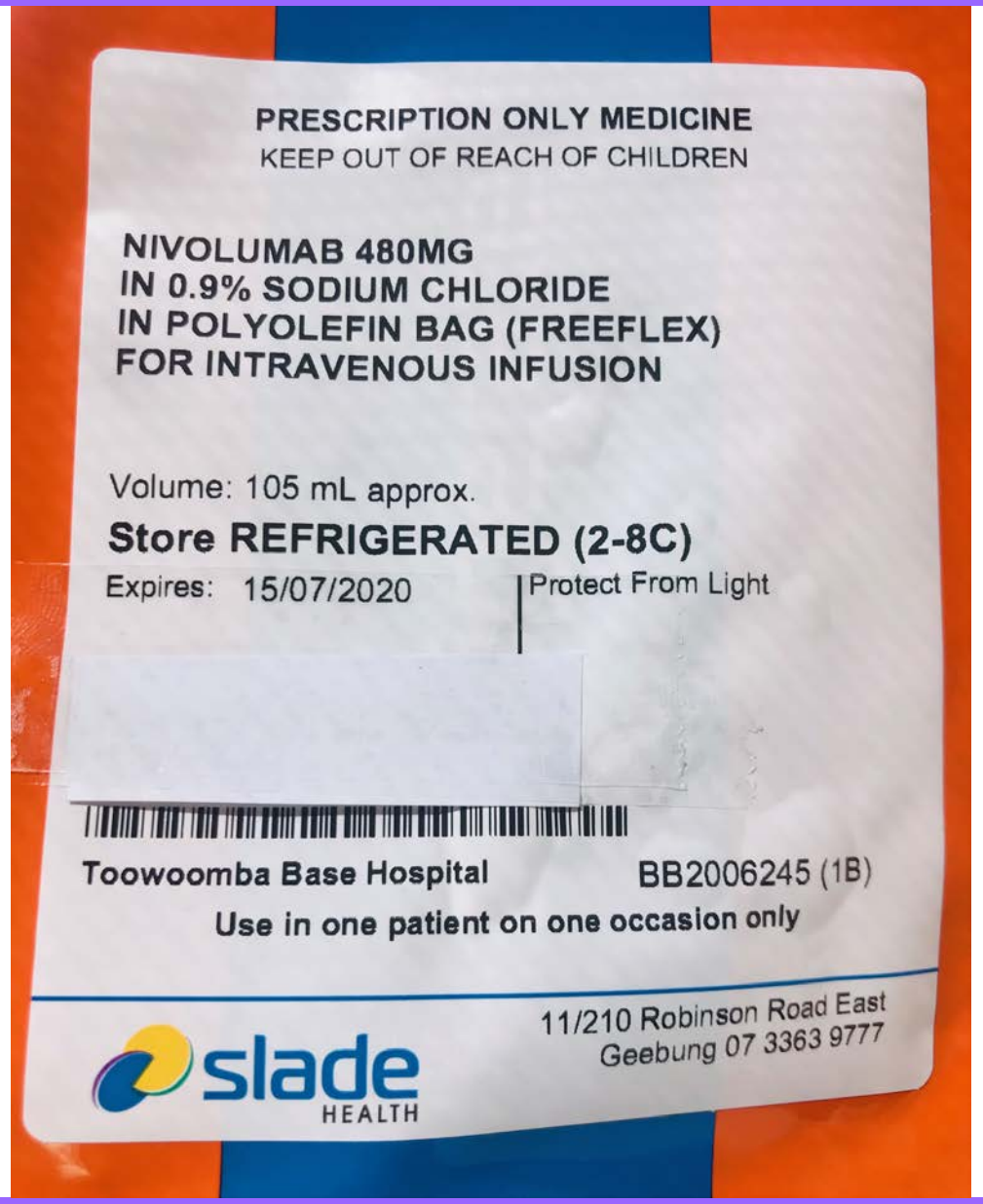
- 86.7% of orphaned drugs recycled

Savings

- 91% of potentially wasted drug products recycled
- Equates to 9.8% of total expenditure on cancer drugs
- $US 203,680 over 6 months

Gilbar PJ et al. Expanding the war on waste: recycling cancer drugs. *J Pharm Pract Res* 2019; 49: 454-459

Nivolumab
42 days expiry



	Canada	New Zealand	United Kingdom	Kenya
Approaches to reduce waste from unused vial contents	Use sterile single-use vial for up to 6 hours if it remains in ISO5 environment.	Similar to Australia.	NHS. Similar to Australia. National dose banding tables.	Limited. Government funded health insurance with capped amounts on treatment costs.
Vial sharing	Yes. Larger sites. Drug days.	Yes. Compounding companies.	Yes.	No.
Assign fiscal value to unused drug in vial	Yes. Have wastage account.	N/A	N/A	No.
Situation to become worse or remain stable if not addressed.	Worse. Significant, increasing costs of new agents. Adopted weight-based dosing for immunotherapy up to flat dose.	Worse. Drug expenditure increasing. More available drugs and increasing patient numbers.	Worse.	Worse. Cancer treatment being decentralised. Potential to pool patients limited. Range of drugs not available.

International Practice

Global Advantages of Drug Sharing

Significant monetary savings

•Billions of $US

Managing drug shortages

Environmental advantages

•Decreased volume of cytotoxic and immunotherapy waste

•Savings on waste disposal

Conclusion

USP Compounding Standards <797>

- Single-dose vials
  - Opened in ISO Class 5 – currently 6 hours
  - ? Possibility of extending this in updated standards

USP Standards adopted by many countries

- Affects ability to introduce vial sharing techniques

Food and Drug Administration (FDA)

- Decisions on drug registration influence other countries
- ? Ability to dictate to Pharmaceutical Industry

Pharmaceutical Industry

- Preserved multi-dose vials; extended stability data
- Vial sizes determined by population modelling

NASEM Drug Vial Study

- Recommendations have important international ramifications


ANY QUESTIONS
DO YOU HAVE?
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