BC CANCER
Provincial Health Services Authority

Pharmacy FAQ

Withdrawal of Drug from Vial with Overfill or Underfill

1. **Does the labelled drug volume on a vial for injection always match the actual volume in the vial? I've withdrawn the full 5 mL listed on the label, but there is still some solution left in the vial.**

   No, the vial contents can slightly exceed what is listed on the product label due to **overfill**. During manufacturing, a very small amount of excess solution may be added as overfill to ensure that the stated dose volume will be fully extractable from the vial. This is allowable per USP guidelines for injections.[1] For example, for a vial labelled to contain 5 mL, there may actually be 5.3 mL of solution in the vial or 5.5 mL if it is a more viscous liquid.[2] This means there can be solution left over in the vial after withdrawing the labelled contents.

   Vials with drug in liquid form tend to have overfill more often than vials that need to be reconstituted, but it is possible with both dosage forms. For example, nivolumab (provided in solution form) and ifosfamide (provided in powder form and reconstituted) can both contain overfill.

   It is important to use a consistent procedure when encountering overfill. At BC Cancer, we follow the Provincial Pharmacy Directive III-50-05 Management of Underfilled and Overfilled Drug Vials. In this instance, if you only require 5 mL for your dose, you would proceed with the withdrawn volume of 5 mL, and leave any excess remaining solution in the vial to be discarded or used for a different dose as applicable.[3]

2. **When we are unable to withdraw the full amount of drug from a vial, can we dispense the amount drawn up, as long as the difference is less than 5%?**

   For example, we could not withdraw the full 30 units of bleomycin from 2 x 6 mL vials. We managed to withdraw 11.8 mL, instead of the required 12 mL. The difference in volume was just 0.2 mL or 0.5 units of bleomycin, which is a difference of 1.7% from the ordered dose. Can we dispense this as the dose ordered, or should we use an additional vial?

   On occasion, it may not be possible to withdraw the stated volume of injectable drug from a vial. This is known as **underfill**, where the drug volume available is less than the labelled volume, and it frequently occurs with drugs such as bortezomib and bleomycin. Underfill is more common with drugs requiring reconstitution, although it can also occur with ready to use liquids. Using a Closed System Drug Transfer Device during preparation may cause some drug volume loss and can contribute to underfill.

   When the total labeled volume of drug cannot be withdrawn from a vial, an additional vial should be used to achieve the correct volume.[3] It is important to use a consistent procedure to ensure the correct dosage is prepared and dispensed for administration to the patient. At BC Cancer, we follow the Provincial Pharmacy Directive III-50-05 Management of Underfilled and Overfilled Drug Vials.

   The dose dispensed should be the **exact** dose ordered by the prescriber. The BC Cancer Policy III-10 Systemic Therapy Treatment Delivery Process[4] allows a maximum 5% variance in dose *calculation*, unless otherwise specified by the protocol. The 5% rule applies to clinical calculations by the pharmacist when checking the dose ordered by the prescriber. This 5% rule does NOT apply to *preparation* of drug doses, and the correct calculated volume corresponding to the drug dose ordered should always be dispensed.

   In rare situations when a drug is in short supply, and it would be deemed wasteful to use a new vial for a very small volume of drug, the prescriber may be contacted to alter the dose accordingly.

References:

1. Health Canada, Health Products and Food Branch. Guidance Document: Quality (Chemistry and Manufacturing) guidance: new drug submissions (NDSs) and abbreviated new drug submissions (ANDSs) [Internet]. [Ottawa]: Health Canada; 2017 Oct 30 [effective 2018 Jan 30; cited 2021 July 7]; p.57. Available from: https://www.canada.ca/content/dam/hc-sc/documents/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/chemical-entity-products-quality/guidance-document-quality-chemistry-manufacturing-guidance-new-drug-submissions-ndss-abbreviated-new-drug-submissions.pdf

2. United States pharmacopeia (USP) compounding compendium [Internet]. Rockville (MD): United States Pharmacopeial Convention; 2020. General Chapter <1151>, Pharmaceutical dosage forms; [cited 2021 Jun 30]; p. 361. Available from: https://www.usp.org/products/usp-compounding-compendium

3. BC Cancer. Management of underfilled and overfilled drug vials [Internet]. Vancouver (BC): BC Cancer; 2014 [revised 2019 Apr 3; cited 2021 Jun 30]. Provincial pharmacy directive no. III-50-05. Available from: Available from: http://shop.healthcarebc.ca/phsa/bc-cancer/document-index

4. BC Cancer. Systemic therapy treatment delivery process [Internet]. Vancouver (BC): BC Cancer; 1999 [revised 2021 May 1; cited 2021 Jun 30]. Policy no. III-10. Available from: Available from: http://shop.healthcarebc.ca/phsa/bc-cancer/document-index

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