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A further strategy to combat the high price of anticancer drugs

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In their insightful Perspectives piece published in the June 2017 issue of this journal (The high price of anticancer drugs: origin, implications, barriers, solutions. *Nat. Rev. Clin. Oncol.* **14**, 381–390 (2017))[1], Prasad and colleagues discussed a number of possible solutions to the increasing global problem of rising costs associated with medications for the treatment of cancer. Their solutions are principally aimed at reducing the price of anticancer drugs; however, other approaches have also been proposed[2,3]. The objective of these alternative strategies is to achieve savings, not by reducing drug acquisition prices, but rather by making better use of the drugs to ensure greater value for money, primarily by minimizing wastage. In this context, waste has been defined as the appropriate and/or inappropriate disposal of unused or partially used ampoules, vials, or syringes of drugs[4]. Waste can also occur with parenteral products that have been prepared for administration to the patient by diluting drugs in bags, bottles, or other vessels[2]. This concern is particularly relevant to products that have limited stability following preparation, with short expiry dates that reduce the possibility of the products being used at a later date.

Waste is commonly generated when expensive injectable medications, particularly those dosed according to the body size (body weight or surface area) of the patient, are provided only in single-strength, single-use vials. Unless a wide range of vial sizes are available, the actual dose required seldom matches the amount of drug provided in a single vial, or combination of vials; the variable quantity of leftover drug is typically discarded. To examine the magnitude of this problem, Bach *et al.*[5] analysed expenditure on the top 20 best-selling anticancer drugs packaged in single-use vials and dosed based on body size in the USA, estimating the total amount of leftover drug and associated revenues to the pharmaceutical manufacturer for each drug. The extent and cost of drug wastage varied according to the available vial concentrations and market size[5]. The proportion of leftover drug ranged from 1–33%[5]. For example, the authors estimated that 7% of all rituximab sold in 2016 was ultimately discarded, equating to an unnecessary expenditure of US$254 million[5]. This figure is for only one drug, in one country, over a 1-year period — extrapolating the wastage associated with the use of all drugs across the global market reveals potential losses in the billions.

A study with results published in 2017 identified numerous injectable anticancer drugs that are potentially amenable to strategies for reducing expenditure by avoiding drug wastage[2]. To provide a global perspective, information was obtained from 20 diverse countries across Europe, Asia, North and South America, Africa, and Australasia, on 45 anticancer drugs, comprising 29 cytotoxic agents and 16 monoclonal antibodies[2]. Data on a number of factors, including the range of vial sizes available and the stability of the products after preparation for administration, were sourced from the product information, if marketed, in each country[2]. The available vial sizes varied substantially between countries; however, numerous medications were often supplied in only a single vial size[2]. Stability data were inconsistently and variably reported by the manufacturer between countries, with most drugs given only a 24 h expiry period[2]. The authors proposed a number of strategies to reduce spending on these anticancer drugs[2,3], which are also applicable to other parenteral medications (including antibiotics), and are particularly important in these times of increasingly frequent drug shortages[6].

Firstly, a reasonable range of vial sizes should be available in all countries in which a drug is marketed. If a range of drug vial sizes are already available in one country, it would seem reasonable that all countries in which the drug is approved should have access to the same range.

Secondly, vial sharing, a proven cost-saving method[7], should be encouraged. By making batches of doses of the same drug, the quantities of drug left in a single-use vial — that would normally be discarded — can be used across multiple administrations. Closed-system drug-transfer devices can be used to extend the microbiological stability of anticancer medications, facilitating vial sharing and subsequent cost savings. For example, in Australia, compounding pharmacy charges for commonly used drugs are calculated on a per milligram basis, rather than on the standard per vial cost basis. Thus, customers pay for only the quantity of drug that is actually used, resulting in substantial cost savings. Unfortunately, the practice of vial sharing is discouraged in a number of countries, including Japan and the USA, for multiple reasons (predominantly concerns regarding the sterility of the unused prepared product, and reimbursement issues).

Thirdly, the use of dose-rounding and dose-banding options should be explored. Dose rounding is the practice of rounding the prescribed dose of drug, either up or down, to that of the nearest available whole-vial concentration. This strategy has been proposed to be appropriate when multiple vial sizes are available and rounding results in a difference from the recommended dose of no greater than ±5% for cytotoxic agents and ±10% for monoclonal antibodies[8,9]. This approach has been criticized, however, because patients can receive a dose that is either too high or too low[5]. Another important concern is that dose rounding does not actually reduce spending on leftover drug[5]. Dose banding is a variation on dose rounding, whereby doses within defined ranges or bands are rounded up or down to predetermined standard doses, with the maximum deviation set at 5%. This approach enables a range of pre-filled syringes or infusion products containing the standard doses to be manufactured or purchased. NHS England is implementing a national system of dose banding for chemotherapeutic agents, and has introduced 'National Dose Banding Tables' to ensure a standard approach across all Hospital Trusts[10].

Finally, reliable stability data should be provided with all manufactured medicines. The pharmaceutical industry invests huge sums of money in research and development to get new anticancer drugs into the marketplace. This research should include stability studies to enable extended expiry dates for all injectable drugs after preparation. Study results should be published and made available in the product information for use by compounding pharmacies and accredited manufacturing pharmacies.

I believe that, by considering these suggestions, in addition to those proposed by Prasad *et al.*[1], and with the aid of policy makers, substantial reductions in expenditure on anticancer drugs are achievable.

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Competing interests statement
The author declares no competing interests.