

“Breakthrough” drugs and growth in expenditure on prescription drugs in Canada

Steven G Morgan, Kenneth L Bassett, James M Wright, Robert G Evans, Morris L Barer, Patricia A Caetano, Charlyn D Black

Driven by increased use of prescription drugs and by shifts from old to new products, spending on drugs in Canada doubled between 1996 and 2003.¹ Which drugs drove this expenditure growth? The Canadian Patented Medicine Prices Review Board appraises the therapeutic novelty of every patented medicine in Canada to distinguish “breakthrough” drugs from other medicines. Since 1990, the board has published these appraisals in annual reports.² We applied the board’s classifications for breakthrough drugs to total expenditures on and use of prescription drugs in the province of British Columbia (population 4.2 million).

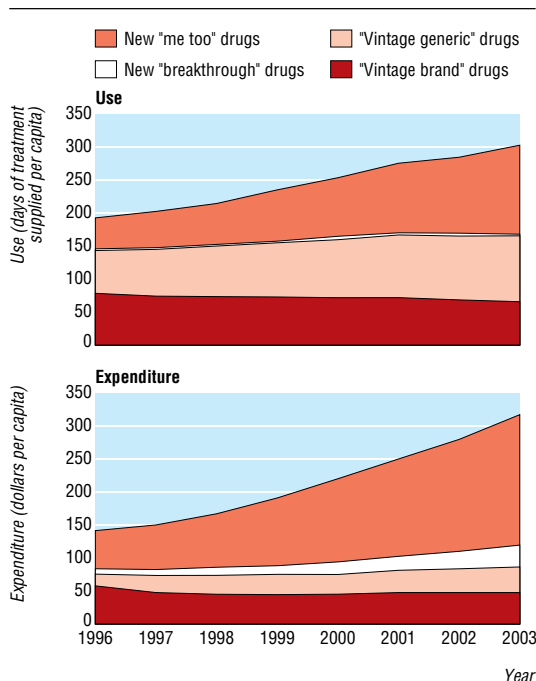
Methods and results

Between 1990 and 2003, the board appraised 1147 newly patented drugs (identified by active ingredient(s), formulation, and strength), including derivatives of existing medicines, such as esomeprazole. Of these new drugs, 68 (5.9%) met the regulatory criterion of being a breakthrough drug (“the first drug to treat effectively a particular illness or which provides a substantial improvement over existing drug products”).² These included, for example, filgrastim, donepezil hydrochloride, and infliximab. We expanded the criterion for being a breakthrough drug, however, to include all subsequent formulations and dosages of a classified breakthrough drug, as well as all competing drugs to enter the chemical subgroup³ established by a classified breakthrough drug. All variants on a breakthrough drug were therefore also classified as breakthroughs. This increased the number of breakthrough products in our study to 142.

The remaining 1005 new drugs did not provide a “substantial improvement over existing drug products.” We classified them as “me-too” drugs. The Patented Medicine Prices Review Board’s breakthrough assessments are not available for drugs first marketed before 1990; we therefore classified these only as “vintage brand” or “vintage generic” drugs. Generic versions of drugs marketed before 1990 were classified as vintage regardless of year of introduction.

From 1996 to 2003, per capita expenditure on prescription drugs in British Columbia more than doubled (from \$141 (£78; €115) to \$316) and per capita days of treatment supplied increased by just over half (from 194 to 301 days) (figure). Cost per day supplied rose from \$0.73 to \$1.05.

Breakthrough drugs accounted for 6% of expenditure and 1% of use in 1996, and 10% of expenditure and 2% of use in 2003. Vintage brand and vintage generic drugs combined accounted for 75% of total use in 1996 and 54% in 2003, but only 53% and 27% of total annual expenditure for those two years respectively. In contrast, me-too drugs accounted for 44% of use and 63% of expenditure by 2003. Their average cost per day of treatment was twice that of vintage brand drugs and four times that of vintage generic drugs.



Use of prescription drugs and expenditure per capita, by product classification, British Columbia, Canada, 1996-2003. Data were extracted from BC PharmaNet, a computer network into which a record of all filled prescriptions (including the data field for days of treatment supplied) must be entered by law

Comment

In British Columbia most (80%) of the increase in drug expenditure between 1996 and 2003 was explained by the use of new, patented drug products that did not offer substantial improvements on less expensive alternatives available before 1990. The rising cost of using these me-too drugs at prices far exceeding those of time tested competitors deserves careful scrutiny. Approaches to drug pricing such as those used in New Zealand⁴ may enable savings that could be diverted towards other healthcare needs. For example, \$350m (26% of total expenditure on prescription drugs) would have been saved in British Columbia if half of the me-too drugs consumed in 2003 were priced to compete with older alternatives. This saving could pay the fees of more than a thousand new doctors.

Given that the list of top 20 drugs in global sales⁵ includes newly patented versions of drugs in long established categories (that is, marketed before 1990)—such as angiotensin converting enzyme inhibitors, statins, selective serotonin reuptake inhibitors, and proton pump inhibitors—me-too drugs probably dominate spending trends in most developed countries.

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Centre for Health Services and Policy Research, University of British Columbia, 429-2194 Health Sciences Mall, Vancouver, BC, Canada V6T 1Z3
Steven G Morgan
assistant professor
Robert G Evans
professor
Morris L Barer
professor
Patricia A Caetano
Post-doctoral fellow
Charlyn D Black
director

Department of Family Practice, Centre for Health Services and Policy Research, University of British Columbia
Kenneth L Bassett
associate professor

Department of Pharmacology and Therapeutics, Centre for Health Services and Policy Research, University of British Columbia
James M Wright
professor

Correspondence to: S G Morgan
morgan@chspr.ubc.ca

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What is already known on this topic

Expenditure on prescription drugs is rising rapidly in Canada

Shifts from old to new products are a common cause of expenditure growth

What this study adds

Eighty per cent of the recent expenditure growth in British Columbia, Canada, is attributable to new drugs launched in established chemical subclasses

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DRUG POINTS

Epirubicin for breast cancer may cause considerable venous sclerosis

Paula Bolton-Maggs, Aileen Flavin

Department of
Clinical
Haematology,
Manchester Royal
Infirmary,
Manchester
M13 9WL

Paula Bolton-Maggs
consultant
haematologist

Clatterbridge
Centre For
Oncology,
Bebington, Wirral,
Merseyside
CH63 4JY

Aileen Flavin
consultant oncologist

Correspondence to:
P Bolton-Maggs
paula.bolton-maggs@
manchester.ac.uk

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The use of the adjuvant epirubicin for breast cancer in the United Kingdom has increased since initial data from the national epirubicin adjuvant trial (NEAT) were presented in 2003.¹ Two women, aged 53 and 55 years, developed pain and restriction of movement of the arm due to venous sclerosis after having infusions of epirubicin. They both had grade 3 invasive ductal carcinoma and had had surgery and axillary node dissection followed by eight courses of adjuvant chemotherapy using the epirubicin, cyclophosphamide, methotrexate, and fluorouracil regimen. This includes four cycles of epirubicin 100 mg/m² given at 21 day intervals.

Neither woman experienced extravasation or pain at the sites of infusion. The first woman had the first two injections into a large antecubital vein. At the time of the second infusion, two other ipsilateral antecubital veins had thrombosed. The infused vein became hard, swollen, and tender 18 days after the second infusion. Subsequent doses were given into two different veins in the back of the hand. The vein used for the third infusion thrombosed together with associated nearby veins, leading to painful symptoms within a week or two in the network of veins further up the arm. The fourth infusion was given into the back of the hand and resulted in sclerosis of veins on the anterior surface of the arm proximal to the wrist, but not directly involving the infused vein.

The second woman described similar symptoms, with aching and pain in the arm days after the second infusion. Both patients experienced pain on extension of the elbow due to tightening of the affected veins and developed puckering of the skin over most of the venous networks in the arm (figure). Similar symptoms developed around the wrist; extension and flexion became painful, lasting more than three months. The second woman gave up driving her car.

This complication had not previously been reported to the Committee on Safety of Medicines or the drug company, although the serious effects of extravasation of



Left arm of the first woman showing puckering of the skin due to a sclerosed network of forearm veins

the drug are known.²⁻³ The medical information for epirubicin contains a limited statement indicating venous sclerosis occurs if small veins are used or with repeated use of the same vein. Irritant drugs are those defined as causing symptoms such as these, which are described as self limiting with no long term sequelae.² The experience of these women indicates that venous sclerosis may be more extensive and troublesome than has previously been recognised and that extravasation injury is merely the tip of the iceberg.

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