Financial Effect of a Drug Distribution Model Change on a Health System

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Abstract

Background: Drug manufacturers change distribution models based on patient safety and product integrity needs. These model changes can limit health-system access to medications, and the financial impact on health systems can be significant. **Objective:** The primary aim of this study was to determine the health-system financial impact of a manufacturer's change from open to limited distribution for bevacizumab (Avastin), rituximab (Rituxan), and trastuzumab (Herceptin). The secondary aim was to identify opportunities to shift administration to outpatient settings to support formulary change. **Methods:** To assess the financial impact on the health system, the cost minus discount was applied to total drug expenditure during a 1-year period after the distribution model change. The opportunity analysis was conducted for three institutions within the health system through chart review of each inpatient administration. Opportunity cost was the sum of the inpatient administration cost and outpatient administration margin. **Results:** The total drug expenditure for the study period was \$26 427 263. By applying the cost minus discount, the financial effect of the distribution model change was \$1 393 606. A total of 387 administrations were determined to be opportunities to be shifted to the outpatient setting. During the study period, the total opportunity cost was \$1 766 049. **Conclusion:** Drug expenditure increased for the health system due to the drug distribution model change and loss of cost minus discount. The opportunity cost of shifting inpatient administrations could offset the increase in expenditure. It is recommended to restrict bevacizumab, rituximab, and trastuzumab through Pharmacy & Therapeutics Committees to outpatient use where clinically appropriate.

Keywords

hospital formulary, drug formularies, formulary committee, hospital financial management, hospital drug distribution systems, drug utilization review

Background

Introduction

The pharmacy supply chain is a complex system revolving around product transition from the manufacturer to the patient with various discounts, rebates, and fees that flow between parties. Chargebacks, rebates, and discounts are pricing incentives between a manufacturer and a wholesaler or direct purchaser. Chargebacks allow wholesalers to purchase products from manufacturers at wholesale acquisition cost (WAC). When a hospital or health system purchases from the wholesaler, the wholesaler is then able to “charge back” the manufacturer for any difference between negotiated prices paid by the institution and the wholesaler's cost of goods. Rebates are a form of retrospective price concession that is based on volume purchased from a manufacturer. Direct discounts mainly occur between institutions that purchase straight from a manufacturer.¹

When purchasing from a wholesaler, hospitals and health systems purchase drugs through a group purchasing

organization (GPO) contract, which leverages aggregate buying power of many institutions to negotiate lower prices. Drugs are also purchased from a wholesaler without a GPO contract, which can be utilized when a manufacturer has the main market share and thus minimal competition to negotiate GPO contract pricing. Wholesalers earn revenue from discounts and fees from manufacturers based on services provided. In turn, the wholesaler returns part of their revenue streams to their purchasers in the form of a “cost minus” distribution discount which they negotiate for market share. The magnitude of the cost minus discount is typically based on the terms of payment and the volume of

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drugs purchased from the wholesaler. This results in purchasers paying less than contract cost or WAC for noncontracted products.²

In addition to the various pricing and strategies, manufacturers determine the most optimal distribution strategy to ensure product integrity for patient safety. Manufacturers transition between distribution strategies to fit the needs of patients and providers as products mature in the market. When a specialty drug is brought to market, manufacturers typically limit access to the product through exclusive distribution to ensure they are meeting US Food and Drug Administration (FDA) requirements. Utilizing exclusive distribution also allows manufacturers to educate distributors and providers on the proper handling and administration of the drug. Manufacturers will transition from exclusive distribution to limited or open channels as distributors and providers become more knowledgeable with the handling and administration requirements. Limited distribution may be utilized for specialty products finding their place in therapy and in instances where distributors are learning how to best handle a product. Once a specialty drug has been released through open channel distribution, it usually becomes the mainstay of treatment. Market maturity is reached when a product is distributed through an open channel because distributors and providers are readily familiar with the product handling and administration requirements.³

Bevacizumab (Avastin), rituximab (Rituxan), and trastuzumab (Herceptin) are three drugs that were within the top 10 drugs by expenditure in nonfederal hospitals in 2014.⁴ They account for roughly 6% of the total nonfederal hospital drug expenditure. These agents are the mainstay for treatment of various oncologic and nononcologic diseases. Bevacizumab is a vascular endothelial growth factor-specific angiogenesis inhibitor indicated for the treatment of colorectal cancer, non-small cell lung cancer, glioblastoma, renal cell carcinoma, cervical cancer, and select breast and ovarian cancers.⁵ Rituximab is a CD-20-directed cytotoxic monoclonal antibody indicated for the treatment of non-Hodgkin's lymphoma, chronic lymphocytic leukemia, rheumatoid arthritis, and aggressive glomerular injury.⁶ Trastuzumab is a HER2/neu receptor antagonist indicated for the treatment of HER2-overexpressing breast cancer and HER2-overexpressing metastatic gastric or gastroesophageal adenocarcinoma.⁷

The manufacturer of these agents, Genentech, announced it would be shifting its distribution models for all 3 drugs from open channel to a limited distribution model through authorized specialty distributors beginning October 1, 2014.⁸ The manufacturer cited a 2012 incident of bevacizumab counterfeiting, stating the change was implemented to improve the overall security of their supply chain. Genentech concluded limiting access to the supply chain would protect product integrity and reduce opportunities for counterfeiting outside of legitimate distributors.⁹

At the time of the transition, hospitals and health systems believed the shift in Genentech's drug distribution model for these agents could cause delays in drug acquisition affecting patient therapy and leading to less than acceptable patient outcomes.¹⁰ In a 2015 survey conducted by Novation, 93% of organizations stated they did not experience a drug shortage prior to Genentech's distribution model change. After the change, organizations noted they were ordering medications more frequently (77%) and encountering variable and unreliable delivery times (63%).¹¹

Prior to the announcement, institutions were able to purchase these 3 drugs from traditional wholesalers at WAC price with cost minus discounts based on sales volume. With the shift to specialty distributors, this discount was lost for purchasers. Various institutions across the United States estimated they would spend an additional \$200 000 to \$4 million per year to purchase these agents under this new distribution model.^{8,12}

Problem

A not-for-profit health system consisting of 8 hospitals utilizes bevacizumab, rituximab, and trastuzumab in both inpatient and outpatient infusion environments. The health system includes an academic medical center, a centralized services center, and community hospitals. Of the 8 entities, 3 are eligible for 340B pricing. In addition, 7 entities have infusion clinic services. When Genentech announced the shift to a limited distribution model for these agents on October 1, 2014, the health system projected a \$2 million increase in drug expense per year due to the loss of cost minus discount. The primary aim of this study was to determine the health-system level financial impact of Genentech's new limited distribution model for the 3 medications. The second aim was to characterize the inpatient and outpatient infusion utilization and identify opportunities to shift, where clinically appropriate, administration of rituximab, bevacizumab, and trastuzumab from inpatient to outpatient settings. This would determine potential opportunities to offset increased drug expenditure in the purchasing of these products for inpatient administration. Finally, this study aimed to support the development of policies and procedures that provide additional guidance regarding optimal utilization of these 3 products within the health system.

Methods

Financial Analysis

To assess the financial impact of the distribution model change on the health system, the cost minus discount calculated from just prior to October 1, 2014, was applied to total drug expenditure during a 1-year period after the distribution model change.

Figure 1. Algorithm to determine opportunity for outpatient administration of rituximab.

R-HCVAD: Rituximab, cyclophosphamide, vincristine, doxorubicin, dexamethasone, high dose methotrexate, and high dose cytarabine; R-MVP: Rituximab, Methotrexate, Procarbazine, Vincristine; RICE: Rituximab, Ifosfamide, Carboplatin, etoposide; R-HDMTX: Rituximab, High-Dose Methotrexate; R-MTX-ARAC: Rituximab, Methotrexate, Cytarabine; DA-R-EPOCH: Dose-Adjusted EPOCH (Etoposide, Prednisone, Vincristine, Cyclophosphamide, Doxorubicin), Rituximab; R-CVP: Rituximab, Cyclophosphamide, Vincristine, Prednisone; R-CHOP: Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, Prednisone; R-BAC: Rituximab, Bendamustine, Cytarabine; VIPER: Bortezomib, Ifosfamide, Dexamethasone, Etoposide, Cisplatin, Rituximab; R- DHAX: Rituximab, Dexamethasone, Cytarabine, Oxaliplatin; R- DHAP: Rituximab, Dexamethasone, Cytarabine, Cisplatin.

Historical purchasing information obtained from the primary wholesaler of the health system was utilized to determine the total expenditure for trastuzumab, rituximab, and bevacizumab in each period. The purchasing information provided by the wholesaler included 7 of the 8 entities within the health system and included 340B purchases for all eligible entities. During the period studied, the 3 drugs evaluated did not have GPO contracts with the health system; therefore, the acquisition costs were limited to WAC and 340B.

The cost minus discount was obtained mathematically due to the inability to access the terms of the wholesaler cost minus discount contracts for each entity. The purpose of analyzing purchasing information in the period prior to October 1, 2014, was solely to obtain the cost minus discount mathematically. The cost minus discount was calculated by dividing the difference between WAC and vial purchase price by WAC, where WAC and purchasing price were obtained directly. To determine the financial effect of the distribution change, the calculated cost minus discount was applied to the study period expenditure.

$$\text{Cost Minus Discount} = \frac{(\text{WAC} - \text{Price Per Vial})}{\text{WAC}}$$

$$\text{Study Period Price Per Vial} = \text{Study Period WAC} - \left(\text{Study Period WAC} \times \text{Cost Minus Discount} \right)$$

Opportunity Analysis

An opportunity cost analysis was conducted for 3 institutions within the health system that had the same Electronic Health Record (EHR) implemented (EPIC, Version 2014, Verona, Wisconsin) to facilitate consistent data collection and review of information. The analysis was performed to characterize inpatient utilization of trastuzumab, rituximab, and bevacizumab, and identify potential methods to compensate for the financial burden caused by Genentech's change in distribution model. Patients who received at least one dose of trastuzumab, rituximab, or bevacizumab within the 3 health system entities between April 1, 2014, and September 30, 2015, were included in the opportunity cost analysis. These dates were determined based on EPIC implementation at each respective entity. Two of the health system entities included in the cost analysis implemented EPIC in April 2014, while the other entity implemented EPIC in July 2014. Data collected from the EHR included medication, dose, admission date and time, discharge date and time, medication administration time, service on administration, and *International Classification of Diseases, Ninth Revision (ICD-9)* code. Data collected for each entity before the October 1, 2014, distribution model change was annualized for performing the opportunity cost analysis. In total, the opportunity cost analysis was over a 2-year period.

A chart review was conducted utilizing algorithms developed by investigators for identifying doses with opportunity to shift from inpatient to outpatient administration. The algorithms were developed in consultation with hematology/oncology pharmacy specialists (Figures 1 and 2). Information

Figure 2. Algorithm to determine opportunity for outpatient administration of bevacizumab or trastuzumab.

retrieved during the chart review included associated diagnosis, chemotherapy regimen information (if applicable), and established outpatient presence. Established outpatient presence was defined as receiving chemotherapy or prechemotherapy laboratory work in a health system clinic. Inpatient administrations of the 3 agents were evaluated by an investigator during the chart review and secondarily by another investigator. If there were discrepancies between the investigators, the group had to discuss and come to consensus regarding the administration opportunity. Interrater agreement was assessed upon completion of the chart review.

To calculate opportunity cost, wholesaler information was used to ascertain the cost of each medication. Acquisition costs of each medication nearest to the end of each time period were used in the analysis and truncated to cost per milligram.

Opportunity cost was defined as the potential cost avoidance of inpatient administrations deemed feasible for outpatient administration combined with the anticipated outpatient margin for these administrations.

$$\text{Estimated Outpatient Margin} + \text{Inpatient Drug Cost} = \text{Opportunity Cost.}$$

Thus, opportunity cost was the sum of the inpatient administration cost and outpatient administration margin. Inpatient cost was determined using GPO pricing. Outpatient cost was calculated using 340B pricing for 340B eligible institutions and GPO pricing for non-340B eligible institutions; 1 of the 3 institutions was 340B eligible. Institutional

charge was calculated by multiplying outpatient cost by markup and adding the institutional flat fee. The chemotherapy Intravenous (IV) bag and injection flat fee was applied for all 3 agents. The institutional markup and flat fee did not change during the study period. The shift in distribution did not affect inpatient purchasing; therefore, inpatient revenue was excluded from the opportunity cost calculation.

For outpatient administrations identified by the algorithm, reimbursements were categorized into private payers and government payers (Medicare and Medicaid). Patients with outpatient administrations reimbursed from private payers had the outpatient cost multiplied by historical payer percentage. Outpatient reimbursement for government payers was the dose multiplied by the Healthcare Common Procedural Coding System (HCPCS) payment limit per milligram (updated November 2015). Finally, outpatient margin was calculated by subtracting outpatient cost from outpatient reimbursement.

$$\text{Outpatient Drug Reimbursement (based on WAC)} - \text{Outpatient Drug Cost} = \text{Estimated Outpatient Margin.}$$

Results

Financial Analysis

The total drug expenditure for the study period of 1 year after distribution model change was \$26 427 263. The study period expenditure with cost minus discount applied was \$25

Table 1. Doses Identified as Opportunities for Outpatient Administration by Entity.

Drug	Entity 1			Entity 2			Total		
	Opportunities	Doses	%	Opportunities	Doses	%	Opportunities	Doses	%
Rituximab	305	969	31.5	56	131	42.7	361	1100	32.8
Bevacizumab	4	8	50	8	10	80	12	18	66.7
Trastuzumab	6	7	85.7	8	8	100	14	15	93.3
Total	315	984	32	72	149	48.3	387	1133	34.2

Table 2. Doses With Opportunity for Outpatient Administration and Established Outpatient Presence by Entity.

Drug	Entity 1			Entity 2			Total		
	Outpatient presence	Total	%	Outpatient presence	Doses	%	Outpatient presence	Doses	%
Rituximab	196	305	64.2	25	56	44.6	221	361	61.2
Bevacizumab	3	4	75	6	8	75	9	12	75
Trastuzumab	5	6	83.3	6	8	75	11	14	78.6
Total	204	315	64.7	37	72	51.4	241	387	62.3

033 657. Thus, the financial effect of the distribution model change was \$1 393 606.

Opportunity Analysis

The doses identified as opportunities using the algorithm are displayed in Table 1. Of the 3 entities included in the analysis, Entity 3 did not have any administrations with opportunity for administration for outpatient setting. A total of 387 (34.2%) administrations of rituximab, bevacizumab, and trastuzumab were determined to be opportunities to be shifted to the outpatient setting. One of the institutions did not have any inpatient administrations within the 2-year period.

The majority of administrations identified as opportunities for administration in the outpatient setting were rituximab, with 361 doses identified. For all 3 drugs, a total of 387 administrations were determined to be opportunities, and 62.3% of patients who received one of the agents had established outpatient presence in a health system clinic. These results are described in detail in Table 2. Interrater agreement was 100% after discussion for all identified discrepancies. During the study period, the total opportunity cost was \$1 766 049.

Discussion

Access to products as they reach market maturity is key for patients to receive optimal care. However, individual priorities between manufacturers and providers may conflict. Hospitals and health systems seek to provide their patients with extensive access to care using the most clinically effective and affordable treatment options. On the contrary, manufacturers want to ensure the integrity of their product and

maintain prices at a level that can sustain the drug development process. It is critical that manufacturers and providers work together to optimize access to drugs and maintain fair pricing to minimize costs throughout the pharmacy supply chain.

The change in Genentech's distribution model on October 1, 2014, for rituximab, trastuzumab, and bevacizumab raised strong concerns among hospitals nationwide that it would cause an increase in drug expenditure that significantly outweighed Genentech's claim for patient benefits. Our health system financial analysis demonstrates results consistent with nationwide concerns.

There are study limitations to note regarding both financial and opportunity analyses. Financial analyses were limited to historical information from a single wholesaler used by the health system. In addition, the cost minus discount could not be calculated for entities which did not have any purchases prior to the distribution model change. Therefore, a standard cost minus was applied to these entities in the study period with the lower limit of the calculated cost minus. It is also important to note that this study only assessed the financial impact of the loss of the cost minus discount on rituximab, bevacizumab, and trastuzumab and not on the total cost of goods sold for the health system. Because rituximab, bevacizumab, and trastuzumab could no longer be purchased from the wholesaler, they did not contribute to the volume component of the cost minus discount. This may have reduced the cost minus discount in the study period for all purchases. By only assessing the financial impact of the loss of the cost minus discount on the 3 drugs, the total financial impact of the distribution model change is underestimated. In addition, the cost of the opportunity analysis was limited to assessment of administrations based on EHR implementation timelines for

the 3 health system entities for data availability. Finally, inpatient reimbursement was not factored into cost opportunity.

With the results of this study combined with current guideline use, the health system seeks to support the development of policies to guide appropriate inpatient utilization of bevacizumab, trastuzumab, and rituximab. Changes to health-system formularies take significant effort over a long period of time while expenditures continue to rise. It is important to recognize that despite identification of opportunities to shift, the consequences are impacted immediately. Institutions will need to take this into account when beginning to evaluate opportunities.

Conclusion

Drug expenditure related to the change in the Genentech distribution model for bevacizumab, trastuzumab, and rituximab increased by approximately \$1.4 million for the health system. The opportunity cost of shifting inpatient administrations of bevacizumab, trastuzumab, and rituximab for the 3 health-system entities during the study period is approximately \$1.7 million. Thus, in the study period, the opportunity cost of \$1.7 million to shift infusions from inpatient to outpatient can offset the increase in expenditure due to the distribution model change.

Declaration of Conflicting Interests

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