

# Evaluating Drug Profitability before Market Launch using Pharmacoeconomic Data: A Study of Generic Warfarin used for Long-Term Anticoagulation

S Bucurescu\*

*Department of Neurology, Klinikum Ansbach, 91522 Ansbach, Germany*

\*Corresponding author: Dr. Septimiu Bucurescu, Klinikum Ansbach, Escherichstr. 1, 91522 Ansbach, Germany, E-mail: [s\\_bucurescu@yahoo.com](mailto:s_bucurescu@yahoo.com)

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## Abstract

The profitability of a new drug can be calculated as drug revenue minus drug cost. Drug revenue can be calculated based on prospective consumption using a mathematical equation. As an example, in this review we have evaluated the profitability of a generic copy of warfarin intended to be put on the market in United States of America. A pharmaceutical company can increase the profitability of a new drug by optimizing factors that influence drug consumption and drug concept to market cost.

**Keywords:** Drug profitability; Drug revenue; Drug cost; Disease frequency; Disease duration; Dispensing status; Drug prescribing; Compliance; Warfarin; Pharmacoeconomy

## Introduction

The profitability (i.e. revenue minus cost) of a new drug is an important factor that should be used for managing the drug portfolio [1]. Before adding a new innovative or generic drug to the portfolio, each manufacturer should assess this financial issue. This evaluation can help pharmaceutical companies increase their economic benefits in a strongly regulated and highly competitive pharmaceutical market. Drug regulatory agencies can also use information on drug profitability while including cost-efficient drugs, with low cost and high therapeutic efficiency, in prescription guidelines. Cost-efficient drugs maintain and improve the population's health by judiciously using existent financial resources of both patients and healthcare insurers [2]. In this paper we describe a mathematical equation for calculating the profitability of a new generic drug based on pharmaceutical medicine criteria. Based on personal clinical experience and pharmacoeconomic studies we have chosen warfarin as an example because this drug is underused in patients with atrial fibrillation for ischemic stroke prevention [3] and venous thromboembolism [4].

## Factors that Influence Drug Profitability

Drug profitability depends on revenue and cost. Drug revenue is obtained through drug sale, which is determined by drug consumption. There are several factors that influence drug consumption, such as frequency of diseases, duration of diseases, drug dispensing status, prescribing habits, drug substitution, patient compliance and daily dose. Drug cost includes concept to market cost.

Frequency of diseases is monitored in almost each country by a national epidemiology agency, by collecting data about infectious and non-infectious diseases. These data can be used for detecting unmet medical needs, which are diseases with high mortality rates, associated with high morbidity rates (i.e. frequent diseases) or low morbidity rates (i.e. rare diseases) that are not addressed adequately by existing therapies. Important unmet medical needs in developed countries are cardiovascular diseases (48%), tumors (19%) and respiratory diseases (7.5%). Important

unmet medical needs in developing countries are infectious diseases (24%), cardiovascular diseases (16%) and respiratory diseases (15%). Using these data, the number of diagnosed patients in one country that can receive a drug treatment can be calculated [5].

A disease is caused by an etiologic agent through a pathogenetic mechanism. Disease duration depends on the natural history of the disease; that is the disease evolution in the absence of any treatment. In acute and sub-acute diseases the natural history is recovery or complication and death. In case of complication, drug treatment can lead to recovery and prevent death. In chronic diseases the natural history is complication and death, drug treatment can only prolong survival. Drug treatment duration is shorter in acute (i.e. on average 2 weeks) and sub-acute (i.e. on average 3 months) diseases as compared to chronic diseases (i.e. more than 6 months) [6].

Most drugs are not available on the free market; they must be prescribed by physician and dispensed by pharmacist (i.e. prescription only medicines or Rx). There are also drugs that can be bought by patients without a prescription (i.e. over the counter or OTC). For the same therapeutic indication, OTC drugs have higher profitability over Rx drugs due to higher consumption, because patients have easier access to OTC drugs. Physicians' willingness to prescribe is measured as a percentage of physicians that are willing to prescribe a new drug; it depends on prescribing budget and favors generic over innovative drugs [7].

Drug substitution by pharmacist means replacing a prescribed drug with another drug; it can be therapeutic (i.e. replacing the prescribed drug with a drug from another therapeutic class upon physician's approval) or generic (i.e. replacing the prescribed drug with a generic copy without physician's approval). Drug substitution favors generic over innovative drugs [8].

Compliance means the rigorous execution of the drug treatment by patient according to healthcare professionals' indications, it is measured as the percentage of prescribed doses taken by the patient (e.g. in

developed countries on average 50%). Compliance depends on patient-physician/pharmacist interaction, patient education, drug formulation, drug accessibility and drug affordability [9].

Daily dose depends on number of doses per day and amount of milligrams per dose; it is measured in mg/day. Daily dose depends on the drug's pharmacological properties, i.e. pharmacodynamics and pharmacokinetics [10].

Drug concept to market cost for an innovative drug is approximately 1,5 billion US dollars, of which circa 25% is spent on research, 45% on development, 2% on approval and 28% on marketing [11]. For a generic drug the cost is approximately 4 million US dollars, of which circa 10% is spent on development, 9% on approval and 80% on marketing [12].

### Calculating Drug Profitability Based on Prospective Consumption

The profitability of a new drug can be calculated as revenue minus cost. The revenue of a new drug is determined by prospective consumption in mg multiplied with cost per mg. The quantity of a new drug consumed (QDC) equals number of diagnosed patients (NDP) multiplied with drug treatment duration (DTT), physicians' willingness to prescribe (PWP), compliance (C) and daily dose (DD):  $QDC (mg) = NDP (\text{number}) \times DTT (\text{days}) \times PWP (\%) \times C (\%) \times DD (\text{mg/day})$ .

A pharmaceutical company can calculate the profitability of a generic copy of warfarin before adding it to its portfolio. The target population would be patients with atrial fibrillation who need long-term anticoagulation after ischemic stroke and patients with venous thromboembolism. In United States, the number of diagnosed patients with ischemic stroke due to atrial fibrillation is approximately 140000 [13]. With a median survival after ischemic stroke of 1.8 years, drug treatment duration would be approximately 660 days [14]. Physicians' willingness to prescribe is 43.5% [15]. Compliance is on average 50% [9]. The average maintenance dose is 4 to 6 mg per day, although dose must be adjusted in each patient to maintain the International Normalized Ratio (INR) at 2 to 3 [16]. In United States, the average price of warfarin per mg is 0.5 US dollars. Using the above described mathematical equation, the prospective average consumption for patients with atrial fibrillation can be calculated:  $QDC (mg) = 140000 \times 660 (\text{days}) \times 43.5 (\%) \times 50 (\%) \times 4 \text{ to } 6 (\text{mg/day})$ , which gives a value of 80388000 to 120582000 mg. The average revenue would be approximately 40 to 60 million US dollars. In United States the number of diagnosed patients with venous thromboembolism is estimated between 300000 to 600000 [17]. Drug treatment duration is at least 3 months, or approximately 90 days [18]. The prospective average consumption for patients with venous thromboembolism would be 234900000 to 704700000 mg. The average revenue would be approximately 117 to 352 million US dollars. The profitability of warfarin would be minimum 36 and maximum 348 million US dollars.

Pharmacoeconomic studies have demonstrated that warfarin is underused in patients with atrial fibrillation for ischemic stroke prevention, which represents an opportunity for generic manufacturers [19]. Cost-minimization, cost-effectiveness and cost-utility studies conducted in United States have demonstrated the benefit of warfarin therapy over no stroke prophylaxis in patients with atrial fibrillation [3]. In patients with venous thromboembolism, pharmacoeconomic studies conducted also in the United States have proved benefits of warfarin therapy over no prophylaxis [4]. Benefits of warfarin therapy can be increased and costs can be reduced by avoiding out-of-range INR values. In settings with poor quality of INR control benefits of warfarin therapy are reduced and complications frequent, making a switch to a novel more expensive oral anticoagulant, for example dabigatran, attractive. If consumption of warfarin declines due to a decrease in physicians' willingness to prescribe and patients' compliance, profitability will decrease [20].

### Means of Increasing Drug Profitability

Drug profitability can be increased by increasing revenue and/or decreasing cost. Revenue can be increased by acting on factors that influence drug consumption. A pharmaceutical company can increase the number of diagnosed patients by sponsoring programs of diagnostic screening. Changing the dispensing status increases drug access but can cause interactions problems if the patient takes also other medications and does not inform the pharmacist. This risk should be taken into consideration if a pharmaceutical company intends to apply at a national drug regulatory agency for changing the dispensing status. Improved patient-physician/pharmacist interactions (e.g. empathy), improved patient education (e.g. disease awareness and drug information leaflets), improved medication (e.g. oral dosage forms, combination drugs and selective drugs) and increased drug affordability (e.g. partial reimbursement of drug treatment) can increase compliance. A pharmaceutical company can improve only patient education and medication. Drug concept to market cost can be decreased by externalizing a part of research and development in developing countries where costs are lower, but extrapolation of clinical studies from one population to another might be sometimes difficult.

### Conclusions

The revenue of a new drug can be calculated based on prospective drug consumption. Factors that influence drug consumption are known and can be compiled into a mathematical equation. Data can be obtained from various sources: morbidity data from national epidemiology agencies, treatment duration from clinical studies, prescribing habits from physician surveys and compliance from patient feed-backs. The preciseness of calculated new drug profitability depends on data accuracy. Drug concept to market cost can be reduced through externalization.

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