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Pharmacoeconomics and the Medicinal Chemist

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ABSTRACT: Pharmacoeconomics is a rational, scientific approach to compare the value (in terms of both cost and patient outcome) of one medication or drug therapy regimen to another. The impact of this new approach on both the practicing medicinal chemist and broader drug discovery efforts is considered.

KEYWORDS: *Pharmacoeconomics, cost benefit, outcomes*

The medicinal chemist has always been mindful of economics in the course of drug discovery campaigns, from project-associated costs to early market assessment; however, there is now excessive scrutiny on drug pricing, set not by the company that developed the drug, but determined by governments, insurance companies, and physicians based upon the value of the new drug to the healthcare system as they struggle with rising costs. While it is well accepted that the overall cost for research and development leading to a new drug may exceed one billion dollars,[1] companies can not necessarily expect to recoup their costs as in the past, but must rather demonstrate value for the resulting patient outcome upon treatment. These emerging economic criteria require the medicinal chemist to better understand the competitive landscape and desired patient outcomes necessary to produce a new drug for a particular disease that will qualify for reimbursement by governments and insurance networks.

Pharmacoeconomics has evolved as a separate discipline from health economics to assess both costs and associated benefits, or outcomes, of drug therapy to aid governments, hospitals, and insurance providers with scientific data to inform decisions regarding health benefit for a particular intervention (Figure 1).[2−4] Pharmacoeconomics examines outcomes (clinical benefits, survival, reduced hospitalization, patient satisfaction/preference/compliance, and quality of life) in terms of cost of the drug. There are four methods of economic/cost evaluation: cost minimization analysis (assesses the cost of drug A to drug B), cost effectiveness (assesses the cost of drug per life year gained, cost per patient cured, etc.), cost utility analysis (assesses cost per quality of life year gained), and cost benefit analysis (net health benefits relative to total costs of the drug).[2−4] The quality of life year gained (QALY) is an important component worthy of further discussion, as it has come to replace a simple quality of life determination. QALY equates the expected gain in life years in terms of quality of health and operates along a scale of 1 (perfect health) and 0 (death). As an example, assume if treated with a drug A, a patient will survive five years with an estimated quality of life (relative to perfect health) of 0.7, which leads to a QALY of (5 × 0.7) = 3.5. Without drug A, the estimated survival is 1 year with a quality of life of 0.5, or a QALY of (1 × 0.5) = 0.5. Therefore, the QALY gain from treatment with drug A is 3.5−0.5 = 3.0 QALYs, and if the drug A costs $15,000, then then the cost per QALY is $5,000.[2−4] Have we as a society placed a monetary value on QALYs? In the United Kingdom, the National Institute for Health and Clinical Excellence values a year lived at ∼$50,000 USD, and in the United States, a similar value is arrived at, though these are not absolutes in terms of enabling or disallowing treatment, at least not yet.[5] In essence, pharmacoeconomics shift the burden on drug discovery from purely evidence-based medicine (novel mechanism of action with a focus on efficacy) to one with a focus on value-based medicine (drug effectiveness with a focus on value to the patient and reimbursement networks). In the near future, all new medicines will require appropriate pharmacoeconomics to qualify for reimbursement and to be prescribed within many health networks.[2−5] This fact requires medicinal chemists and drug discovery organizations to plan early and consider the monetary value their future drug therapy will afford. Moreover, this adds an additional challenge of cost effectiveness to drug development, beyond the classical efficacy, safety, and tolerability challenges.

Why now? Health care costs reflect more than 18% of the gross domestic product (∼$2.7 trillion) as compared to 6−9% in Europe where there are cost containment measures in place for prescription drugs.[2−5] As a result, drug prices in Europe and many other countries are 30−60% less than drug costs in the United States, suggesting geopolitical and socioeconomic pressures on pricing. In fact, when drug prices are perceived

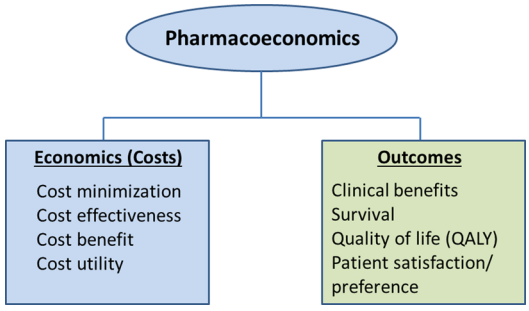

Figure 1. Major components of pharmacoeconomics, a subdiscipline of health economics that attempts to quantify the value and comparison of drug therapy options in terms of costs and outcomes.

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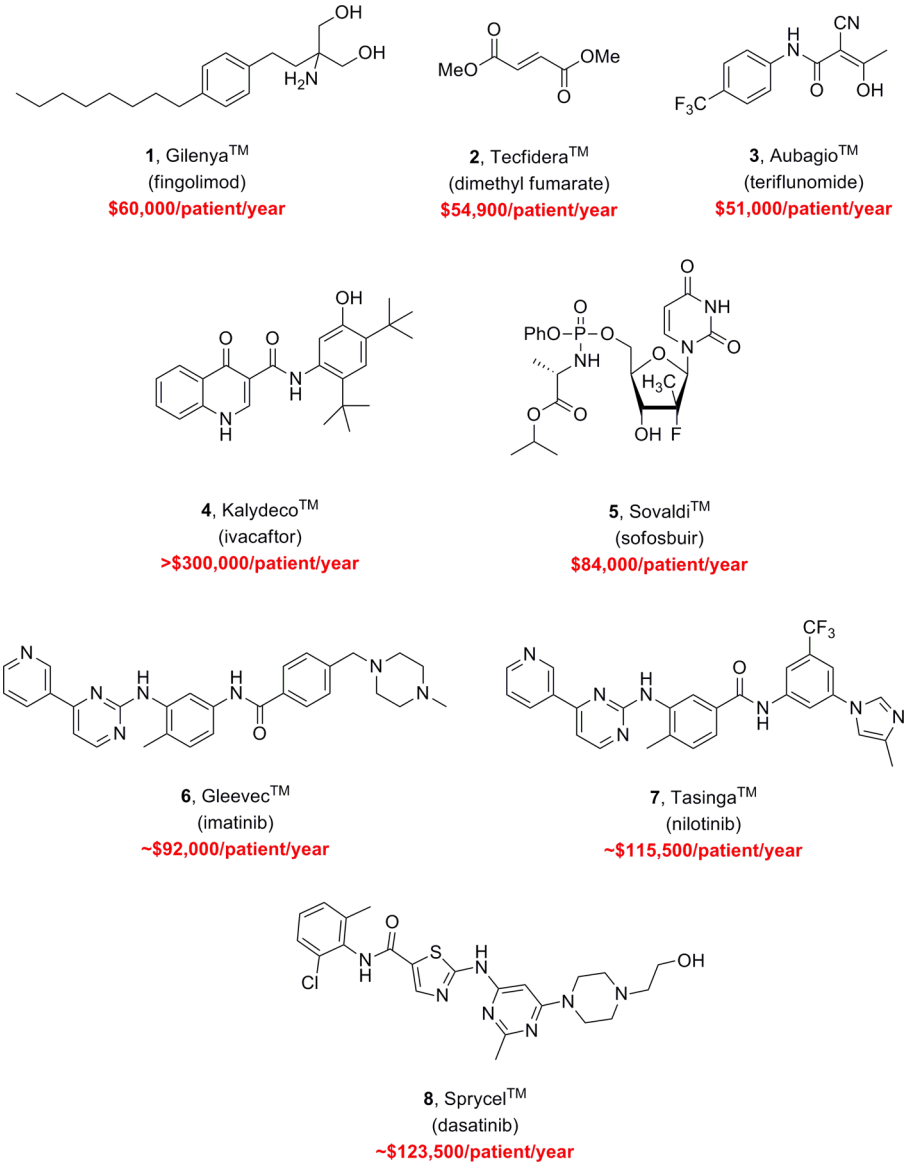

Figure 2. Structures and cost/patient/year of representative medicines that have recently been the subject of pharmacoeconomic debate in the lay and scientific literature.

to be too high, some countries, such as India, grant a compulsory license to a company within the country to manufacture the drug leading to costs <10% of the price in the United States.[2−5] Historically, because of the free market economy, prices have been based upon the economic doctrine of *justum pretium*, or just price, and guided by charging what the "market will bear".[5] With the Affordable Care Act in the United States, an Independent Payment Advisory Board was established, consisting of pharmacoeconomic experts, with a mandate from President Obama to monitor excessive payments for prescription drugs, where significant attention is focused on the price of new drugs.[1−5] Indeed, many new drugs, especially those for cancer or rare and neglected diseases, cost over $100,000/year and have been coined "sticker shock" by many physicians and payer networks (Figure 2) and have been the subject of pharmacoeconomic debate in the lay and scientific literature.[1−5] In many instances, despite the high cost and sticker shock, the new drugs do offer value to the patient community by lowering overall healthcare costs (hospitalizations, surgeries, work days lost, etc.) and improving QALYs, and thus possess favorable pharmacoeconomics to qualify for reimbursements.

For example, Biogen Idec priced its new multiple sclerosis (MS) drug Tecfidera (**2**) at $54,900/patient/year, between the prices for existing MS therapies **1** ($60,000/patient/year) and **3** ($51,000/patient/year).[1] The price of **2** does not reflect the overall research and development costs incurred to discover **2**, nor the costs of goods (the active ingredient in **2** is dimethyl fumarate, which costs $56/kilogram), but rather the value to the MS community and overall costs savings to the health care system versus no treatment in this patient population.[1] The same situation exists for Kalydeco (**4**), a new treatment for an ∼4% subpopulation with a rare mutation of the ∼300,000 cystic fibrosis patients in the United States. Drug therapy with **4** offers significant improvement on patient health and QALYs and relieves hospitalization and other incurred health care costs, and once again, despite concerns of the cost, represents solid pharmacoeconomics.[6] Finally, as Sovaldi (**5**) represents a cure for HCV infected patients and eliminates the need for hospitalization and liver transplants, the $84,000/patient/year

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is similarly viewed as possessing favorable pharmacoeconomics.[1] In all of the above instances, the costs for caring for these patient groups, in the absence of an effective drug regimen is millions of dollars/year; so, despite the high cost, patients, insurers, and healthcare systems do save money, highlighting the *VALUE* the new drug brings to the patient population.

In the case of new tyrosine receptor kinase inhibitor drugs **6**−**8** for chronic myeloid leukemia (CML), passions run very high, as life and death hangs in the balance.[5] A recent article in *Blood*, authored by 100 CML experts, states that the price of **6**−**8** (>$90,000/patient/year) for treating CML in the United States is unsustainable. These drugs have revolutionized CML treatment, increasing the >10 year survival rate from <20% to >80% enabling normal life spans; however, these are life-long, daily drug regimens to afford the long-term survival. Thus, patients can be viewed as financial victims, as they pay on average a 20−30% out-of-pocket copay (~$25,000/year). Still, most hospital and insurers reimburse for **6**−**8** due to the value the drugs reap on the patient population, e.g., favorable pharmacoeconomics due to the outcome of significantly enhanced survival. In Europe and across the world, many countries negotiate prices of drugs if they are to become part of the national health care system. Whereas **6** costs $92,000/patient/year in the United States, the cost is $33,500/patient/year in the United Kingdom, $29,000/patient/year in the Mexico, and $43,000/patient/year in Japan. Without exception, the United States reflects the high cost extreme for prescription medications.[5]

Today and moving forward, all pharmaceutical companies will be required to justify that the value (outcome) for a new drug is worth the cost to patients, insurers, and hospital networks. Pharmacoeconomics can clearly demonstrate how the availability and use of a drug can reduce the overall healthcare cost and patient burden while improving QALYs and other positive outcomes. Pharmacoeconomics does not attempt to instill price constraints, as shown by the favorable pharmacoeconomics for **1**−**8** (Figure 2), despite high cost. It does appear that future drugs with unfavorable pharmacoeconomics, and no clear value beyond existing treatment options, will not be viable in the marketplace. Thus, medicinal chemists must consider the target, patient population, and pharmacoeconomics of novel targets/mechanisms very early on in the discovery process in order to launch a successful drug and move beyond just evidence-based medicine (efficacy, safety, and tolerability) to value-based medicine (not only drug efficacy, safety, and tolerability but also significant value to the patient and reimbursement networks). Pharmacoeconomics is here to stay, and it will impact drug discovery moving forward.

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Notes

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