To What Extent are Pharmaceutical Prices Determined By Patents? A Case Study of Oncology Medicines in Thailand

Inthira Yamabhai†1 and Richard D Smith2

1Health Intervention and Technology Assessment Program (HITAP), Ministry of Public Health, Nonthaburi, Thailand
2Faculty of Public Health and Policy, London School of Hygiene and Tropical Medicine (LSHTM), London, UK

Received 10 February 2015; accepted 10 March 2015

This study seeks to assess the relative impact of patent status as a component of pharmaceutical prices while controlling other market and medicine characteristics on the retail prices of oncology medicines in Thailand. Ordinary Least-Squares (OLS) regression model of log prices as a function of supply and demand factors was developed and data fitted to establish the relationship and the effects for each factor. The main finding of the model is that patented status is associated with a price of approximately 144-206% that of an equivalent generic. Market characteristics also affect price, e.g. larger sales volumes, a more competitive market and a longer product life are associated with price around 3-30% higher. The scale of the influence of patent status over other factors confirms the view that addressing patent policy is the most effective option to bring down price, and proves support for invoking TRIPS-flexibilities such as, compulsory licensing, parallel importation or other exceptions to patentability.

Keywords: TRIPS Agreement, patent, pharmaceuticals, medicines, compulsory licensing, parallel importation, oncology medicines, National List of Essential Medicine, Thai pharmaceutical market

There is increasing attention being paid to the rising cost of health care in low- and middle-income countries (LMICs), where treatment prices as a proportion of income are often high.¹ This cost pressure is often linked to the high price of medicines faced by these countries, in particular the treatment of cancer which has seen exponential increase in incidence and prevalence in such countries. In higher income countries, such as, US² and UK³, the costs of care have doubled over the past two decades. Such expense is clearly a barrier to many, but is especially pronounced within LMICs, where two-thirds of the global burden of cancer mortality now exists.⁴

In 2012, the Thai pharmaceutical market was valued at US$ 3.5 billion.⁵ Medicine expenditure accounted for 46% of overall health expenditure and the greatest proportion was from the household sector (58%).⁶ Most oncology medicines are imported and many new chemotherapy medicines are not listed on the National List of Essential Medicine (NLEM) since their prices are not deemed to be affordable by the government.⁷ Cancer patients therefore, often pay out of their own pocket for non-NLEM medicines which are generally expensive. The use of patents has been argued to be a key driver, driving a considerable margin between the cost of the medicine and the price the patent-holder may charge. For instance, in China, some patented medicines are priced at 18 times that of the lowest generic price.⁸

Concern over the impact of patents on price led the Thai Ministry of Public Health in 2008 to issue compulsory licenses (CL) for four anti-cancer medicines: Letrozole, Docetaxel, Erlotinib and Imatinib.⁷ However, this was criticised by pharmaceutical companies on the basis that, unlike HIV/AIDS where previous CLs were issued, cancer, as a non-communicable disease, was not seen to constitute a national emergency, as required under the TRIPS Agreement.⁹ It is also not clear to what extent the patent actually drives price (and hence the benefit to be derived from issuing a CL) since half of cancer medicines selling in Thailand in 2008 were not patented, and despite this they remained expensive.

As policy, such as CL, is largely driven by an assumption that price is the major determinant of access, and that price is largely determined by patent status, it is critical to determine the extent to which price is actually determined by patent status, as if it is not, then CL may be an inappropriate policy lever, possibly leading to more harm than benefit. If it is the

---

¹Corresponding author: Email: inthira.y@hitap.net
most significant determinant of price then this confirms the importance of measures focused on patents. This study seeks to assess the relative impact of patent status as a component of pharmaceutical prices while controlling for other factors.

**Patents and Prices: Theory and Evidence**

Three common factors of note in setting medicine prices were found to be: the costs incurred in bringing the product to market, from production to marketing; the value of the new medicine in terms of its incremental effectiveness in comparison to other available therapies; and external price referencing defining the economic capacity of nations into similar groupings. The monopoly rights granted through the patent are not explicitly mentioned. However, patenting clearly gives the patent holder an exclusive legal right authorising monopoly power to set price much higher than the marginal cost, i.e. the supplier of a product has more flexibility over the price they can charge.

Previous studies show that patent protection appears to increase price by some 26%-277% depending on which approach to estimation is used and country setting the data. Most studies observe price changes after patent expiry. For instance, price fell by 51-69% one year after patent expiry in the Netherlands. To less magnitude, price was found to fall in Germany and the UK, where three years after patent expiration the price index decreased approximately 20%. However, for France, the price index has been found to be stable following patent expiry. Conversely, two US studies showed that an original product can have an increase in price of 7% after one year and 11% after two years following generic entry.

Some studies have sought to estimate price as a function of the price elasticity of demand, in order to estimate the likely effects of the enforcement of TRIPS on the price of eligible medicines. Using this methodology, it was estimated for instance, that the entire patentable medicine price in India would increase by 26%-417%. However, although this approach could be useful if the price elasticity of demand is known and correct, the pharmaceutical market’s demand function is thus often distorted, given that the consumption decision commonly involves physicians and hospital committees or government rather than ‘consumers’. In addition, there seems to be no effect from the introduction of product patent protection time on the price of patentable medicines in the market before 1992 when the Thai patent law was amended to include protection for pharmaceutical products in 1992, eight years ahead of the requirement in the TRIPS Agreement and 13 years ahead of the end of the transitional flexible period for developing countries.

In another approach, Borrell (2007) used regression analysis of possible explanatory factors on medicine price, of which patent status was one factor, to estimate the impact of patent protection of 14 ARV molecules in 34 low- and middle-income countries. The results showed that combination therapy containing at least one patented medicine was on average priced 70% higher than combination therapy containing only generic medicines. However, this analysis also did not include wider market characteristics.

Evidence thus suggests that the size of impact varies across a huge range, depending on what methods are employed in the studies and in what country. Current evidence therefore, makes it difficult for a specific country, such as Thailand, to come to a conclusion on advice to national policy makers to make decisions, such as concerning invoking a CL, which may trade-off health or access impacts with wider economic issues.

**Price Data**

The price data for all oncology medicines, in each form, in 2008 were obtained from the IMS Health database (calculated from the results of a survey of purchase price from 276 general and 22 specialized hospitals across Thailand). There were 88 chemical substances, contributing to 249 products in 418 forms. Prices at the hospital level were chosen for the analysis since the hospital is the major channel for medicines in Thailand, accounting for 80% of pharmaceutical market. Prices were calculated on the price per daily maintenance dosage adapted from the defined daily dose (DDD) as suggested by WHO guidelines. However, the data for DDD is not available for anti-cancer medicines, since treating the majority of chemotherapy drugs is dosed based on body surface area (BSA) or the patient’s weight. As a result, the cumulative dose received during treatment in cycles needed were calculated based on the average BSA at 1.51m² and patient’s weight at 60.88 kg.

The recommended dose for each medicine in each indication was retrieved from MICROMEDEX, a
database of drug indication, dosage, interactions and side effect information. Based on this information, the cumulative dose received during the cumulative number of days that the patient received that medicine was estimated. The price per daily maintenance dose was computed at the average daily dose and at product level using the volume-weighted average of all forms available in 2008; therefore, it has 249 observations (sum of a product of quantity and price for each strength divided by quantity).

**Medicine Price Determinants**

From the supply side, there are three important factors determining price. First, the number of competitors, which should theoretically reduce price, and empirically has been found to be the case for increasing the number of substitutes from one to two leads on average to a 38% reduction in the price and increasing from 2-3 to 19% reduction. This effect is expected to be positively related to price. Second, product age (the number of years that the product has been on the market). This factor is a proxy for therapeutic effectiveness, assuming that more recent compounds are generally more effective. This variable may also reflect life-cycle pricing strategies. With increasing years on the market, the product owners may decrease the price in order to cover the mature stage of the product life-cycle. The coefficient is expected to be negatively related to drug price. Third, the number of forms or strengths available provides the prescriber with greater flexibility to prescribe the product that most suits their patients’ need. Ellison and Ellison (2011) suggested the use of presentation proliferation as a strategic tool of entry deterrence. By increasing the number of presentations available, the branded firm increases the cost to the generic entrant of reproducing the entire product line thereby deterring entry, which allows the branded firm to charge a higher price. Therefore, the number of presentations available is expected to be positively related to drug price.

Demand side factors also determine the price level. The higher the sales volume (the higher the number of cases) the lower the individual drug price. Scherer and Watal for example, found that drug prices decreased with the number of HIV/AIDS cases, although the magnitude of the effect was small. Sales volume is expected to be inversely related to medicine prices.

One would also expect a more effective medicine to be able to charge a price premium. For the effectiveness of medicine, Quality Adjusted Life Years (QALYs) gained, life years saved and important adverse effects were selected as proxies. Life years saved and QALYs gained were selected to represent the health benefit of taking the treatment. They are expected to have a positive effect on the medicine’s price. The Health Economic Evaluations Database (HEED) and Cost-Effectiveness Analysis Registry at the Centre for Reviews and Dissemination were databases used to find QALYs gained and life years saved when compared with best supportive care available on the market. This study also includes two severe complications of chemotherapy, neutropenia (low white blood cell counts) and thrombocytopenia (low platelet counts). It is expected that both of these indicators would have a negative impact on price since they are life-threatening and also costly to manage. Data for the percentage of severe neutropenia and thrombocytopenia were retrieved from DRUGDEX database which reports the percentage of adverse effect of particular medicines.

With regards to medicine characteristics, the marginal cost of production represents the complete process of production and cost of material in manufacturing. Some studies have employed the lowest unit cost of a generic medicine on the market as a proxy of marginal cost. However, often there is no generic competition on the domestic market since the market is protected by a patent. Therefore, this study employed the Indian procurement price as a benchmark to represent the marginal cost variable and expected that it has a positive relationship with price. Indian pricing, with adjustment for the same strength, was mainly obtained from the Tamil Nadu Medical Services Corporation Ltd (TNMSC), a public sector organisation in India with the primary objective of ensuring the availability of essential medicines in government medical institutions. For medicines not available from this source, the average price from Medindia was used. The average exchange rate for 2008 at 0.82 Baht per Indian Rupee was used to convert into Thai currency.

**Patent Status**

Similar to many developing countries, there is no updated public database of patented medicines in Thailand. Patent status of each medicine was therefore obtained from a specific study, as previously reported by the authors. There were 27 patented medicines and seven medicines that are suspected to
have patent protection since they are under protection in either the United States or Canada but their patent filing have not been found from the Thai patent office. Patent expiry date was collected and was estimated as the number of years to expiry; from this the average patent life from 2008 was estimated to be 11.30 years. It is hypothesized that a patent shifts price up, and that price is expected to be higher with the greater the number of years remaining of patent protection.

Statistical Analysis
A model of log prices as a function of supply and demand factors was developed and data fitted to establish the relationship and the effects for each factor, as illustrated below.

\[ P_i = \alpha_i + \beta_i x_i + \epsilon_i \]

Where \( P_i \) is the log of price for daily dose of medicine \( i \), \( x_i \) is a vector of observable characteristics of the individual medicines (i.e. patent status, years to expiration, log of sales, number of competitors, number of forms, product age, log of Indian price, life year saved and quality of life gained, and adverse effect) and \( \epsilon_i \) is the effect of the unobservable variables.

Impact of Patent on Prices of Oncology Medicines
Table 1 reports separate regressions by a different set of supply and demand characteristics. Model 1 represents the influence of market characteristics variables but excludes this marginal cost variable,
whereas model 2 includes the marginal cost variable proxied by the Indian price to avoid a biased underestimate of manufacturing cost. The second group of specification, models 3 and 4, represent medicine characteristics which separate QALYs gained and life years saved. The last group of specifications (model 5-8) include all explanatory variables, accounting for the different manufacturing cost and medicine benefit variables.

In the first model, sales volume and number of competitors have a negative and statistically significant coefficient at $\alpha = 1\%$. For example, one percentage increase in purchased volume would decrease price by 0.2%, and entrance of a new seller would decrease price by 18%. As expected, patent status and product variety have a positive and significant effect on prices at the same level. Patented products are priced 144% higher than non-patented medicines. However the number of exclusive years left has an effect opposite to that expected. It seems the more patent life a medicine has, the cheaper it is; one year less in patent life leads to a price increase of approximately 2% but this effect is not significant.

The number of competitors has a negative and significant effect on price, as expected; only in the model 7 is this variable not significant and this seems likely to be because of the small number of observations. In general, one more competitor would reduce the price by around 13%-30%. The coefficient estimates on the number of forms available is positive and statistically significant in model 2, 5 and 6 suggesting that the more variety in choices, the higher price. The estimated coefficient on product age is negative and statistically significant in the model 2. This suggests that the longer the product is on the market the lower the price. However, the impact is minimal.

When the marginal cost variable was included in the model 2, although the number of observations dropped to 186, the sign of every variable was unchanged and followed a priori expectation. However, the magnitude of explanatory variables was less significant than the first model results. The impact of patent on price was similar at around 145%. Marginal cost has a positive significant impact on price: one percent increase of cost would increase price by approximately 0.26%. In model 3, with a very small sample size (46 observations), investigation toward how medicine efficacy and adverse effects affect the price of medicines suggests that life years saved has a positive and significant coefficient: one life year saved could increase price by around 65%. The event of thrombocytopenia has a negative and significant effect on price. The percentage of severe neutropenia shows a positive relationship with price which is not as expected. With a small $R^2$ in model 4, QALYs gained has a positive correlation with price; however, this variable is not a significant price determinant.

When both markets and medicine characteristics are included (models 5-8) some of the market characteristics turn out to be insignificant but still show the expected signs. Although models 6 and 8 specifications show high R-square, this is from a very small data set, determined by the availability of QALYs information, as shown in Table 1. Most of the medicines included in these models are not patented medicines. It is therefore, suggested that models 1-3 be seen as the core, most reliable, results.

With regards to the effect of patent on price, monopoly rights protection from a patent for the particular medicine generates a price of patented medicines some 144-200% higher than medicines without a patent. This effect is statistically significant and shows an expected sign. Pharmaceutical companies appear to use a penetration pricing strategy, initially set at a lower price than the eventual market, to launch new products in Thailand. Over the time, as brand loyalty increases, the low introductory price is often raised. Price is negatively correlated with patent years left, as seen from the experience in the US.

**Conclusion**

The result in a qualitative sense is not surprising; patenting is associated with higher prices relative to a regime where patents are not available. From the literature reviews, the impact could range anywhere from 26-277%. This study shows that the impact of patent on the price of oncology medicines in Thailand is within the range, 144-206%, forms a tighter range, which is very clearly towards the top end of the other estimates from the literature. This relatively high patent impact in Thailand could be the result of pricing freedom, with no patented price monitoring and control in Thailand. Many countries that regulate manufacturer prices, either directly or indirectly, are likely to have a patent impact on price that is lower.

This study has three potentially significant limitations. First, prices in this model do not take...
discounts or promotions from pharmaceutical companies into account. Therefore, the patent effect may be overestimated. However, the most available data source that represents the price was used and the study aims to assess the intent of the patent owner to exploit the monopoly. Second, the method employed in this study is cross-sectional, which looks at price at a specific point of time. It does not take the price trend into account if the product owner decreases or increases price during the period from introduction to the year 2008. This was because budget limitations meant that it was not feasible to obtain a time series of medicine prices in Thailand. However, product age was chosen to proxy price trend to capture the relationship between price and time. Third, there is a lack of systematic data on the benefits and adverse effects from medicines. This information was retrieved from clinical trials that were performed on specific indications. However the results of the same medicine in different indications could yield different results. Of course, the population samples included in clinical trials also differ. As a result, this factor might not represent the actual benefits and costs of treatment by that medicine.

It is concluded that with respect to market characteristics, most of them have a significant impact on price. For instance, the higher the sales volume, the more suppliers selling the same medicine in the market and the longer time that product has been on the market, the cheaper the medicines are. However, the magnitude of their impacts is minimal, i.e. a policy related to market characteristics would have a small impact on oncology medicine use. The Thailand experience is typical for other LMICs where there is no direct price control mechanism for medicines prescribed or sold through hospitals and clinics, and the power to set prices, for both patented and non-patented medicines, rests with the pharmaceutical companies themselves. This study supports the view that policies relating to patenting are probably the most effective options to decrease the price of oncology medicines. The use of TRIPS flexibilities may therefore be needed.  

Acknowledgement

The authors acknowledge the support from Health Intervention and Technology Assessment Program (HITAP) funded by the Thailand Research Fund under the Senior Research Scholar on Health Technology Assessment (RTA5580010) and Thai Health Global Link Initiative Program (TGLIP), by Thai Health Promotion Foundation.

References