CANCER CARE AND ACCESS TO CANCER DRUGS IN ASIA-PACIFIC

Pricing policies for off-patent drugs in Asia-Pacific

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PRICING POLICIES FOR OFF-PATENT DRUGS IN ASIA-PACIFIC

Sub-report 5 of the main report “Cancer care and access to cancer drugs in Asia-Pacific”

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Report summary

In general, most payers and authorities adopt cost-containment policies to increase market uptake of generics and biosimilars, and thus curb pharmaceutical spending. As such, generics and biosimilars have become fundamental to pharmaceutical cost control, but many markets could better leverage such policies to control pharmaceutical expenditure more effectively, freeing up resources to improve patient access to more advanced cancer treatment options.

One such policy lies within the pricing of off-patent drugs. Once a patent expires, market exclusivity is lost, and generic copies of the originator can enter the market. This stimulates competition between manufacturers and should cause the price of the originator drug to fall. Pricing policies for off-patent medicines affect the magnitude of price decreases following patent expiry of originator drugs, and larger price drops could generate substantial savings particularly for widely prescribed drugs.

In general, markets in Asia-Pacific react as anticipated with prices of originator drugs overwhelmingly falling after patent expiry (or loss of exclusivity), but the magnitudes of price drops vary substantially across drugs and markets. Drawing on a limited sample of 11 major cancer drugs with patent loss between 2010 and 2020, the analysis in this report indicates that all markets could save from 3% to 20% of total cancer drug expenditure, if more effective off-patent pricing mechanisms are adopted. In middle-income markets where access to originator drugs is low, price drops associated with effective pricing mechanisms on off-patent drugs would likely trigger increased sales volumes, thus compounding the savings.

While there may not be a one-size-fits-all approach, markets in Asia-Pacific should invest in learning from each other to develop policies on off-patent drugs that are effective in their local market. This could play a crucial role in increasing access to innovative drugs for the growing population of cancer patients. Ensuring effective pricing policies for off-patent drugs and stimulating availability of and competition between generics/biosimilars, which provide “equal” clinical value as originators can lead to substantive savings. An effective reduction of prices creates budget headroom for reimbursing new innovative drugs. Ultimately, an effective re-channeling of resources from off-patent drugs to new innovative drugs could offer a more sustainable financing model of innovative drugs.

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1. Pricing mechanisms and off-patent cancer drugs

In general, across most countries, payers and authorities adopt cost-containment policies to increase market uptake of generics and biosimilars, and thus curb pharmaceutical spending (1-3). As such, generics and biosimilars have become fundamental to pharmaceutical cost control, but many markets could better exploit such policies to more effectively control pharmaceutical expenditure, freeing up resources to improve patient access to cancer drugs (1-3).

One such policy lies within the pricing of off-patent drugs. Once a patent expires, market exclusivity is lost, and generic copies of the branded drug enter the market, causing the price to fall. The introduction of generics to the market following patent expiry of originator cancer drugs is a key means of savings for healthcare budgets (4). Healthy off-patent pricing mechanisms allow for cost containment (5), and thus for markets to off-set the financial cost of granting patients access to new originator products (6). While patent expiration is generally associated with price drops in originator products, the magnitudes of these drops vary between drugs and markets (6). Policies surrounding off-patent pricing mechanisms likely have a direct influence on the magnitude of price decreases following patent expiry of originator drugs, and larger price drops could generate substantial savings for widely prescribed drugs.

1.1 Aim of the sub-report

The aim of this sub-report is to present current patterns in market price reactions to patent expiry of cancer drugs in Asia-Pacific[1], and to estimate the potential savings associated with effective off-patent pricing mechanisms adopted for cancer drugs.

- Section 2 presents the price control mechanisms across markets and explores the impact of patent expiry on the price of branded cancer drugs within these markets.
- Section 3 presents the savings opportunities associated with effective off-patent pricing mechanisms.

[1] Asia-Pacific consists in this report of 7 high-income markets – Australia, Hong Kong, Japan, New Zealand, Singapore, South Korea, Taiwan – and 7 middle-income markets – China, India, Indonesia, Malaysia, the Philippines, Thailand, Vietnam.

2. Price response to patent expiry across markets

2.1 Method and data

Changes in price of originator drugs following patent expiry were explored across 13 markets across Asia-Pacific. The analysis primarily focused on drugs used for the same five cancer types as discussed in previous sub-reports (breast cancer, gastro-esophageal cancer, head & neck cancer, liver cancer, lung cancer), but drugs for the treatment of other cancer types were also selected in order to create a representative sample of biologics and small-molecule drugs. 11 drugs (bevacizumab (Avastin), capecitabine (Xeloda), erlotinib (Tarceva), fulvestrant (Faslodex), gefitinib (Iressa), imatinib (Glivec/Gleevec), letrozole (Femara), pemetrexed (Alimta), rituximab (Mabthera/Rituxan), sorafenib (Nexavar), and trastuzumab (Herceptin)) with patent loss between 2010 and 2020 were selected. Data on sales volumes of these drugs across 13 markets from Q1 2010 to Q3 2020 were obtained from the MIDAS® database, an international database containing comparable pharmaceutical sales data (7). For Indonesia, data were only available from Q1 2014 to Q3 2020 from the International Pharmaceuticals Manufacturer's Group (IPMG) (8). The largest 40 pharmaceutical companies share data with IPMG, and these companies contribute to around 70% of the market. India was excluded from this analysis due to data limitations associated with both sales data and information on patent expiry.

Quarterly sales data were obtained in both local currencies and ex-manufacturer US dollars, and corresponding sales volumes were obtained in what IQVIA refers to as "counting units". Counting units were converted to milligrams (mg) using methods described in Appendix 3. The price per mg was calculated per market, per drug, per quarter.

Data on patent expiry dates were available from local industry contacts in Australia, New Zealand,and Taiwan (9-11). For all other markets, no local public source on patent expiry dates was identified. Instead, the date of the first generic/biosimilar approved was obtained from national regulatory agencies (see Table A2 in sub-report 3). In Japan, where the latter information was not available, the date of first sales of generics/biosimilars within the MIDAS® database was used (7). Patent expiry dates (or their proxies) for each drug and market are presented in Appendix 1.

For each market-drug, the data were normalized around date of patent expiry, with the quarter of patent expiry serving as quarter-zero (Q_0). The price per mg the quarter before patent expiry (Q_{-1})

served as a benchmark against which quarterly prices were indexed for each market-drug. Prices were analyzed 1 year pre- and 2 years post-patent expiry.

It should be noted that IQVIA data does not capture the impact of confidential price negotiations between manufacturers and governments and other payers. In cases where confidential price negotiations were made, the associated price decreases are not detected in the MIDAS data. The database may have other limitations; however, we based our analysis on best available data, which in this case, is the MIDAS database.

2.2 Results

In general, the selected Asia-Pacific markets reacted as anticipated with prices overwhelmingly falling after patent expiry. The magnitude of price drops varied substantially across drugs and markets, and while it is difficult to tease out a perfect mechanism, markets could invest in learning from one another to develop effective policies for their local context.

It is important to note how differences between biologics and small-molecule drugs impact post-expiry prices of originators and their predecessors. Biologics are more complicated and expensive to produce, and they are therefore more difficult to reverse engineer, including generic forms (called “biosimilars”). Biosimilars are typically developed at a cost of $10-40 million, while generics usually cost $1-2 million to develop (12). Additionally, the fixed costs associated with building manufacturing facilities for the production of biologics lies in the range of $100-200 million (12). Therefore, off-patent biologics, facing fewer and higher-cost competitors as compared to small molecules, experience smaller price drops (12, 13). Figure 1 presents the mean price drop of all small-molecule branded drugs for each high-income market, and Figure 2 presents the same for biologics. Consideration should be taken to approach cost-containment policies for handling off-patent competition separately for biosimilars and small molecules, including pricing (14).

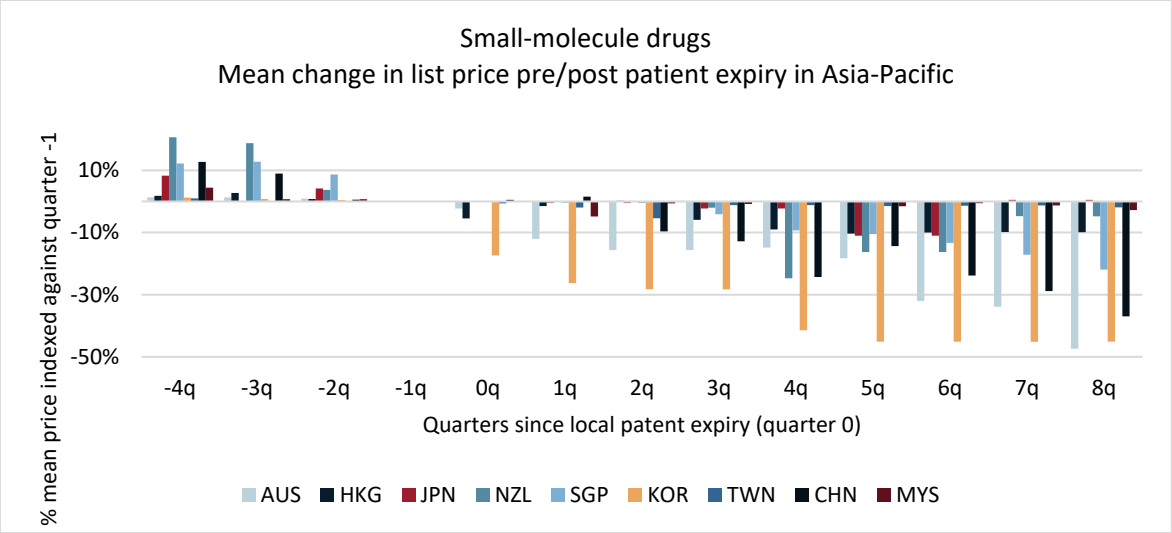


Figure 1: Indexed price per mg changes in list price pre/post patent expiry for small molecule drugs

Notes: Eight major small-molecule cancer drugs with patent loss between 2010 and 2020 were included in the analysis. Quarter 0 refers to the quarter during which a drug's patent expired or (if the former information was not available) to the quarter during which the first generic version received regulatory approval or started being sold.

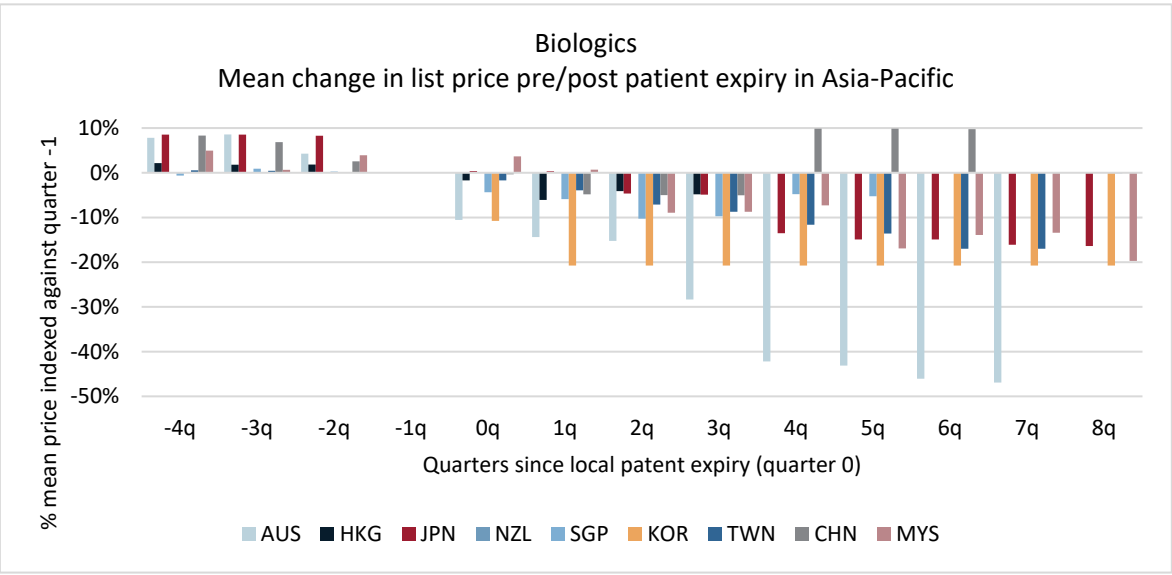


Figure 2: Indexed price per mg changes in list price pre/post patent expiry for biologics

Notes: Three major biologics with patent loss between 2010 and 2020 were included in the analysis. Quarter 0 refers to the quarter during which a drug's patent expired or (if the former information was not available) to the quarter during which the first generic version received regulatory approval or started being sold.

Australia

Australia implements mandatory price cuts combined with price-disclosure policies on off-patent drugs (15-17). In 2007, two separate formularies were created for PBS drugs, and price disclosure and statutory price reductions were introduced, which have been accelerated and expanded since. There is currently a mandatory price reduction of 25% (16% until September 2018) when the first generic was added to the PBS, and the originator went off patent (18, 19). The price of the first generic would be 25% cheaper than the originators' original price. Subsequent price reductions are based on a price-disclosure policy for off-patent originator drugs. Avastin, Mabthera, Herceptin, and Glivec all experienced the expected 25% mandatory price drops expected with post-2016 patent expiry, and Xeloda and Femara experienced the expected pre-2016 16% price drops.

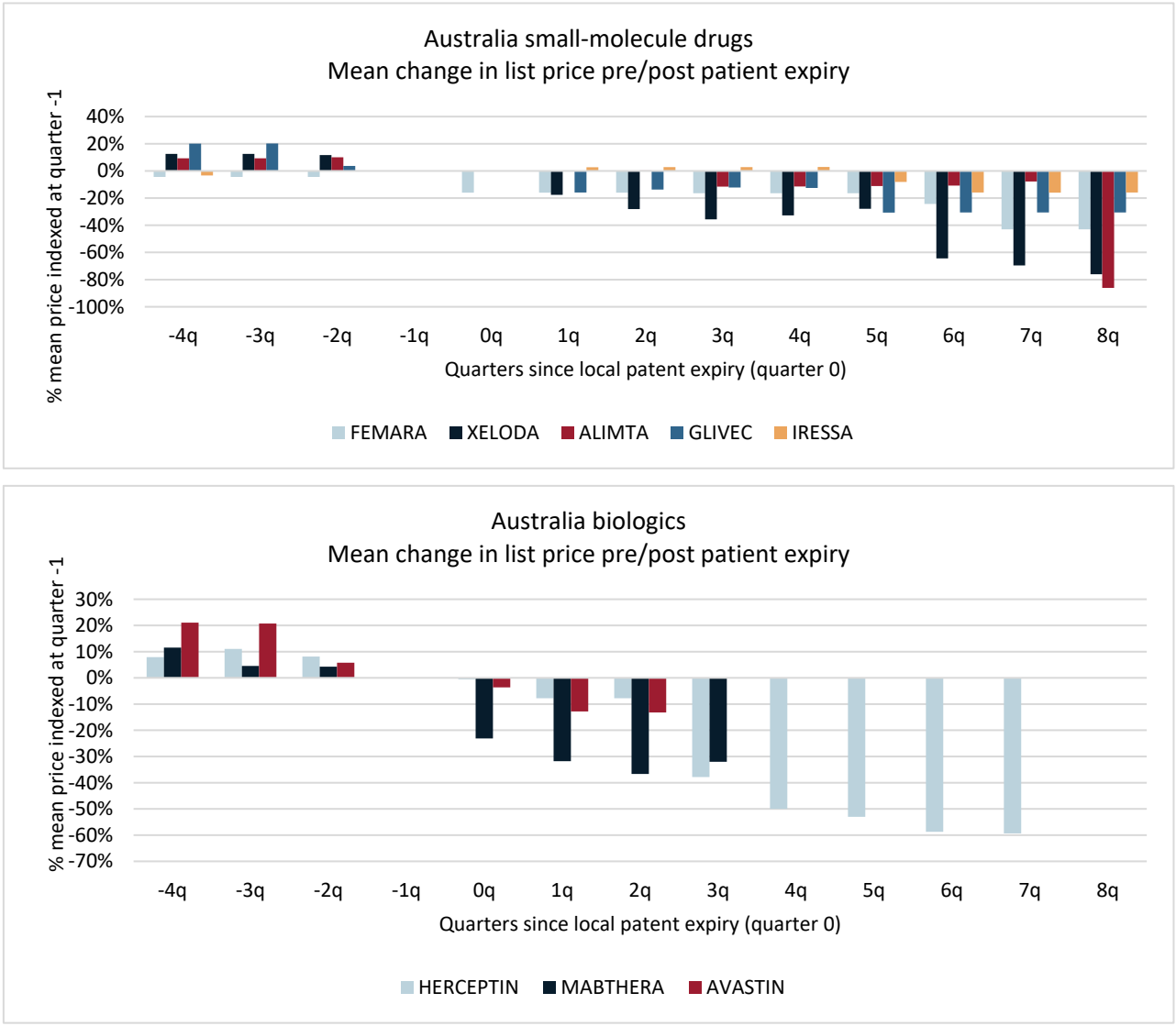


Figure 3: Australia, price changes pre- and post-patent expiry

Hong Kong

Price negotiations and tendering lie at the core of drug pricing policy in Hong Kong, and prices go free of direct regulatory control to allow for competition within the market. In the public sector, tender-based procurement of multi-source drugs (including non-originator drugs) limits public physician choice and increases prescription of generics and biosimilars. However, in the private sector, original brand drugs and biologics are continuing to be widely prescribed even after generics and biosimilars enter the market (20). In Hong Kong, the data did not allow for differentiation in sales data between the public and private sector. Among high-income markets, Hong Kong has a relatively high share of private spending (see Figure 3 in sub-report 2). Prescribers and citizens in Hong Kong are reported to be brand conscious due to lingering historical safety concerns associated with the bioequivalence of generic products, and prices of branded drugs could thus be more resistant to entry of generics into the market (20). The Hospital Authority places strong focus on drug safety with generic purchasing, which could also hinder the entry of generics into the public market. Specifically, it was mandated that generics undergo good manufacturing practice certification and delivered with bioequivalence/bioavailability data and a sample for testing. This could explain why several drugs did not see expected price drops following patent expiry. These policies were loosened in 2016 when Hong Kong joined the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S) and began purchasing generics from PIC/S member markets in 2017. Prior to joining PIC/S, Hong Kong purchased generics from manufacturers stationed in member markets of the International Conference of Harmonization (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use. Generics from markets affiliated with the ICH were treated with caution, as compared to suppliers based in PIC/S affiliated markets. Expected expansion of tender-based purchasing contracts for generics are yet to take hold, but low-cost generics are expected to step up competition in coming years (20).

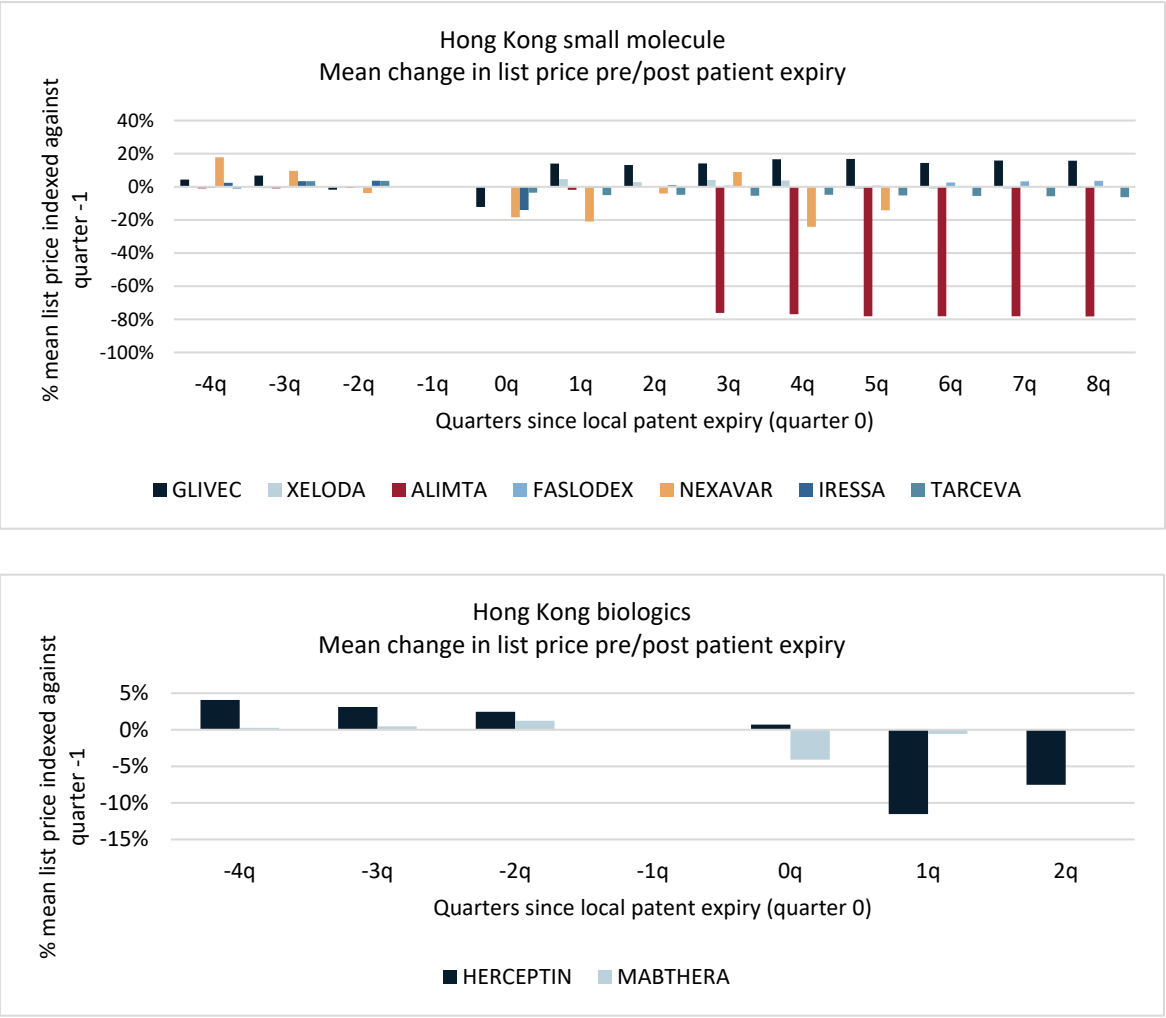


Figure 4: Hong Kong, price changes pre- and post-patent expiry

Japan

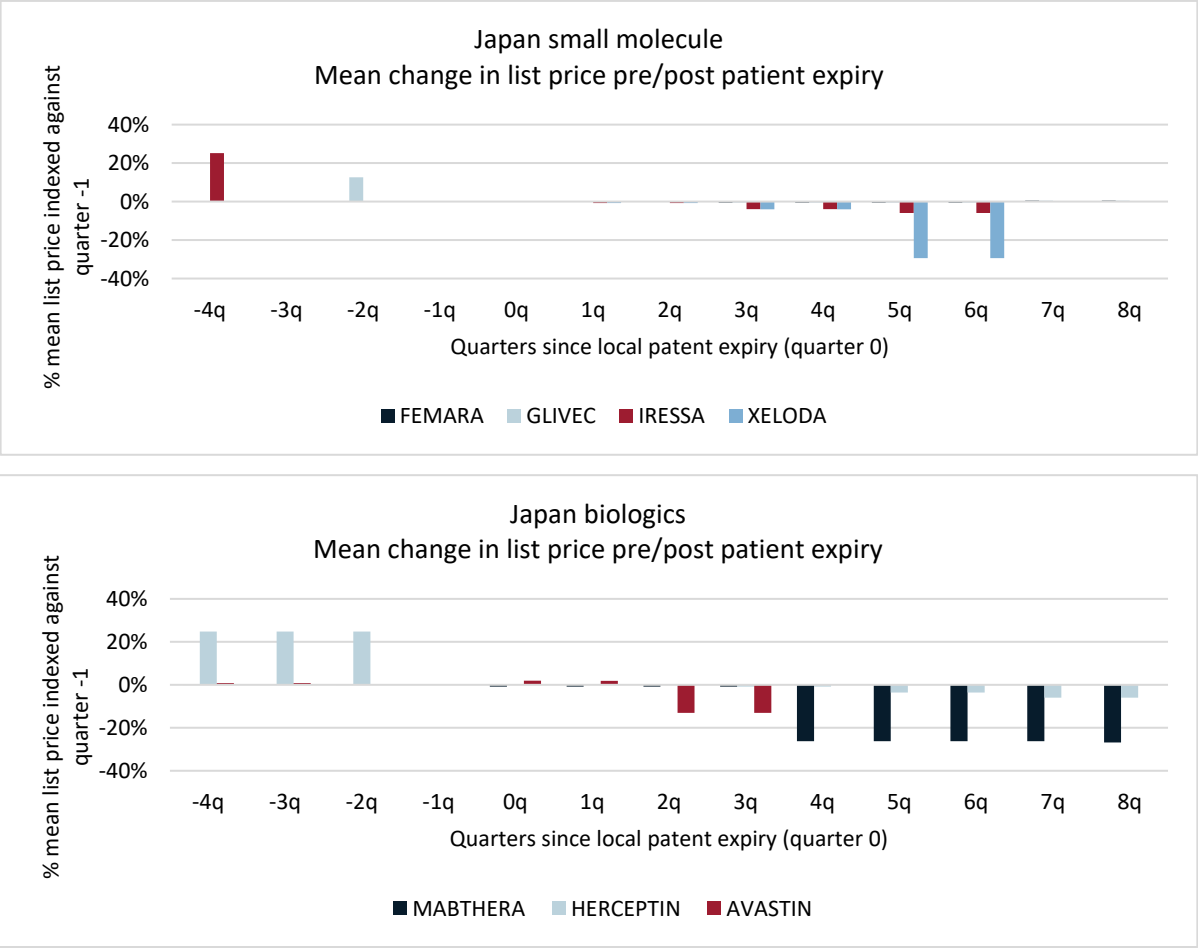
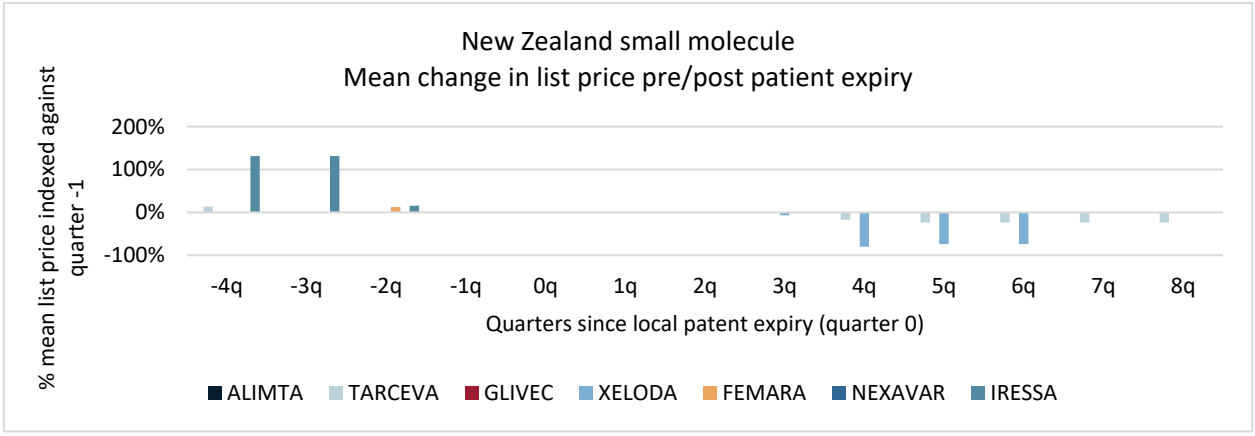


Figure 5: Japan, price changes pre- and post-patent expiry

Of the markets included in this report, Japan has the highest share of public spending, and employs a range of pricing policies to control costs and to support pharmaceutical innovation. The price of generics is set to 50% of the original product, and 40% if the number of already approved brands exceeds ten generic products. The price of new biosimilars is set to 70% of the original product (60% if the number of already approved brands exceeds ten). Twice a year (June and December), generic drugs have the opportunity to be included in the Japan's National Health Insurance reimbursement list. To help free up resources from spending on pharmaceuticals, a national volume target of 80% generics was set to be met by September 2020 by the MHLW (it was 40% in September 2011) (21). The largest insurer had reached 79% by 2019, and of the 47 prefectures, 20 had reached 80% by the end of 2020 (22). As a larger percentage of generics and biosimilars have been incorporated into the market, originators experiencing patent expiry more recently also experience larger price drops. More recent cancer drugs, like Iressa, Herceptin, and Mabthera, experienced expected price cuts after patent expiry. Older drugs like Femara did not experience a price fall for several years after generics entered the market.

New Zealand



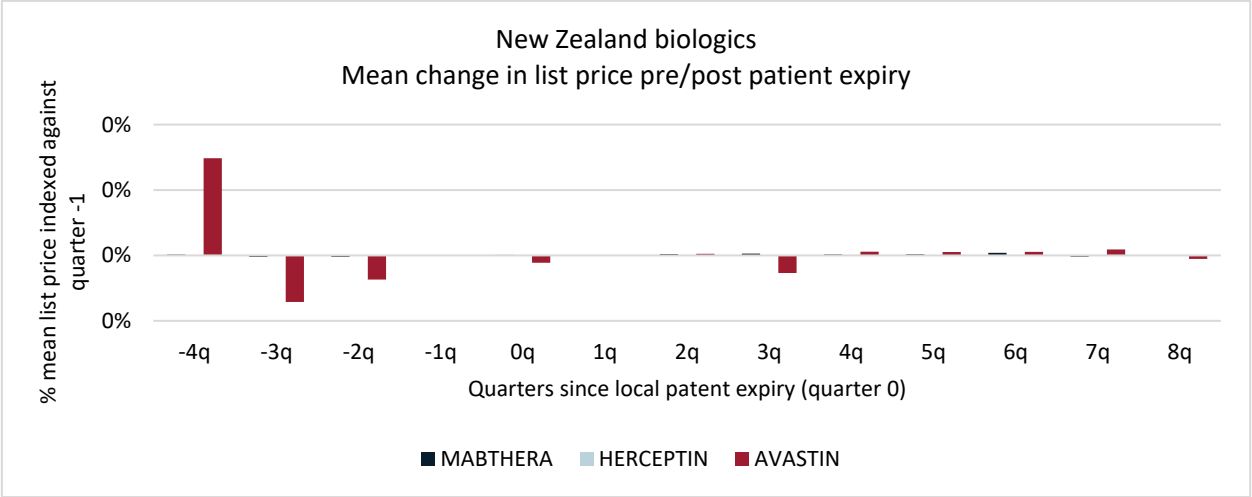


Figure 6: New Zealand, price changes pre- and post-patent expiry

New Zealand uses a competitive tender across therapeutic areas to decide on brands that will be subsidized, and historically effective price negotiations with manufactures have led to significant reductions in brand prices well before patent expiry (16). Since 1997, the Pharmaceutical Management Agency of New Zealand (PHARMAC) has been tendering out sole supply contracts for generic drugs, for a limited period, to encourage the development of cheaper generic versions of off-patent drugs (15, 23). Effective negotiating prior to listing originator products has led to significant price reductions in New Zealand, and is reflected in the price for Tarceva, Mabthera, and Iressa. However, the expected price drops because of generic entry into the market are not seen in the results. This is most likely a limitation of data availability. IQVIA sales data is unable to capture the price impact of confidential agreements across markets. PHARMAC keeps the specifics of price negotiations confidential from other buyers, and thus the rest of the world, introducing a lack of transparency to the actual price of drugs in New Zealand's Pharmaceutical Schedule (23, 24). This may be why price drops are not always detected in the dataset, and New Zealand almost certainly achieves lower prices than those presented in this analysis.

Singapore

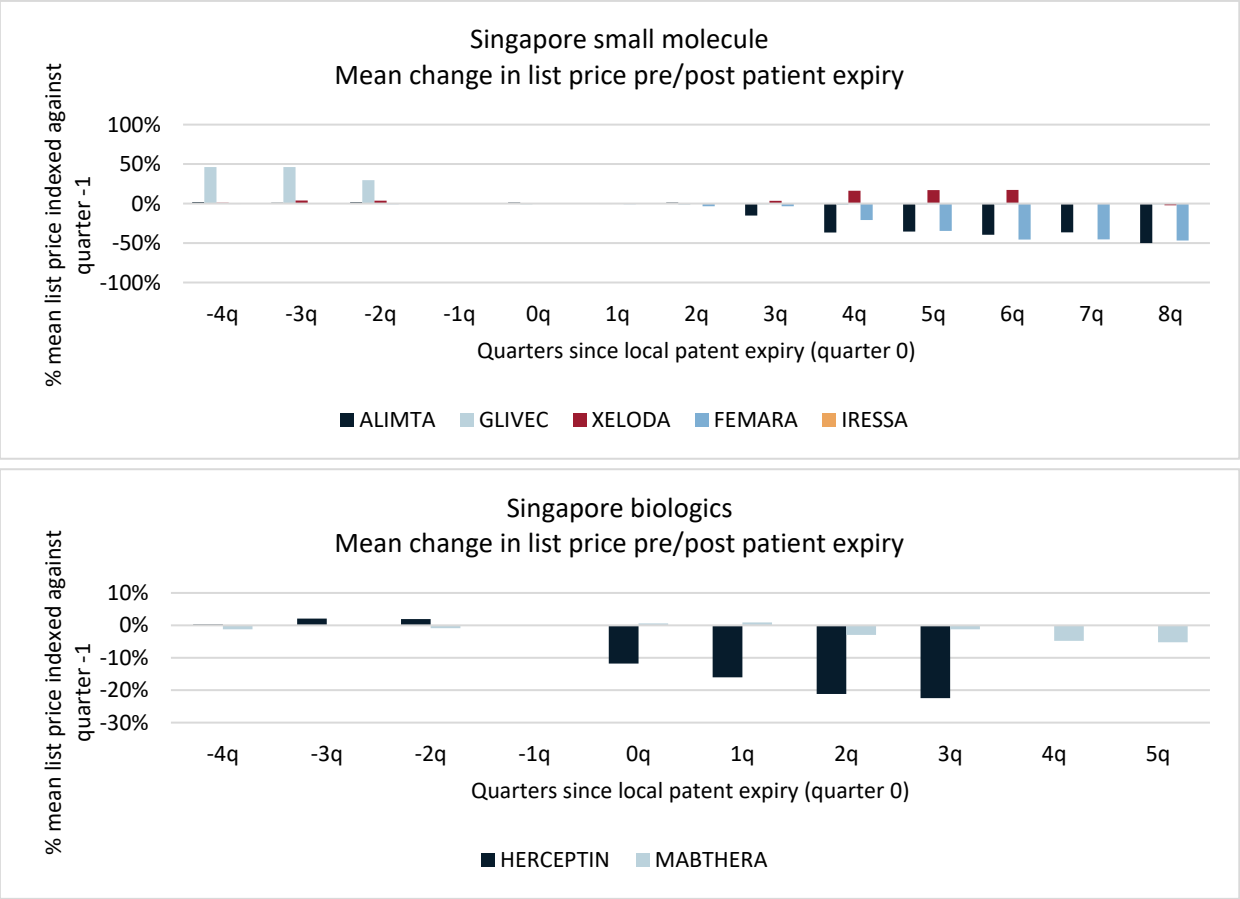
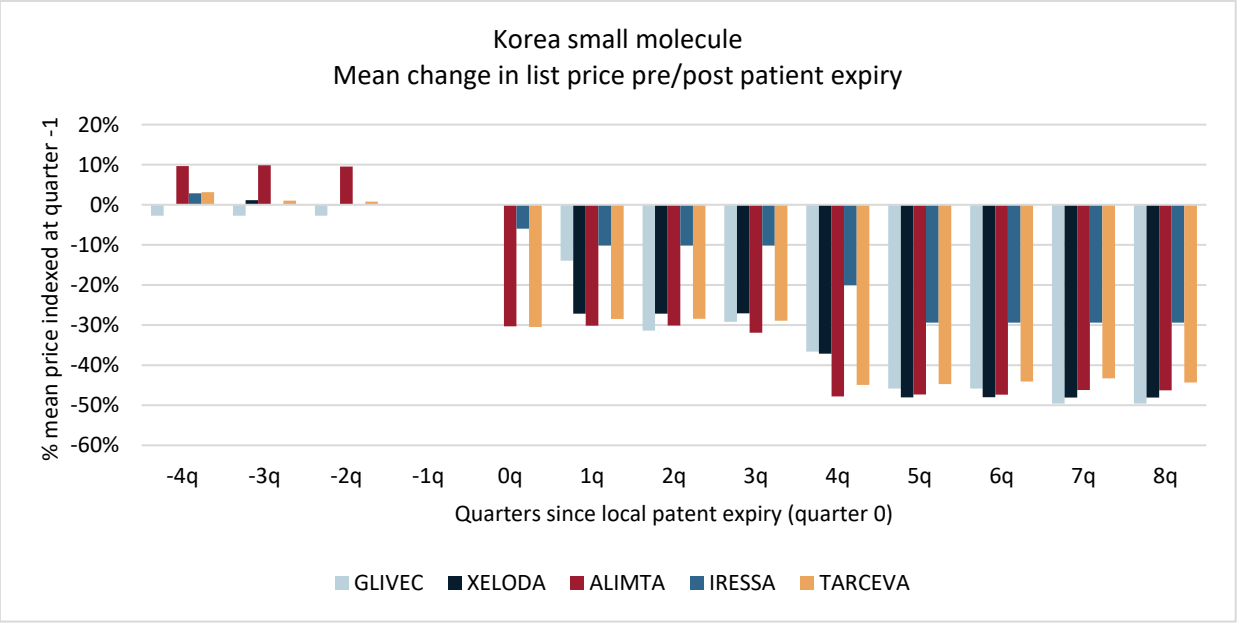


Figure 7: Singapore, price changes pre- and post-patent expiry

In Singapore, prices are set by manufacturers, and are controlled for public providers through a tendering process, which has been shown to reduce prices in both public and private markets after generic entry (16). Private providers also engage in bulk purchasing practices, which has successfully kept private sector prices comparable to, if not slightly higher than, publicly tendered products in the public sector (25). The prices set through negotiations in the public and private sector are heavily impacted by the availability of generics on the market, thus recently off-patent drugs should experience reductions in price. Historically, general practitioners and private providers have adhered to prescribing originator products even after generic entry, but this trend has shifted, and continues to shift in recent years (25). In Singapore, prices consistently drop following patent expiry, but not as dramatically as what is seen in other markets. This could be because of brand-conscious prescribing practices, and also that tendering and bulk purchasing practices in Singapore successfully set the prices of originator drugs at a low level from the outset.

South Korea



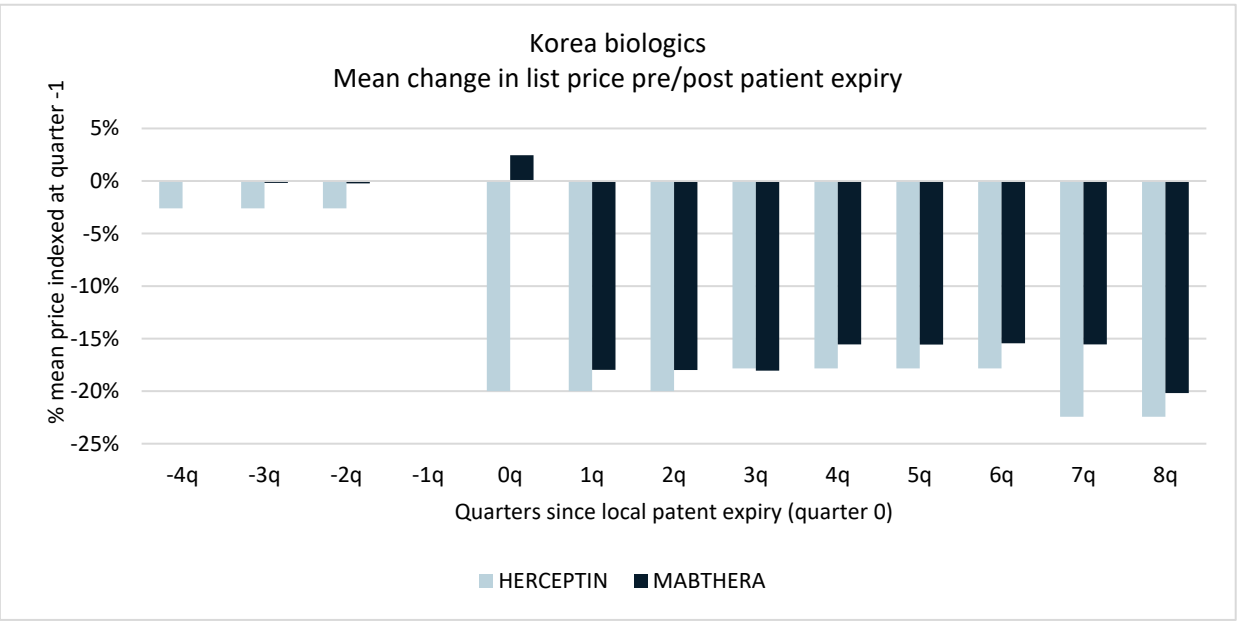


Figure 8: Korea, price changes pre- and post-patent expiry

South Korea exercises mandatory price discounts internally referenced to the originator product when generics enter the market, and a subsequent percentage reduction two years after generic entry (16). As a result, prices can be expected to experience reductions of around 30% and 10% in the first and second years following generic entry, respectively (16). The results align well with the expected first- and second-year price drops (16)

Taiwan

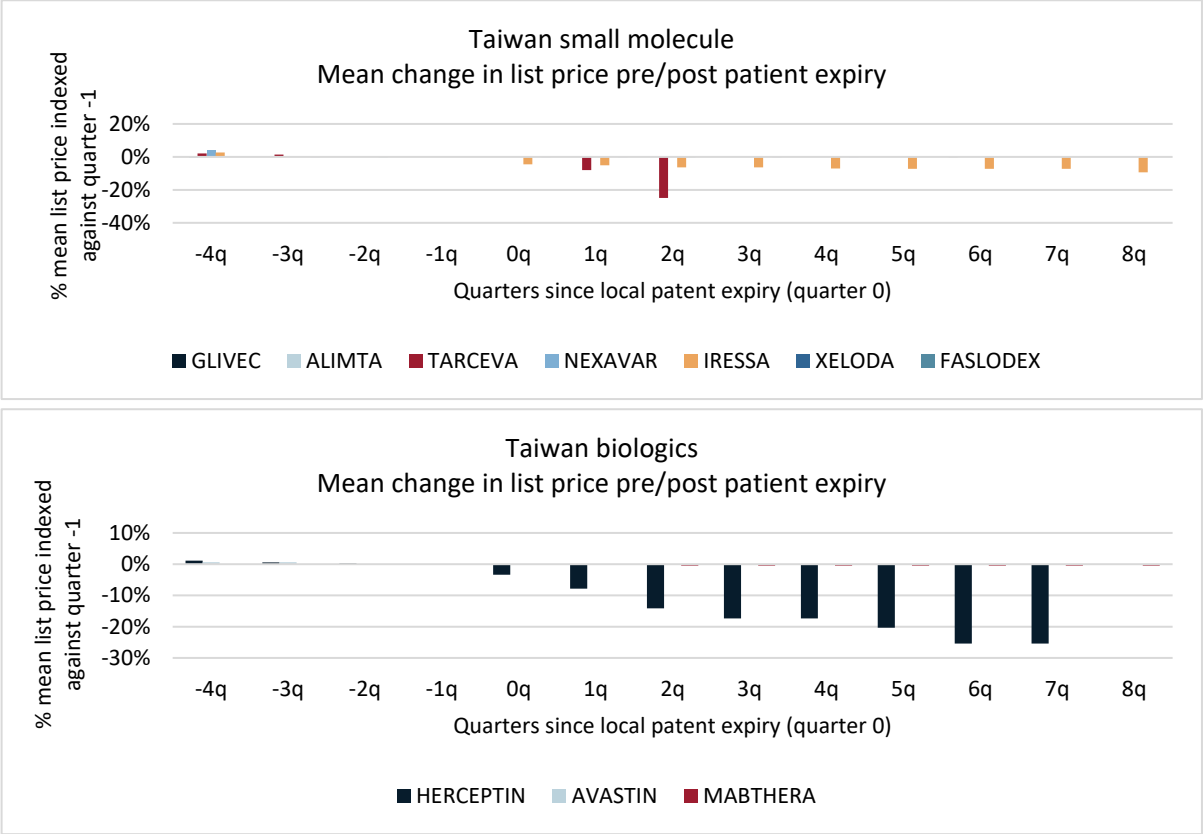


Figure 9: Taiwan, price changes pre- and post-patent expiry

Taiwan uses reference pricing, drawing on a basket of ten reference markets: the United States, the United Kingdom, Canada, France, Belgium, Germany, Japan, Sweden, Australia, and Switzerland (26). The designated reference price is set in accordance with the level of evidence and efficacy of the treatment. However, many manufactures often apply with prices lower than the required reference prices in order to secure a place on the approval list, and to reduce review time (26). The National Health Insurance Administration monitors differences in procurement and reimbursement prices and makes price adjustments in cases where the prices differ by more than 30%. Further, prices are monitored and adjusted every two years. Since 1999, the price of brand drugs with bioequivalent generic alternatives must not exceed 85% of the designated reference price (27). Originators that went off patent within one year are set equal to the minimum price of the 10 reference markets. After one year, prices are set to a weighted average price of all generic competitors plus 15%. Expected substantial price drops are seen in Tarceva, Nexavar, Iressa, and Herceptin, but the other six drugs facing patent expiry – Avastin, Xeloda, Faslodex, Glivec, Alimta, and Mabthera – see no change in price in subsequent quarters. Given the clear policies in place in Taiwan that go beyond the downward pressure of market competition, it can be assumed that this is due to limitations surrounding data availability.

China

In 2009, China began to explore policies to close the gap between the price of originator drugs that go off patent and their generic counterparts. In 2010, the State council decided that prices of recently off-patent drugs will be revisited every two to three years, which result in price reductions of generally no less than 15% (28). In 2015, China began piloting price negotiations with manufactures pre-patent. Iressa was selected as one of these drugs, all of which experienced price drops greater than 50% pre-patent expiry (28). Iressa was followed by Tarceva, Avastin, Mabthera, Nexavar, and Herceptin, all experiencing price drops of 40 to 60%, all before patent expiry. Further drops were also seen in quarters immediately following patent expiry in all drugs but Mabthera.

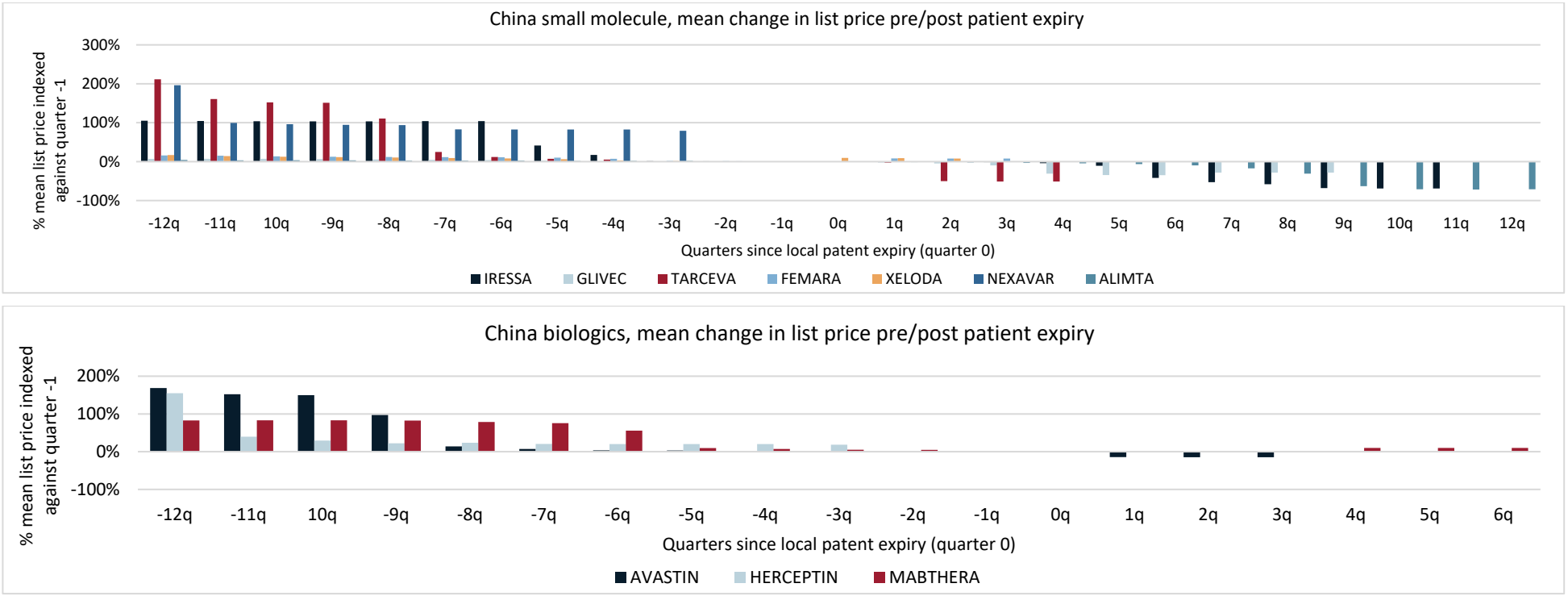


Figure 10: China, price changes pre- and post-patent expiry

Malaysia

In Malaysia, the Ministry of Health (MOH) procures drugs to public providers. To gain listing status in the national formulary, manufactures must present evidence of efficacy and reasonable price, and are selected through a tendering process (29). Prices are then monitored to maintain affordability for the MOH. Drug prices within the private sector are not regulated and there are no mechanisms in place to control prices within private pharmacies at the retail level (30). The private sector has a markets share of around 60% (31), and limited price controls paired with brand-conscious prescribing mean that drug prices in Malaysia remain comparatively high (30). The MOH is discussing the implementation of international reference pricing, setting a ceiling price at the median level of the average of the lowest of three reference prices. However, the basket of markets is yet to be specified, and this along with other price control policies are still under discussion. It is unclear when they will come into effect, but are expected to hit the public sector first (29).

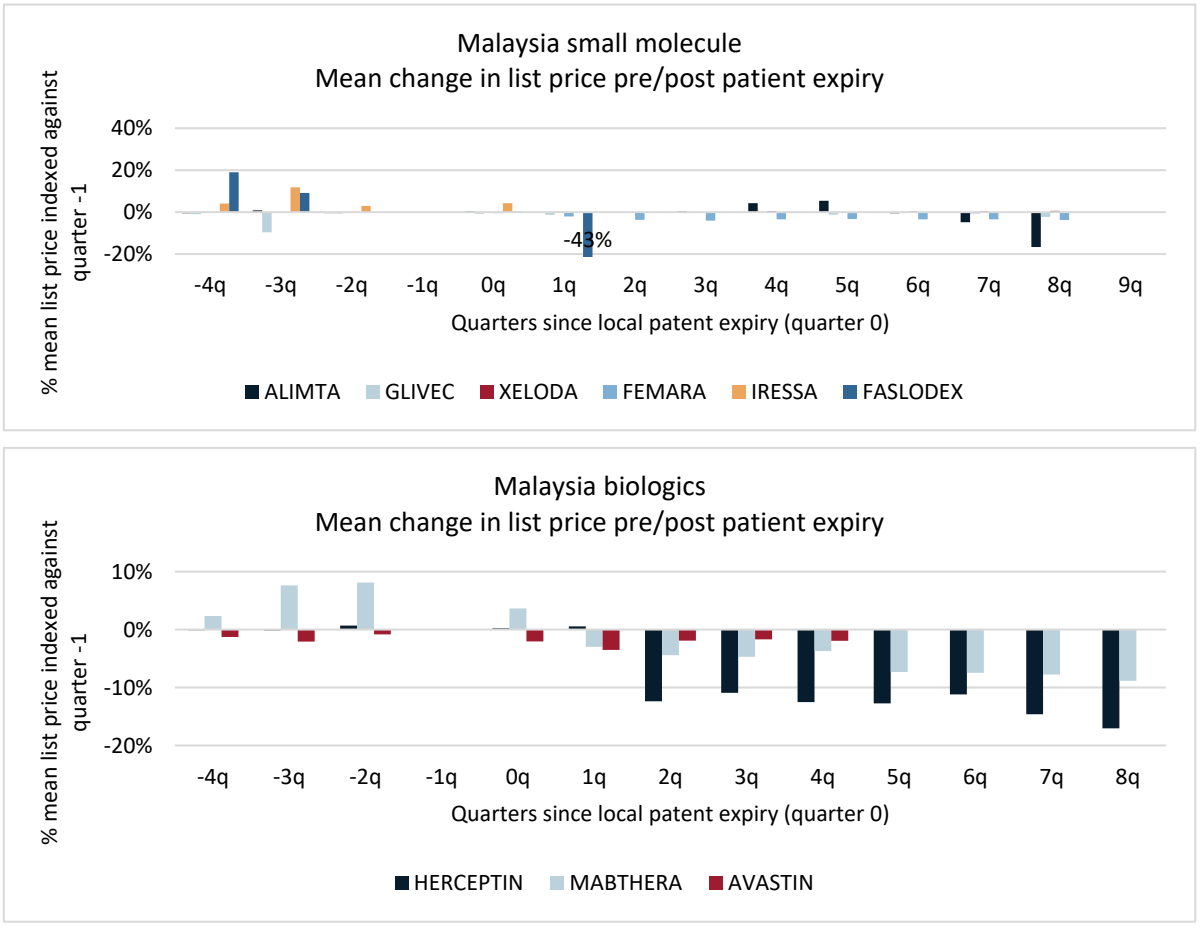


Figure 11:Malaysia, price changes pre- and post-patent expiry

For Malaysia, the MIDAS dataset allowed for differentiation between public and private sales. For most drugs, following patent expiry, the price of branded products falls in the public sector following patent expiry, and returns to original price levels in the quarters that follow, indicated generic takeover of the market – see the example of Alimta in Figure 12. This is also the case for Avastin,

Faslodex, Glivec, Alimta, and Mabthera. Public sector prices of Femara and Herceptin drop and stay down after the entry of generics, and sales of Iressa cease after patent expiry. The lack of changes in private sector prices could be in part due to brand-conscious prescribing behavior in the private market. The quality of data coming out of the private sector is also reported as less reliable, although, the MOH is taking steps to collect data more accurately and broadly from the private sector in coming years (29). Finally, in Malaysia, it can take time for the government to put tenders into place after generic approval, which may explain some of the delay seen in price drops.

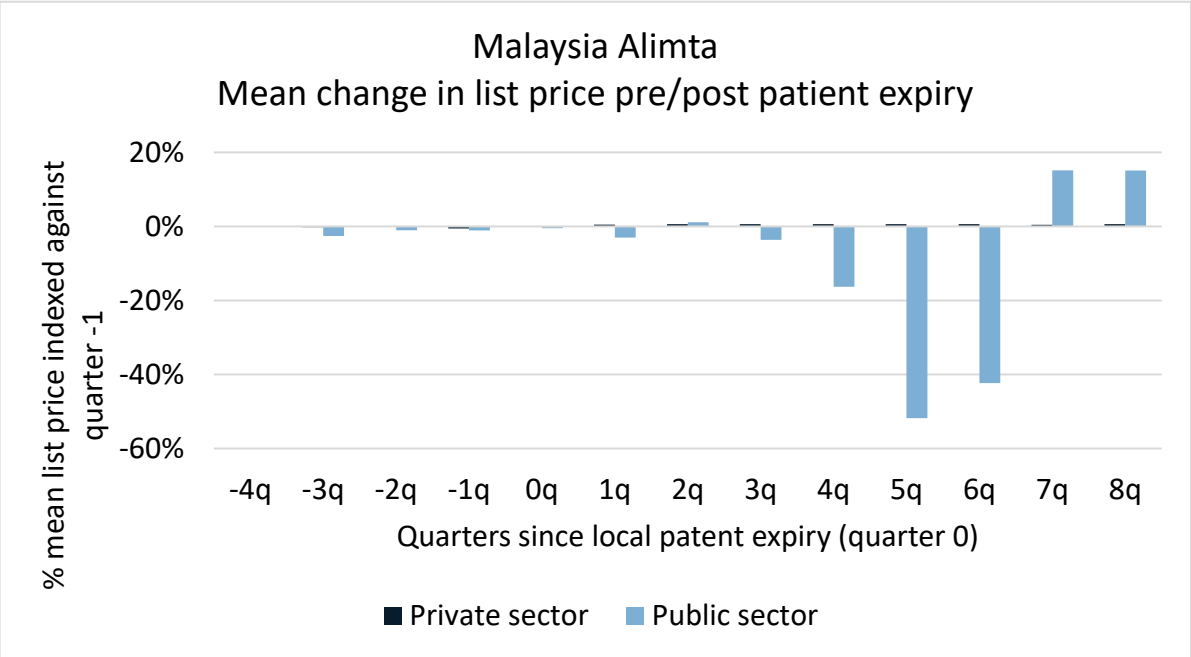


Figure 12: Case example of Alimta price changes in Malaysia

Thailand, the Philippines, Indonesia, and Vietnam

In all four of these markets, increased price control policies are expected in the coming few years. In Indonesia, the Philippines, and Vietnam, the private sector accounts for a large proportion of the market and goes largely unregulated. In Thailand, median pricing and other strict pricing negotiations limit the successful entry of originator drugs into the market (32). For off-patent drugs facing competition from generics and biosimilars, median pricing obtained from the average price of all versions of the drug (generic and original). The median pricing leads to cuts ranging from 10%-90% and averaging on 50% (32). Post patent expiry, in this analysis Thailand experiences no price change in originator products in the quarters following patent expiry. Among middle-income markets, Thailand has the largest share of public financing (see sub-report 2, Figure 3), and under these policies generic competition should bring originator prices down considerably. The current policy environment surrounding off-patent drugs is inconsistent with unaffected prices of originator products, so we must conclude that the IQVIA data is not capturing pricing events that likely have happened.

In Indonesia, after drugs are listed on the national formulary, they are most often purchased through the e-catalogue and priced using a cost-plus approach. These prices serve as the basis of a price ceiling system (33). This ceiling process is multi-source and also involves locally produced generic products, and resulting competition drives prices very low. For single-source products, prices are set through negotiations between MOH and manufacturers. These negotiations often involve budget impact analysis, and resources available to spend on high priced products, allowing limited room for negotiation. As a result, many single-source products are not available in the e-catalogue, and prices in Indonesia remain relatively low (33). Vietnam, Thailand, and the Philippines all experience relatively high drug prices, comparable to those seen in European markets.

In all cases, generic entry into an unregulated private sector should lead to price drops in originator products. Within the outputs of the analysis of MIDAS and IPMG data, however, prices in all four markets remain essentially unchanged before and after patent expiry. Some possible exceptions are Femara in Indonesia, Mabthera in the Philippines, and Faslodex, Femara, Iressa, Nexavar, and Mabthera in Vietnam. However, in all of these cases the trends are unstable, distorted, and generally uninterpretable. As was the case with Thailand, these results are inconsistent with expected price drops of originator products associated with generic entry into the market. We therefore assume that the IQVIA data is not capturing pricing events associated with generic entry to markets.

However, in each of these markets (Indonesia, Thailand, Vietnam, and the Philippines), price levels are consistent with those seen in other markets, and sales volumes appear to respond as expected, as seen in the following analysis.

3. Potential savings from efficient pricing mechanisms

3.1 Method and data

Focusing on the same 11 drugs, the prices of the originator drugs were analyzed across markets to estimate the savings associated with effective off-patent pricing mechanisms. Effectiveness is here defined as achieving the lowest possible price.

For the year following patent expiry, total currency sales were divided by the total mg sales for each market to estimate the annual price per mg of originator drugs the year following patent expiry. For each drug, market specific annual prices were benchmarked against the market with the absolute lowest price per mg. Candidates for benchmarking included both the 13 markets excluding India in Asia-Pacific and a set of OECD markets for which MIDAS data were also available (Belgium, Canada, France, Germany, Italy, the Netherlands, Norway, Spain, Sweden, Switzerland, and the UK). For each drug, the price difference between the benchmark price and each market's off-patent price was multiplied by the volume sold (mg) in the respective market the year after patent expiry to estimate potential savings.

3.2 Results

The estimated savings per drug per market are presented in Appendix 2. Estimated total savings per newly diagnosed cancer case in the respective markets are presented in US dollars in Figure 13. All markets included in this analysis could theoretically achieve considerable amounts of savings. Compared to total cancer drug expenditure (see Figure 3 in sub-report 4), potential savings range from 3% to 20% of cancer drug expenditure across the markets; see Figure 14.

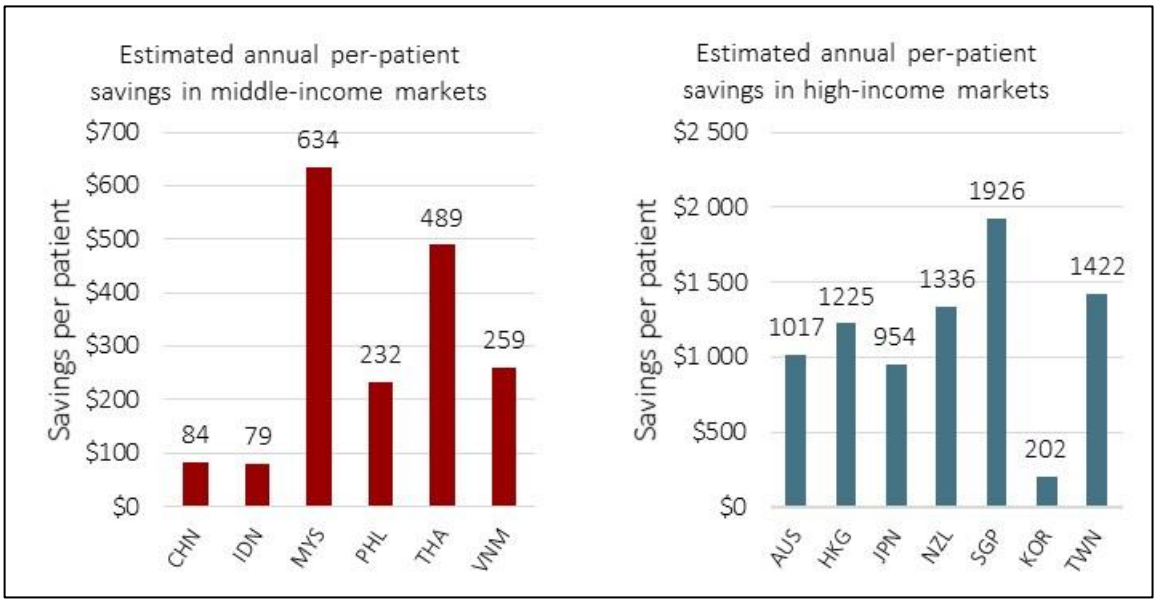


Figure 13: Estimated savings per newly diagnosed cancer case (US$) from more effective off-patent pricing outcomes of 11 cancer drugs

Notes: No data available for India. Effectiveness is here defined as achieving the lowest possible price for the originator drug after patent expiry or loss of exclusivity. The analysis is based on list prices, which typically do not fully capture confidential rebates and arrangements granted by drug manufacturers to payers.

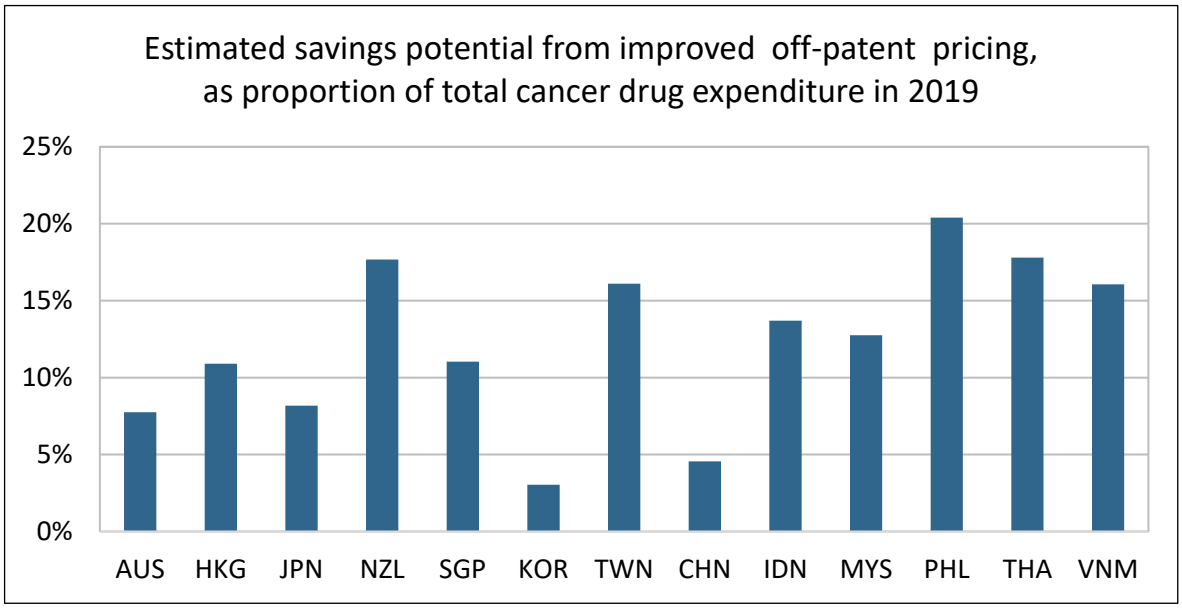


Figure 14: Estimated savings from more effective off-patent pricing outcomes of 11 cancer drugs as a proportion of total expenditure on all cancer drugs

Notes: No data available for India. Effectiveness is here defined as achieving the lowest possible price for the originator drug after patent expiry or loss of exclusivity. The analysis is based on list prices, which typically do not fully capture confidential rebates and arrangements granted by drug manufacturers to payers.

The analysis in section 2 concluded that the IQVIA data likely did not capture price reductions following patent expiry in Indonesia, Thailand, Vietnam, and The Philippines. Prices during the year following patent expiry in these markets would likely be overestimated, and thus savings may be overestimated as well. In these same middle-income markets, however, where originator drugs are often unaffordable, price reductions associated with effective off-patent pricing mechanisms would likely trigger increases in sales volumes, thus compounding the savings and improving access to drugs. Therefore, savings estimates in middle-income markets are likely underestimated. Under current market conditions, sales volumes in these markets already increase post-patent expiry; see Figure 15 where Australia, New Zealand, and South Korea are also included as reference markets where these drugs are reimbursed. Thus, sales volumes are already maximized at patent expiry. The observed increase in sales volumes implies that an expansion of patient access to these drugs in middle-income markets. The possibility that these increases were due to either confidential agreements or reimbursement pricing actions following self-payment across all these markets is unlikely. Thus, it can be assumed that there were actions in the self-pay sector that were not captured by the MIDAS database.

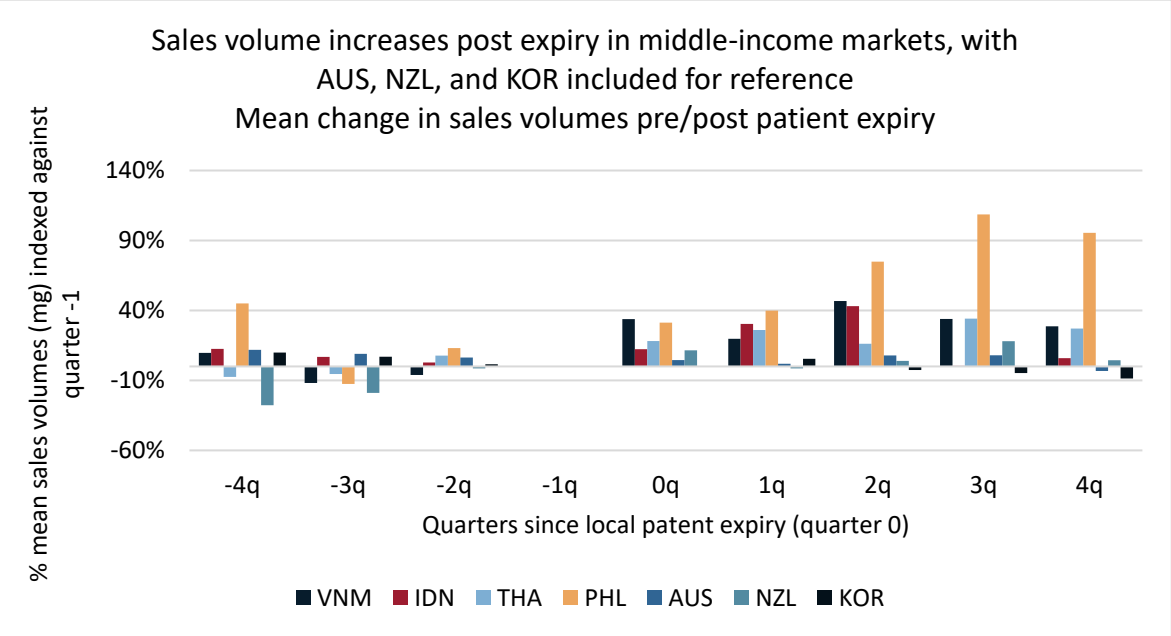


Figure 15: Sales volumes in select middle-income markets, with high-income markets as reference

Notes: Middle-income markets where IQVIA data did not detect off-patent originator price changes.
AUS, NZL, and KOR included for reference.

In New Zealand, price changes that likely occur were not present in the dataset. Many price discounts remain confidential in New Zealand, and if they were truly reflected in the dataset, the potential savings in New Zealand would be proportionally decreased.

While there is likely no one-size-fits-all approach, governments and policy makers across the Asia-Pacific should aim to maximize potential from pricing policies on off-patent drugs and adopt those that are effective in their individual market. This analysis involves only a sample of 11 drugs, and more savings can be expected if a broader scope of drugs were included. Finally, the savings estimated from this analysis are theoretical estimates, and do not represent empirical findings. The analysis highlights the potential to free up limited health resources to better address the unmet needs of cancer patients.

A recent study in South Korea found that patent loss could save 20% of expenditure on cancer drugs over five years, freeing up resources for innovative treatments and to treat more patients (4). Affordable access to off-patent treatments is one of the most valuable assets for patients in market when achieved (34), and should be a priority in these middle-income markets where there is potential for expansion. Ensuring effective pricing policies for off-patent drugs stimulates the availability of and competition between generics/biosimilars, which provide “equal” clinical value to originator drugs and can lead to substantive savings. Patent expiry should be viewed as an opportunity where effective policy can improve access to drugs and free up resources to re-invest in more effective and innovative treatments for patients (4, 6, 35).

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Appendix 1. Patent expiry dates by drug and market

	AUS (10)	HKG	JPN (7)	NZL (10)	SGP	KOR	TWN (9)	CHN	IND	IDN	MYS	PHL	THA	VNM
Bevacizumab	Q1 2020	n/a	Q4 2019	Q2 2018	n/a	n/a	Q4 2019	Q4 2019	Q1 2016	n/a	Q3 2019	n/a	Q1 2019	n/a
Capecitabine	Q2 2014	Q2 2014	Q1 2019	Q4 2013	Q3 2014	Q1 2012	Q4 2013	Q1 2020	X	Q1 2017	Q4 2017	Q4 2012	Q3 2014	Q1 2012
Erlotinib	n/a	Q3 2017	n/a	Q1 2016	n/a	Q1 2013	Q1 2020	Q3 2019	Q3 2010	Q2 2019	n/a	Q4 2013	Q3 2018	Q4 2013
Fulvestrant	n/a	Q3 2018	n/a	n/a	n/a	n/a	Q3 2019	n/a	X	n/a	Q1 2019	n/a	Q2 2020	Q3 2019
Gefitinib	Q4 2017	Q3 2019	Q1 2019	Q1 2013	Q3 2020	Q2 2015	Q2 2017	Q4 2017	X	Q2 2019	Q3 2020	Q1 2017	Q1 2020	Q4 2015
Imatinib	Q3 2016	Q4 2013	Q3 2010	Q1 2013	Q4 2016	Q1 2013	Q1 2013	Q2 2018	X	Q2 2019	Q3 2013	Q1 2016	Q3 2014	Q4 2015
Letrozole	Q2 2012	n/a	Q3 2010	Q3 2010	Q1 2011	n/a	n/a	Q4 2019	X	Q2 2016	Q3 2010	Q3 2011	n/a	Q1 2013
Pemetrexed	Q2 2015	Q3 2016	n/a	Q1 2013	Q2 2014	Q2 2012	Q1 2011	Q3 2017	X	Q2 2019	Q3 2017	Q2 2016	Q2 2019	Q4 2012
Rituximab	Q4 2019	Q4 2019	Q2 2017	Q4 2013	Q2 2019	Q3 2015	Q4 2013	Q1 2019	Q3 2012	Q4 2018	Q3 2018	Q1 2019	Q2 2018	Q4 2012
Sorafenib	n/a	Q2 2019	n/a	Q1 2020	n/a	n/a	Q2 2020	Q3 2020	Q2 2010	n/a	n/a	n/a	n/a	Q4 2019
Trastuzumab	Q4 2018	Q1 2020	Q3 2018	Q3 2014	Q4 2019	Q1 2014	Q4 2018	Q3 2020	Q3 2012	Q2 2018	Q3 2018	Q1 2017	Q2 2018	Q3 2019

Source: Patent expiry date obtained from government sources where available. If the latter was not available, date of first generic/biosimilar approved was obtained from regulatory agencies. If the latter was not available, date of first sales of generic/biosimilar in IQVIA MIDAS database was used.
Data and data period for analysis of price patterns: IQVIA MIDAS data Q1 2010 to Q3 2020
n/a = still on patent at the end of Q3 2020 or patent expiry/first generic version approved/sold before Q1 2010
X = no patent expiry date or date of first generics approved/sold identified

Appendix 2. Estimated savings per drug per market

Table 1: Estimated savings in million US$ per drug per market

	Reference	AUS	HKG	JPN	NZL	SGP	KOR	TWN	CHN	IDN	MYS	PHL	THA	VNM
Bevacizumab	CHN	14	on patent	270	1	on patent	on patent	18	reference	on patent	2	on patent	11	on patent
Capecitabine	KOR	3	1	33	1	1	reference	5	60	4	0	1	2	2
Erlotinib	CHN	on patent	4	on patent	0	on patent	3	10	reference	3	on patent	2	3	6
Fulvestrant	NWY	on patent	1	on patent	on patent	on patent	on patent	2	on patent	on patent	0	on patent	1	0
Gefitinib	MYS	2	6	18	1	2	11	16	52	12	0	2	15	4
Imatinib	IDN	31	8	341	14	4	32	42	93	reference	7	9	14	17
Letrozole	BEL	7	on patent	80	0	1	on patent	on patent	38	0	1	1	on patent	0
Pemetrexed	KOR	9	1	on patent	0	2	reference	17	24	no sales	1	2	2	no sales
Rituximab	KOR	26	6	143	4	6	0	10	73	6	0	3	12	3
Sorafenib	CHN	on patent	1	on patent	0	on patent	on patent	22	reference	on patent	on patent	on patent	on patent	2
Trastuzumab	KOR	49	13	81	12	11	reference	45	17	2	3	12	22	10
Total Savings		140	40	967	33	26	46	188	357	27	15	33	82	42

"no sales" indicates that no sales occurred in the respective market during the year following patent expiry.
"reference" indicates that this is the reference market specific to the corresponding drug.
"on patent" indicates that the drug is still on patent at the end of Q3 2020 or patent expiry/first generic version approved/sold occurred before Q1 2010.

Appendix 3. Handling of data unit variables

Within the extracted MIDAS dataset used in this analysis, there were some hurdles to overcome associated with the unit of analysis surrounding sales volumes. Sales volumes were provided both in terms of counting units (CU) and standard units (SU). Depending on the dosage form, CUs were defined as either the number of tablets in a package, the number of mL in a vial, or the number of mg in a vial. The CUs were then divided by a "standard unit factor" to obtain SUs.

The standard unit factor was equal to 1 for all solid dosage forms; one SU was equal to one CU. Across quarters within the same drug/market, the unit count changed in intervals equal to the pack size, and it was therefore suspected and later confirmed by IQVIA that one unit (SU or CU) was equal to the standard unit factor, or one tablet. The mg per tablet remained unchanged for each drug, so the counting units for solid dosage forms were acceptable for our analytical purposes.

For liquid forms where concentration and volume were defined, the CU was total volume in mL, the standard unit factor was the volume of the vial in mL, and the resulting SU was the number of vials of the specified volume. For vial dosage mediums where the volume and concentration were not specified, the CU was total mg, the standard unit factor was the number of mg in the vial, and the resulting SU was one vial.

This information was used to convert all units into milligrams for the purposes of our analysis. In some cases, the price per mg can vary substantially. For example, sub cutaneous vials are generally priced lower than infusion vials due to added administration and production costs associated with infusion treatments. To account for these differences in our analysis, thresholds were set up to detect cases where the price per mg deviates substantially, and in these cases, comparisons were made as if they were separate drugs.

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