Bioequivalent Drugs: Worth the Risk?

Chile's pharmaceutical market is worth US$2 billion, but in recent years it has cost patients both their pesos and their trust. The government's recent decision to certify bioequivalent drugs in Chile aims to increase access for consumers by providing an affordable alternative to branded products. But industry specialists wonder whether bioequivalent drugs are paving the way to risky industry innovations.

By **Olivia Crellin**

In Chile healthcare, like education, is expensive. This is, in part, due to the high cost of medication. In 2010 the average family spent 1.8 percent of their total monthly household budget on medicines, according to the Ministry of Economy. This represents 60% of their total spending on healthcare, which is a hefty proportion that the country's Institute of Public Health (ISP) aims to reduce with the introduction of bioequivalent drugs.

Currently there are only 70 approved bioequivalent drugs in Chile but the ISP and the newly created national drug regulator, Anamed, plan to increase this to around 236 by the end of the year.

A bioequivalent drug is "a copy of an original innovator drug which contains the same active ingredient. This ingredient operates at the same molecular rate and concentration in the bloodstream as the original to achieve an identical therapeutic effect," according to the ISP, which bases its definition on that of the World Health Organization (WHO).

"By the end of 2014 every generic drug in Chile is going to have the bioequivalence seal."

Jaime Mañalich,
Minister of Health

Bioequivalent drugs can be between five and 20 times cheaper than the original. For example Zotran, a drug used to help alleviate anxiety, costs 11,540 pesos (around US$24) in Chile if sold as a branded product. The bioequivalent version of the same drug sells for 540 pesos, just over US$1, a savings of 95.3 percent.

Once the patent on an original drug has expired, other companies can produce bioequivalent drugs more cheaply, not needing to recoup the financial costs already incurred by the original manufacturer for research, development and testing. This introduces competition into the market, driving down the retail price of the drug for consumers and enhancing access to the product.

Affordable medication

The scheme has been welcomed by Chileans, who, unlike in countries with free public healthcare such as the U.K., have to pay for medicine. It will also help ensure the supply

of medicine in the public health system and, in turn, generate further savings for patients; something urgently needed according to Dr. Enrique Paris, president of the Chilean College of Physicians.

In Chile 90 percent of primary healthcare clinics are operated by municipalities, not the state. In recent years the mismanagement of this system has resulted in a "chain of debt" between clinics and the laboratories that supply them, which has ultimately left the patient to foot the bill. Despite 80 percent of people in Chile having access to free drugs under FONASA, the public health insurance system, there are many times when the necessary drugs are not in stock.

"What does a person do then?" Paris asks. "They go to buy the medicine at the pharmacy on the corner, and spend their own money. This is why the public's spending on medicine is very high."

The bioequivalence plan will leave government finances in a healthier state too. If, on average, a bioequivalent drug costs a third of the price of its original, three times as much can be purchased, thereby enlarging stock, improving access and saving the public money. In addition, Cenabast, the government agency that supplies medicines to the public health system, receives an additional 30 percent discount from laboratories, which means that the price of drugs could fall by at least 50 to 60 percent.

According to Jaime Mañalich, Chile's Health Minister, President Piñera's administration has reduced the amount owed to laboratories by Cenabast from US$160 million to US$70 million and aims to pay off the rest by the end of the year, leaving the public health system free to do what it was created for – provide healthcare and medicines to the public.

"We are moving very fast in the direction of making drugs part of the health guarantee," Mañalich said at a press conference held to coincide with the visit to Chile of WHO Assistant Director-General Keiji Fukuda, who considered the government's thinking on the matter "future-orientated and solid".

Health benefits

Bioequivalent drugs are not just about saving money though – in fact studies show that the savings generated by bioequivalent drugs plateau after the first initial drop in price.

Instead, "bioequivalent drugs are about economy in general and about improving health," says Dr. Iván Saavedra, director of the Center of Equivalence at the University of Chile, one of ten laboratories that currently test drugs for their bioequivalence in Chile.

Unlike generic drugs, bioequivalent drugs need to be certified before they can be approved for sale; a long and costly undertaking that in Chile falls to the ISP. But once this task has been completed, patients can be sure that the drug they are consuming is exactly what it says it is.

This was not the case previously. When the quest for cheaper medical alternatives began in Chile during the presidency of Eduardo Frei in 1964, the drugs that were introduced were generic, not bioequivalent. Generic drugs, like bioequivalent

"Unlike generic drugs, bioequivalent drugs are certified to be identical to the original drug on a molecular level."

Iván Saavedra, Center for Equivalence, University of Chile

"In Chile people often take medication that someone recommends without consulting a doctor, but this is a cultural shortcoming."

Dr. Enrique Paris, Chilean College of Physicians

"People will need more help than ever to navigate the medicine market after the arrival of bioequivalent drugs."

Héctor Rojas, Chile's Association of Independent Pharmacists

drugs, are cheaper and fulfill the same medical function more or less as their patented ancestors, but they are not identical on a molecular level. This makes it dangerous for doctors and pharmacists to calculate the appropriate dosage when prescribing and selling them, points out Saavedra.

Generic drugs still account for 38 percent of industry sales in Chile, but the system of certification gives bioequivalent drugs an "extra", says Hector Rojas, the president of the Association of Independent Pharmacists. "If the drug is good for patients, it's good for my pharmacy," he says. But securing the confidence of customers, to encourage them to buy the new drugs, is one of the biggest challenges facing the initiative.

Trusting in bioequivalence

It is no wonder that the public thinks twice before swallowing new pharmaceutical schemes. In March last year a price-fixing scandal revealed that Chileans had been cheated by the country's three biggest pharmacies.

Then, earlier this year, the media brought attention to economic incentives that persuade pharmacy workers to recommend some drugs over others. Even the practice of keeping harmless products like make-up in display cabinets fosters an environment of mistrust.

In addition, Chileans have an unshakable belief in the quality of branded products. "It is very psychological. Here in Chile, people think that cheap things are bad. They want the Rolls Royce of products," says Paris.

Luckily, Chile's bioequivalent drugs will be getting a branding all of their own. The drugs will come in packaging with a bright yellow band and the word "Bioequivalent" in red. The drugs will also keep their generic name, known as the International Nonproprietary Name, which allows customers to recognize the product anywhere in the world.

So if bioequivalent drugs are healthy, cheap and have been around in most developed countries for decades, why is their introduction into the Chilean market so controversial?

"Chile is new to this," says Rojas. "We are more backward than the European countries, the U.S., Brazil, Canada and Japan, which immediately started to accept the recommendations of the WHO with regards to the quality, safety and efficacy of medicines in the late 1980s."

In many ways it is admirable that the government is racing ahead with bioequivalence policies - Mañalich has promised that by the end of 2014 every generic drug in Chile "will have the bioequivalence seal" as well. But there are those in the medical profession and pharmaceutical business that think Chile is trying to run before it can walk.

Certified manufacturing practices

From a technical standpoint only 40% of laboratories in Chile are fully GMP (Good Manufacturing Practice) certified, which is a significant drawback for a scheme that requires laboratories to prove the safety and efficacy of new drugs.

"GMP is the first floor of the building and the second is bioequivalence. Obviously we are not going to prescribe medicines that are bioequivalent if they don't also demonstrate good practices," says Paris.

This concern is shared by Pfizer Chile's general manager, Mónica Zerpa. "Our main concern with this policy is how bioequivalence will meet international pharmaceutical standards and that laboratories do not cut corners for a faster compliance with basic requirements."

Many choose to see a silver lining, however. With an increased focus on the manufacture and certification of bioequivalent drugs, the ISP may be forced to scrutinize manufacturing practices more closely.

"The whole bioequivalency program is a safety step," says the WHO's Fukuda. "This entire effort is really to increase scrutiny and ensure both the quality and the safety of the drugs being use."

Culturally as well the Ministry's policies to increase access could risk doing more harm than good. These plans, which consist of increasing the number of 24/7 pharmacies and introducing a fleet of mobile pharmacies, also include a bill to legalize the sale of drugs in places like supermarkets – a bill denounced by Rojas as "criminal".

Mañalich says the bill would improve access, especially in the 50 of Chile's 320 municipalities that don't have a single pharmacy, but Rojas is against the idea of selling medicines "like candy" in places other than pharmacies. He cites the example of Argentina which tried something similar in 1991, only to reverse the decision almost two decades later following problems with self-medication.

One of the fears of making drugs available in every corner store, even seemingly mild ones like paracetamol – a drug that incidentally kills around 900 Chileans a year – is that levels of public awareness about medicine are not yet sufficiently developed.

"The benefit of pharmacies is that advice is free and you won't get that in an ordinary shop," says Rojas.

Bioequivalence is about improving access to pharmaceutical drugs, a grueling and lengthy process of testing and certification, but one that opens up more affordable options for the patient. As with many scientific and social advances, changes such as this one often prompt more questions than they answer, but if done properly Chileans will finally be able to afford something money supposedly cannot buy – health. bUSiness CHILE

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