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Japanese Wholesalers Challenged as Generics Gain Ground

(Source: An article prepared by Masayuki Yasuda and Published by Pharma Japan)

The Japanese government approved its economic and fiscal policy guidelines in June, calling for increasing the rate of generic penetration in Japan to 70% on a volume basis by mid-2017, and to 80% at the earliest possible date between April 2018 and March 2021. As this will certainly speed up the market's shift to generics in the coming years, both original and generic drug makers are bracing for the huge impacts the 80% target will have on their businesses, but drug wholesalers are the most concerned of all.

In recent years, wholesalers have been taking a hit from what they call a "category change," which means a shift in the ethical drug market from long-listed drugs, or off-patent original medicines, to generics and drugs receiving the premium for new drug development and elimination of off-label use. Up to now, long-listed drugs have been the biggest moneymaker for wholesalers due to their high profit margins. However, with the rise of generics and premium-granted products, which resulted in decreased revenues from long-listed drugs, wholesalers have lost this mainstay and their earnings have deteriorated.

The decline of long-listed drugs is clear from the figures announced by Medipal Holdings (combined results for Mediceo, Everlth, and Atol) and Toho Holdings (pharmaceutical wholesale business), both of which announce sales in each ethical drug category. For the fiscal year ended March 2014, long-listed drugs and generics respectively accounted for 32.7% and 7.9% of Medipal's sales and for 35.0% and 8.9% of Toho's sales. However, the category shift that was already underway suddenly accelerated since a number of government measures to actively promote generics, including incentives for DPC hospitals, were introduced in April 2014. For the fiscal year ended March 2015, the sales ratio for long-listed drugs fell below 30% at both Medipal and Toho, with long-listed drugs and generics respectively constituting 29.2% and 9.4% at Medipal and 28.4% and 9.9% at Toho. Generics are expected to represent over 10% of their sales in the current fiscal year ending March 2016.

Sliding revenues from long-listed drugs have arguably hurt wholesalers, but growth in sales of generics should not be a bad thing in itself. The problem is the low prices of generics and the high cost of distributing so many brands. First generics generally receive NHI prices that are 60% those of the original products, but this is reduced to 50% if 10 or more products of the same active pharmaceutical ingredients, dosage forms, and specifications are listed together. As a result, most first generics of major products receive NHI prices that are only 50% those of the original products. Since these generics start out with low NHI prices, wholesalers' sales and profit margins fall when they replace long-listed products. A final blow is the intense price competition.

Adding to this predicament is a serious inventory issue. According to a distribution manager at one multiregional wholesaler, the number of products increases by an average of 15 to 20 each time generics of an original product are launched. Due to the recent increase in their product volumes, generics account for roughly half of inventory at distribution centers despite

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In Brief . . .

- The consolidated net sales of the **Galenica Group** rose by 7.9% to CHF 1.8 billion / US$1.9 billion in the first half of 2015. On a comparable basis (without currency exchange losses and accounting components of IAS 19) net profit before deduction of minority interests rose by 13.8% to CHF 170.2 million / US$178.3 million and net profit after deduction of minority interests increased by 6.4% to CHF 143.2 million / US$150 million. On 1 September 2015, **Galenica Santé** – the Group's pharmacy, logistics and healthcare information business - will introduce a new organizational and management structure with three Business sectors: Products & Brands, Retail and Services.
- **Toho Pharmaceuticals** (Japan) reported a 4.9% increase in net sales to ¥295,159 million / US$2.46 billion and ordinary income of ¥4,309 million / US$35.9 million for its fiscal 1st quarter ended June 30th.
- **IMS Health** has launched *IMS Health Insights* — a free application that delivers the company's extensive thought leadership materials from 19 major countries directly to Apple and Android tablet devices. The IMS Health Insights app can be downloaded via the Apple iTunes store for iPads as well as Google Play for Android devices.
- **Shire** (UK) has made a US$30 billion / £19 billion takeover bid for rare-disease specialist **Baxalta** (US).

Dr Reddy's Laboratories is to market and distribute 3 Amgen therapies – including *Repatha* (evolocumab), *Kyprolis* (carfilzomib) and *Blincyto* (blinatumomab) – on the Indian market. Dr. Reddy's will provide a "full range" of regulatory and commercial services to seek approval and launch the products in India. No indication of potential pricing plans was provided.

- **Pfizer Inc.'s** acquisition of injectables and biosimilar specialist **Hospira Inc.** has received US competition authorities' approval, with stipulations that certain sterile injectable assets be divested. Pfizer said the takeover will close in early September, seven months after it initially agreed to a price with Hospira of US$17 billion-which valued Hospira at US$90 per share.
- Korean pharmaceutical companies are gaining international recognition for their drug development capabilities and partnering with a growing number of internationally renowned drug manufacturers to better export their newly developed drugs. As an example, **Hanmi Pharmaceutical** signed an exclusive US$730 million agreement with **Boehringer Ingelheim** to sell the development and global commercialization rights to its 3rd-generation lung cancer treatment drug and signed a similar deal (valued at approximately US$690 million) will Eli Lilly for an autoimmune disease therapy still in Phase II trials.

(Sources: Galenica, IMS, Korea Herald, Scrip, The Guardian and Toho)

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their sales ratio of less than 10%. Drug wholesalers have selected "recommended generic makers" and are taking steps to encourage pharmacies to adopt their products, but the results have been disappointing. The sense of crisis wholesalers are feeling is strongly expressed in a petition the Federation of Japan Pharmaceutical Wholesalers Association submitted to the Ministry of Health, Labor and Welfare's Ryukaikon council for the improvement of ethical drug distribution in June. Among other things, the petition calls for the enforcement of generic-name prescribing and steps to curb co-development, which has led to an increase in the number of products. In addition, it points out the "extreme price competition being seen among some products." An official at one regional wholesaler warns, "If the number of generics continues to rise at the current rate, drug wholesalers will be the one to take the biggest hit. Measures of some sort need to be taken with respect to generics."

The government's new target ensures that generics' inroads will continue to gather pace. If wholesalers are to make a profit under their current business model, it may be necessary to create a system that allows wholesalers to receive fees from generic makers or to address the problem of negative primary sales margins (wholesalers' losses on sales without factoring in rebates and allowances), an unresolved issue in distribution reform. If they opt to adopt new business models, wholesalers will have to strengthen their initiatives in the field of nursing in the context of the regional comprehensive care system and reinforce their overseas operations.

Drug wholesalers have been buffeted by changes in the market environment for some time, but an increase in generic drug volume is likely to cause an even greater upheaval. The author concludes that the time is coming when wholesalers will have to choose either to muster the determination to raise profits within their existing business models or adopt new business models that leverage their core competencies.

Drug Regulatory Changes in Russia

(Sources: An article prepared by Ian Schofield and published by Scrip; Baker & McKenzie)

Pharma firms in Russia are facing major regulatory changes and new legal responsibilities despite a last minute attempt by the authorities to postpone the provisions until next year to allow more time to prepare for their introduction. Among the measures are shorter approval times for new medicines, and new rules on biologics, pharmacovigilance and product interchangeability.

The measures were approved last December in the form of legislation amending the existing federal law on the circulation of medicines in order to rectify a number of inconsistencies and shortcomings in the law. Most of the measures were scheduled to come into effect on 1 July this year, while others, such as those on the data exclusivity period and the format of the drug registration dossier, were slated to apply from January 2016. However, as the July deadline approached the Russian authorities tried unsuccessfully to push through legislation postponing the implementation of all the measures until January 2016.

According to Baker & McKenzie in Moscow, there has been no official explanation for this effort, but it would appear the authorities were not ready for the implementation of these measures and felt they needed time to put the necessary infrastructure in place. The fact that the provisions did come into effect as scheduled may cause some problems with their implementation. For multinational companies, from a compliance standpoint, they will have to ensure they are following the new law, but in terms of the implementation of the legislation it will be most likely somewhat chaotic for the rest of the year.

The key changes under the December 2014 law (No 429FZ):

- As of 1 July the timeframe for registration of medicines has been cut from 210 to 160 business days. However, the expedited registration process timeline has been increased from 60 to 80 days. The reason for this is that whereas the expedited procedure originally applied only to generic products, it has now been extended to orphan and pediatric drugs. In the case of generics, the procedure will only be open to the first three generic versions of a given reference drug, with any subsequent generics being subject to the standard assessment period; It will not apply to biosimilars.
- The clinical trials process has now been fully separated from the drug approval procedure.
- A new definition of the owner or holder of the registration certificate (marketing authorization holder) has been introduced, together with new legal responsibilities. This is seen as a significant move because the holder of the certificate will now be expressly responsible for the quality, safety and efficacy of the medicine, and will have to implement a pharmacovigilance system and ensure it works properly. The holder will also have to submit safety monitoring reports to the competent state authority once every six months for the first two years after approval, once a year for the following three years, and then once every five years. Failure to take steps to ensure the safety of medicines may result in the registration being cancelled. The move also means that the transfer of marketing authorizations among companies will take on added legal significance.
- Under the law a statutory basis is given to the concept of interchangeability among products, which is defined as "proven therapeutic equivalence or bioequivalence with respect to a reference drug, including an equivalent qualitative and quantitative composition of the active substances, the composition of excipients, the pharmaceutical form and the mode of administration." The main objectives of this change are to increase competition in the public procurement sector and keep down costs of medicine tenders by more clearly identifying which products can be used in place of others, and to help in the application of competition law. Interchangeability of a particular product will be determined by an expert committee, as part of the state registration process.

Also introduced is a legal definition of a "biological medicinal product" and a "biosimilar". This provision also states that biosimilars cannot be approved on the basis of just a bioequivalence study, and that some clinical trials will be necessary.

- The new law reintroduces the "grace period" regarding products whose registration dossier has been amended. Products manufactured within 180 days of such changes to the dossier in accordance with the "old" dossier can now remain on the market until their expiry date.
- With regard to the pricing of drugs on the vital and essential medicines list, the amendments have reduced the very detailed provisions and the law will now only provide a very general framework for the state regulation of prices, with detailed regulations to be adopted by the government. It is understood that the provision will require the health ministry to consider whether, in establishing prices, the interests of consumers are properly

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balanced against those of the manufacturers.

- A new single "GxP" inspectorate is to be set up to oversee compliance with Russian good practices, including the conduct of Good Manufacturing Practices (GMP) compliance audits of foreign manufacturing sites. The law introduces more circumstances in which a product's registration can be cancelled: for example if it is not marketed for three or more years, or if the company refuses to amend the use instructions where there is newly confirmed data showing that the risk outweighs the benefit.

The Pharmacist's Role in Diabetes Care

(Source: Edited excerpt from an article prepared by Jay Gitomer and published by Zuellig Pharma)

Diabetes is a growing threat to the health of populations around the world. In 2013, the number of diagnosed diabetics globally reached 382 million, a prevalence of 8.3% of the world's population. Asia is particularly impacted by the disease with Asian countries contributing more than 60% of the world's diabetic population, as Southeast Asia and the Western Pacific are home to 213 million diabetics – one in 12 of their adult populations. China alone contains a quarter of the world's diabetic population, and half of its population is pre-diabetic. The outlook is for an increase in these numbers and by 2035 the diabetic population in Southeast Asia and the Western Pacific is expected to reach 325 million (+53%).

The critical medical and healthcare needs of diabetic patients are many, but the most fundamental need is education. Patients need to learn to manage the disease, as outcomes rely heavily on a clear understanding of the consequences of non-adherence to their care plan, but they cannot manage their health alone. Nevertheless patients need to adhere to their medication schedule, measure and track blood sugar levels, and administer insulin injections. Understanding how to manage daily self-care activities can be difficult though and these patients often need both support and assistance.

Diabetes treatment is complicated. It requires a healthcare team that includes at least one professional who is aware of all treatment efforts, a registered dietitian, an exercise professional, and possibly endocrinologists as well as an ophthalmologist or optometrist. A pharmacist plays an important role in the care of a diabetic patient and today can and does do more than simply fill prescriptions. Those who are trained well are highly qualified professionals who maintain a profile on each patient that enables them to track the various medications a patient may be taking, educate the patient on possible drug interactions between prescriptions, and warn the patient about the side effects of existing and new prescriptions. Pharmacists are also capable of doing eye and other diagnostic tests required under a patients care plan and support drug adherence, one of the top challenges in managing diabetes.

Today, community pharmacists increasingly play a critical role in diabetes care and adherence. The reasons for this evolution are multiple: Diabetes patients may see their doctor only a few times a year; Visits to the doctor can be hard to schedule or costly, and some patients have a general reluctance to enter a medical office; Pharmacists are easier to access - patients can walk into a local pharmacy and talk to a pharmacist without having to wait weeks for an appointment or spend a morning in a waiting room; and Patients tend to trust their pharmacists and they are perceived as approachable and knowledgeable.

Patients are not the only ones who recognize the benefits that a pharmacist can provide in the treatment of diabetes. Increasingly, healthcare organizations use pharmacists to assist in the monitoring and management of patients with diabetes. Pharmacists themselves are also stepping up to help their patients improve self-care practices. Pharmacies can benefit from running diabetic care programs, either by becoming eligible for government funding or simply by increasing foot traffic into their businesses and thereby growing their sales of non-medical products.

Best practices for pharmacies offering diabetes care include a clinical protocol, access to an integrated team of healthcare professionals, specific and up-to-date knowledge of diabetes care, and auditing and evaluation procedures. A pharmacy offering such care should also be easily accessible to patients and provide payment options that make the care affordable.

Some examples of pharmacy diabetes programs include a health resource center in a US chain's retail outlets where each center offers health information, monitoring services, wellness classes, and referrals to local health resources. Another chain pharmacy has teamed up with a diabetes center to deliver diabetes care across all of its consumer channels, including its nationwide network of pharmacies. In the UK, a chain pharmacy offers in-store risk assessments for Type 2 diabetes which consists of a series of questions based on risk factors, as well as body measurements and body mass index (BMI) calculations. A Singapore pharmacy chain now offers monitoring and counseling, goal-setting, and medication management programs for its diabetic patients.

Adoption of technology is another tool used by pharmacies in providing diabetic care. For example, the US chain, CVS, offers a software app that provides enhanced prescription management tools, as well as discounts on diabetes-related products. Walgreens has a registration enabled site that helps users track their nutrition and medications. Other sources of help in managing diabetes are also available on the internet.

The role of governments and manufacturers are essential in managing this growing healthcare challenge. However, the role of pharmaceutical wholesaler/retailer/service providers cannot be underestimated. With scope of scale it has the opportunity to serve as an integrator of services to include education, technology, manufacturer and government programs, and that of professional and diabetes societies.