HONG KONG PHARMACEUTICAL JOURNAL

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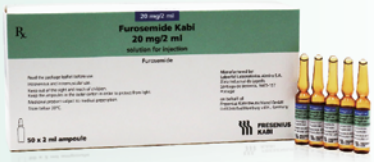

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INSTRUCTIONS FOR AUTHORS

The Hong Kong Pharmaceutical Journal is a journal of the pharmacists, for the pharmacists and by the pharmacists. Submissions are welcome for the following sections:

- Pharmacy Education & Practice
- Drugs & Therapeutics
- Primary Care
- OTC & Health
- Pharmaceutical Techniques & Technology
- Medication Safety
- Herbal Medicines & Nutraceuticals
- Society Activities
- New Products

Comments on any aspects of the profession are also welcome as Letter to the Editor.

There is no restriction on the length of the articles to be submitted. They can be written in English or Chinese. The Editorial Committee may make editorial changes to the articles but major amendments will be communicated with the authors prior to publishing.

It is preferable to have original articles submitted as an electronic file, in Microsoft Word, typed in Arial 9pt. Files can be sent to the following address:

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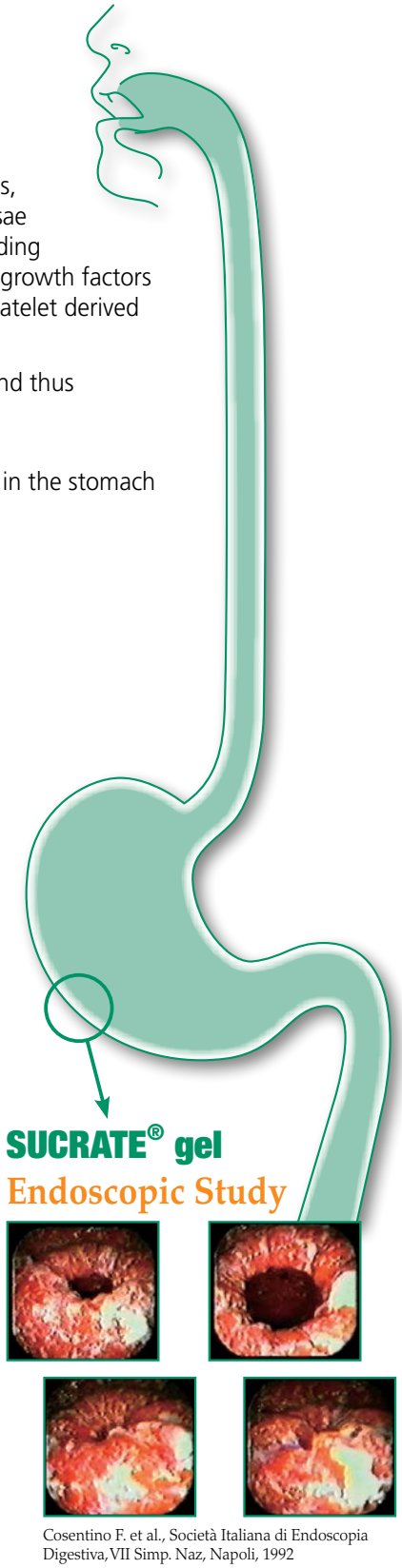

Cosentino F. et al., Società Italiana di Endoscopia Digestiva, VII Simp. Naz, Napoli, 1992

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Continue to fight the Covid 19 Virus and new frontiers for pharmacists

The emergence of Omicron variant Covid-19 poses new risks to Hong Kong. In response to the threat of an outbreak of Omicron variant, restrictions on travel and social activity have been tightened. This variant, compared to the original virus and the Delta variant, replicates faster and is highly transmissible. Although people who are fully vaccinated against Covid-19 may still be infected, vaccination still remain the best public health measure to combat the infections. Together with proper personnel hygiene and wearing of face masks, let's hope that life can get back to normal as soon as possible.

In this issue, an article written by AU-YEUNG, Gordon Tsz Fung; HO, Justin Chun-Ting; CHOI, Angus Yiu-Ting and CHONG, Donald Wing-Kit (page 87) interviewed Mr. Cheng Wai Chung ("Chung"), a graduate from The University of Hong Kong, who is now working as an non-governmental organizations (NGO) pharmacist at Lok Sin Tong (LST). In this article, Chung explains the service model and development of LST and shares his journey in becoming an NGO pharmacist. In addition, he describes some challenges he encountered at work and provides suggestions to our Pharmacy students or graduates.

Drug reclassification, as stated in the article on "Overview of Worldwide Drug Reclassification Policy" written by CHAN, Philip Pan; LI, Johnny Chun Wing and CHONG, Donald Wing-Kit (page 92), is a process of changing the legal classification of a medication. This article provides an overview of drug reclassification guidelines/policies established across the globe, the implications of drug reclassification to public health, the current process in Hong Kong as well as the roles of pharmacists in reclassification. There is no doubt that drug reclassification can improve access to medication and reduce healthcare burden. Yet, concerns of the reclassification cannot be neglected. Misuse or abuse of medications, reduced opportunistic screening and delayed diagnosis may happen. Pharmacists can play a key role in the process of drug reclassification and promote the safe use of reclassified medications.

The article on "Survey of Physicians' Perceptions on the Use of Oral Anticoagulants among Patients with Atrial Fibrillation" (page 99) written by NG, Vanessa WS *et al.*, reports the attitudes and perceptions of local physicians on the barriers to prescribing oral anticoagulants (OACs) to patients with atrial fibrillation (AF). Under-prescribing of OACs among patients with AF is common and the findings of this article echoed such behavior. It also identifies some potential barriers (e.g. insufficient counseling time, over-worrying about the occurrence of adverse events) and highlights the importance of better communication between patients and healthcare professionals.

I hope you enjoy reading this issue. As always, you may provide suggestions and give feedbacks on any aspect of the Journal by contacting me or other members of the Editorial Committee.

May PS Lam
Editor-in-Chief
9 January 2022

Prepared by Branson Fok and Chloe Ip

Ticagrelor versus Clopidogrel in CYP2C19 Loss-of-Function Carriers with Stroke or TIA

Date: October 28, 2021

Clopidogrel is a prodrug requiring conversion into active metabolite by hepatic CYP450 enzymes. It has shown less effectiveness for the secondary prevention of stroke in carriers of CYP2C19 loss-of-function alleles, which are present in 60% of Asian patients.

A randomized, double-blind, placebo-controlled trial at 202 centres in China involving patients with a minor ischemic stroke or transient ischemic attack (TIA) who carried CYP2C19 loss-of-function alleles. Patients were assigned in a 1:1 ratio, to receive ticagrelor (180mg on day 1 followed by 90 mg twice daily on days 2 through 90) and placebo clopidogrel or to receive clopidogrel (300 mg on day 1 followed by 75 mg once daily on days 2 through 90) and placebo ticagrelor; both groups received aspirin for 21 days. Primary efficacy outcome was new stroke and primary safety outcome was severe or moderate bleeding, both within 90 days.

11,255 patients were screened and 6,412 patients were enrolled, with 3,205 and 3,207 assigned to ticagrelor and clopidogrel groups respectively. The median age of the patients was 64.8 years, and 33.8% were women; 98.0% belonged to the Han Chinese ethnic group.

Within the 90 days, stroke occurred in 191 patients (6.0%) and 243 patients (7.6%) in the ticagrelor and clopidogrel groups respectively (hazard ratio, 0.77; 95% confidence interval, 0.64 to 0.94; P=0.008). Severe or moderate bleeding occurred in 9 patients (0.3%) and 11 patients (0.3%); bleeding events of any severity occurred in 170 patients (5.3%) and 80 patients (2.5%) in the ticagrelor and clopidogrel groups respectively.

In conclusion, Chinese patients with minor ischemic stroke or TIA who were carriers of CYP2C19 loss-of-function alleles, had a modestly lower risk of stroke at 90 days with ticagrelor than with clopidogrel. The risk of moderate-to-severe bleeding did not differ between the two treatment groups, but ticagrelor was associated with more total bleeding events than clopidogrel.

Source: www.nejm.org

FDA Authorizes Pfizer-BioNTech COVID-19 Vaccine for Emergency Use in Children 5 through 11 Years of Age

Date: October 29, 2021

The U.S. Food and Drug Administration (FDA) has authorized the emergency use (EUA) of Pfizer-BioNTech COVID-19 Vaccine for the prevention of COVID-19 to include children 5 through 11 years of age. The vaccine for this age group is administered as a two-dose primary series, 3 weeks apart using a lower dose of 10 microgram (mcg) than that used for individuals 12 years and above (30 mcg).

Effectiveness data to support the EUA was based on an ongoing randomized, placebo-controlled study that has enrolled approximately 4,700 children 5 through 11 years of age. The study is being conducted in the U.S., Finland, Poland and Spain. Children in the vaccine group received two doses of the Pfizer-BioNTech COVID-19 Vaccine containing 10 mcg of messenger RNA per dose. The FDA compared the immune response of 264 participants from this study to 253 participants 16 through 25 years of age who had two 30 mcg of mRNA vaccine doses. The immune responses of children 5 through 11 years of age were comparable to those individuals 16 through 25 years of age.

Additionally, the vaccine was found to be 90.7% effective in preventing COVID-19 among children 5 through 11. The FDA determined the vaccine effectiveness after conducting a preliminary analysis of cases of COVID-19 occurring seven days after the second dose. The analysis included 1,305 vaccine recipients and 663 placebo recipients who did not have evidence of prior infection with SARS-CoV-2.

Safety data included approximately 3,100 vaccinated children aged 5 through 11 from the ongoing study. Commonly reported side effects included injection site pain, fever, fatigue, headache and more. Side effects were generally mild to moderate in severity and occurred within two days after vaccination. Most were transient and went away within one to two days. No serious side effects have been detected.

Source: www.fda.gov

FDA Approves First Drug to Improve Growth in Children with Dwarfism

Date: Nov 19, 2021

The United States Food and Drug Administration (FDA) has announced its approval to Voxzogo (vosoritide) injection for improving growth in children aged at least 5 years old with achondroplasia and open epiphyses.

Achondroplasia is a genetic disorder that causes children to have disproportionate growth and short heights with an average of approximately four feet, which has affected more than 10,000 children in the United States. This is owing to a gene mutation on fibroblast growth factor receptor 3 which is responsible for growth regulation. The overactivity of the gene results in inhibition of normal bone growth. Vosoritide binds to natriuretic peptide receptor-B for inhibiting the activity of the growth regulation gene and thus stimulating bone growth.

The safety and efficacy of Voxzogo were proved in a double-blind, placebo-controlled, phase 3 study that recruited 121 participants with 5 years of age and older with achondroplasia and who have open epiphyses indicating the potential of further bone development. In the study, participants were randomly assigned to receive Voxzogo subcutaneous injections or placebo and had their annualized growth velocity measured at the end of the year. Results of the study showed that participants who received Voxzogo injections had an average of 1.57 centimetres taller in height comparing to the placebo group. The common side effects of Voxzogo include injection site reactions, vomiting as well as hypotension, which was also indicated in the labeling as a warning and precaution.

Voxzogo was approved under the accelerated approval pathway which allows an earlier approval of drugs for treatment of serious conditions like dwarfism and fulfil unmet medical need. The manufacturer, BioMarin, will have to conduct a post-marketing study assessing the final adult height after treatment of vosoritide injection as a condition of this accelerated approval.

Source: www.fda.gov

Serving the Community as an NGO Pharmacist in Lok Sin Tong - Interview with Mr. Cheng Wai Chung

AU-YEUNG, Gordon Tsz Fung[a]; HO, Justin Chun-Ting[a]; CHOI, Angus Yiu-Ting[a]; CHONG, Donald Wing-Kit[a]*

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*(*Corresponding author)*

ABSTRACT

The Lok Sin Tong Benevolent Society, Kowloon (LST) is one of the few local non-governmental organizations (NGO) providing community pharmaceutical service. Initially solely enrolled in a government scheme to collaborate with visiting medical officers (VMO) to provide residential care homes (RCH) healthcare services, Lok Sin Tong Community Pharmacy Services (LSTCPS) has also been providing affordable, accessible and quality pharmaceutical services to the public since 2020 through its team of dedicated community pharmacists. Recently, another LSTCPS pharmacy has begun operation in Prince Edward, broadening its patient reach and service scope.

In this issue, we interviewed Mr. Cheng Wai Chung, a passionate community pharmacist and the Head of Pharmacy Services at LSTCPS, about its service model and development. He also shared his journey in becoming an NGO pharmacist and his view on the post-COVID-19 landscape of the pharmacy profession.

Keywords: *Lok Sin Tong Community Pharmacy Services, Community Pharmacist, Non-Governmental Organization, Primary Care, Affordability, Accessibility*

INTRODUCTION TO THE LOK SIN TONG AND LOK SIN TONG COMMUNITY PHARMACY SERVICES

The Lok Sin Tong Benevolent Society, Kowloon, commonly known as Lok Sin Tong (LST), was established as a charitable organization in the late-19th century. Even before its official registration, LST had been providing free medical services to the needy as a regional volunteer group. Gradually, they would expand their services to cover education, social welfare and a multitude of medical services while sponsoring numerous other community projects. With a growing demand for healthcare services, LST is expanding its footstep via a variety of community and corporate health promotional programmes, including smoking cessation programmes and outreach health services.

In establishing its first community pharmacy in Kowloon City in 2019, LST has become one of the few local non-governmental organizations (NGO) to provide community pharmaceutical service. Initially set up to solely collaborate with visiting medical officers (VMOs) to provide residential care homes (RCH) healthcare services in a government scheme, Lok Sin Tong Community Pharmacy Services (LSTCPS) has also been providing affordable, accessible and quality pharmaceutical services to the public since 2020. LSTCPS is managed by a team of dedicated community pharmacists, including Mr. Cheng Wai Chung, its Head of Pharmacy Services, with the ultimate goal of strengthening primary care. As a testimony to their successful sustainable, non-profit and patient-oriented service model, a second community pharmacy was opened in Prince Edward in late 2021, furthering its patient reach and ability to provide an even more diverse set of services.

INTRODUCTION TO MR. CHENG WAI CHUNG

Figure 1. Portrait of Mr. Cheng Wai Chung. *Mr. Cheng is currently the Head of Pharmacy Services of LSTCPS.*

After graduating from The University of Hong Kong (HKU) with a Bachelor of Pharmacy in 2015, Mr. Cheng became a pharmacy intern in the Queen Mary Hospital and Watson's The Chemist. Upon the end of the internship, he first worked as a community pharmacist in Watson's The Chemist for more than 3 years, before joining LSTCPS with a vision to promote and expand the role of pharmacists in the community. During this time, he also attained a Master of Public Health and a Master of Social Science, Behavioural Health at HKU, while actively involving himself in the development of the pharmacy profession outside his job, being a founding committee member of Pharmacists Connect, an association of young pharmacists.

INTERVIEW WITH MR. CHEUNG WAI CHUNG

PJ: Why did you choose to pursue a career in LST?

Studying the Master of Public Health at HKU after my graduation, I had the opportunity to connect with different NGOs who are planning on setting up community pharmacy services, which stimulated my interest in becoming an NGO pharmacist.

I was greatly impressed by the high level of autonomy offered by LST to develop new services based on patients' needs. Having familiarized myself with patient counselling and other frontline duties at chain community pharmacies, I have been longing to take on more goal setting and strategic planning roles, which were plentiful in LSTCPS. The shift in responsibility can be challenging yet deeply rewarding. Similarly, being more involved in decision-making in LSTCPS means I can better align our overall development with my vision of promoting the role of pharmacists and establishing a professional image among the public. Exploring all these uncharted territories helps me expand my skillsets and gain a deeper understanding of how our profession can contribute to society.

PJ: What is the vision of LSTCPS?

Our vision is to enhance health and medication access, improve health literacy and awareness in the general public, promote the roles of community pharmacists in primary care and provide training for the pharmacy industry to aid continuous future development.

First, we provide affordable medications to all members of the public with pharmaceutical care to ensure that even people with limited financial capability can acquire medication necessary for the management of chronic disease without sacrificing other aspects of livelihood, recognizing the cost of SFI has long been a burden for many patients and their families. We achieved this mostly via a mix of brand drug discount programmes and advocation of generic substitution. In addition, we pride ourselves on offering detailed counselling and second opinion, understanding that patients often cannot receive comprehensive information in public institutions due to limited time.

Second, we aim to help the public achieve a better quality of life by raising their health literacy and awareness. Both can help promote medication adherence and a healthy lifestyle, which are crucial in disease prevention and treatment. We engage the public via various approaches and platforms. Other than face-to-face consultation, education materials are regularly published on our Facebook page.

Third, we hope to increase usage and understanding of community pharmacist services via active contact with the public. For instance, we are well-positioned to serve as the first point of contact for patients for free consultation and medications for symptomatic relief. By guiding patients in minor ailments management and offering medical devices, we promote self-care, an important component of primary care.

Fourth, we support continuous education of community pharmacists and pharmacy students. Other than encouraging sharing of experience and collaborative decision-making among pharmacists, we offered clerkship and volunteering positions for pharmacy students. They are welcome to take on different roles under supervision and join study groups hosted by our pharmacists.

PJ: What is the daily routine of LSTCPS?

When I first joined LSTCPS, we mainly collaborated with VMOs on providing service for RCHs. Whilst VMOs diagnosed and prescribed medications for sub-acute disease management, we provided centralized drug dispensing. Throughout the dispensing process, pharmacists verified the prescriptions against medication errors to ensure patient safety and provide drug information whenever there are enquiries from prescribers. Afterwards, medications are delivered to RCHs directly. This operation model separating prescribing and dispensing has some unique advantages over other outreach physician programmes. VMOs do not have to limit their choices to the few medications carried with them to the RCHs and can select from a far more comprehensive drug formulary. Moreover, as physicians only need to concern themselves with diagnosis and prescribing, the overall process is more efficient and more patients can benefit from the service. On the other hand, our formulary is actively managed by pharmacists. Adjustments are made according to physician needs and pharmacists' recommendations. As medication experts, we hope to promote evidence-based drug use by modifying our formulary.

In 2020, we began launching several services to the public as well. We provide prescription medications from reputable manufacturers to all patients with eligible prescriptions at a nominal price in the hope of relieving their financial burden. Supplying medication aside, detailed counselling on medications and lifestyle modification are provided to optimize overall disease management. We use a combination of face-to-face interactions, hotline and instant messaging apps for this purpose. By raising their health literacy, we hope that their adherence will be improved, and medication safety can be ensured. Moreover, we give second opinions to patients to educate them on the rationale behind various treatment options to improve medication adherence, especially since the many burdens on our public healthcare system often create time constraints impeding comprehensive patient counselling.

Apart from the above services, we provide free consultations to all customers and perform preliminary differential diagnoses for minor ailment management. For episodic illnesses such as common cold, gastrointestinal discomfort and eczema, appropriate medications are dispensed directly if indicated and professional advice will be provided. If we identify severe

conditions, patients will be referred to physicians for further diagnosis and treatment.

Empowering patients to better manage their health via self-care is yet another key objective. Other than education, we achieve this via the provision of compliance aids and medical devices, from pill cutters and pillboxes to blood pressure monitors and compression stockings. Since last year, a trade-in programme has been set up to let patients acquire blood glucose meters with up-to-date accuracy standards at virtually no cost, improving their ability in managing their chronic diseases.

Additionally, our pharmacists operate beyond the boundaries of our pharmacy to support LST-operated District Health Centre (DHC) Expresses in Yau Tsim Mong and Kowloon City. Funded by the government, DHC Expresses leverage on private healthcare networks in the community to enable members of the public to receive necessary care and services as part of a prevention-focused healthcare system. Our pharmacists are involved in services as diverse as providing talks on various health issues and medication review. In the future, we expect our roles to grow further as the DHC Expresses evolve into full-fledged DHC.

PJ: What makes the operation model of LSTCPS unique?

First, we go to great lengths to provide affordable medications to the general populace by keeping medication costs low. For brand medications, our pharmacists liaised with pharmaceutical companies to provide patient assistance programmes and discount schemes. Whenever the patent of a brand medication has expired and a stable source of supply from a reputable company can be identified, we strongly encourage generic substitution to patients and doctors alike, recognizing that it lowers patents' financial burden without compromising the efficacy, safety and quality of medications. We customize letters guiding willing physicians to allow for generic substitution directly when writing prescriptions for individual patients. We believe that the extra steps we took to advocate for substitution were well-worth it for patients and their families.

Our second advantage is the accessibility of our service. To enjoy our service, patients need not make appointments or go through financial tests. Our medication dispensing service is open to both patients with public or private prescriptions. For those with enquiries, our pharmacists can be easily reached via hotline, instant messaging apps, social media and email, and we are more than willing to provide consultation over the phone. In addition, our pharmacy is staffed by at least one pharmacist across all business hours, including lunch hours and whole Saturdays, so that patients can always receive quality pharmaceutical services whenever they visit, especially for those who work on workdays.

Another unique feature seldomly seen in community pharmacy is that we generally arrange multiple pharmacists to work together at any given time. This offers more chances for the junior pharmacists to observe the work of the more experienced pharmacists, and for them to complement one another in any shared decision-making processes. We can all learn at a faster rate. Of course, there is an additional benefit of having a larger team. Due to our sufficient manpower, we have implemented a five-day working week to offer our full-time colleagues a greater work-life balance.

PJ: How is LSTCPS organized and what are the roles of different employees?

Our workforce consists of the Head of Pharmacy Services, pharmacists, dispensers, part-time pharmacy assistants and student volunteers. In addition, a clerk and other colleagues from LST Medical Services Department often support our administrative work, while medication delivery to RCHs is handled by our delivery team.

My role as the Head of Pharmacy Services involves extensive decision-making and managing. By conceiving and pitching new projects to our superiors in LST, I set the development plan of LSTCPS. Changes in our operation model and allocation of manpower and resources to ensure smooth incorporation of new services are decided by me. Furthermore, I supervise the pharmacists in our daily operations.

Meanwhile, our pharmacists are responsible for all aspects of our daily operation and services, from verification of VMOs' prescription, SFI dispensing and counselling, to supporting LST-operated DHCE. Each full-time pharmacist oversees some specific development projects, such as our upcoming ambulatory care service. We once arranged locum pharmacists to support our operations when our full-time pharmacists are on leave. All pharmacists supervise our dispensers and students.

Pharmacy assistants and dispensers form another part of our workforce. Aside from full-time assistants, we have pharmacy students with long service records and exceptional performance serving as our part-time pharmacy assistants. In RCH service, they are responsible for screening prescriptions and contacting VMOs or RCH staff whenever clarification is warranted, dispensing medications and inventory management. In our services to the public, they answer patients' inquiries and provide counselling on prescription drugs and medical devices alike under pharmacists' supervision.

As part of our collaboration with the two local pharmacy schools, we have been offering clerkship and volunteering positions for pharmacy students in the past two years to let them experience a unique NGO practice model and gain hands-on experience in communicating with patients. Students are welcome to take part in a wide variety of activities according to their learning objectives, guided by our pharmacists. These range from dispensing medications to developing patient education materials and social media marketing campaigns. More senior students can counsel patients in prescription medication or make recommendations for minor ailments directly under supervision. To further

their knowledge and skills, we arrange for study groups involving case discussions and role-playing sessions as well as other on-the-job training.

PJ: How do you engage eligible patients for your service?

We look to different professionals involved in a patient journey as well as the patient and his/her caregivers for our service. In the upstream and midstream portion, we notify the public, private and LST doctors as well as para-medical staff working in hospitals of our services by sending them our electronic catalogues. Besides, we also maintain good relationships and an extensive network with all healthcare professionals and social workers we communicate with.

In the downstream, it is of utmost importance that we reach patients and their caregivers directly. Our strategy has evolved significantly over time. At the beginning of the pandemic, we secured sponsorship from different companies to offer surgical masks and other personal protective goods at a nominal fee with a quota for each participating individual in promotional campaigns. In return, we saw the subscription of our Facebook page rising, and participants got to know our services as they visited our pharmacy to collect the goods. As the pandemic winded down, we have been making even more extensive use of our website and social media. Our website provides a list of our medications, while we regularly publish education materials or host other promotional campaigns on Facebook. Instant messaging apps have also proved to be a valuable tool for us to resolve customer enquiries, provide follow-up information and maintain good relationships with patients, though the number of ongoing conversations can be overwhelming from time to time. Nonetheless, as we realize after our operation has taken off, it is the quality and impact of our pharmaceutical services and the word-of-mouth that truly attracts patients to come to and stick with us, which is why we are constantly adding to our service model.

PJ: What do you enjoy the most about working in LSTCPS?

First, with LST's support, I can transform my plans into actions and develop new pharmaceutical services for the public. In LSTCPS, our pharmacists have both the platform and the manpower to initiate projects for the sake of improving public health. The launching of our patient-orientated pharmaceutical service is one such example. We are now dispensing self-financed items (SFI) regularly under a model that involves deal-making with pharmaceutical companies and marketing. We also modify our operation model further to better suit our goal. One such modification is that we encourage generic substitution to keep medication costs at a minimum for patients. By also providing detailed counselling to raise the health literacy of patients, our multifactorial approaches help patients to cease choosing between medication and livelihood.

Another aspect I really enjoy in LSTCPS is that I can help train a new generation of pharmacists and pharmacy students. Since I am always working with more junior pharmacists in the pharmacy, I can directly share with them my relevant experience and lead them in decision-making processes. Our pharmacists also support and provide feedback to students concerning the way they carry out various assigned duties, such as patient counselling. It is very satisfying to see my fellow pharmacists and students grow in both knowledge and skills under our on-the-job guidance.

PJ: What were some challenges you encountered at work?

Greater autonomy comes with more responsibility. Unlike in a chain community pharmacy where many aspects of operations are handled by other departments, in LSTCPS, I developed our marketing, procurement and SFI dispensing model from scratch, a process that requires comprehensive planning, clear communication to colleagues and meticulous execution on a scale I hadn't encountered before.

As a decision-maker, timely response to the rapidly changing situation is yet another challenge. The unexpected outbreak of Coronavirus Disease (COVID-19) pandemic at a time when our SFI dispensing service has not been well known, necessitated a dramatic shift in our marketing plan. We scrapped the original plan of promoting our services by informing doctors in public hospitals in face-to-face meetings. Instead, we turned to securing sponsorship and offering surgical masks via Facebook promotional campaigns, attracting the attention of many people at a time when masks were in shortage.

Lastly, setting the price of the medications is another extremely challenging task. To ensure the sustainability of our pharmaceutical service, I have to balance the affordability of the medications and our operation cost. The difficulty is greatly compounded by the multitude of companies providing the same medication and non-transparent information regarding medication origin and drug cost. Our financial forecast is also impacted unexpectedly when supply proves unstable or when wholesale prices shifted without warning.

PJ: What does LSTCPS have in mind for the future?

As our pharmacy in Prince Edward comes into full operation, we are ready for a number of new initiatives.

First, our pharmacist-led ambulatory care service for diabetic patients on insulin will be launched. We expect to provide regular follow-up sessions, detailed review and counselling on medication use, blood glucose monitoring and lifestyle intervention. Our new private consultation room in Prince Edward will be used for this purpose. Having access to Electronic Health Record Sharing System (eHRSS), our pharmacists can offer more personalised recommendations based on

individuals medical and drug history. As a community pharmacy, we can directly offer necessary blood glucose self-monitoring products including test strips to patients, which in turn, will help us maintain our service in a self-sustaining manner. Our ultimate goal is to ensure medication safety and empower patients in the self-management of diabetes.

Our second plan aims to increase the transparency of our product pricing to both patients and healthcare professionals. To offer a clearer overview of our available medications, their prices, and the availability of various assistance schemes, we are revamping our website with the help of a third-party company. Eventually, our Chinese educational material will be hosted on the website alongside an eCommerce platform, transforming it into a one-stop purchasing and information centre. For eligible healthcare professionals, electronic catalogues will be sent with clearly listed prices.

Third, we look forward to medical-social collaboration initiatives outlined in the Chief Executive's 2021 Policy Address. According to the government's plan, DHC Express will gradually develop into DHC, with a potential enlargement of the scope of service. Our pharmacist team is expected to play an even greater role in supporting pharmaceutical services by LST-operated DHC in the future.

PJ: How can the pharmaceutical services in Hong Kong be improved?

First, in terms of training, I believe continuing education should be encouraged to equip pharmacists with updated pharmaceutical knowledge. As for pharmacy students, I am glad to observe that there are more and more opportunities for experiential learning in different sectors, allowing them to develop their soft skills early, while applying their knowledge. Second, the role of pharmacists should be promoted to reach a greater portion of the public. Many citizens still do not understand the role of pharmacists, resulting in the underutilization of pharmaceutical services provided by pharmacists in Hong Kong. Third, and most importantly, policy or systematic changes should be imposed. For example, Electronic Health Record Sharing System (eHRSS) and Public-Private Partnership (PPP) are significant changes expanding the role of pharmacists in the local healthcare system. It would be great if The Health Care Voucher Scheme could also cover pharmaceutical care services offered by pharmacists in the future.

PJ: As an enthusiastic pharmacist, what changes do you anticipate in our profession in the coming years?

Changes brought about by the COVID-19 pandemic will certainly have far-reaching implications for community pharmacy. The unprecedented scale of travel restrictions and a sharp decline in tourist number implies that many community pharmacies can no longer rely on retail sales of general goods to tourists. They must now look to offer sustainable healthcare services to the public. Even though these services do not directly generate revenue as lucrative, they can promote the role of community pharmacists to the public.

In addition, when NGOs get to recognize the contribution and roles of pharmacists, they will be more willing to establish pharmacies. When pharmacists are widely recognized as medication and health experts, their remuneration can be sustained by healthcare services rather than retail sales to tourists. NGO pharmacies, well-known for their social conscience and patient-orientated service, play an important role in achieving this goal. I hope to see that more NGO pharmacies will be set up in the future and more passionate pharmacists willing to accept new roles and take on new challenges in this sector.

PJ: What suggestions do you have for our Pharmacy students or graduates?

Try exposing yourselves to different sectors and don't limit yourselves to a single career option. This has always been one of the key messages in my own guest lectures to HKU and CUHK pharmacy students. Pharmacy in Hong Kong is developing in a dynamic fashion, and we all need to adapt and diversify, leading to multiple career paths. Another message I have is that soft skills are just as important as knowledge, so don't just focus on studying, but actively step out of your comfort zone and treasure all internship and volunteering opportunities.

"Work hard together for our profession and uphold our professionalism for a better tomorrow for all pharmacists!" has always been my motto in my career.

Figure 2. *Lok Sin Tong Community Pharmacy Services (LSTCPS) at Prince Edward.*

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Overview of Worldwide Drug Reclassification Policy

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ABSTRACT

"Drug Reclassification", also known as "Rx-to-OTC Switch", is a process of changing the legal classification of a medication. In view of the prevalence and indications for reclassification, international regulatory authorities have devised drug reclassification guidelines and policies to ensure a simple, speedy and transparent process.

This article will review the implications of drug reclassification to public health, the current process in Hong Kong and the role of pharmacists in reclassification. In addition, an overview of international drug reclassification policy will be provided to help inform the future development of relevant guidelines in Hong Kong.

Keywords: *Drug Reclassification, Rx-to-OTC Switch*

INTRODUCTION

"Drug Reclassification" is defined as a process of changing the legal classification of a medication. In some countries such as the United States, medications are only classified as "Prescription Only Medication" or "Over-the-Counter (OTC) Medication". Therefore, drug reclassification is also known as "Rx-to-OTC Switch".

However, one must not miscomprehend that drug reclassification is always about loosening the control on medications. In fact, it also allows restricting the access to certain drugs after considering various factors such as the risk of abuse and misuse and their severity.

When first approved, medications are usually restricted for use under medical supervision and are available only with prescription. As time goes by, experience is gained with use and evidence may emerge to suggest that the medication is safe for use without prescription control and/or medical supervision. Under these circumstances, the medication can be reclassified into pharmacy-only medicine or OTC medicine to allow better access by the general public.

Drug reclassification brings both positive and negative implication to the public health. According to an article published in the *Hong Kong Pharmaceutical Journal (HKPJ)* in 2018,[1] drug reclassification provides benefits to patients and countries, such avs greater accessibility of medications,[2-4] cost-savings for the healthcare system,[5,6] and other economic benefits.[7,8] On the other hand, it may increase the risk of errors in self-diagnosis[9] and self-medication by patients.[10] **(Table 1)**

Table 1: Summary of Impact of Drug Reclassification (Rx-to-OTC Switch)[1-10]

Positive Impact	Negative Impact
More rapid and convenient access to medications, facilitating quicker relief of disorder	Worsened patient outcome due to self-management
Cost-savings for the healthcare system	Misuse and noncompliance of OTC medications
Economic benefits (e.g. improve labor productivity by reducing absences from work due to physician visit)	Shift of healthcare costs from insurance companies to consumers
Increased profitability for pharmaceutical companies	

A NEW ERA OF INFORMATION ACCESSIBILITY

A survey conducted by the American Pharmaceutical Association in 1998 revealed that one third of consumers exceeded the maximum dose of OTC products. This casts doubt on consumers' ability to self-medicate safely.[10]

However, emergence of the internet has revolutionized the way information is shared and accessed. Access to and retrieval of health-related information is easier now than ever before. Although internet information may be unreliable, more trustworthy and recognized health information platforms such as WebMD in US, National Health Service (NHS) in UK and Dingxiang Yisheng (丁香醫生) in China have emerged to fill in the gaps. These sources help to increase the knowledge and competency of patients in making correct health-related decisions such as buying OTC products to treat minor ailments. With more trustworthy sources of information to support

patient self-care, it is an opportune time to review the current policies of drug reclassification in Hong Kong.

DRUG RECLASSIFICATION IN HONG KONG

In Hong Kong, Pharmacy and Poisons Board (PPB) Poisons Committee is responsible for the review of the classification of pharmaceutical products regulated under the Pharmacy and Poisons Regulations, while Hong Kong Department of Health provides professional executive support to PPB for handling drug-related regulatory affairs including drug reclassification application. Examples of successful reclassification in Hong Kong include Loratadine, Omeprazole, Ranitidine and Salbutamol.**(Table 2)**[11]

Table 2: Example of Successful Reclassification in Hong Kong[11]

Medication	OTC Status Requirements
Loratadine	**When contained in pharmaceutical products labelled for the relief of the symptoms of allergic rhinitis only**
Omeprazole	**Not for human parenteral administration except in mixture with insulin**
Ranitidine	**Not for human parenteral administration except in mixture with insulin**
Salbutamol	**When contained in aerosol dispensers**

However, no concrete drug reclassification guideline is currently available in Hong Kong, which may complicate the application process for both applicants and the Department of Health.

CURRENT DRUG RECLASSIFICATION ACROSS THE GLOBE

Some countries have already established relevant guidelines to facilitate the application and process of drug reclassification. They are similar in most criteria for application but differ in application procedures and requirements on safety data. It is beneficial to compare and contrast the various countries' guidelines as a reference for Hong Kong in developing a pragmatic drug reclassification process.

1. The United States (US)

In the US, medications are classified as either "Prescription Only" or "Over-the-Counter". However, some OTC medications may actually be available behind the counter due to other considerations. Examples include codeine to reduce the risk of abuse, emergency contraceptives for age verification and human insulin for its refrigerated storage requirements.[12]

In 1951, Durham-Humphrey amendments to the Food, Drug, and Cosmetic Act stated that in the absence of a medical need to restrict distribution, non-prescription availability is the default status for drug products regulated by the US Food and Drug Administration (FDA).[13]

To switch a drug product from Rx to OTC status, it must undergo the same process and fulfill the same requirements as New Drug Application (NDA) which is managed by the US FDA. The central issue of any Rx-to-OTC Switch is whether the drug product is safe and effective for OTC use. It requires consideration of consumers' ability to successfully self-recognize and self-treat a condition, particularly whether consumers understand product label uses, directions and warnings.[14]

Notably, everyone can submit a Citizen's Petition to FDA to switch a product from Rx to OTC status. However, NDA holders who developed the drug and have the most product information on hand are in the best position to determine whether and under what circumstances it would be appropriate to request a switch.[14]

There are 4 criteria for switching **(Table 3)**:

a) Safety and efficacy data for the original prescription drug;
b) Information on adverse events reported in association with prescription use of the drug;

Table 3. Criteria and Required Information in FDA Rx-to-OTC Switch Application[14]

Criteria	Question Concerns	Information Required
Safety and efficacy data for the original prescription drug	▪ Does the product have an acceptable safety and efficacy profile for the OTC setting, in the potential absence of a learned intermediary? ▪ Does the benefit of OTC availability of the proposed product outweigh the potential consequences of some consumers not complying with label directions and warnings or inappropriately self-selecting the product?	▪ **Safety and efficacy data**
Information on adverse events reported in association with prescription use of the drug	▪ Does the product have low potential for misuse and abuse?	▪ **Post-marketing safety surveillance and literature reports**
Consumer behavior	▪ Can the condition be adequately self-recognized? ▪ Can the consumer appropriately select and use the product in accordance with product labeling?	▪ **Label Comprehension Study** ▪ **Self-selection Study** ▪ **Actual Use Study** ▪ **Human Factors Study**
Information pertaining to OTC use in other countries	▪ N/A	▪ **N/A**

Table 4. Examples of Rx-to-OTC Switch in the US in 2020[15]				
Product	**Active Substance**	**Strength**	**Dosage Form**	**Indication**
Voltaren Arthritis Pain	Diclofenac sodium	1%	Gel	**Temporary relief of arthritis pain**
Pataday Twice Daily Relief	**Loratadine hydrochloride**	0.1%	Ophthalmic solution	**Temporary relief of itchy and red eyes due to pollen, ragweed, grass, animal hair, or dander**

c) Consumer behavior; and
d) Information pertaining to OTC use in other countries.

The US FDA is among the few regulatory authorities that deem consumer behavior crucial for switching, which is difficult to be quantified.

2. The United Kingdom (UK)

Unlike in the US, medicines are classified into "General Sale List (GSL)", "Pharmacy (P)" and "Prescription Only Medicine (POM)" in the UK.[16] Due to the flexibility in switching, the UK health authority, Medicines and Healthcare Products Regulatory Agency (MHRA), executes the Reclassification Policy instead of Rx-to-OTC Switch.

There are 3 types of reclassification, namely Major, Standard and Simple Applications, which are determined during the Scientific Advisory Meeting (SAM) between the MHRA and the applicant before application submission.

Reclassification process differs among the three types of reclassification. For example, Major Application requires referral to expert advice from different stakeholders such as therapeutic expertise and patient group and from the Commission on Human Medicines (CHM), while Standard and Simple Applications do not. Their features and timelines are summarized in **Table 5**.

The MHRA undertakes benefit-and-risk assessment on all reclassification application. All medication must be in prescription status if they present the below risk and whether they are classified into "GSL" or "P" depends on whether access to professional advice from pharmacist is required for safe use of the medicine:[17]

a) It is likely to present a direct or indirect danger to human health, even when used correctly, if used without medical supervision;
b) It is frequently and to a very wide extent used incorrectly, and as a result is likely to present a direct or indirect danger to human health;
c) It contains substances or preparations of substances of which the activity requires, or the side effects require, further investigation; and
d) It is normally prescribed by a doctor for parenteral administration (that is, by injection).

Compared to other countries, MHRA stands out for their focus on implementation and lifecycle

Table 5. Comparison of Different Reclassification Application in UK[17]			
Application Type	**Features**	**Timelines**	**Examples**
Major Application	▪ Must seek expert advice	Indicative timelines will be set during the scientific advisory meeting between MHRA and reclassification applicant.	**First in a new therapeutic category**
Standard Application	▪ Only applies to applications previously submitted as a Major application. (i.e. Conversion of Major Application into Standard Application) ▪ Seek expert advice when necessary	Indicative timelines will be set during the scientific advisory meeting between MHRA and reclassification applicant. It is usually shorter than Major Application as expert advice may not be sought.	**Second product in a therapeutic category with no significant differences in the safety profile.**
Simple Application	▪ Known as "Me-too Application" for reclassification of an analogous product. ▪ Analogous products are a product which (a) Has a UK marketing authorization or a marketing authorization granted through EU Centralized Procedure; (b) has the same active ingredient, route of administration and use; (c) has the same strength or a higher strength; (d) has the same dosage or daily dosage, or a higher dosage or daily dosage; and (e) is for sale or supply at the same quantity or a greater quantity, as the medicinal product in relation to which the application is made. ▪ Different pharmaceutical forms will be considered on an individual basis and may not be eligible to be considered an analogous product.	Follow Type IB or Type II variation procedure, depending on the nature of the proposed changes to the product information.	**N/A**

Table 6. Examples of Drug Reclassification in UK in 2019[18]					
Product	**Active Substance**	**Strength**	**Dosage Form**	**Indication**	**Type of Switches**
Acnecide Face Gel	Benzoyl Peroxide	5% per Gram	Gel	For the treatment of mild acne affecting the face, when comedones predominate, and there are few or no papules and pustules and no inflamed spots, in adults and adolescents aged 12 years and over	**From P to GSL**
Sildenafil Film-Coated Tablets	Sildenafil Citrate	50 mg	Film-Coated Tablet	For the treatment of adult men with erectile dysfunction.	**From POM to P**

maintenance. A reclassification may be granted with conditions, such as requiring the applicant to undertake a specific risk management plan (RMP) comprising training, education, pharmacy sales protocol, consumer supporting programs, and monitoring of actual non-prescription use.

Based on the outcome of RMP, additional restrictions to the product may be required, such as further post-marketing surveillance and revision to labelling. Alternatively, the new data may support loosening of requirements such as removal of pharmacy sales protocol and supporting reclassification from Pharmacy Medicine (P) to General Sale Medicine (GSL).

3. Canada

In Canada, drugs are classified into four categories, namely Schedule 1, Schedule 2, Schedule 3 and Unscheduled **(Table 7)**. In brief, Schedule 1 is Prescription Only Medicine, Schedule 2 is Pharmacy Only Medicine while Schedule 3 and Unscheduled can be considered OTC drugs.[19]

Table 7. Drug Classification in Canada (reproduced from Outline of the Schedules, NAPRA)[19]	
Category	**Definition**
Schedule 1	**Requires a prescription for sale and is provided to the public by a licensed pharmacist.**
Schedule 2	**Does not require a prescription but requires an assessment by a pharmacist prior to sale.** **These drugs are kept in an area of the pharmacy where there is no public access**
Schedule 3	**Does not require a prescription but must be kept in an area under the supervision of a pharmacist.** **These drugs are kept in an area of the retail outlet where self-selection is possible, but a pharmacist must be available to assist in the self-selection of medication if required.**
Unscheduled	**Does not require a prescription and may be sold in any retail outlet.**

Health Canada, the health authority of Canada, issued a guidance document of "Data Requirements for Switching Medicinal Ingredients from Prescription to Non-Prescription Status".[20] Despite not a legal document, it is a useful reference for the industry and healthcare professionals on how to comply with governing statutes and regulations.

The Guidance suggested nine criteria for assessing the eligibility of switching. Depending on the extent of compliance to these criteria, applicants can submit the proposal as either Full or Partial Switch Application. The criteria and the two types of application are summarized in **Table 8** and **Table 9** respectively.

Table 8. Criteria for switching medicinal ingredients from prescription to non-prescription status in Canada[20]	
No.	**Criteria Description**
1	The use of the product is amenable to self-diagnosis
2	The use of the product is amenable to self-treatment.
3	The use of the product is amenable to self-monitoring.
4	The use of the product is associated with an adequate margin of safety.
5	The consequences of misuse of the product are minor
6	The use of the product does not lead to dependence.
7	The use of the product does not have potential for diversion, addiction or abuse, leading to harmful nonmedical uses to either the individual or the public at large.
8	There is adequate market experience with the product.
9	The use of the product does not present a significant risk to human, animal or public health.

Table 9. Comparison between Full and Partial Switch Applications[20]		
Type of Switching	**Definition**	**Examples**
Full Switch Application	The medicinal ingredient and all approved conditions of use are removed from prescription status.	Paracetamol or its salt
Partial Switch Application	The medicinal ingredient remains in prescription drug list, but certain conditions of use are removed from prescription status.	Indication for management of heartburn for famotidine or its salts is under non-prescription status.

China

Medications in China are classified into "Prescription Only Medicine", "Type A OTC" (甲類 OTC) and "Type B OTC" (乙類 OTC). Type A OTC refers to Pharmacy Only Medicine while Type B OTC is General Sales Medicine.

National Medical Product Administration (NMPA) (國家藥品監督管理局) is responsible for managing drug reclassification in China. Instead of a formal protocol or policy, NMPA issued a memorandum (《關於做好處方藥轉換為非處方藥有關事宜的通知》) to illustrate the framework for regulation on OTC.[21]

Table 10. Example of Drug Reclassification in China in 2020[22]				
Product	**Active Substance**	**Strength**	**Dosage Form**	**Type of Switches**
Adapalene gel	Adapalene	0.1%	Gel	**From Prescription Only Medicine to Type A OTC**

Currently, NMPA focuses heavily on product safety profile, including

a) Toxicology Study;
b) Adverse Drug Reaction;
c) Dependence Study (依賴性研究);
d) Tolerance Study (耐受性研究);
e) Drug-Drug Interaction & Drug-Food Interaction;
f) Safety Study of consumer Self-diagnosis, self-treatment (消費者進行自我診斷、自我藥療情況下的安全性研究); and
g) Safety Data Under Generalized Usage (廣泛使用情況下的安全性研究).

4. Taiwan

Medications in Taiwan are classified into "Prescription Only Medicine (處方藥)", "Instruction Drugs (指示藥)" and "Over-the-Counter Drugs (成藥)",[23] where "Instruction Drugs" is equivalent to Pharmacy Only Medicine.

Taiwan FDA provides application checklists. Manufacturers or distributors can apply through "Reclassification Application (藥品類別變更申請)". The checklists are available online for public reference so that the companies can prepare documents correspondingly.

There are principles of reclassification that have to be met before application, such as:

a) The product has been used in Taiwan for not less than 10 years;
b) The active ingredients being registered as OTC drugs has been in more than 3 specified developed countries for more than a year; and
c) The product is used for minor ailments.

Taiwan FDA also requires safety data including ADR reports, prescribing information and Pharmacist Training Program. Manufacturers are obligated to provide their contact information, knowledge of the indication, product knowledge (e.g. mechanism of action, adverse drug reaction and precaution) and direction of use to pharmacists.[24,25]

5. Singapore

The Health Science Authority (HSA) is the local health authority of Singapore. The drug classification system is the same as that of the UK where drugs are also classified into "General Sale List (GSL)", "Pharmacy Only Medicines (P)" and "Prescription Only Medicines (POM)".

Normally, Major Variation Application-2 (MAV-2 Application) is the standard reclassification application for drug products. Should there be a previous reclassification of an analogous product, applicants may opt for "Me-too" Reclassification which has simpler documentary requirement. For example, summary of clinical safety is required for MAV-2 Application but not "Me-too Reclassification".

Similar to "Full Switch" and "Partial Switch" in Canada, after drug reclassification, HSA may either reclassify a medicine into GSL or P, or just allow certain exemptions for supply of POM without prescription.[26] Reclassified medicines are listed on the HSA website for public acknowledgement, and some examples are illustrated in **Table 11**.

HSA mainly considers four criteria when deciding on eligibility for reclassification:

a) The use of the product has been sufficiently extensive;
b) The product has been marketed for a sufficient period of time to establish a post-marketing adverse event profile;
c) The product's safety profile gives no cause for concern during the marketing period; and
d) The product is presented in an appropriate pack size with consumer-friendly labelling (package leaflet/ outer carton).

Table 11. Examples of Drug Reclassification in Singapore[27]					
Part 1: Reclassified Medicine					
Year	**Product**	**Active Substance**	**Strength**	**Dosage Form**	**Type of Switch**
2020	Bifen	Ibuprofen	100mg/5ml	Suspension	**From P to GSL**
2019	Derm-aid	Hydrocortisone	0.5%	Cream	**From P to GSL**
Part 2: Exemptions for supply of prescription only medicine (POM) without prescription					
Year	**Active Substance**	**Exemptions for supply of POM without prescription**			
2017	Fluticasone Furoate	As an intranasal spray not exceeding 27.5 mcg/actuation ▪ Indication: Prevention and treatment of allergic rhinitis ▪ Maximum daily dose: 110 mcg ▪ Maximum supply: 3 months ▪ Minimum age: 18 years			

Comparison of Current Drug Reclassification Policy across the Globe

Drug reclassification policies in different regions of the world are compared in **Table 12** below.

RECOMMENDATIONS FOR DEPARTMENT OF HEALTH

A guidance document on application for drug reclassification issued by the Department of Health will help to ensure a simple, efficient and transparent drug reclassification process to improve public access to medication. In particular, it is recommended that the local health authority provide criteria and document checklists for the reclassification application procedure.

To facilitate reclassification evaluation, local health authority may consider the medicine classification in other countries. Specifically, Taiwan FDA requires applicants to consolidate the current classification of the medicine in "The Top Ten Advanced Healthcare Countries (十大醫藥先進國家)" consisting of Germany, the US, the UK, France, Japan, Switzerland, Canada, Australia, Belgium and Sweden. With the experience from these reference countries, it may help justify the application and make evaluation easier.

HOW PHARMACISTS CAN CONTRIBUTE TO DRUG RECLASSIFICATION

Pharmacists can contribute to drug classification in the following ways:

1. Assist the General Public for Self-Medication of Minor Ailments

With drug reclassification, there will be more visits to the pharmacy for OTC medication, including both general sales medicines (i.e. Non-Poisons, Part II Poisons) and pharmacy-only medicines (i.e. Part I Poisons).

As drug experts who are familiar with community members, pharmacists can help enhance the level of health knowledge and provide therapy-related medication advice to patients to assist in self-medication of minor ailments.

When the public reaches a higher drug literacy with adequate awareness of drug safety, a wider range of products can be accepted for self-medication.

2. Provide Valuable Opinion on Drug Reclassification

One of the most crucial criteria of drug reclassification is consumer behavior – whether consumers can correctly recognize minor ailments by themselves and whether they can select the appropriate therapeutic product according to the product label.

Since community pharmacists work at the healthcare front line and provide medication therapy advice to patients, they receive direct patient feedback on drugs and know how well they can use the medications. They also know the public's demand and expectation for drug reclassification.

With their valuable experience and knowledge of drug safety profile, community pharmacist can provide useful insights on drug reclassification. This can help the authority to make better assessment and evaluation of every Rx-to-OTC switch.

3. Safety Monitoring After Reclassification

Pharmacists play an important role in pharmacovigilance, as they are trained to detect various signals, such as drug-herb or drug-drug interactions,[28,29] adverse events and hypersensitivity.

Table 12. Comparison of Current Drug Reclassification Policy across the Globe

Items	US	UK	Canada	China	Taiwan	Singapore
Part 1: General Characteristics						
Authority	US FDA	MHRA	Health Canada	NMPA	Taiwan FDA	**HSA**
Policy / Guidance / Memorandum	Policy	Policy	Guidance	Memo	Guidance	**Policy**
Different types of application	No	Yes	Yes	No	No	**Yes**
Part 2: Criteria for Drug Reclassification						
Extensive use	No	No	Yes	No	Yes	**Yes**
Post-marketing surveillance	Yes	Yes	Yes	Yes	Yes	**Yes**
Safety profile	Yes	Yes	Yes	Yes	Yes	**Yes**
Assessment in risk of misuse	Yes	Yes	Yes	Yes	No	**No**
Ease in self-medication	Yes	No	Yes	Yes	Yes	**No**
Requirement on labelling	Yes	Yes	No	No	Yes	**Yes**
Pharmacist training programme	No	Yes	No	No	Yes	**No**
Reference to the medication legal status in other countries	Yes	No	No	No	Yes	**Yes**

Since community pharmacists engage with patients directly and are easily accessible, they can participate in post-reclassification safety surveillance by detecting and reporting any adverse drug reaction occurring in their patients.

These can help enable the Market Authorization Holder (MAH) and the healthcare authorities to detect safety signals and evaluate if consumers can select the appropriate product for use according to product labels.

CONCLUSION

Drug reclassification is a double-edged sword. It can bring you numerous benefits such as improved access to medication and reduced healthcare burden. On the other hand, careful evaluation must be in place to assess and lower the risk of misuse. Nevertheless, with the increased accessibility to reliable health-related information, it may reduce the risk of incorrect self-diagnosis and self-medication.

To ensure a simple, efficient and transparent drug reclassification process, it is suggested that the local health authority make reference to other countries' experience in developing a guidance document for Hong Kong.

Finally, to implement drug reclassification, the role of pharmacists should not be overlooked. Pharmacists can contribute by assisting the public with medicinal advice, providing insights on drug reclassification and participating in safety monitoring of reclassified medicines.

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Survey of Physicians' Perceptions on the Use of Oral Anticoagulants Among Patients With Atrial Fibrillation

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ABSTRACT

Despite the increasing evidence of the superior efficacy of oral anticoagulants (OACs) compared to antiplatelet therapy (aspirin and/or clopidogrel) for stroke prevention, their improved safety profiles and current clinical recommendations, OACs are underused whereas antiplatelet therapy remains high in Asia compared to western countries. The attitudes of physicians towards prescribing OACs versus aspirin to patients with atrial fibrillation (AF) in Asia are unclear. This cross-sectional observational study investigated the attitudes and perceptions of physicians on the barriers to prescribing OACs to patients with AF. An anonymous survey was sent to 33 physicians in two regional hospitals in Hong Kong. 20 out of 31 participating physicians had the experience of prescribing aspirin to patients with AF for stroke prevention. Factors which influenced physicians to prescribe aspirin were patient-related factors such as the high risk of bleeding, frailty and poor adherence to treatment, in order of importance. Physician-related factors related to prioritizing concerns of bleeding over stroke prevention benefits, insufficient consultation time to adequately explain treatment options in detail, and to educate patients regarding the lifestyle adjustments necessary resulting from the use of OACs, which could be viewed as potential barriers to using OACs. The barriers to prescribing OACs perceived by physicians relate to clinical and psychosocial factors of patients with AF, concerns of adverse effects of anticoagulation, and limitations of healthcare settings. The findings highlight a need for a better communication platform between physicians and patients to achieve optimal stroke prevention management.

Keywords: *atrial fibrillation, oral anticoagulants, aspirin, barriers, perceptions, physicians*

INTRODUCTION

Atrial fibrillation (AF) is a common cardiac dysrhythmia associated with a 5-fold higher risk of ischemic stroke which often leads to long-term disability and mortality.[1] The consequences of AF-related stroke pose a significant burden to patients, their families and society. Therefore, stroke prevention therapy is important in AF management.

Over the past decade, there has been emerging evidence of superior efficacy of reducing the risk of having a stroke with oral anticoagulants (OACs) compared to antiplatelet (aspirin and/or clopidogrel) from randomized controlled trials and observational studies.[2-4] The use of OACs, including warfarin and non-vitamin K oral anticoagulants (NOACs), has been associated with a significantly lower risk of stroke compared to antiplatelet therapy but demonstrated a similar risk of gastrointestinal bleeding in both Caucasian and Asian populations.[3,5] Aspirin monotherapy was no longer recommended for AF patients regardless of the stroke risk and OACs are recommended for patients with moderate to high risk of stroke ($CHA_2DS_2VASc \geq 2$) in the current international clinical guidelines.[6-9]

Under-prescribing of OACs to patients with AF for stroke prevention aroused concerns from physicians and researchers over many years, although this issue has improved since the introduction of NOACs. Prior studies conducted in Denmark and the UK reported an increase in prescribing of OACs to patients with AF since 2010.[10,11] However, the prescribing of OACs in Asia are still much lower than that of western countries and the proportion of patients receiving antiplatelet therapy is substantially higher, reflecting the problem of underuse of OACs among AF patients.[3,12] Therefore, understanding the underlying reasons for not prescribing OACs is crucial for optimal AF management in Asia.

A recently published qualitative meta-synthesis summarized the views and attitudes of prescribing OACs from physicians' perspectives [13]. It highlighted the potential difficulties of physicians transferring guideline recommendations into clinical competency, namely the application of evidence-based medicine into practice, differences in healthcare settings, patients' medical conditions and personal opinions, and communication with patients. However, all studies included in the review were conducted in western countries. The education training for physicians and healthcare systems might differ in various geographical locations, thus influencing the prescribing habits in Asia. Furthermore, previous studies either focused on the barriers to prescribing OACs generally or only a particular kind of OACs (warfarin or NOACs).[14-16] Much less is known about how physicians' views might vary when comparing different OACs with aspirin.

To the best of our knowledge, no study has yet explored the perception of physicians regarding the use of OACs versus aspirin for stroke prevention. Our study aimed to identify the barriers to prescribing different types of OACs among patients with AF who were prescribed aspirin.

STUDY DESIGN and RECRUITMENT

This is a cross-sectional survey study investigating the perceptions of physicians in relation to the barriers to prescribing OACs among patients with AF.

Participants were eligible to participate in this study if 1) they are medical doctors who have had the experience of prescribing any medications for stroke prevention in patients with AF including warfarin, NOACs, aspirin and/or clopidogrel, and 2) are currently practicing in the public hospitals in Hong Kong. Participants were excluded if they were unable to comprehend written Chinese or English. Convenience sampling was used for recruiting participants. All eligible physicians from the Division of Geriatrics and Cardiology Division from the two acute public hospitals managed by the Hospital Authority - Queen Mary Hospital and Ruttonjee and Tang Shiu Kin Hospital were invited to complete the questionnaires. Surveys were delivered to the respective hospitals together with the information sheet and consent form between 20 August 2019 and 20 September 2020. The division representatives separately collected the signed consent forms and completed surveys from the physicians who had voluntarily participated. All completed surveys were anonymous. The reason why we chose our participants from the Division of Geriatrics and Cardiology Division was that they were the groups who often prescribe medications for stroke prevention among patients with AF. To maximize the response rate, our researcher sent a reminder email to the division representatives one month after the initial invitation.

Ethics approvals were sought and obtained from the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster (UW18–580) and Hong Kong East Cluster Research Ethics Committee (HKECREC-2019-007).

SURVEY DEVELOPMENT

The survey aimed to identify the factors affecting their prescribing decisions in relation to OACs, and their attitudes to prescribing OACs to patients with AF. The survey had 4 sections: Section A) demographics of participating physicians, Section B) adherence to the international clinical guidelines, Section C) characteristics of patients with AF who were likely to receive aspirin for stroke prevention, and Section D) barriers that affect physicians' decisions when prescribing warfarin and NOACs respectively.

For Section B, participants were asked about their experience of prescribing aspirin monotherapy using closed questions. Participants who have never prescribed aspirin for stroke prevention were not required to answer the questions in Sections C and D. For Section C, participants were asked to rank the top 3 most influential clinical characteristics of patients with AF that make physicians more likely to prescribe aspirin in the order of importance. For Section D, participants were asked to rate their level of agreement with the given potential barriers to prescribing OACs using a 5-point Likert scale (1: strongly disagree; 5: strongly agree). All survey questions were developed based on current literature findings, previous semi-structured interviews conducted with patients with AF in Hong Kong and validated by our multidisciplinary team of researchers, pharmacists and physicians to ensure the content was clinically relevant **(Appendix 1)**.[17]

DATA ANALYSIS

For Sections A and B, participants' responses were analyzed using descriptive statistics. For Section C, a weighted score was assigned to the ranked attributes in reverse order. A score of 3 was assigned to the attributes that were ranked first while a score of 2 and 1 was assigned to those ranked second and third respectively. Those attributes not selected as being in the top 3 were given a score of 0. The total weighted scores of each attribute were calculated. For Section D, a score was assigned to each response using a 5-point Likert scale. The median score of each response was then compared to the hypothesized median of the Likert scale, which is the midpoint of 3 representing neutrality. Cronbach's alpha was used to assess the internal consistency and reliability of each of the statements.[18] All data analyses and manipulation were conducted by two investigators (VN and ML) using SAS (version 9.4) and Microsoft Excel.

RESULTS

Study sample

33 questionnaires were sent to eligible physicians from both hospitals and 31 of them participated in this study, yielding an overall response rate of 93.9%. Cronbach's alpha for Section D was 0.87. More than half of the participants (67.7%) were males and the majority were resident specialists level or above **(Table 1)**. 20 out of 31 physicians prescribed aspirin to patients with AF before participating in this study.

Table 1. Respondents' characteristics

Characteristics	Total (n=31)	Prescribed aspirin (n=20)	Never prescribed aspirin (n=11)
Males (%)	21 (67.7)	13 (65)	8 (72.7)
Age distribution, n (%)			
21-30 years	6 (19.4)	1 (5)	5 (45.5)
31-40 years	11 (35.5)	7 (35)	4 (36.4)
41-50 years	6 (19.4)	5 (25)	1 (9.1)
51-60 years	8 (25.8)	7 (35)	1 (9.1)
Position ranking, n (%)			
Intern	3 (9.7)	1 (5)	2 (18.2)
Resident	7 (22.6)	2 (10)	5 (45.5)
Resident specialist	2 (6.5)	2 (10)	0 (0)
Associate consultant	15 (48.4)	12 (60)	3 (27.3)
Consultant	4 (12.9)	3 (15)	1 (9.1)
Specialty, n (%)			
Cardiology	8 (25.8)	7 (35)	3 (27.3)
Geriatric	13 (41.9)	9 (45)	4 (36.4)
Internal medicine	10 (32.3)	4 (20)	4 (36.4)
Years of experience, n (%)			
≤10	15 (48.4)	6 (30)	9 (81.8)
11-20	8 (25.8)	7 (35)	1 (9.1)
21-30	8 (25.8)	7 (35)	1 (9.1)

Adherence to the International Clinical Guidelines

Among all participants, 77.4% of physicians (24 out of 31) in our study self-reported that they strictly follow the recommendations of stroke prevention in international clinical guidelines and make a formal assessment of patients' stroke risk and bleeding risk estimation (e.g. CHA_2DS_2VASc and HAS-BLED scores) when making prescribing decisions in their clinical practice. The remaining participants claimed that they take patients' past medical history, comorbidities and lifestyle factors into consideration based on their clinical experience.

Evaluation of the characteristics of patients with AF who were prescribed antiplatelet monotherapy for stroke prevention by the physicians

Among the 20 respondents who have ever prescribed aspirin for stroke prevention to patients with AF, 3 did not provide valid answers so their responses for this section were omitted. Overall, according to the total weighted score, a high risk of bleeding was perceived to be the most important characteristic in patients with AF that physicians would consider when prescribing aspirin, followed by frailty and poor adherence to treatment.

Although physicians from all three specialties commonly perceived the risk of bleeding and frailty as the top two characteristics to be considered, only geriatricians prioritized frailty over the former. Physicians from internal medicine and geriatricians prioritized patients' preferences as the third influential factor while only the cardiologists considered chronic renal and/or hepatic impairment **(Table 2)**.

Table 2. Physicians' perspectives of the top three most influential characteristics of patients with atrial fibrillation who were more likely to receive aspirin

Rank	Characteristics of patients with atrial fibrillation	Total weighted score
Total (n=17)		
1	High risk of bleeding	25
2	Frailty	21
3	Poor adherence to treatment	14
Cardiology (n=5)		
1	High risk of bleeding	9
2	Poor adherence to treatment	6
	Frailty	6
3	Chronic renal/liver diseases	4
Geriatrics (n=8)		
1	Frailty	11
2	High risk of bleeding	10
3	Patients' preferences*	7
Internal medicine (n=4)		
1	High risk of bleeding	6
2	Frailty	4
3	Patients' preferences*	3
	High risk of fall	3

* Patients' preference was self-defined by the physicians in the 'others' option

Perception of the potential barriers of prescribing OACs to patients with AF of physicians from different specialties was assessed according to patient-related and physician-related factors. Participants' responses were reported in **Tables 3a** and **3b**. Overall, the majority of the barriers to prescribing OACs were patient-related factors. Respondents commonly agreed that they were unlikely to prescribe OACs when patients had prior

bleeding events, a high risk of having a fall or were non-adherent to their treatment. Furthermore, physicians also perceived patients' worries about the adverse events of OACs and their unwillingness to experience the unpredictable adverse events from OACs as the barriers to prescribing OACs, especially when patients were long-term aspirin users. Physicians also reported difficulty in persuading patients to consider OACs within the short consultation time. Drug choices had some influence on physicians' decisions. Food restrictions, regular blood tests and drug interactions were perceived as barriers to prescribing warfarin while medication cost was the only barrier to prescribing NOACs.

Table 3a. Percentage of respondent's agreement with statements describing potential barriers of prescribing oral anticoagulants

	Warfarin		NOACs	
	N (%)[a]	Median score[b]	N (%)[a]	Median score[b]
Total (n=20)				
Patient-related factors				
Patient reluctance to have food restrictions	14 (70)	4	4 (20)	1
Patient reluctance to have regular blood tests	16 (80)	5	5 (25)	2
Medication cost	2 (10)	1	16 (80)	4
Drug interactions	13 (65)	4	3 (15)	2
Prior bleeding events	16 (80)	4	14 (70)	4
High risk of falls	15 (75)	4	13 (65)	4
Non-adherent to treatment	15 (75)	5	14 (70)	4
Unwilling to bear unforeseeable adverse events of other oral anticoagulants when patients have been taking aspirin for long time	13 (65)	4	11 (55)	4
Over-worried about the adverse events (e.g. bleeding)	17 (85)	4	14 (70)	4
Unrealistic or irrational pre-conceived ideas	8 (40)	3	6 (30)	3
Personal preference for aspirin	10 (50)	3.5	8 (40)	3
Lack of knowledge on AF/stroke prevention	9 (45)	3	7 (35)	3
Influence from relatives and/or peers	10 (50)	3.5	8 (40)	3
Physician-related factors				
Not the regular doctor who follows up patients' case at each consultation	5 (25)	3	5 (25)	3
Aspirin is perceived as a safer alternative because it has a lower bleeding risk	5 (25)	1.5	4 (20)	1
Constant changes to scientific evidence and clinical guidelines	4 (20)	1.5	3 (15)	1.5
The risk of bleeding overrides the benefits of stroke prevention	9 (45)	3	5 (25)	2.5
Prior negative experience of prescribing respective medicines	6 (30)	2	3 (15)	2.5
Difficult to explain to patients about the respective medicines and persuade them to make the decision within short consultation time at each follow-up	11 (55)	4	10 (50)	3.5

[a] Number of respondents who agreed with respective statements; [b] Median score=3: no opinion; Median score>3: agree; Median score<3: disagree

When stratifying by different specialties, similar responses were recorded **(Table 3b)**. However, there was some variation in the level of agreement on the potential barriers across specialties. For patient-related factors, most cardiologists agreed that high risk of fall and non-adherence to treatment were the barriers to prescribing warfarin only while geriatricians and the physicians' from internal medicine considered them as barriers to prescribing all OACs. More than half of the cardiologists agreed that they were more concerned with the bleeding risks than the risk of stroke and prior negative prescribing experience affected their decision not to prescribe warfarin. Geriatricians and physicians from internal medicine additionally considered patients' preference for aspirin and opinions from patients' relatives and/or peers as barriers to prescribing OACs.

DISCUSSION

In this study, we surveyed physicians from two regional hospitals in Hong Kong to explore their attitudes towards prescribing OACs versus aspirin and the potential barriers to prescribing OACs for stroke prevention. Our findings were reported in three aspects: 1) clinical factors and beliefs of patients with AF; 2) the limitations of healthcare setting; and 3) lifestyle changes and concerns associated with the respective OACs.

Patients' physical conditions and beliefs towards OACs often affected physicians' prescribing decisions. In our study, high risk of bleeding and frailty were perceived as the two most important factors which made physicians more likely to prescribe aspirin. Our findings were consistent with the current evidence.[13] Frail patients with AF were reported to have a higher predicted risk of stroke and bleeding as evidenced by higher mean scores using various risk assessment tools than those who were non-frail.[19] Prior studies also showed that frailty was associated with elevated risks of stroke and bleeding complications among the AF population.[20,21] The rate of OACs prescribing was much lower in frail patients than the non-frail.[21] There has been limited evidence on the efficacy and safety of OACs in frail patients as they have always been excluded in clinical trials. The clinical practice guidelines have not yet explicitly assessed frailty. The under-prescribing of OACs in this population might be due to the fear of causing idiopathic harm to patients and lack of guidance for optimal treatment plans. Therefore, physicians may prefer alternatives, such as aspirin, as reflected in this study.

Bleeding complications have been a major safety concern for physicians and patients, hence influencing the uptake of anticoagulation. From physicians' perspective, there is a dilemma in striking a balance between stroke prevention and the risk of bleeding. It is well known that patients who had a previous bleeding event were one of the key barriers to prescribing OACs.[22,23] The concept of 'do not harm' proposed by Aberegg et al. might be at the forefront of the physicians' mindset so they might avoid treatments which could potentially cause harm to patients.[24] Most cardiologists in our study agreed that previous negative experience adversely affected their prescribing decisions and they appeared to be more concerned with the risk of bleeding when prescribing warfarin. Having

Table 3b. Percentage of respondent's agreement with statements describing potential barriers of prescribing oral anticoagulants stratified by different specialties

	Cardiology (n=7)				Geriatrics (n=9)				Internal Medicine (n=4)			
	Warfarin		NOACs		Warfarin		NOACs		Warfarin		NOACs	
	N (%)[a]	Median score[b]	N (%)[a]	Median score[b]	N (%)[a]	Median score[b]	N (%)[a]	Median score[b]	N (%)[a]	Median score[b]	N (%)[a]	Median score[b]
Patient-related factors												
Food restrictions	6 (85.7)	4	1 (14.3)	1	5 (55.6)	4	1 (11.1)	1	3 (75)	4	2 (50)	3.5
Regular blood tests	5 (71.4)	5	1 (14.3)	2	8 (88.9)	4	2 (22.2)	1	3 (75)	4.5	2 (50)	3.5
Medication cost	1 (14.3)	1	5 (71.4)	4	0 (0)	1	7 (77.8)	4	1 (25)	1.5	4 (100)	5
Drug interactions	4 (57.1)	4	0 (0)	2	6 (66.7)	4	1 (11.1)	2	3 (75)	4.5	2 (50)	3
Prior bleeding events	7 (100)	4	4 (57.1)	4	6 (66.7)	4	7 (77.8)	4	3 (75)	4.5	3 (75)	4.5
High risk of falls	5 (71.4)	4	2 (28.6)	3	7 (77.8)	4	8 (88.9)	4	3 (75)	4.5	3 (75)	4.5
Non-adherent to treatment	4 (57.1)	4	3 (42.9)	3	7 (77.8)	5	8 (88.9)	4	4 (100)	5	3 (75)	4.5
Unwilling to bear unpredictable adverse events of other oral anticoagulants when patients have been taking aspirin for long time	5 (71.4)	4	4 (57.1)	4	5 (55.6)	4	4 (44.4)	3	3 (75)	4.5	3 (75)	4
Over-worried about the adverse events (e.g. bleeding)	6 (85.7)	4	4 (57.1)	4	8 (88.9)	4	8 (88.9)	4	3 (75)	4.5	2 (50)	4
Unrealistic or irrational pre-conceived ideas	2 (28.6)	3	1 (14.3)	3	4 (44.4)	3	4 (44.4)	3	2 (50)	3.5	1 (25)	2.5
Personal preference for aspirin	2 (28.6)	3	0 (0)	3	6 (66.7)	4	6 (66.7)	4	2 (50)	3.5	2 (50)	3.5
Lack of knowledge on AF/stroke prevention	2 (28.6)	3	1 (14.3)	3	5 (55.6)	4	4 (44.4)	3	2 (50)	3.5	2 (50)	3.5
Influence from relatives and/or peers	3 (42.9)	3	2 (28.6)	3	6 (66.7)	4	5 (55.6)	4	1 (25)	2.5	1 (25)	2.5
Physician-related factors												
Not the regular doctor who follows up patients' case at each consultation	1 (14.3)	3	0 (0)	3	3 (33.3)	3	4 (44.4)	3	1 (25)	2.5	1 (25)	2.5
Aspirin is perceived as a safer alternative because it has a lower bleeding risk	2 (28.6)	1	1 (14.3)	1	2 (22.2)	2	2 (22.2)	2	1 (25)	1	1 (25)	1
Constant changes to scientific evidence and clinical guidelines	2 (28.6)	3	1 (14.3)	2	1 (11.1)	1	1 (11.1)	1	1 (25)	2	1 (25)	2
The risk of bleeding overrides the benefits of stroke prevention	5 (71.4)	4	3 (42.9)	3	2 (22.2)	2	1 (11.1)	2	2 (50)	3.5	1 (25)	3
Prior negative experience of prescribing respective medicines	4 (57.1)	4	1 (14.3)	3	1 (11.1)	2	1 (11.1)	2	1 (25)	2	1 (25)	3
Difficult to explain to patients about the respective medicines and persuade them to make the decision within short consultation time at each follow-up	3 (42.9)	3	2 (28.6)	3	5 (55.6)	4	5 (55.6)	4	3 (75)	4.5	3 (75)	4.5

[a] Number of respondents who agreed with the respective statements; [b] Median score=3: no opinion; Median score>3: agree; Median score<3: disagree

prior negative prescribing experience might amplify the potential occurrence of bleeding complications in physicians' minds.[15] This might explain why our finding was in contrast to some of the current evidence that geriatricians put more focus on the risks.[25] Patients' fear of bleeding complications from anticoagulation was given as a reason for refusing OACs as reflected in our study that patients over-worrying about the occurrence of adverse events was a barrier to prescribing OACs.[17]

Lack of adequate time in the consultation was perceived as another obstacle to prescribing anticoagulation. A consultation provides patients with an opportunity to express their concerns about their illness and treatment to their doctors. However, physicians in this study found it difficult to have an in-depth discussion with patients, which leads to a poor understanding of the importance of stroke prevention management. This might affect shared decision-making for optimal treatment plans. The same concern was raised by the UK specialists that a less time-pressured interaction process with patients could prevent patients from information overload and allow them to contemplate the issues discussed in one consultation.[14] Our previous study found that most patients had minimal involvement in the treatment decision-making and delegated trust to their doctors.[17] Therefore, it is important to enhance the communication with the patients.

Undoubtedly, specific drug choices of OACs play an important role in deciding which might be more appropriate for patients. The lifestyle changes necessitated by different OACs have been another consideration for patients. Most physicians in our study agreed that food restrictions, regular therapeutic drug monitoring and drug interactions were the barriers for prescribing warfarin, which is consistent with prior studies.[14] The inconvenience arising from lifestyle adjustments might hinder patients' adherence to warfarin compared to aspirin, leading to the suboptimal effects

of stroke prevention and potentially increasing the risks of adverse events. Some of the physicians in our study also identified poor adherence to treatment as a barrier to prescribing OACs. The cost was the only obstacle to prescribing NOACs. This was also observed in other countries under different healthcare systems as the cost of NOACs is generally higher than that of warfarin and aspirin.[16,26] In Hong Kong, the use of NOACs is under the Special Drug Scheme and patients are charged for NOACs if they do not meet certain criteria. Since 2019, the criteria for prescribing NOACs to patients with AF has been relaxed so it is predicted that more patients with financial difficulties might benefit in the near future.

To tackle some of the aforementioned barriers, the use of multidisciplinary collaborations with different healthcare professionals might be a starting point. In many other countries, anticoagulation clinics led by multidisciplinary teams were set up decades ago.[27,28] The clinical pharmacists and/or specialist nurses play different roles in the anticoagulation clinics to ensure patients receive sufficient care and optimize anticoagulation control. They are responsible for following up on the anticoagulated patients, including checking their adherence to treatment, and adjusting the doses of OACs if necessary depending on the protocols in various healthcare systems. They also serve as an educator enhancing patients' awareness of the consequences of a stroke if not well-managed. More importantly, they act as a communication channel for patients to express their concerns and enable a joint decision-making process to optimize the therapy. Physicians provide some backup clinical support if changes of treatment are warranted. This could help reduce the workload of physicians so they could spend more time on patients who are severely ill and require more complex treatment. Prior studies showed that anticoagulation clinics effectively improved patients' anticoagulation control, reduced bleeding rates and hospitalization, compared to usual medical care provided by physicians, with a resultant saving of medical costs.[27, 29] In Hong Kong, anticoagulation clinics have been established in some of the public hospitals but have developed underway. The current scope of service is limited to warfarin users only. Thus, more promotion of the anticoagulation clinics utilizing a multidisciplinary approach is recommended to build up trust between patients and other healthcare professionals, which could help enhance the service utilization and lead to optimal anticoagulation control in the future.

There are notable strengths of this study. The high response rate (93.9%) could potentially minimize the effect of non-response bias on the results.[30] Furthermore, we obtained a value of Cronbach's alpha of 0.87 which is higher than the threshold of 0.7, showing that the design of our survey is highly reliable and consistent.[18] There are some limitations to this study. Firstly, resource limitations precluded a larger sample size. The recruitment of physicians from two regional public hospitals in Hong Kong would affect the generalizability of the findings as the prescribing habits of physicians might differ by the established protocols in different public and private hospitals, the socio-economic status of patients that they encounter, all of which cannot be accounted for in this study. However, our findings are consistent with those of previous studies conducted in various countries and hence reflect the barriers of anticoagulation from physicians' perspectives. Another limitation is that our survey only includes the more common reasons for not prescribing OACs. Future research using in-depth interviews is warranted to further explore potential barriers of OACs from specialists in various settings.

CONCLUSION

This study reflects the current practice behavior and beliefs of doctors when prescribing anticoagulation for stroke prevention. Physicians had some concerns regarding the use of OACs, especially relating to patients' clinical and psychosocial factors, actual and perceived risks of bleeding and felt there was insufficient consultation time. Importantly, our findings implicate the need for a better communication platform between patients and healthcare professionals allowing sufficient time to educate patients in order to achieve optimal AF management.

DECLARATION

Ethics approval and consent to participate:

Ethics approvals were sought and approved by the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster (UW18-580) and Hong Kong East Cluster Research Ethics Committee (HKECREC-2019-007).

Competing interests

The author(s) declare(s) that they have no competing interests.

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Authors' contributions

IW initiated the conception and design of this study and led to the development of the protocol and securing of the funding. CWS, PC, CK contributed to the protocol, recruitment of participants and study administration. VN and ML were responsible for the study administration, recruitment, data collection, data analysis, and interpretation of results. VN and ML have the full access to all the study data and take responsibility for the integrity and accuracy of data analysis. EJ provided advice on the methodology. VN wrote the initial draft of the paper, to which all authors contributed. All authors read and approved the final manuscript.

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CE Questions Answer for 282(D&T)

Tumour Lysis Syndrome

1. A 2. A 3. D 4. C 5. B 6. A 7. D 8. B 9. D 10. C

Appendix 1

Questionnaire

Section A

Basic demographics

1. Please indicate your gender.
   ☐ Male ☐ Female

2. Please indicate your age range.
   ☐ 20-30 ☐ 31-40 ☐ 41-50 ☐ 51-60 ☐ >60

3. What is your current position?
   ☐ Intern ☐ Resident ☐ Resident Specialist ☐ Associate consultant ☐ Consultant
   ☐ General Practitioner (Please skip Q4) ☐ Others (Please specify:_____)

4. What is your main specialty? _____

5. How many years of experiences have you practiced as a medical practitioner in your main specialty after obtaining the qualifications?
   ☐ 0-5 ☐ 6-10 ☐ 11-15 ☐ 16-20 ☐ 21-25 ☐ 26-30 ☐ 31-35 ☐ 36 or above

6. Where did you finish your training of your specialty?
   ☐ Hong Kong ☐ China ☐ United Kingdom ☐ Australia ☐ United States ☐ Canada
   ☐ Others (Please specify:_____)

7. Where do you spend most of your time practicing your main specialty?
   ☐ Hong Kong ☐ China ☐ United Kingdom ☐ Australia ☐ United States ☐ Canada
   ☐ Others (Please specify:_____)

Section B

8. Do you usually rely on current clinical guidelines when deciding whether OACs/aspirin should be prescribed for AF patients?
   ☐ Yes, I strictly follow the clinical guidelines and make formal assessment of CHA_2DS_2VASc and HAS-BLED score.
   ☐ No, I make my own judgement depending on each patient's past medical history, comorbidities and other lifestyle factors based on my clinical experience.
   ☐ No (Please state the reason:_____)

9. Have you ever prescribed aspirin to AF patients for stroke prevention?
   ☐ Yes (please answer Q10, Q11) ☐ No

Section C

10. What are the first **THREE** dominant characteristics of AF patients you would take into consideration when prescribing **aspirin** for stroke prevention? Please rank them. (1 is the most influential factor and 3 is the least)
    ☐ Advancing age (Please define 'advancing age'=_____) ☐ High risk of bleeding
    ☐ Polypharmacy ☐ Chronic renal/liver diseases ☐ High risk of fall ☐ Psychiatric disorders
    ☐ Low literacy skills ☐ Poor adherence to treatment ☐ Fragility ☐ Fail to attend follow-up
    ☐ Others (Please state:_____)

Appendix 1

Section D

11. How much do you agree with the following barriers of using OACs (both initiating and changing from aspirin to OACs) on AF patients when they are **eligible for anticoagulation** (i.e. CHA_2DS_2VASc or $CHADS_2 \geq 2$)? (1: strongly disagree; 5: strongly agree) Please complete **BOTH** columns.

Barriers	Warfarin	NOACs
1. Patients are reluctant to have food restriction.	1 2 3 4 5	1 2 3 4 5
2. Patients are reluctant to take regular blood tests.	1 2 3 4 5	1 2 3 4 5
3. Patients are unable to afford the cost of stated medications.	1 2 3 4 5	1 2 3 4 5
4. There are more significant drug interactions between patient's medications and the stated medication than with aspirin.	1 2 3 4 5	1 2 3 4 5
5. Patients have prior bleeding events.	1 2 3 4 5	1 2 3 4 5
6. Patients have high fall risk.	1 2 3 4 5	1 2 3 4 5
7. Patients are non-adherent to treatment.	1 2 3 4 5	1 2 3 4 5
8. Patients have been taking aspirin for many years without experiencing any serious adverse events so they are not willing to take OACs with unforeseeable adverse effects.	1 2 3 4 5	1 2 3 4 5
9. Patients are over-worried about the adverse effects (e.g. bleeding) of stated medications.	1 2 3 4 5	1 2 3 4 5
10. Patients have unrealistic or irrational pre-conceived ideas on OACs from other sources, e.g. hearsays, peers, family, TV programs or Internet.	1 2 3 4 5	1 2 3 4 5
11. Patients have personal preference for aspirin.	1 2 3 4 5	1 2 3 4 5
12. You are not the regular doctor who follows up patient's case at each consultation.	1 2 3 4 5	1 2 3 4 5
13. Patients lack knowledge on AF/stroke prevention management.	1 2 3 4 5	1 2 3 4 5
14. Aspirin is a safer alternative because it has a lower bleeding risk compared to OACs.	1 2 3 4 5	1 2 3 4 5
15. Constant changes to scientific evidence and clinical guidelines make you less likely to prescribe OACs to AF patients.	1 2 3 4 5	1 2 3 4 5
16. Patients heard of bad experience of using OACs from families and peers.	1 2 3 4 5	1 2 3 4 5
17. The risk of bleeding overrides the benefits of stroke prevention	1 2 3 4 5	1 2 3 4 5
18. You have prior negative experience of prescribing OACs affecting the prescribing decision of OACs to other AF patients.	1 2 3 4 5	1 2 3 4 5
19. It is difficult to explain to patients about OACs thoroughly and persuade them to take OACs within short consultation time at each follow-up.	1 2 3 4 5	1 2 3 4 5

2022 General Council of Pharmaceutical Society of Hong Kong and Pharmaceutical Society Charitable Foundation Limited

We are pleased to announce that the Annual General Meeting of The Pharmaceutical Society of Hong Kong (PSHK) and The Pharmaceutical Society Charitable Foundation Limited (PSCF) has been held at PSHK Clubhouse on 16th December 2021. The following members were elected for the tenure from 16th December, 2021 onwards for 2021-2022 term.

President:	Mr. Dick SUNG		
Vice-presidents:	Ms. Beverley TAM	Mr. Edward YAU	
Hon. Secretary:	Mr. Jonathan NG		
Hon. Treasurer:	Mr. Paul LAM		
Council Members:	Mr. CHEUNG Wai Keung	Mr. Vincent LAU	Ms. Sandra TSANG
	Ms. CHEW Leng Leng	Mr. Raymond LUK	Mr. Edwin WONG
	Mr. Ian CHEUNG	Mr. Rex NG	
	Ms. Kathleen KUNG	Mr. Patrick TAM	
Pharmacy & Poisons Board Members:	Mr. Dick SUNG	Ms. Beverley TAM	Ms. Sandra TSANG

2022 - The 35th Anniversary of SHPHK

Next year is the 35th Anniversary of the Society of Hospital Pharmacists of Hong Kong (SHPHK)!

In 2022, SHPHK is hoping to organise various activities, not only to celebrate its anniversary, but also connect pharmacists of different hospitals together and foster communication between members and the Society. We welcome any comments, suggestions and feedback from pharmacists, pharmacy students and our collaborators, so that we can continue to improve and do more for the profession and the city!

Activities Highlights: Q4 2021

When Pharmacists Meet the Epee Fencing Athlete Miss Vivian Kong - The Value of Life

It is one of the aims of SHPHK to bring motivational and inspirational insights to its pharmacists and pharmacy students through different activities. This time, the Society has invited Miss Vivian Kong, Hong Kong Epee Fencing Athlete to join the Facebook Live session of SHPHK. The General Committee of SHPHK would like to thank Vivian for spending the afternoon with us despite her super busy schedule, and sharing with us her vegan life and how fencing has been influencing her life and value.

SHPHK Facebook Live session on 20th November 2021. From left: Mr. William Chui, President of SHPHK; Miss Vivian Kong, Hong Kong Epee Fencing Athlete; Miss Amy Chu, General Committee Member of SHPHK; and Miss Michelle Zheng, General Committee Member of SHPHK.

Archive can be found at the SHPHK facebook page: www.facebook.com/shphk.

Hiking Trip to Tai Tam Reservoir

The SHPHK Hiking is back this year!

A hiking trip to Tai Tam Reservoir was organised on 4th December 2021. The weather on the day was perfect for hiking, and the view of the surrounding hills is spectacular! Overall, it was an enjoyable hike, suitable for hikers of all levels.

Educational Events

In the final quarter of 2021, the Society has organised two educational events – A hybrid seminar on anaesthesia and a webinar on HR+/HER2- advanced breast cancer. In the coming years, the Society hopes to organise more face-to-face events as long as the pandemic situation in Hong Kong is under control. We look forward to meeting our members in person very soon in our future events.

SHPHK Activities: 2021 In Review

January	1. Webinar: Migraine, Secondary Progressive Multiple Sclerosis & Therapeutics
	2. Webinar: Eosinophilic Inflammation in COPD
April	3. Hybrid Seminar: RAS-targeting Cancer Therapies: Past, Present and Future
June	4. Workshop: 藥劑職場攻略 - 面試篇
	5. Lunchtime Webinar: Liquid Biopsy for Early Cancer Detection - the Nasopharyngeal Cancer Model
	6. The 34th SHPHK Annual General Meeting
July	7. Online Workshop: 藥劑師如可解答COVID-19疫苗問題的技巧分享
August	8. Webinar: Latest insights on COVID-19 Vaccines
	9. Lunchtime Webinar: What's New in GINA 2021?
October	10. Online Conference: FRANC Asia: Paediatrics 2021
November	11. Facebook Live: 當藥劑師遇上劍擊天后江旻憓 - 人生的價值
December	12. SHPHK Hiking Trip to Tai Tam Reservoir
	13. Hybrid Seminar: Update in Anaesthesia
	14. Webinar: Updated evidence on the treatment and management of HR+/HER2- advanced breast cancer in patients with PIK3CA mutation

The 3rd micro-movie of SHPHK

In November, the Society has released its 3rd micro-movie on the SHPHK Youtube channel. The key message that the production team would like to deliver is that, no matter what your role in the profession is, you should never forget your original intention of being a pharmacist. We share the same beliefs, and we are sure that there is always something extra we can do for the city.

Group photo: Actors, actresses and producers of the 3rd SHPHK micro-movie.

You may scan the QR code below to watch the micro-movie now:

The SHPHK Website (www.shphk.org.hk)

We are pleased to announce that the SHPHK website was successfully revamped and launched in December 2021.

From now on, Members can renew their membership, enroll for SHPHK activities, track record of attended events with SHPHK, access information on SHPHK previous educational events, and keep abreast of pharmacy related news online.

Members should now have received an email from the Society regarding the activation of their SHPHK account. Should you have any enquires regarding your SHPHK account, please do not hesitate to contact the SHPHK Membership Team at: info@shphk.org.hk.

The President of SHPHK would like to take this opportunity to thank the General Committee Members for their dedication and hard work throughout the year, and the Members of SHPHK for their continuous support to the Society.

Wish you all a Happy New Year!

More activities to come in 2022 to celebrate the 35th anniversary of SHPHK! Please stay tuned!

You are most welcome to follow the Society's Facebook page (**@SHPHK**) and the SHPHK Instagram (**@shphk1987**) to know more about the Society's development and activities. You may also visit the Drug Education Resources Centre (DERC) Website: www.derc.org.hk to keep abreast of the latest news and development of pharmaceutical services in Hong Kong. Join us now as new member or renew your membership at the Society's website: www.shphk.org.hk.

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數量 ____ 盒/套

升級版

維新烏絲活髮洗髮露 250ml

零售價~~$199~~

- 升級版加入活髮成分咖啡因
- 維特健靈專業研配的配方：製何首烏、靈芝、墨旱蓮、女貞子、菟絲子、咖啡

單盒訂購價 $159/樽
買5送1套裝 平均 $133/樽
數量 ____ 樽/套

升級版

維新烏絲活髮精華 100ml

零售價~~$350~~

- 升級版加入活髮成分咖啡因
- 維特健靈專業研配的配方：人參根、墨旱蓮、余甘子、假馬齒莧、咖啡

單盒訂購價 $300/樽
買3送1套裝 平均 $225/樽
數量 ____ 樽/套

如欲訂購 96814689 wilfred.wong@vitagreen.com

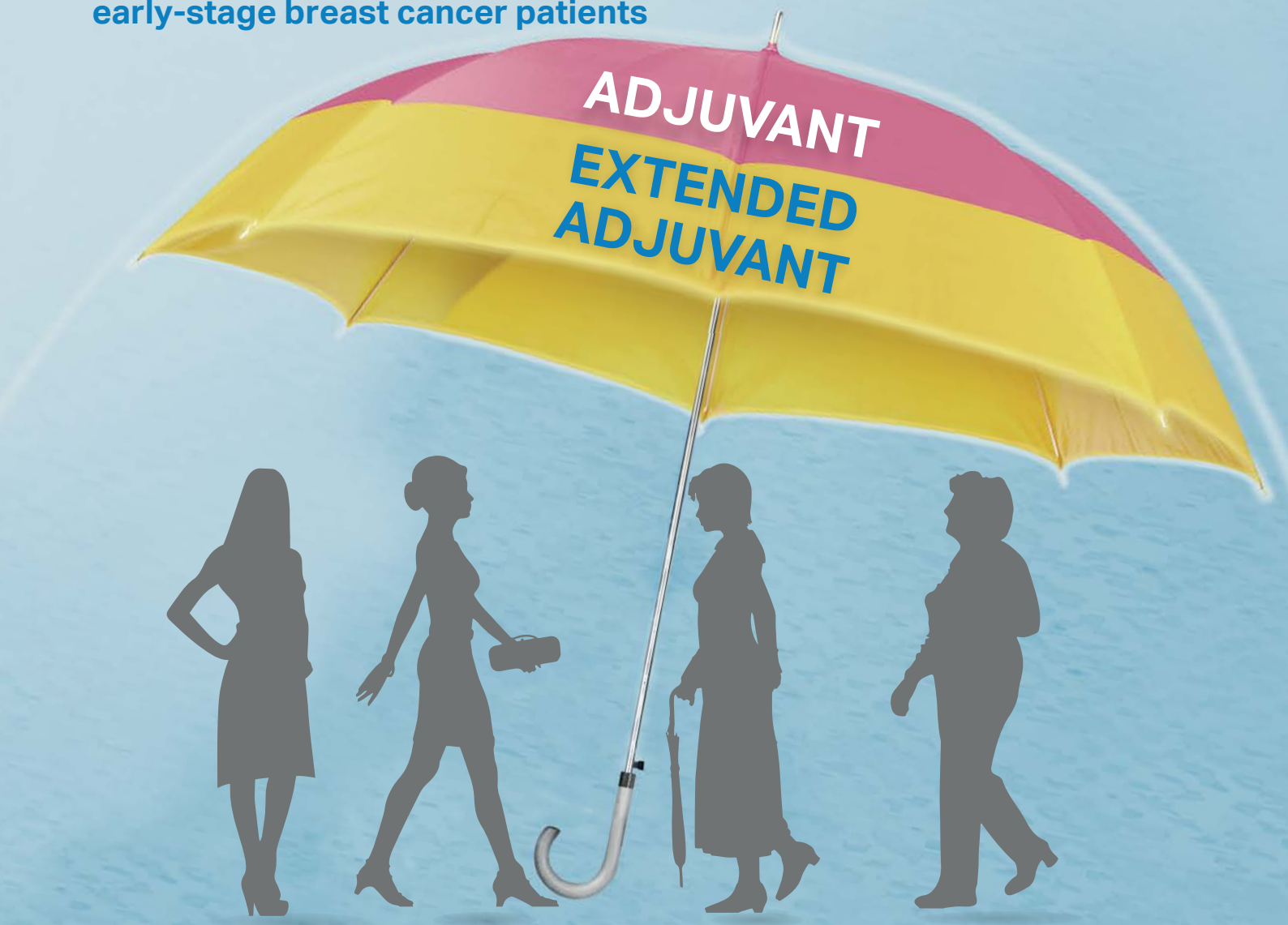
條款及細則: 1. 優惠只限藥劑師 2. 優惠期至2021年12月31日 3.有關產品優惠，維特健靈健康產品有限公司擁有最終決定權

CANbridge

nerlynx® (neratinib) tablets

FOLLOWING ADJUVANT TRASTUZUMAB-BASED THERAPY

NERLYNX offers Extra Protection to your HER2+ HR+ early-stage breast cancer patients



In an analysis from the phase III ExteNET trial, Nerlynx demonstrated significant improvement in HER2+, HR+ early-stage breast cancer patients who completed adjuvant trastuzumab-based therapy ≤ 1 year[1,2], in the following :

Consistent iDFS with △7.4%, 56% reduction of relative risk of recurrence at 5 years in patients who completed therapy[2]

Significant OS benefit with △5.8%, 51% reduction of relative risk of death at 8 years in patients who completed therapy[2]

Significant CNS benefit, 59% reduction of relative risk of CNS recurrence at 5 years[1]

HER2=human epidermal growth factor receptor 2, HR=hormone receptor, iDFS=invasive disease-free survival, CNS=Central Nervous System; OS=Overall Survival

References:
1 : Chan A, et al. Lancet Oncol. 2016;17(3):367-377;
2 : Moy B, et al. 2021 ASCO Annual Meeting. Poster #540

Nerlynx® 40 mg film-coated tablets ABBREVIATED PRESCRIBING INFORMATION

ACTIVE INGREDIENT(S): Each film-coated tablet contains neratinib maleate, equivalent to 40 mg neratinib.

INDICATION(S): Extended adjuvant treatment of adult patients with early-stage hormone receptor-positive HER2-overexpressed/amplified breast cancer and who completed adjuvant trastuzumab-based therapy less than one year ago. ADMINISTRATION: The recommended dose of Nerlynx is 240 mg (six 40 mg tablets) taken orally once daily, continuously for one year. Nerlynx should be taken with food, preferably in the morning. Patients should initiate treatment within 1 year after completion of trastuzumab therapy. See the Full Prescribing Information for dose modification information. CONTRAINDICATIONS: Co-administration with the following medical products that are strong inducers of the CYP3A4/P-gp isoform of cytochrome P450: carbamazepine, phenobarbital, phenytoin (antiepileptics), St John's wort (Hypericum perforatum) (herbal product), rifampicin (antimycobacterial). Co-administration with moderate CYP3A4/P-gp inhibitors: fluconazole (antifungal), diltiazem, verapamil (calcium-channel blockers), erythromycin (antibiotic), Severe hepatic impairment (Child-Pugh C).

SPRCIAL WARNINGS AND PRECAUTIONS: • Diarrhea: The diarrhea may be severe and associated with dehydration. Diarrhea generally occurs early during the first or second week of treatment with Nerlynx and may be recurrent. •Elderly: Elderly patients (≥65 years of age) are at a higher risk of renal insufficiency and dehydration which may be a complication of diarrhea and these patients should be carefully monitored. •Patients with a significant chronic gastrointestinal disorder: Patients with a significant chronic gastrointestinal disorder with diarrhea as a major symptom were not included in the pivotal study, and should be carefully monitored. •Renal impairment: Patients with renal impairment are at a higher risk of complications of dehydration if they develop diarrhea, and these patients should be carefully monitored. •Hepatic impairment: In patients with severe hepatic impairment (Child-Pugh C) there is a 2.8-fold increase of exposure to neratinib. •Left ventricular function: Left ventricular dysfunction has been associated with HER2 inhibition. Nerlynx has not been studied in patients with less than lower limit of normal left ventricular ejection fraction (LVEF) or with significant cardiac history. In patients with known cardiac risk factors, conduct cardiac monitoring, including assessment of LVEF, as clinically indicated. •Proton pump inhibitors, H2-receptor antagonists and antacids: Co-administration with proton pump inhibitors (PPIs) and H2-receptor antagonists are not recommended. If an antacid is taken, separate the dosing of Nerlynx and the antacid by at least 3 hours. •Pregnancy: Neratinib may cause fetal harm when administered to pregnant women. •Skin and subcutaneous tissue disorders: Nerlynx is associated with skin and subcutaneous tissue disorders. Patients with symptomatic skin and subcutaneous tissue disorders should be carefully monitored. •Concomitant treatment with inhibitors of CYP3A4 and P-gp: Concomitant treatment with strong CYP3A4 and P-gp inhibitors should be avoided due to risk of increased exposure to neratinib •Grapefruit juice should be avoided during treatment with Nerlynx. ADVERSE EFFECTS: Most common adverse reactions (>20%) of any grade were diarrhea, nausea, fatigue, vomiting, abdominal pain. PREGNANCY & LACTATION: Pregnancy: Nerlynx should not be used during pregnancy unless the clinical condition of the woman requires treatment with neratinib. Lactation: It is not known whether neratinib is excreted in human milk. A risk to the breastfed infant cannot be excluded.

PLEASE REFER TO FULL PRESCRIBING INFORMATION BEFORE PRESCRIBING.
Prescribing information last revised: December 2019

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