# HONG KONG PHARMACEUTICAL JOURNAL

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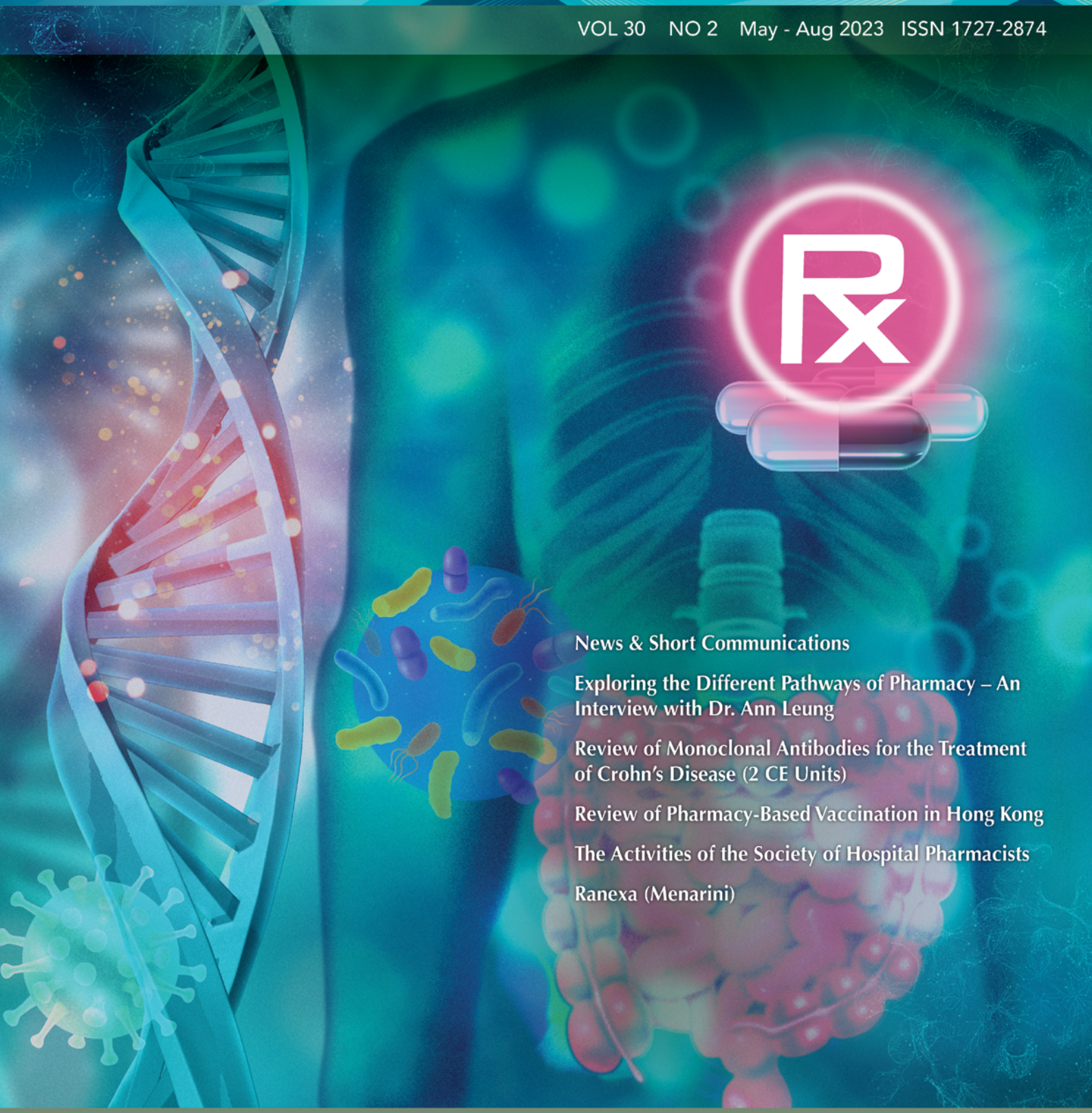



*The Pharmaceutical Society of Hong Kong*
*The Practising Pharmacists Association of Hong Kong*
*The Society of Hospital Pharmacists of Hong Kong*

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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.

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For detail instructions for authors, please refer to the first issue of each volume of HKPJ.

# Breakthrough in the Primary Care Services for Pharmacists in Hong Kong

I have just completed the 6 months' Certificate Course in Primary Healthcare for Pharmacists offered by HKU Department of Pharmacology and Pharmacy. It is a comprehensive course with Module 1 covering the social determinants of health, health equity and medical social collaboration, the services offered by some of the District Health Centres based on a multi-disciplinary team, transdisciplinary and family healthcare management approach, health screening and assessment, telehealth and use of technology. After completion of Module 1, an on line test consisting of multiple choice questions must be completed. Module 2 consists of pre-recorded on line lectures of different chronic diseases and the pharmacotherapies. The topics covered include management of hypertension, dyslipidemia, stroke, heart failure, myocardial infarction, stable angina, atrial fibrillation and use of anticoagulants; the management of osteoporosis and fall, asthma and COPD, diabetes mellitus; pharmacotherapy in special population including renal and hepatic impairment, pregnancy and breastfeeding, paediatric, geriatrics, men's and women's health and lifestyle medicines. The most update guidelines of USA, Europe and Hong Kong are taught and referred to. After that there were 2 clinical case studies with 1 week for preparation and then zoom on line assessments with a passing mark of 70%.

Module 3 consists of health-related issues and advice such as evidence-based medicine, history taking and medication reconciliation and motivational interviewing. Module 4 consists of Basic life support with assessment, Smoking cessation online lectures and workshop with oral assessment and Immunization training for pharmacists with assessment. Finally, everyone has to attend an oral assessment on a clinical case. You are given 10 minutes to look up information on line and then 10 minutes for presentation in which you have to identify 2 most significant drug-related problems, suggest solutions to the problems and to provide appropriate counselling to the patient based on the provided solutions.

Based on the topics covered and the assessments required, I am confident that the pharmacists will be equipped with the update knowledge to provide medication counselling, conduct medication review, medication reconciliation, smoking cessation services and provide immunization services in the District Health Centres and Community Pharmacies. Moreover, it is envisaged that the pharmacists who have taking the certificate course can have their names entered into the Primary Care Register of Pharmacists and eligible for payment of services by the Government in the near future.

In this issue on page 38, "Exploring the Different Pathways of Pharmacy –An Interview with Dr. Ann Leung" written by CHAN, Stephanie Nok Yan; CHONG, Donald Wing-Kit, Dr. Ann Leung talks about her experience as a clinical pharmacist in Canada and her views on Hong Kong's pharmacy education. In addition, she shares her teaching experience at the University of Hong Kong and discusses the new Master of Advanced Pharmacy program, which consists of four streams through which students can tailor their course selection and experience depending on their professional needs.

The article on page 42, "Review of Monoclonal Antibodies for the Treatment of Crohn's Disease" written by AU-DOUNG, Phillip Lung Wai; CHAN, Jason Chi Hin; CHENG, Andrew Foon Yu; LAU, Anna Pak Yan; LEE, Dawn Kei Yan; WU, Jason Tsun Sing, SUN, Wai Yan Kiwi aims to summarize the four monoclonal antibodies (mABs): adalimumab, infliximab, ustekinumab and vedolizumab, in terms of indications, mechanisms of action, pharmacokinetics, dosing regimen, efficacy and adverse effects. The key clinical features of the mABs in treating Crohn's disease are also discussed.

The article on page 54, "Review of Pharmacy-Based Vaccination in Hong Kong" written by CHAN, Philip Pana; LI, Johnny Chun-Wing; WONG, Janet Kit-Ting pointed out that in overseas healthcare systems, the high accessibility of community pharmacies and community pharmacists can promote immunization rates. In Hong Kong, despite recent advancement in the training pathway for pharmacist-led vaccination, the territory-wide implementation of pharmacy-based vaccination still faces crucial barriers with regard to vaccine access, expectation of pharmacists' roles and the difficulties for community pharmacies to fulfil infrastructure-related requirements. Overcoming these obstacles requires a constant supply of trained pharmacists, widespread distribution of vaccination-ready pharmacies, and potential updates in legislation or policies. Continuing collaborations and engagement among healthcare providers, academia, professional bodies, pharmaceutical industry and regulatory authorities will undoubtedly accelerate the introduction of pharmacy-based vaccination in Hong Kong.

I hope you enjoy reading the articles and look forward to your comments and active participation in submission of articles.

*Mary Catherine Cheng*
*Managing Editor*
*17 September 2023*

*Prepared by Branson Fok, Chloe Ip & Candice Leung*

## Intravenous Ketamine Demonstrated Non-Inferiority to Electroconvulsive Therapy in Patients with Non-psychotic Treatment-Resistant Major Depression

**Date: June 22, 2023**

Patients with major depression who fail to respond adequately in 2 or more antidepressant trials are regarded as treatment-resistant or refractory. Electroconvulsive therapy (ECT) is generally considered an effective option for this group of patients. Intranasal esketamine was approved by the U.S. Food & Drug Administration (FDA) in 2019 while intravenous (IV) ketamine is still being investigated by clinicians for its efficacy and safety in treating treatment-resistant major depression.

In this prospective, open-label, randomized trial conducted in the United States, a total of 365 patients with treatment-resistant major depression without any psychotic features participated in the study. Eligible participants were randomly assigned to receive a 3-week treatment of either IV ketamine (at a dose of 0.5 mg/kg of body weight) twice weekly (n=195) or right unilateral ECT thrice weekly (n=170), followed by a 6-month follow-up period. The primary endpoint was the drop in patient-rated Quick Inventory of Depressive Symptomatology-Self-Report (QIDS-SR-16) score by at least 50% at the end-of-treatment visit compared with their first visit as baseline. The predetermined non-inferiority margin was set at -10 percentage points between the two study groups.

Treatment responses were recorded in 55.4% of patients receiving IV ketamine and 41.2% of patients undergoing ECT, which indicated a difference of 14.2 percentage points (95% confidence interval [CI], 3.9 to 4.2; P<0.001 for non-interiority) in terms of changes in their QIDS-SR-16 scores. Fewer patient-reported memory dysfunction were documented in the IV ketamine group (mean between-group difference = 9.0 points; 95% confidence interval [CI], 5.1 to 13.0) based on the Squire Memory Complaint Questionnaire (SMCQ). Higher incidence of dissociative symptoms was observed in the IV ketamine group while more patients receiving ECT reported musculoskeletal adverse effects.

The clinical study demonstrated the non-inferiority of IV ketamine to ECT in managing non-psychotic treatment-resistant major depression when subanesthetic ketamine was given in a primarily outpatient setting.

Source: www.nejm.org

## Fruquintinub Improves Overall Survival for Refractory Metastatic Colorectal Cancer Patients

**Date: July 1, 2023**

About 50% of colorectal cancer patients develop distant metastases with an overall 5-year survival rate of 15%. Current treatment options available for metastatic colorectal cancer patients include chemotherapy and targeted therapies, in which trifluridine-tipiracil and regorafenib are oral agents that have shown promising effect on median overall survival. However, these agents are often found to induce treatment-related toxicities, necessitating subsequent dose reductions. Fruquintinib is an oral tyrosine kinase inhibitor that is highly selective in vascular endothelial growth factor 1, 2, and 3. This newly developed drug agent targets at the key regulators of angiogenesis during the development of metastases.

The multicenter, randomized, double-blind and placebo-controlled phase 3 FRESCO-2 study had recruited 691 patients from 14 countries to assess the efficacy and safety of fruquintinib in refractory metastatic colorectal cancer patients. Eligible participants were randomly assigned in 2:1 ratio to receive either fruquintinib 5 mg capsule (n=461) or matched placebo (n=230) once daily on day 1-21 in 28-day cycles alongside best supportive care until disease progression, death, unacceptable toxicities or study termination. The primary endpoint was overall survival from the day of randomization to death from any cause, while progression-free survival was a key secondary endpoint of this clinical trial.

An absolute difference of 2.6 months in median overall survival were observed between the fruquintinib (7.4 months; 95% confidence interval [CI], 6.7-8.2) and placebo (4.8 months; 95% confidence interval [CI], 4.0-5.8) group (hazard ratio=0.66; 95% confidence interval [CI], 0.55-0.80; P<0.0001). The fruquintinib group also had a longer median progression-free survival compared to the placebo group (absolute difference=1.9 months; hazard ratio=0.32; 95% confidence interval [CI], 0.27-0.39; P<0.0001). However, a higher percentage of participants in the fruquintinib group (63%) reported grade 3 or worse adverse events, including but not limited to hypertension and asthenia, against the placebo group (50%).

In conclusion, the study unveiled the potential of fruquintinib as a new treatment option to prolong overall survival of refractory metastatic colorectal cancer patients.

Source: www.thelancet.com

## Dupilumab Reduces Moderate-to-Severe Exacerbations in COPD Patients with Type 2 Inflammation

**Date: July 20, 2023**

Chronic Obstructive Pulmonary Disease (COPD) refers to the long-term lung inflammation that causes airflow restriction. Approximately 20-40% of the disease population possess type 2 inflammation, which is characterized by elevated blood eosinophil counts. Current studies have also shown that COPD patients with type 2 inflammation have higher risk of exacerbations. Dupilumab is a fully humanized monoclonal antibody which blocks the receptor components of interleukin-4 and interleukin-13, which are responsible for type 2 inflammatory reactions.

In this multicenter, double-blind, randomized and placebo-controlled phase 3 study, 939 COPD patients (with an absolute blood eosinophil count ≥ 300 per microliter) who have been using standard triple inhaler (inhaled glucocorticoid + long-acting muscarinic antagonist + long-acting $\beta_2$-agonist) therapy were randomized to receive either subcutaneous dupilumab 300 mg (n=468) or matched placebo (n=471) once every 2 weeks as add-on therapy for 52 weeks across 24 countries. Upon completion of the trial period, participants were enrolled in a 12-week follow-up period to assess drug safety. The major primary endpoint was the annualized rate of moderate-or-severe exacerbations during the study period.

The dupilumab group attained an annualized rate of moderate-or-severe exacerbations of 0.78 (95% confidence interval [CI], 0.64-0.93), meanwhile the rate was 1.10 (95% confidence interval [CI], 0.93-1.30) for the placebo group (rate ratio=0.70; 95% confidence interval [CI], 0.58-0.86; P<0.001). Functional improvements in terms of prebronchodilator forced expiratory volume in 1 second (FEV1) were also more significant in the dupilumab group (least-squares mean difference=83 ml; 95% confidence interval [CI], 42-125; P<0.001). The safety profile for both study groups was similar, with comparable rates of adverse events.

As has been demonstrated by the study, the use of dupilumab lowered the annualized rate of moderate-or-severe exacerbations in COPD patients presenting type 2 inflammation. Patients who underwent dupilumab as add-on therapy also showed greater improvements in lung function and quality of life.

Source: www.nejm.org

## FDA Approves Zurzuvae (Zuranolone) as The First Oral Treatment for Postpartum Depression

**Date: August 4, 2023**

Zurzuvae (zuranolone) has been approved by the U.S. Food and Drug Administration (FDA) on August 4th, 2023, as the first oral medication specifically indicated for the treatment of postpartum depression (PPD) in adults. Previously, the only available treatment for PPD was Zulresso (brexanolone), which was administered as an intravenous injection.

PPD is a type of major depressive episode that commonly occurs after childbirth but can also present in later stages of pregnancy. It shares similar symptoms with other forms of depression, including feelings of sadness, loss of interest in previously enjoyed activities, cognitive impairment, feelings of inadequacy, or even suicidal ideation.

The efficacy of Zurzuvae in treating PPD in adults has been demonstrated in two randomized, double-blind, placebo-controlled, multicenter studies. These studies enrolled women with PPD who met the criteria for a major depressive episode according to the Diagnostic and Statistical Manual of Mental Disorders and symptoms which began in the third trimester or within four weeks of delivery. In the first study, patients received 50mg of Zurzuvae or placebo once daily in the evening for 14 days. In the second study, patients received an equivalent of 40mg of Zurzuvae or placebo, also for 14 days. Both studies monitored patients for at least four weeks after the 14-day treatment period. The primary endpoint was the change in depressive symptoms assessed by the total score on the 17-item Hamilton depression rating scale (HAMD-17) on day 15. In both studies, patients in the Zurzuvae groups demonstrated significantly greater improvements in their depressive symptoms compared to those in the placebo groups. The positive effects of treatment were maintained at day 42, which was four weeks after the last dose of Zurzuvae.

Zurzuvae carries a boxed warning to alert individuals about the potential impact on their ability to drive or perform other potentially hazardous activities. Patients should refrain from driving or operating heavy machinery for at least 12 hours after taking Zurzuvae. The most common side effects include drowsiness, dizziness, diarrhea, fatigue, nasopharyngitis, and urinary tract infection. Use of Zurzuvae may also increase the risk of suicidal thoughts and behavior.

The recommended daily dose of Zurzuvae is 50mg, to be taken once daily for a duration of 14 days. It is recommended to take the medication in the evening with a fatty meal.

Source: www.fda.gov

# Exploring the Different Pathways of Pharmacy – An Interview with Dr. Ann Leung

**CHAN, Stephanie Nok Yan; CHONG, Donald Wing-Kit[a]***

*[a] GlaxoSmithKline Ltd., 23/F, Tower 6, The Gateway, 9 Canton Road, Tsim Sha Tsui, Kowloon, Hong Kong SAR, China*

**ABSTRACT**

**In this interview, Dr. Ann Leung talks about her experience as a clinical pharmacist in Canada and her views on Hong Kong's pharmacy education. In addition, she shares her teaching experience at the University of Hong Kong (HKU) and discusses the new Master of Advanced Pharmacy (MAP) program, which consists of four streams through which students can tailor their course selection and experience depending on their professional needs. In the future, she hopes to continue to align the program with the evolving needs of the healthcare system and connect with more pharmacy professionals to promote experiential learning.**

***Keywords:*** *Master of Advanced Pharmacy, Clinical Pharmacy, Pharmacist, Experiential Learning*

## INTRODUCTION TO DR. ANN LEUNG


Dr. Leung is currently a lecturer and one of the program coordinators of the Master of Advanced Pharmacy program at HKU Department of Pharmacology and Pharmacy. She is also a section editor for the Hong Kong Pharmaceutical Journal. She graduated from the University of Toronto with a Bachelor of Science in Pharmacy in 2009, subsequently working as a pharmacy resident at St. Michael's Hospital. After completing residency, she continued as a clinical pharmacist at St. Michael's Hospital and specialized in cardiology and critical care pharmacotherapy. Dr. Leung has rich experience as a preceptor for undergraduate pharmacy students and pharmacy residents on clinical rotations. In 2017, she finished her Doctor of Pharmacy at the University of Florida. Before returning to Hong Kong, she worked as a hospital clinical pharmacist in Canada for ten years.

## INTRODUCTION TO MASTER OF ADVANCED PHARMACY

To support the evolving needs of pharmacy professionals in Hong Kong, HKU initiated the Master of Advanced Pharmacy (MAP) program in 2022. The program provides student-centered postgraduate training that allows students to customize their course selection and exposure based on their professional aspirations and interests in different pharmacy sectors. The program consists of four streams, namely Clinical Practice, Community Health, Pharmaceutical Medicine, and Generalist. All four streams include the option of completing a practicum that provides hands-on experience and networking opportunities to students. The program is currently offered as a 1-year full-time or a 2-year part-time program. Candidates holding a Bachelor's degree in pharmacy or other relevant disciplines are eligible to apply. You can scan the QR code to learn more about the MAP program.

## INTERVIEW WITH DR. ANN LEUNG

**Q: Why did you choose to study pharmacy?**

**Dr. Leung:** I have always been interested in life sciences in school. I was drawn to a healthcare-related career with plenty of interaction with patients. In addition, you can be an entrepreneur and build your own pharmacy in the community. After studying pharmacy, I discovered even more pathways, including hospital, industry, consultant and education roles. At graduation, I realized that I especially enjoyed the clinical aspect of pharmacy, so I chose to pursue a hospital residency after I graduated.

**Q: What is the curriculum like in Canadian or United States pharmacy schools?**

**Dr. Leung:** In North America, students typically complete at least 2 to 3 years of undergraduate studies prior to applying for pharmacy school. Most schools now offer the entry-level Doctor of Pharmacy degree. For example, the University of Toronto PharmD program is a 4-year program that combines coursework, laboratory instruction, and at least 40 weeks of hands-on experiential learning in a variety of practice sites, ranging from community, hospital, research and education settings. Students spend 5 weeks at each rotation so that there is enough time to immerse and hone their knowledge and skills. Compared to the old Bachelor's degree with only 1 semester of dedicated rotation time, I definitely see the value of increased experiential learning on students' ability to apply knowledge and handle patient scenarios in a real-world setting.

**Q: Do you see any differences in how students choose their professional degrees when comparing Hong Kong and Canada?**

**Dr. Leung:** In Canada, most professional degrees do not offer direct entry from high school. Students must go through at least 2 to 3 years of undergraduate studies, and many will complete an undergraduate degree first. During this time, students are expected to explore different career options through volunteering or summer work. Professional programs not only consider academic achievement, but also extracurricular involvements to select well-rounded individuals. By the time Canadian students get into pharmacy school, they typically have a better idea of what being a pharmacist is about. The Canadian university system wants students to gain more life and work experience before choosing their career direction. On the contrary, students in Hong Kong enter professional degrees straight from high school. It's hard to know what you want to do at such a young age.

The downside of the Canadian system is the uncertainty during the first few years of university, as you are not guaranteed a professional degree and will need to compete. I remember feeling very uncertain at that time, but looking back now, I think it is wise to spare some time to get to know yourself first. There is no need to rush into anything and you will not know what you want to do until you have had some exposure and experiences first.

**Q: Can you share about your work experience in Canada?**

**Dr. Leung:** After I graduated from the University of Toronto, I became a pharmacy resident at St. Michael's Hospital. Residency is a 1-year intensive accredited training program, which includes structured rotations to drug distribution, drug information, and around six clinical areas. It was a great opportunity to polish my therapeutic thought process and deepen my knowledge and ability to apply it in various patient populations under the guidance of wonderful mentors. I also presented patient case presentations monthly and took a research project from design to manuscript. With the structured residency program, the 1-year experience is generally considered equivalent to 3 to 5 years of working experience as a clinical pharmacist.

After my residency, I started my first job at the same hospital, covering various areas including the neurosurgery and trauma intensive care unit (ICU), cardiovascular ICU, operating room pharmacy satellite and pre-admission clinic for 3 years. Then I took on my permanent role as a clinical pharmacist in the cardiac ICU, working with patients with acute coronary syndrome, severe heart failure, arrhythmia, and after resuscitation for cardiac arrest.

My work consisted of 70% direct patient care on the ward and 30% project time. I worked on many interesting assignments such as preparation for hospital accreditation and protocols and education leading up to the legalization of cannabis. Looking back now, my 10 years at St. Michael's Hospital gave me a strong clinical background, project management skills, the ability to deal with ill-defined problems, and many other soft skills that are so important for my role now at HKU.

**Q: How did you become a specialist pharmacist in cardiology and critical care?**

**Dr. Leung:** It's a combination of learning on the job and seeking additional training. In Canada, you are assigned to a specific clinical area. At my hospital, the department will also assign a senior mentor in that area to guide your development and review patient cases with you. It's a lot of self-directed learning. You also learn every day on multidisciplinary teaching rounds. I would say it takes about 1 year to gain familiarity and feel comfortable in any specific area, and you continuously learn. It wasn't until I returned to Hong Kong that I obtained the Board of Pharmacy Specialties certification for cardiology. It's not that common in Canada but in retrospect, the structured materials would have been very helpful when I first started in the cardiac ICU.

**Q: What was your daily work routine in the cardiac ICU ward?**

**Dr. Leung:** On a typical day, I start work at 8 am to prioritize and see patients in preparation for rounds. Then, from 10 am to 1 pm, I join the bedside round with the doctors, nurses, respiratory therapist, and dietitian. ICU rounds are very systematic to ensure the team reviews all the issues for each patient. As the pharmacist, I was responsible for summarizing the active medications, providing recommendations on how to optimize the medication regimen, supporting drug monitoring and

reconciling home medications. I loved being on rounds because I can proactively contribute to the orders of the day rather than retrospectively resolving issues. In the afternoon, I follow up on less urgent issues and address any drug information questions.

**Q: After working in Canada, what is your view on the future of clinical pharmacy in Hong Kong?**

**Dr. Leung:** Hong Kong's clinical pharmacy services are rapidly developing. In the hospital setting, pharmacist roles are expanding on the ward beyond high-risk areas such as oncology and pediatrics. Pharmacists are now serving in many new specialized outpatient clinics. It is only a matter of time before pharmacists are regularly expected in every ward and clinic as we see in North America. With the rapid development of primary care, we are already seeing the expanding role of community pharmacists in sharing the load of outpatient prescriptions and providing essential education to the public to keep the population healthy. Pharmacists will need varied knowledge and skills to expand their role depending on their setting, and we will continue to evolve the Master of Advanced Pharmacy curriculum and courses to support this exciting growth of clinical pharmacy in Hong Kong.

**Q: Are there any challenges or unforgettable memories from your hospital work?**

**Dr. Leung:** The first few years were challenging. I had a good base from pharmacy school, but it took lots of practice and feedback to get to a point where I could efficiently apply my knowledge and handle a full patient load. I stayed an hour or two behind almost every day and tackled additional learning in the evenings and weekends. My first job as a pharmacist in the neurosurgery and trauma ICU also presented a lot of sad patient cases that taught me how to have empathy without being too emotional.

As for the memorable part, the first thing that comes to mind is my wonderful multidisciplinary work team. I value the positive team dynamics and am glad to have worked with such a harmonious team. Also, I am thankful for all the mentors at St. Michael's Hospital who have become dear friends. There were many good role models in terms of both professional and personal attributes. By observing my mentors, I learnt how to communicate with patients, how to deal with stress, how to be a good coworker, and many other things. I truly loved my job as a clinical pharmacist.

**Q: Why did you start teaching in Canada?**

**Dr. Leung:** St. Michael's Hospital is a teaching hospital that provides rotation spots to the University of Toronto and Waterloo every year. All pharmacists in the department are expected to take students and that's how I got started. It's such a rewarding experience to support and see how students grow over the course of 4 to 5 weeks. Experiential learning is so crucial to a pharmacy student's transition into practice, and I'm honored to play a small part. As I got more experienced in critical care and cardiology, I was invited to teach a few lectures at the university and to guide international pharmacy graduates. Teaching in Canada was mainly conducted in small groups, so that has really shaped my teaching style.

**Q: What made you come back to Hong Kong?**

**Dr. Leung:** I moved back to Hong Kong for family reasons. I took some time to network and met some great colleagues who helped me understand the pharmacist job opportunities in Hong Kong. Since I had already worked for 10 years in hospital pharmacy, I decided to develop myself in the field of teaching. Time flies, and now I have been teaching at HKU for three years and have become the course coordinator for the MAP program.

**Q: Why did HKU decide to transition from the Master of Clinical Pharmacy to the Master of Advanced Pharmacy program?**

**Dr. Leung:** The Master of Clinical Pharmacy (MCP) program had been running for over 10 years and it was primarily focused on hospital pharmacy practice. Students complete mostly the same courses with the difference of only one elective course. Over the years, we noticed that MCP lacked flexibility and did not fully satisfy the learning needs of individual students, especially in community and industry settings. At the same time, we wanted to increase the exposure of our students to important skills and topics, such as health informatics and big data, primary care and public health, and advanced therapy products. As such, we introduced the MAP program which absorbed the MCP as its Clinical Practice stream. With its 4 streams of study, we greatly expanded the scope of our courses and flexibility so that students can tailor their exposure according to their career goals and interests.


*Teaching team and students of the Master of Clinical Pharmacy program at the 2023 Poster Presentation Day*

**Q: What are the new features of the MAP program that you would like to highlight?**

**Dr. Leung:** In addition to the student-centered curriculum, the MAP program introduces the option of practicum. Students gain hands-on experience and competencies at different practice sites in the hospital, community and industry. Also, they gain project management and other soft skills by completing an on-site project to improve medication management. They work on solving real-world issues that benefit the practicum organization and the clients served. It is a great way to develop our students' critical thinking skills, so they can identify and deal with ill-defined problems. The MAP is a hub that connects the various sectors of pharmacy practice and fosters collaboration and networking.

Another key focus of the MAP program is local application. We want our students to be able to apply the knowledge and skills the next day at work. We have built a community of experienced local pharmacists who collaborate with our academic staff on course design and assessment so that the courses capture what pharmacists need to know most in Hong Kong practice.

**Q: As the course coordinator, how are you feeling about the new MAP program after a year? What are the future directions for the program?**

**Dr. Leung:** It has been a smooth transition and we're receiving great feedback from students and employers! In the future, we hope to expand our role in connecting pharmacy professionals in various sectors. We will continue to introduce new courses and public seminars to respond to evolving issues and skills needed in pharmacy practice. For instance, we organized a public seminar in collaboration with The Society of Hospital Pharmacists of Hong Kong last year, and over 100 people registered to learn about the latest developments in ambulatory care clinic pharmacy practice. This in turn identified the need for including clinical assessment skills in our curriculum to prepare pharmacists to seize new opportunities in the workplace. Through our close links with external stakeholders, we will continue to align the program to prepare our graduates to advance our profession.

**Q: After three years of teaching, how are you finding your work at HKU?**

**Dr. Leung:** What I like about this job is that there are new tasks and challenges every year. Our department head, Professor Wong, empowers us to try new things and to push pharmacy education forward. In addition to teaching skills, my job constantly challenges me to grow. In my first year, I led the process to bring the Master of Advanced Pharmacy program to approval at HKU. I gained experience with promoting MAP and events, both through social media and in collaboration with multimedia companies. This year, I received a teaching development grant to build a new educational electronic health record platform that will help students bridge the gap to practice.

**Q: What advice do you have for our pharmacy students and graduates?**

**Dr. Leung:** To fellow pharmacy students and graduates, I encourage you to stay open-minded about your future career. Get exposed to various sectors during your training so that you can figure out what you're most interested in and good at. Make good use of the summer holidays to gain experience, and this will help you stand out during future interviews. In addition, prepare yourself for future opportunities before they come. Seek ways to upskill and it doesn't always have to be pharmacy related. For example, I've had great students who developed great programming and social media promotion skills that they were able to apply beautifully in pharmacy. This really helped them shine amongst the crowd.

Most importantly, do not just focus on pharmacy knowledge, because you need more than that to be successful in the workplace. Learn how to be helpful and valuable in your team. As mentioned, I had many amazing mentors along the way. Do not be shy to seek out senior colleagues because they are happy to share their experiences and knowledge with you.

## CONCLUSION

As a lecturer and course coordinator for the MAP program at The University of Hong Kong, Dr. Ann Leung shares her experiences as a clinical pharmacist in Canada, and how she found her path as a pharmacist in Hong Kong. She now focuses on coordinating the MAP program to ensure that the program allows for students to shine in their respective fields in pharmacy practice.

**Author's background**

***CHAN, Stephanie Nok Yan*** *is a pharmacy intern at Consumer Health, GlaxoSmithKline Hong Kong. Her email address is: stephanie.x.chan@haleon.com*

***CHONG, Donald Wing-Kit*** *is currently the Regulatory Affairs Director, Consumer Health at GlaxoSmithKline in Hong Kong. For enquiries, please contact him through the email address: donald.w.chong@haleon.com*

# Review of Monoclonal Antibodies for the Treatment of Crohn's Disease

**AU-DOUNG, Phillip Lung Wai[a]; CHAN, Jason Chi Hin[a]; CHENG, Andrew Foon Yu[a]; LAU, Anna Pak Yan[a]; LEE, Dawn Kei Yan[a]; WU, Jason Tsun Sing[a]; SUN, Wai Yan Kiwi[a]***

*[a]School of Pharmacy, 8/F, Lo Kwee-Seong Integrated Biomedical Sciences Building, Area 39, The Chinese University of Hong Kong, Shatin, N.T., Hong Kong*

*(*Corresponding author)*

## ABSTRACT

**Over the past 20 years, a rising prevalence of Crohn's disease (CD) has been observed in Asian countries including Hong Kong. Apart from anti-TNF agents adalimumab and infliximab, some newer agents such as vedolizumab for anti-α4β7 integrin receptors, and ustekinumab for anti- interleukin (IL)-12 and anti-IL-23 are also available in Hong Kong. This review aims to summarize the four monoclonal antibodies (mABs): adalimumab, infliximab, ustekinumab and vedolizumab, in terms of indications, mechanisms of action, pharmacokinetics, dosing regimen, efficacy and adverse effects. The key clinical features of the mABs in treating CD are also discussed.**

***Keywords:*** *adalimumab, infliximab, ustekinumab, vedolizumab, Crohn's disease, monoclonal antibody*

## INTRODUCTION

Crohn's disease (CD) is a type of inflammatory bowel disease (IBD) that was diagnosed by Dr. Burrill B. Crohn and team in 1932.[1] CD is characterized by chronic inflammation that can occur in any part of the mucosal area of the gastrointestinal tract. The presenting symptoms include diarrhea, abdominal pain, weight loss and fever.[2] The median onset time of CD is between the age of 20 and 30 years old, and with a peak at around 50 years old.[3] The prevalence of CD is around 50 to 200 cases per 100,000 people globally.[4] In Hong Kong, the most recent registry showed that the local prevalence of CD is 18.6 cases per 100,000 people.[5]

The pathogenesis of CD involves a complicated mechanism between the innate and adaptive immune system. Gut microbiota is also described to have a role.[6] Conventional treatments include 5-aminosalicylates (5-ASA), corticosteroids, azathioprine or methotrexate that aim to delay the progression of CD.[7] Despite a lifelong therapy, the progression or relapse of CD still occur in most patients. A meta-analysis showed the relapse rate in 1 year and 2 years was 38% and 52% respectively in patients who received anti-tumour necrosis factor (TNF) after CD remission.[8] The development of mABs aims to provide an alternative treatment option to overcome the high relapse rate.[9] Thus, it is important for healthcare professionals to acquire the knowledge of pharmacological treatment options for CD.

## PATHOPHYSIOLOGY

CD is characterized by tissue inflammation that is triggered by the dysregulation of the innate and adaptive immune systems.[10] In the inflammation stage, more IL-34 is released in patients with CD via extracellular signal-regulated kinase (ERK)-mediated mechanism, therefore it increases TNF-α and IL-6 production.[11] In addition, $CD4^+$ T cells are increased and lead to the production of type 1 T helper ($T_H1$) and type 17 T helper ($T_H17$) cells-associated proinflammatory cytokines, such as interferon (IFN)-γ, IL-12, IL-23 and TNF-α.[12, 13] For instance, IL-12 induces $T_H1$ cell activity to further enhance the production of IFN-γ.[14] Excessive $T_H1$ immune response is known to cause intestinal inflammation in CD. Furthermore, CD patients also have a high amount of IL-2 which binds to $CD4^+$ T cells and activate the differentiation of plasma cells in the mucosa.[10] As a result, it triggers the activity of cytotoxic mediators on the intestinal mucosa and damages the epithelial cells.[15]

Good balance of gut microbiota in the intestinal tract can be key to control the inflammatory response.[10] A cohort study found that a higher percentage of dysbiosis occurs in patients with CD when compared to healthy individuals.[16] It usually accompanied by excessive growth of *Enterobacteriaceae* (i.e. *Salmonella, Shigella and Escherichia coli*) that activates the inflammatory response in guts.[17]

Moreover, smoking is a risk factor of CD induction or deterioration as cigarettes affect colon mucus production and delay mucosal repairment in the guts.[18, 19] Smoking also changes the autophagy-related gene *ATG16L1* expression resulting in dysfunction of recognition, handling and clearance of invading pathogens.[20] Another risk factor is chronic use of high dose NSAIDs that inhibit COX1 and COX2 enzymes resulting in a high risk of intestinal ulcer.[21, 22] Genetic mutation is shown to contribute to the pathogenesis of CD. Nucleotide-binding oligomerization domain 2 (NOD2) mutation is found in one-third of the patients with CD, which the inhibitory effect on Toll-like receptor 2 (TLR2) is lost and causes the activation of inflammatory pathways via excessive $T_H1$ responses.[23]

## USE OF MONOCLONAL ANTIBODIES (mABs) IN CD

Corticosteroids, 5-ASA, azathioprine and methotrexate are the conventional treatments for CD. However, some patients are either not responding or intolerant to them.[24] With the advancement in the drug discovery, biologics (mABs) have been shown to be effective.[9] They are classified into anti-TNF agents (infliximab, adalimumab) and other selective agents such as anti-integrin (vedolizumab) and anti-IL agent (ustekinumab) **(Table 1 and Table 2)**. As per the American Gastroenterological Association (AGA) 2021 guideline, these mABs are indicated for patients with moderate to severe CD.[25] In terms of safety, patients are required to screen for latent tuberculosis (TB) and hepatitis B virus before using mABs. Live vaccinations are generally not recommended in all mABs except vedolizumab, to prevent overacting immune response, patients should discuss with physicians the risk versus benefit of the live vaccination. Although mABs are effective in CD management, they are costly.[26] In Hong Kong, they are under the safety net at the Hospital Authority Drug formulary **(Table 1)**.

The goal of CD therapy is divided into two aspects: inducing remission and preventing a relapse of CD.[27] Compared to the conventional regimens, there is no concrete consensus on the selection of first-line mABs. This is likely due to the limited head-to-head trials to compare the efficacy and safety between mABs.[9] Clinically, anti-TNF agents are considered as the first-line mABs treatment because of more evidence.[9] However, approximately two-third of patients experienced a recurrence of CD within 1 year post anti-TNF treatment.[28] Also, these patients tended not to have a good response to another anti-TNF agent after failing with one anti-TNF.[29] AGA 2021 guideline emphasizes that selection of mABs should be based on patient's conditions, such as history of failure to anti-TNF agents, allergic reaction any mABs, and screening results of latent TB and hepatitis B virus.[25]

## INFLIXIMAB (Remicade®)

### Approved Indication

Infliximab (Remicade®) is registered in Hong Kong since 2006 and is classified as P1S1S3 poison.[30] It is indicated for adult and pediatric patients with moderate to severe active CD.[31]

### Mechanism of Action

TNF-α is a key proinflammatory cytokine leading to CD. Overexpression of TNF-α amplifies the inflammatory process and causes the induction and perpetuation of intestinal inflammation.[32] Infliximab is a genetically engineered immunoglobulin 1 (IgG1) murine–human chimeric monoclonal antibody by binding to transmembrane and soluble forms of the protein and preventing the interaction between TNF-α and its receptor.[33] Other than the blockade of TNF, infliximab can inhibit the production of IL-1 and IL-6, which reduces leukocyte migration and adhesion molecule expression by the endothelial cells to help suppress inflammation.[34] The levels of soluble CD40L was elevated in plasma and surface CD40L was increased in platelets and T cells of CD patients. Infliximab also regulates the CD40L signaling pathway that contributes to the systemic anti-TNF-α action.[35]

Other than the known mechanisms of action of infliximab in humans, a recent study suggested that the efficacy of infliximab is correlated to the expression of Annexin A1 (AnxA1) on formyl peptide receptors (FRRs) by using dextran sulfate sodium colitis model in mice.[36] AnxA1 is a mediator produced by epithelial cells and mobilized to the membrane after the cell activation to trigger anti-inflammatory pathways of FRRs, which is a possible mechanism of infliximab.[36]

### Evidence from Clinical Trials

A recent trial that recruited luminal CD patients with Asia background to show an increase of 60% remission rate by infliximab. The remission rate further increased to more than 90% in week 54 of infliximab.[37] Other than luminal CD patients, there was a prominent effect on the fistulizing CD patients as the remission rate reached 56.2%. Furthermore, the remission rate increased to 97.1% by week 54.[37] Only 6% of patients had serious adverse effects, such as severe infusion reactions (7 cases), serum sickness (2 cases), intra-abdominal abscess (2 cases), and active tuberculosis (2 cases).[37]

In pediatric CD patients, a study conducted in Japan found that infliximab is effective in refractory cases when compared to cyclosporin and tacrolimus.[38] Upon remission, 54.7% and 69.6% of the pediatric CD patients can reduce or discontinue the dose of steroids, respectively.[38]

### Dosing Regimen

The recommended dose is 5 mg/kg through intravenous

(IV) injection at 0, 2, and 6 weeks and then started the maintenance dose at 5 mg/kg every 8 weeks for adult or pediatric patients with moderate or severe active CD or fistulizing CD.[31]

If adult patients showed partial response, infliximab can be increased to 10 mg/kg. However, if no response is observed by week 14, it should be discontinued and other treatment options should be considered.[31]

**Adverse Drug Effects (ADRs)**

Common ADRs include fever, shortness of breath, coughing and rash which may occur during the treatment in adult and pediatric patients.[31] It is more likely to increase the risk of infection, such as cytomegalovirus infection, re-activation of latent TB in adult patients.[37, 38]

**Management of ADRs**

Infusion related reactions (IRRs) to infliximab are common and acute that usually occur within 15 to 30 mins post-infusion. The symptoms of IRRs include pruritus, urticaria, fever and bronchospasms.[39] There are four different types of IRRs: complement activation-related pseudo-allergy (CARPA), cytokine release syndrome, anaphylactoid reaction and immunoglobulin E-mediated anaphylaxis.[39] CARPA and cytokine release syndrome are well described as IRRs, but the latter two syndromes are often considered as allergic reactions.[39] Physicians can prescribe prophylactic medications, such as prednisolone, hydrocortisone and antihistamine, to prevent the IRRs.[39] However, if patient's IRR symptoms exist despite the use of prophylactic medications, changing the regimen is needed, such as dosage adjustment and change of another class of drug.[40]

## ADALIMUMAB (Humira®)

**Approved Indication**

Adalimumab (Humira®) is registered in Hong Kong since 2017 and is classified as P1S1S3 poison.[30] It is available in single pen and prefilled syringe form for injection, and is indicated for moderate to severe active CD in adults and pediatric patients 6 years of age or above.[41]

**Mechanism of Action**

Adalimumab is a fully humanized IgG1 monoclonal antibody, which reduces the overexpression of TNF-α by blocking its receptors. Therefore, the associated proinflammatory signals is attenuated.[42] The Fc region of adalimumab can trigger M2-type wound-healing macrophages which may help to promote mucosal healing.[33] In addition, it induces antibody-dependent cellular cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC). ADCC refers to the binding of Fc receptor to the target cells to trigger the killing action of the natural killer cells.[43] CDC refers to the antibodies binding to the target cells to activate the complement pathway for the killing action.[43]

**Evidence from Clinical Trial**

In the CHARM trial, around 40% of CD patients treated with adalimumab had remission in week 26. A similar percentage of remission remained in week 56, suggesting a good maintenance rate by adalimumab.[28] Also, patients treated with adalimumab had 64% reduction of hospitalization over a 12-month follow-up period.[44] Patients who achieved steroid-free clinical remission increased from 22.3% to 50.0% over a prolonged period of 96 week.[45] Indeed, AGA (2021) guideline recommended that adalimumab can be administered with or without an immunomodulator for patients who have no response to the conventional pharmacological treatment.[25] Adalimumab is also effective for prophylactic therapy in patients with CD following surgical resection to prevent clinical recurrence.[46, 47]

**Dosing Regimen**

For adult patients, adalimumab 160mg is given subcutaneously (SC) on day 1 or split over 2 consecutive days, followed by 80mg SC on day 15 and then 40mg SC once every other week from day 29.[48]

For pediatric patients ≥ 6 years old or less than 40kg, adalimumab 80mg SC is given on day 1, followed by 40mg SC on day 15 and then 20mg SC once every other week from day 29.[48]

For pediatric patients ≥ 6 years old and greater than 40kg, adult dosage of adalimumab is used.[48]

**ADRs**

The most frequent adverse effects are injection site reactions and dermatologic rashes. Other common side effects include headache, sinusitis and upper respiratory infection.[41] Adalimumab can increase the risk of infection, such as TB, invasive fungal infection leading to hospitalization as mentioned in the black box warning.[41] If occurs, immediate discontinuation of adalimumab is needed.[41] Case reports of lymphoma and malignancies in children and teenagers during the treatment of adalimumab are described.[49]

## VEDOLIZUMAB (Entyvio®)

**Approved Indication**

Vedolizumab (Entyvio®) is registered in Hong Kong since 2015 and is classified as P1S1S3 poison.[30] It is available in solution for infusion and is indicated for patients with active status of moderate to severe CD who are intolerant or have insufficient response to TNF-α blocker, or demonstrated dependence on corticosteroids.[50]

### Mechanism of Action

Vedolizumab is a humanized α4β7 integrin monoclonal antibody.[50] It binds to the α4β7 integrin receptor to interfere the interaction with mucosal addressin cell adhesion molecules-1 (MAdCAM-1), resulting in alleviation of chronically inflamed gastrointestinal parenchymal tissue associated with CD.[51] Also, Vedolizumab prevents further inflammatory reaction by inhibiting the movement of memory T-lymphocytes across the endothelium into inflammatory gastrointestinal tissue.[51]

### Evidence from Clinical Trials

The efficacy and safety of using vedolizumab in moderate-to-severely active CD were conducted in the GEMINI 2 phase 3 clinical trial.[52] The post-hoc analysis aimed to access the induction and maintenance phase of Asian and non-Asian patients who were treated with vedolizumab. The disposition of the Asian subgroup was separated into Cohort 1 included 51 patients, 34 were randomized to vedolizumab and 17 to placebo in the induction phase. Cohort 2 included 24 patients who were treated with vedolizumab on open-label. During the induction phase, approximately 15% of the patients in the vedolizumab group achieved remission compared to 0% in the placebo group at week 6.[52] The clinical remission and response rates were higher in vedolizumab compared to placebo. During the maintenance phase, patients with clinical response to vedolizumab during the induction phase were subsequently treated with vedolizumab every 8 weeks, every 4 weeks, or placebo for up to 52 weeks.[52] The clinical remission rate were 41.7%, 36.4% and 0% respectively; while enhanced clinical response rates indicated 41.7%, 63.6% and 42.9% respectively.[52] However, the limitation of the study is relatively small sample size in subgroup analysis.

Vedolizumab is effective in patients with history of failure with anti-TNF as the therapeutic benefits of vedolizumab were detectable in week 10.[53] GEMINI 2 trial showed that patients after receiving vedolizumab every 8 weeks, 83% [n=100/120] and 89% [n=62/70] of patients were in remission after 104 and 152 weeks, regardless of prior anti-TNF exposure.[52]

### Dosing Regimen

For adults, the induction dose of vedolizumab is 300mg IV infusion over 30 minutes at 0, 2, and 6 weeks, and for maintenance, the same dose is administered once every 8 weeks thereafter.[50] Discontinuation of vedolizumab is generally required in patients who show no therapeutic benefit by week 14.[50]

For pediatric patients, the safety and effectiveness of vedolizumab have not been analyzed.[50]

### ADRs

The most common side effects include nasopharyngitis, headache, abdominal pain, arthralgia, upper respiratory tract infection and pain in extremities.[50] Monitoring any hypersensitivity signs and symptoms during and after infusion is recommended.[50] Infections may occur during treatment, infection-relate symptoms need to be recognized, such as fever, chills, muscle ache, cough, pain during urination and shortness of breath.[50] Vedolizumab should be withheld when a serious infection occurs.[50] Monitoring patients for any worsening of neurological signs and symptoms is recommended to minimize the risk of progressive multifocal leukoencephalopathy (PML), a virus induced infection in the central nervous system (CNS) and is considered as a rare but serious side effect reported in patients treated with another integrin receptor antagonist. A referral to neurologist should be made for suspect cases and permanent discontinuation of vedolizumab is needed if diagnosed with PML.[50]

## USTEKINUMAB (Stelara®)

### Approved Indication

Ustekinumab (Stelara®) is registered in Hong Kong since 2011 and is classified as P1S1S3 poison. It is available in solution for infusion and injection.[30] Ustekinumab is indicated for patients with moderate to severe CD who have history of failure or intolerance to corticosteroids or TNF blockers.[54]

### Mechanism of Action

IL-12 and IL-23 are pro-inflammatory cytokines that are involved in the pathogenesis of CD by inducing intestinal inflammation.[55] Ustekinumab is a fully humanized IgG1 monoclonal antibody that selectively binds to the p40 subunit of IL-12 and IL-23, and thereby inhibiting the binding of the respective receptors on the T cells and NK cells surface. As a result, intestinal inflammation is attenuated.[56]

### Evidence from Clinical Trials

Both UNITI-1 and UNITI-2 trials showed a larger remission rate in patients treated with 6 mg/kg of ustekinumab at week 8 when compared to the placebo controls (UNITI-1: 20.9%, UNITI-2: 40.2%, $p<0.001$).[57] Also the clinical response and health-related quality of life (HRQoL) measured by Inflammatory Bowel Disease Questionnaire (IBDQ) and 36-item short form health survey (SF-36) were significantly better in the treatment group of patients (UNITI-1: 37,8%, UNITI-2: 57.9%, $p<0.001$).[57] Regarding the maintenance regimen, the rate of remaining remission at week 44 was significantly higher in patients with ustekinumab at 90 mg every 8 weeks (53.1%, $p=0.005$) and patients with ustekinumab at 90 mg every 12 weeks (48.8%, $p=0.040$) than the placebo groups.[57]

### Dosing Regimen

The induction regimen is administered by IV infusion.[54] For patient whose body weight is <55kg, 55-85kg and >85kg, the dosage is 260mg, 390mg and 520mg respectively.[54, 57] The maintenance dose is injected at 90mg SC once every 8 weeks.[54]

For pediatric patients, the safety and effectiveness of ustekinumab have not been examined.[54]

### ADRs

The common ADRs during the induction therapy were nasopharyngitis (up to 6.8%), arthralgia (up to 6.0%), pyrexia (up to 6.0%), nausea (up to 5.3%) and abdominal pain (up to 5.2%).[57] A similar ADR profile was observed during the maintenance therapy.[57]

Rarely, patients treated with ustekinumab (up to 0.2%) developed non-melanoma skin cancer. Therefore, all patients receiving ustekinumab should be monitored for a new onset of skin abnormality.[54]

**Table 1. Comparison of mABs for the treatment of CD**

| **Monoclonal antibodies** | | **Infliximab[31]** | **Adalimumab[41]** | **Vedolizumab[50]** | **Ustekinumab[54]** |
|---|---|---|---|---|---|
| **Brand name** | | Remicade® | Humira® | Entyvio® | Stelara® |
| **Mechanism** | | TNF-α inhibitor | TNF-α inhibitor | α4β7 integrin receptor antagonist | Anti-IL-12 and IL-23 antagonist |
| **Dosage form and strength in Hong Kong** | | 100mg lyophilized powder per vial | Single use pen 40mg/0.8mL and 40mg/0.4mL single use prefilled syringe 40mg/0.8mL, 40 mg/0.4 mL, 20 mg/0.2 mL | 300mg lyophilized powder per vial | 130 mg/26mL (single dose vial), 45mg/0.5mL (Both pre-filled syringe and solution for injection) 90mg/1mL (Pre-filled syringe) |
| **Indications** | | Moderate to severe Crohn's disease | | | |
| **Route** | | IV | SC | IV | IV, SC* |
| **Dosing regimen** | **Initial** | Adult and Pediatric ≥ 6 years old: 5 mg/kg at week 0, 2, 6 | Adult and Pediatric ≥ 6 years old and ≥40kg: 160 mg on day 1 or 80mg on day 1 and 2, followed by 80 mg on day 15<br><br>Pediatric ≥ 6 years old and 17kg to < 40 kg: 80 mg on day 1, 40 mg on day 15 | Adult: 300 mg at week 0, 2, 6 | A single IV infusion in weight-based dosage Adult ≤ 55kg: 260 mg Adult > 55 to 85kg: 390 mg Adult > 85 kg: 520 mg |
| | **Maintenance** | Adult and Pediatric ≥ 6 years old: 5mg/kg Q8W | Adult and Pediatric ≥ 6 years old and ≥40kg: 40 mg on day 29 and then every other week<br><br>Pediatric ≥ 6 years old and 17kg to < 40 kg: 20 mg on day 29 and then every other week | Adult: 300 mg Q8W | 90mg at week 8* after initial infusion, then Q8W* |
| **Pre-treatment screening** | | Screen for latent tuberculosis (TB) and hepatitis B virus before starting therapy | | | |
| **Vaccination** | | Live vaccines should not be given concurrently | Avoid the use of live vaccines during the therapy | Live vaccines may be administered concurrently only if the benefits outweigh the risks | Avoid the use of live vaccines during the therapy |
| **Black-box warning** | | Serious infection and malignancy | | No data | |
| **Most common adverse reactions** | | Upper respiratory tract infection, infusion-related reactions, headache and abdominal pain | Upper respiratory tract infection, injection site reactions, headache and rash | Infections, arthralgia, rash, pruritis and pain in extremities | vomiting, nasopharyngitis, injection site erythema and abdominal pain |
| **Contraindications** | | Moderate to severe heart failure (NYHA III and IV) | NA | NA | NA |
| **Safety net[58]** | | Yes | Yes | Yes | Yes |

| Table 2. Pharmacokinetic profile of the mABs | | | | |
|---|---|---|---|---|
| **Monoclonal antibodies** | **Infliximab[31]** | **Adalimumab[41]** | **Vedolizumab[50]** | **Ustekinumab[54]** |
| **Brand name** | Remicade® | Humira® | Entyvio® | Stelara® |
| **Mechanism** | TNF-α inhibitor | TNF-α inhibitor | α4β7 integrin receptor antagonist | Anti- IL12 and IL-23 antagonist |
| **Bioavailability** | 100% | 64% | 100% | 100% |
| **Elimination Half-life ($T_{1/2}$)** | 7.7~9.5 days | 10-20 days | 25 days | 19 days |
| **Steady-state trough level ($Css_{trough}$)** | No data | 7 μg/mL | 13.0 μg/mL | FDA: 2.5 μg /mL<br>EMA: 1.97 μg/mL |
| **Clearance** | No data | 12 mL/hr | 6.54 mL/hr | 7.92 mL/hr |
| **Monitoring parameters** | IL-6 and CRP | CRP, MMP-1 and MMP-3 | CBC | IL-12 and IL-23 |

## IMMUNOGENICITY OF mABs

Anti-drug antibodies (ADAbs) can be developed in a patient's body after receiving a specific mAB.[59] ADAbs is classified into neutralizing and non-neutralizing. Neutralizing ADAbs bind to the (Fab′)2 region of the mAB to reduce its therapeutic activity.[60] Non-neutralizing antibodies do not reduce therapeutic activity directly because they do not bind to the Fab region. However, they can affect the pharmacokinetics of mABs such as enhancing the clearance rate.[61]

A higher rate of ADAbs is found in patients who treated with infliximab when compared to adalimumab, vedolizumab and ustekinumab (2.9-60.8 % vs 0.3-35.0%, 1.0-4.1% and 0.7% respectively).[62] It is important to examine the levels of ADAbs periodically because the presence of ADAbs may result in the loss of response to mABs and treatment failure.[63] Moreover, ADAbs can increase the risk of infusion reactions.[64] Therefore, therapeutic drug monitoring (TDM) can be done to optimize the treatment outcomes.

## FUTURE mABs DEVELOPMENT IN CD

The future development of mAB is in two main directions: 1.) New drug candidate with a novel mechanism of action and 2.) oral route of administration. For instance, Risankizumab binds to the p19 subunit of IL23 and which is currently in phase 2 clinical trials.[65] On the other hand, oral anti-TNF is also being investigated to test its effectiveness in rats. Using engineering technique, V565 combines with antibodies to resist protease enzyme, so that it is protected against the gastric environment for subsequent absorption.[66] Oral mABs will provide several advantages including no infusion-related hypersensitivity reaction, and reduced risk of opportunistic infections such as TB, as oral antibodies will not neutralize TNF systematically. Patient compliance should be improved with easy administration of the agent.[66]

Recently, V56B2 is a novel agent which consists of an IL23p19-specific domain antibody, engineered for intestinal protease resistance (V900), and combine with a TNFα-specific domain antibody (V565).[67] The preclinical results showed that V56B2 inhibited the production of TNF by decreasing the phosphorylation of p53, RSK-1 in *ex vivo* culture of colonic biopsies.[67]

## ROLE OF PHARMACISTS IN MANAGEMENT OF CD

One of the roles of a pharmacist in the management of CD is to facilitate medication adherence for a good treatment response and prevent a relapse of the disease.[68, 69] Indeed, 45% of CD patients self-reported to have poor adherence.[70] Pharmacists can enhance medication adherence by educating patients on the background of the disease, rationale and goal of the treatments during patient counselling.[71] Information leaflets and pills cards may also be given to improve adherence.[71]

Apart from medication adherence, pharmacists can also play a role in TDM. Dose intensification can recapture the therapeutic response for patients with low antidrug antibody against adalimumab. For patients with a high antidrug antibody level to adalimumab, switching to the same class infliximab can recapture the therapeutic response in proportion of patients.[72] The Asia-Pacific Working Group on IBD established a consensus statement and recommend checking the plasma concentration of anti-TNF regularly.[73] The recommended steady-state trough levels of infliximab and adalimumab are 3-7 μg/mL and 4-8 μg/mL respectively.[73] However, it should be noted that there is no standardized antibody cut-off

level.[74] More clinical trials are warranted to determine the optimal steady-state trough concentration in Asian population.

As CD is a chronic inflammatory disease, chronic abdominal pain is often reported by the patients.[75] Pharmacists can suggest pain management and optimize the use of analgesics.[76] First line treatments of pain relief include paracetamol and NSAIDs. Low dose of selective COX-2 inhibitors shows less adverse effect of gastrointestinal toxicity when compared to non-selective COX-2 inhibitors. However, cautious use of COX-2 inhibitors should be exercised due to its potential cardiovascular risks.[77] Long term use of opioid is discouraged because there is a risk of developing narcotic bowel syndrome, a side effect related to chronic use of opioid, characterized by unexplained abdominal pain and worsen with increasing opioid dose.[78] Opioid may also increase the risk of serious infection as it masks the early signs of infection.[79] Therefore, pharmacist should help monitor patients' conditions and screen individuals who are at risk for opiate abuse.

Regular monitoring the signs and symptoms of infections is important, as the use of mABs is associated with a risk of TB and hepatitis reactivation.[73] Antiviral treatment should be initiated for patients detected with positive HBV DNA prior to the use of mABs.[73] Prophylactic treatment should also be initiated for patients diagnosed with latent TB to prevent reactivation.[73] mAB is then initiated at least 3 to 4 weeks after the use of anti-TB medications.[73] Chest radiography and interferon gamma release assay (IGRA) should be performed every 6 months to 12 months to detect any active TB infection during the therapy.[73] Monitoring liver function for 6 to 9 months is also recommended after cessation of anti-TNF.[80]

## CONCLUSION

Infliximab, adalimumab, vedolizumab and ustekinumab are the registered biologics in Hong Kong that indicate for moderate-to-severe CD. The selection of mABs depends mainly on patients' conditions, including liver function, infection status, history of allergic adverse effects to mABs. Infliximab and adalimumab also suitable to pediatric patients who are ≥ 6 years old. All four mABs are of similar efficacy but associated with a higher cost than conventional treatments. Evidence from clinical trials and Asian consensus statement can help to guide healthcare professionals in prescribing mABs and monitoring parameters.

**Author's background**

***AU-DOUNG, Phillip Lung Wai*** *is currently a year 4Bachelor of Pharmacy student of The Chinese University of Hong Kong. His email address is phillipaudoung@link.cuhk.edu.hk.*

***CHAN, Jason Chi Hin*** *is currently a year 4 Bachelor of Pharmacy student of The Chinese University of Hong Kong. His email address is 1155142302@link.cuhk.edu.hk.*

***CHENG, Andrew Foon Yu*** *is currently a year 4 Bachelor of Pharmacy student of The Chinese University of Hong Kong. His email address is 1155126919@link.cuhk.edu.hk.*

***LAU, Anna Pak Yan*** *is currently a year 4 Bachelor of Pharmacy student of The Chinese University of Hong Kong. Her email address is 1155143475@link.cuhk.edu.hk.*

***LEE, Dawn Kei Yan*** *is currently a year 4 Bachelor of Pharmacy student of The Chinese University of Hong Kong. Her email address is dawnleekeiyan@gmail.com.*

***WU, Jason Tsun Sing*** *is currently a year 4 Bachelor of Pharmacy student of The Chinese University of Hong Kong. His email address is 1155143854@link.cuhk.edu.hk.*

***SUN, Kiwi Wai Yan*** *is a lecturer of School of Pharmacy, The Chinese University of Hong Kong. She is the corresponding author and her email address is kiwisun@cuhk.edu.hk.*

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# Questions for Pharmacy Central Continuing Education Committee Program

*(Please be informed that this article and answer sheet will be available on PCCC website concurrently. Members may go to PCCC website (www.pccchk.com) to fill in their answers there.)*

**2** CE Units

**Review of Monoclonal Antibodies for the Treatment of Crohn's Disease**

1. ***Infusion related reactions (IRRs) are common adverse events associated with infliximab. Which of the following is not a prophylactic medication of IRRs?***
   a. Prednisolone
   b. Paracetamol
   c. Ondansetron
   d. Chlorphenamine

2. ***The side effects associated with ustekinumab include:***
   a. Dyspnea
   b. Skin rash
   c. Increased risk of viral infections
   d. Nasopharyngitis

3. ***Which of the following maintenance regimen is calculated based on body weight?***
   a. Infliximab
   b. Adalimumab
   c. Vedolizumab
   d. Ustekinumab

4. ***How should an adult patient be advised in proper administration of adalimumab?***
   a. It should be given subcutaneously soon after meal
   b. Pre-treatment screening is needed for those patients who have family history of hepatitis B infections
   c. It is administered every 2 weeks after the initial dose
   d. Annual FluMist (live attenuated intranasal influenza vaccine) can be recommended to the patients to prevent influenza infections

5. ***A 62-year-old Chinese patient weighs 60 kg and has no known drug allergies, who do not have good response to infliximab at 10 mg/kg after 16 weeks of treatment. Which of the following is the most appropriate treatment options?***
   a. Increase infliximab to 15 mg/kg IV
   b. Change to vedolizumab 300 mg IV
   c. Change to adalimumab 80 mg SC
   d. Continue IV infliximab at 10 mg/kg for another 14 weeks

6. ***Which one of the following situations would preclude the patient from receiving ustekinumab?***
   a. Hepatitis B surface antigen negative
   b. Hepatitis B surface antibody positive
   c. Pregnancy test negative
   d. Influenza PCR positive

7. ***IPY is a 43-year-old male with CD, currently managed with adalimumab. However, he was recently hospitalized for a flare up with severe diarrhoea. Upon discharge, IPY expressed that he still prefers using self-injectable or oral drugs at home, instead of having to periodically return to the hospital for infusion. Which one of the following drug options would you recommend?***
   a. Infliximab
   b. Vedolizumab
   c. Ustekinumab
   d. Cyclosporine

8. ***Which one of the following proinflammatory cytokines is the therapeutic target for the initial treatment of moderate to severe Crohn's disease?***
   a. IL12
   b. TNF-α
   c. IL23
   d. IFN-γ

9. ***Which one of the following genetic mutations is commonly found in patients with Crohn's disease, and may be linked with disease pathogenesis?***
   a. NOD2
   b. TYK1
   c. KRAS g12c
   d. TP53

10. ***Which one of the following mABs has the highest risk of developing human anti-chimeric antibodies (HACA) after use, which could reduce its efficacy towards CD treatment?***
    a. Vedolizumab
    b. Infliximab
    c. Adalimumab
    d. Ustekinumab

***Answers will be released in the next issue of HKPJ.***

***CE Questions Answer for 301(D&T)***

**Overview of the Drug Therapy of Psoriasis**

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

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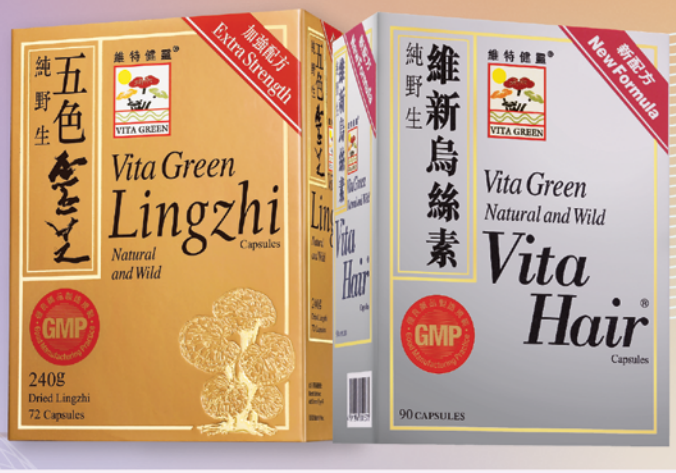


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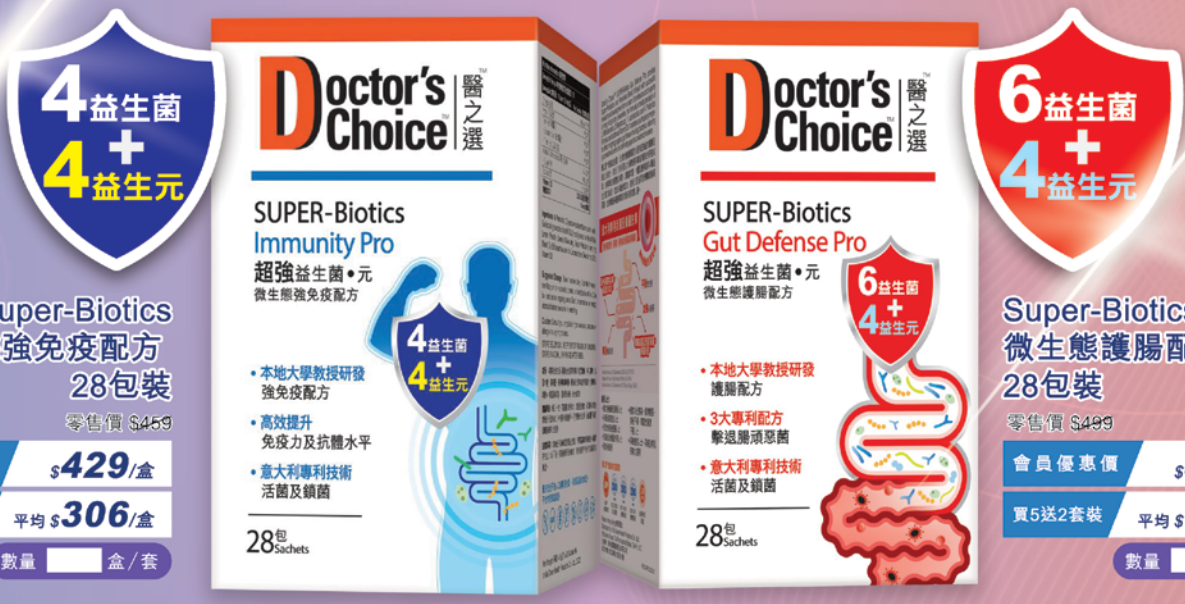


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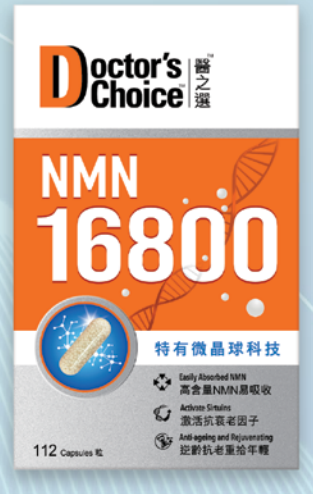


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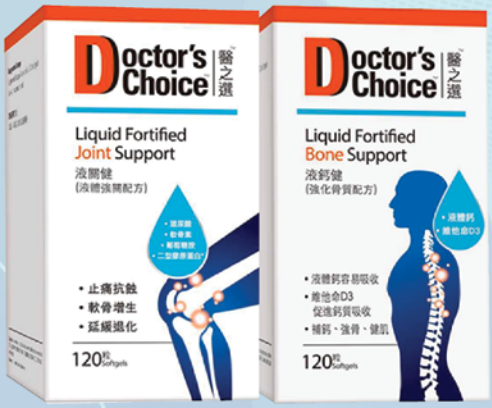


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# Review of Pharmacy-Based Vaccination in Hong Kong

**CHAN, Philip Pan[a]; LI, Johnny Chun-Wing; WONG, Janet Kit-Ting[b]***

*[a] Fortune Pharmacal Co. Ltd., Block A & Block B, 50-68 Wang Lok Street, Yuen Long Industrial Estate, Yuen Long, New Territories, Hong Kong, China*

*[b] Department of Pharmacology and Pharmacy, The University of Hong Kong, Hong Kong, China*

*(*Corresponding author)*

## ABSTRACT

**Community pharmacies as venues for immunisation are not utilised as they should be in Hong Kong. A fully implemented pharmacy-based vaccination scheme can enhance vaccination coverage and minimise health costs. Currently, pharmacists' role in immunisation in Hong Kong is mostly limited to stock management, cold chain assurance, and quality management within community vaccination centres. Even with training programmes in place, there is still a long way for pharmacists in Hong Kong to be authorised as independent vaccinators. With at least 13 countries already enlisting their pharmacists to contribute to immunisation in various ways, Hong Kong can take reference from their policies or programmes to devise local guidance for pharmacy-based vaccination.**

***Keywords:*** *Pharmacy-Based Vaccination, Hong Kong*

## INTRODUCTION

Although immunisation is widely considered to be one of the greatest achievements of public health, the vaccination programme of the COVID-19 vaccine in Hong Kong has brought the issue of vaccine hesitancy to the forefront. Vaccine hesitancy, which is defined as "the reluctance or refusal to vaccinate despite the availability of vaccines", is listed as one of the top ten threats to global health by the World Health Organization.[1]

To address vaccine hesitancy, the 3Cs Model (i.e., Confidence, Complacency, Convenience) and the 5As Model (i.e., Access, Affordability, Awareness, Acceptance, Activation) are usually adopted to analyse the problem and establish relevant measures.[2,4] Being renowned for the accessibility, wide distribution, and expertise in medicines, community pharmacists are in a privileged position to provide vaccination. In at least 13 countries such as the United States (US), the United Kingdom (UK), Australia, Canada, and New Zealand, pharmacists are not only responsible for advocating vaccination and ensuring the safe supply of vaccines, but they are also empowered to play an active role in immunisation programmes where they are legally authorised to administer vaccines.

In Hong Kong, pharmacists are minimally involved in any vaccination programme. Even under the recent community COVID-19 vaccination programme, pharmacists' role is mainly limited to ensuring the safe supply and reconstitution of vaccines. Emerging worldwide evidence demonstrates the cost-effectiveness of pharmacy-based vaccination as well as the potential expansion of vaccination coverage through pharmacies during epidemics. This article aims to review the possible roles of pharmacists in vaccination in Hong Kong by highlighting the benefits of pharmacy-based vaccination, current challenges faced by pharmacists, and the worldwide landscape of pharmacy-based vaccination.

## WHY PHARMACY-BASED VACCINATION?

Pharmacists are well-equipped to provide vaccination services as they possess extensive clinical knowledge and skills including medication management, history taking, health assessment, counselling, and optimising medication therapy. Pharmacists are also among the most accessible and frequently consulted healthcare professionals for health advice. As such, pharmacists can serve as advisors and educators to facilitate vaccine uptake.[2]

Delivering vaccination services at pharmacies in addition to conventional sites offers numerous advantages including expansion of coverage, reduced physician workload and wait times, as well as cost savings for the healthcare system.[3]

### a) Enhance Vaccination Coverage

The wide distribution and the long opening hours of community pharmacies make them an ideal location for people to receive vaccination in a casual and friendly environment which can in turn improve community vaccine uptake.

A study on influenza vaccination in community pharmacies of the US reported an eightfold increase in the number of vaccines administered when pharmacists offered vaccination daily compared to nurses offering vaccination on a single day.[4] Evidence supporting pharmacy-based vaccination in Canada is also growing. A study in Canada comparing the estimated influenza

vaccine coverage before and after pharmacy-based vaccination reported that the vaccine coverage increased from 26% in 2012 – 2013 to 36% in 2013 – 2014.[5]

The studies highlight the potential positive impact of pharmacy-based vaccination services in promoting vaccine uptake rates.

**b) Indirect Cost Savings**

Pharmacy-based vaccination not only costs less than vaccine administration by a general practitioner, but also helps alleviate the burden on other healthcare providers. Pharmacy-based vaccination can bring the flexibility of mobilising the healthcare workforce, which can be crucial in addressing the rapidly evolving demands for health services in peak seasons. In the states and territories of the US where pharmacists are allowed to vaccinate, higher vaccination rates and lower vaccination-related healthcare resource utilisation and costs have been observed.[6]

Utilising an agent-based model and a clinical and economic outcomes model for simulation, a US study has shown that administering vaccines through pharmacies in addition to traditional locations (hospitals, clinic / physician offices, and urgent care centres) during an influenza epidemic can avert up to 23.7 million symptomatic influenza cases. The reduction in influenza cases can be translated to a substantial cost-savings up to $2.8 billion to third-party payers and $99.8 billion to society.[7]

## PHARMACY-BASED VACCINATION WORLDWIDE

The role of pharmacists in vaccination varies in different healthcare systems. In some parts of the world, pharmacists are responsible for vaccine education and supply management; while in other countries, they are legally authorised to administer vaccines.

According to a global survey conducted by the International Pharmaceutical Federation (FIP), 13 out of 45 countries authorise pharmacists to legally administer vaccines. These countries include Argentina, Australia, Canada, Costa Rica, Denmark, Ireland, New Zealand, the Philippines, Portugal, South Africa, Switzerland, the UK, and the US.[8] In these countries, in addition to the requirements on the pharmacies with regard to records, premises, equipment, materials and waste management, there is also a restriction that only accredited personnel could perform the vaccinations.

**a) Accreditation of Vaccinators**

In the UK, pharmacy personnel and other providers who wish to administer vaccines are required to undergo extensive training on immunisation knowledge defined in Public Health England's **"National Minimum Standards and Core Curriculum for Immunisation Training for Registered Healthcare Practitioners"**.

The curriculum covers 12 core areas of immunisation knowledge, among others, includes legal issues, vaccine administration, anaphylaxis and adverse reactions, record keeping and reporting.[9] The training also comprises face-to-face practical training on injection techniques and basic life support. Furthermore, the UK Health Security Agency has developed a "Flu Vaccinator Competency Assessment Tool" to periodically verify competency that includes knowledge, core clinical skills, clinical process and procedures for vaccine administration.[10]

Starting from the 2022/23 flu vaccination season, pharmacists and other vaccinators could determine the frequency of face-to-face training for both injection technique and basic life support instead of every three years, providing that ongoing competence of an individual vaccinator can be demonstrated.[11]

**b) Scope of Pharmacy-based Vaccination Services**

The scope of pharmacy-based vaccination services varies among countries as presented the **Table 1**.[7]

**Table 1. Vaccination Provided at Community Pharmacies in Different Countries**

| Country | Scope of Pharmacy-Based Vaccination Services |
|---|---|
| Argentina | Vaccination included in the National Vaccination Schedule such as influenza and varicella |
| Australia | Vaccinations provided vary across different jurisdictional legislation. For example, some only allow influenza vaccine, while some cover a wider range of vaccines such as measles and pertussis. |
| Canada | Vaccinations provided differ in different provinces. Some only allow influenza vaccine; some cover a wider range of vaccines such as influenza, hepatitis, human papillomavirus (HPV), chickenpox, and rabies post-exposure; Quebec only authorises pharmacists to administer vaccines for demonstration/education purposes |
| Ireland | Seasonal influenza, pneumococcal, and shingles for adults |
| New Zealand | ▪ Vibrio cholerae and enterotoxigenic Escherichia coli vaccine<br>▪ Influenza vaccine (for ≥ 3 years old)<br>▪ Diphtheria, tetanus, and pertussis (acellular, component) vaccine (Tdap) (for ≥ 18 years old)<br>▪ Meningococcal vaccine (for ≥ 16 years old)<br>▪ Varicella (shingles) vaccine (for ≥ 50 years old) |
| Portugal | Vaccinations not included in the National Health Service Vaccination Plan such as Cholera, Herpes Zoster, and Rabies |
| South Africa | Measles, mumps, and rubella (MMR) and influenza vaccine, and vaccination included in the Expanded Programme on Immunisation (EPI) such as Hepatitis B and HPV |
| Switzerland | Vaccination varies across different Cantons in Switzerland |
| The Philippines | Influenza and pneumococcal vaccines for adults |
| UK | Vaccination strategy varies among England, Scotland, Northern Ireland, and Wales. The scope of services can cover most of the vaccines such as influenza and childhood immunisations (measles, mumps, and rubella) under the National Health Service Immunisation Plan |
| US | Vaccination strategy varies across different states in the US. |

### c) Legal Framework for Pharmacy-Based Vaccination

Different countries have developed different legal frameworks to enable pharmacy-based vaccination.

For instance, New Zealand has implemented the reclassification of vaccines since 2011 so that selected vaccines can be supplied at a pharmacy without a prescription when administered by an accredited registered pharmacist, and in compliance to the immunisation standards of the Ministry of Health. For example, varicella (shingles) vaccine does not require a prescription when (a) administered for the prevention of herpes zoster (shingles) to (b) a person 50 years of age or over (c) by an accredited registered pharmacist.[12] The pharmacist accreditation involves the completion of a vaccinator training course approved by the Ministry of Health.

Meanwhile, the UK defined "Patient Group Directions (PGDs)" in the Regulation 213 of the Human Medicines Regulations 2012 as an administrative approach that enables registered health professionals (e.g. registered pharmacists) to supply and administer prescription-only medicines to patients without prescription under specific planned circumstances where patient care can be enhanced without compromising patient safety.[13] PGDs are applied in various scenarios such as routine immunisation programmes, and emergency response. PGDs are written instructions established by a multi-disciplinary group composed of a doctor, a pharmacist, and a representative of any professional group expected to supply the medicines under the respective PGDs. Established PGDs require further endorsement and authorisation by the NHS organisation and signing by all individual health professionals working under the directions. PGDs for immunisation cover aspects of staff authorisation, documentation, audit requirements, and general guidance on best practices required to safely administer vaccines such as COVID-19 vaccine and HPV vaccine.[14] Thus, PGDs serve as a mechanism that allows the administration of prescription-only vaccines by community pharmacists.

## CHALLENGES TO PHARMACY-BASED VACCINATION IN HONG KONG

### a) Access to Vaccination

Despite the absence of legal restriction on personnel administering injectable, registered vaccines are currently classified as prescription-only medicines in Hong Kong (except certain veterinary vaccines).[15] All vaccines are supplied and administered after medical assessment and prescription by medical practitioners.

Under the Vaccination Subsidy Scheme (VSS) which covers vaccination for COVID-19, seasonal influenza, and pneumococcal infection, only doctors listed in the "Primary Care Directory" are eligible to enrol in the scheme. The registered medical practitioner is responsible for the entire vaccination service, from assessing patients' clinical suitability for vaccination, supervising the administration, to managing vaccine-related adverse effects and emergencies. Healthcare professionals such as nurses, pharmacists and other trained personnel can only perform vaccination under doctors' supervision.[16]

The doctor-dependent supply and administration of vaccines can limit the access and scalability of vaccination services in the local community. As in other healthcare systems, vaccines with favourable safety profile can be delivered by other qualified healthcare professionals such as registered pharmacists and nurses. Quality assurance and regulatory framework can be established to empower non-medical disciplines to contribute to the vaccination services while safeguarding patient safety.

### b) Perceived Role of Pharmacist in Vaccination

Pharmacists' primary role in vaccination service sites is to manage the distribution of vaccines and to ensure their quality. However, this division of labour limits the flexibility of sharing workload with other healthcare professionals.

Furthermore, some medical associations in the UK and Australia have raised concerns about pharmacy-based vaccination hindering follow-up care for at-risk patient groups due to a lack of record sharing between pharmacists and physicians. Others have expressed concerns over inadequate experience in injectable administration and training on handling potential anaphylaxis after vaccination.[2,7]

### c) Lack of Ready Pharmacy Infrastructure

According to the VSS Doctor's Guide, service providers should have readily available equipment and medications on-site to manage anaphylaxis. Suitable purpose-built vaccine refrigerators equipped with temperature monitors and cold box picking are also necessary for providing vaccination service.[17] The setup of venue for vaccination services requires space and comprehensive design. Most existing community pharmacies in Hong Kong have not been designed in a way that can fulfil the requirement for vaccination services and conversion can be immensely resource-demanding. The establishment of vaccination-ready pharmacies and the implementation of pharmacy-based vaccination compounds the dilemma of the chicken or the egg.

## WHERE ARE WE?

Various stakeholders have been dedicating efforts to pharmacy-based vaccination in Hong Kong and to overcoming the aforementioned challenges. Pharmacists in Hong Kong are assuming greater roles in vaccination services. Trained pharmacists have been working closely with nurses and doctors in implementing vaccine services and administering vaccines in non-profit non-governmental organisations, chain pharmacy company, private and public medical clinics. The growing involvement of pharmacists in vaccination services offer opportunities to promote cross-disciplinary collaboration and development of expertise in vaccination among pharmacists.

Since 2018, local professional societies and universities have delivered multiple in-person vaccination workshops to local pharmacists and pharmacy students. In 2021, the University of Hong Kong (HKU) and Health in Action, a local non-profit non-governmental organisation which promotes health equity through innovations in primary healthcare services, led the Hong Kong Pharmacists Immunisation Training Working Group and together they established the "Immunisation Training Programme for Registered Pharmacists – Standards and Framework". The document sets out the general standards and framework of immunisation training for Hong Kong to ensure confidence, competence, safety, and effectiveness of the promotion and administration of vaccinations in different healthcare settings. Based on the developed standards and framework, HKU has successfully delivered the immunisation training to over 300 local pharmacists and pharmacy students since early 2021. The local pharmacist immunisation training programme consists of (a) face-to-face immunisation practice, (b) basic life support including cardiopulmonary resuscitation (CPR) in response to an emergency such as anaphylaxis, and (c) clinical skill and competency assessment by qualified vaccinators.

Meanwhile, pharmacy programmes of the Chinese University of Hong Kong and HKU have incorporated immunisation training in the local pharmacy undergraduate curricula since 2021. All graduates would be expected to be qualified for immunisation services.

As current and future pharmacists are becoming equipped for vaccination, professional societies and their management team can advocate for the integration of pharmacist-led vaccination in clinical care pathways to promote the local immunisation coverage. For example, influenza and pneumococcal conjugate vaccines can be inoculated and managed by pharmacists in hospital ambulatory clinics and community vaccination outreach programmes. These are the steps forward that will ultimately bring the pharmacy profession, the regulatory authority, and the healthcare system to better utilisation of pharmacists in the local immunisation programmes.

## CONCLUSION

As demonstrated in overseas healthcare systems, the high accessibility of community pharmacies and community pharmacists can promote immunisation rates. Despite recent advancement in the training pathway for pharmacist-led vaccination, the territory-wide implementation of pharmacy-based vaccination still faces crucial barriers with regard to vaccine access, expectation of pharmacists' roles and the difficulties for community pharmacies to fulfil infrastructure-related requirements.

Overcoming these obstacles requires a constant supply of trained pharmacists, widespread distribution of vaccination-ready pharmacies, and potential updates in legislation or policies. Continuing collaborations and engagement among healthcare providers, academia, professional bodies, pharmaceutical industry and regulatory authorities will undoubtedly accelerate the introduction of pharmacy-based vaccination in Hong Kong.

**Author's background**

***CHAN, Philip Pan*** *is currently a Quality Assurance Manager at Fortune Pharmacal Co. Ltd in Hong Kong. His email address is philipchanpan@gmail.com*

***LI, Johnny Chun-Wing*** *is currently a Registered Pharmacist in Hong Kong. His email address is johnny_pharm@hotmail.com*

***WONG, Janet Kit-Ting*** *is currently a Part-Time Lecturer at the Department of Pharmacology and Pharmacy, the University of Hong Kong, Hong Kong, China. Her email address is janetwkt@hku.hk*

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# The Activities of the Society of Hospital Pharmacists

Over the past few months, the Society of Hospital Pharmacists of Hong Kong (SHPHK) has been actively engaged in various events and activities. These include organizing webinars, participating in a prestigious conference held in Shanghai, and successfully hosting the Annual General Meeting (AGM).

**Webinar on breakthroughs in gene therapy and radio-ligand therapy**

Spinal Muscular Atrophy (SMA) is a rare genetic disorder which has limited treatment options primarily restricted to supportive care. The most severe forms of SMA carry a high incidence of mortality if left untreated. Similarly, metastatic prostate cancer also poses significant challenges in treatment. The webinar "New Breakthroughs in Treatment - Gene therapy and Radio-ligand Therapy" was held on 30th June 2023, featured two presentations that explored innovative treatment options for SMA and metastatic prostate cancer.

Professor Eugenio Mercuri, a specialist in Paediatric Neurology from Polilchinico Gemelli in Rome, Italy, delivered a speech titled "SMA Treatment: Translating Gene Therapy from Research to Reality." Prof. Mercuri introduced Onasemnogene abeparvovec, the first and only gene therapy for SMA. His presentation discussed the findings in clinical trials which reported safety and efficacy profiles using gene therapy in SMA patients.

Dr. Kenneth Chun-wai Wong, Honorary Clinical Associate Professor, Department of Clinical Oncology, The Chinese University of Hong Kong (CUHK), presented on "Theranostics - A Novel Approach in Metastatic Prostate Cancer." Dr. Wong introduced the concept of theranostics, an advanced approach that combines therapeutic and diagnostic elements in the management of metastatic prostate cancer. He highlighted the clinical efficacy and safety of targeted radio-ligand therapy in identifying and treating cancer cells which provides phenotypic precision medicine, leading to improved outcomes for patients.


**The 36th SHPHK Annual General Meeting cum Educational Seminar**

The 36th Annual General Meeting (AGM) of the Society of Hospital Pharmacists of Hong Kong (SHPHK) cum Educational Seminar took place on July 21, 2023, at The Mira Hong Kong in Tsim Sha Tsui. The event was held in-person setting and included a dinner following the educational seminars. Pharmacists were thrilled to have the opportunity to meet face-to-face after a prolonged period of virtual interactions.

One of the key topics discussed during the seminar was the "Challenge and Opportunity of Medication Safety in A&E." Dr. Poon Kin-ming, an associate consultant from the Accident & Emergency Department at Tin Shui Wai Hospital (TSWH), presented the safety measures implemented in TSWH and emphasized the importance of pharmacist involvement in ensuring medication safety. Audiences showed great enthusiasm in exploring more potential roles of clinical pharmacists in the emergency department.

Another seminar titled "From Manual to Prefilled Preparation: A Blessing to all?" was delivered by Ms. Amy Yuen, a clinical pharmacist from Queen Mary Hospital. The presentation focused on the transition from manual medication preparation to prefilled systems and its impact on patient safety, workflow efficiency, and medication administration accuracy. The discussion explored the benefits and challenges associated with this technological advancement in pharmacy practice.

During the AGM, the President of the Society provided an overview of past activities, shared future aspirations for the SHPHK, and expressed gratitude for the contributions of SHPHK pharmacists' contributions during the COVID-19 pandemic. General committee members were elected during the AGM, including a returning member. Mr. So Yiu Wah, former SHPHK President, is expected to bring valuable experiences to the general committee.

In addition, three General Committee Members, namely Ms Amy Chu, Ms Michelle Zheng and Ms Zoey Tsui were awarded the 'President's Award 2023' this year.

SHPHK General Committee Members 2023-2024

1 Ms. Chu Man Wa Amy
2 Mr. Chui Chun Ming William
3 Mr. Chung Wing Fai Kenneth
4 Ms. Lai Oi Lun Ellen
5 Mr. Lam Kam Mo Kemo
6 Mr. Lau Ka Hei Tony
7 Ms. Ng Yi Qing Christy
8 Mr. Ng Man Keung
9 Mr. So Yiu Wah
10 Ms. Tsui Hoi Tung Zoey
11 Mr. Wong Kai Chung Vincent
12 Mr. Wong Po Kwan Bryan
13 Mr. Wong Sze Ho Johnny
14 Mr. Yiu Sui Ki Kenneth
15 Ms. Zheng Sin Man Michelle

If you have missed any of the above webinars/ lectures and you are a member of SHPHK, you can always visit SHPHK homepage and sign in to view all the past webinar recordings (shphk.org.hk > resources > learning activities)

## 第二屆滬港澳台醫院藥學管理論壇

The second 滬港澳台醫院藥學管理論壇 was held on 28th– 29th May, 2023 in Shanghai, China. Organized by the Shanghai Pharmaceutical Association, the forum focused on the theme "Working together to look into the future – Promoting High-Quality Development of Hospital Pharmacy". Hospital pharmacists from Shanghai, Hong Kong, Macao, and Taiwan gathered together to discuss and exchange ideas on promoting the high-quality development of hospital pharmacy. The forum featured selected topics such as precision pharmacy, chronic disease medication management, practical experiences in public health emergencies, and related hospital pharmaceutical management. An interactive forum was included to allow for valuable knowledge exchange and collaboration among participants.

The SHPHK sent nine members to participate in the forum, two of whom were speakers sharing their experiences from Hong Kong. Ms Chiang Sau Chu, a life member of SHPHK and the chairperson from the Hong Kong Pharmaceutical Care Foundation, discussed "Promoting Home Medication Safety through Pharmaceutical Services". Her presentation highlighted the significant contributions of Hong Kong pharmacists in addressing medication issues among elderly communities, delivering professional knowledge to the community, and enhancing public health literacy. Ms. Zoey Tsui, a general committee member of SHPHK, presented a report titled "Hong Kong Pharmacists Join Forces Against COVID-19," outlining measures taken to address medication issues during the pandemic.

On the second day of the forum, two hospital visits were arranged. Participants had the opportunity to visit the outpatient pharmacies, intravenous medication compounding centers, and clinical research centers at the Pharmacy Department of 復旦大學附屬中山醫院 and 上海交通大學醫學院附屬仁濟醫院. The Chief Pharmacists from both hospitals introduced the recent developments and fruitful achievements of their respective hospitals. Core personnel from each hospital participated in the exchange and learning activities. The remarkable achievements in marine drug innovation research and clinical pharmacy research at Renji Hospital have greatly impressed us.

The successful organization of this forum has established a platform for the development and cooperation of hospital pharmacy in Shanghai, Hong Kong, Macao, and Taiwan. It comprehensively promotes the development of hospital pharmacy and the innovative capabilities of clinical pharmacists. It has made an important contribution to forming a regional collaboration and sharing of pharmaceutical service information resources. Let us look forward to meeting again next year!

You are most welcome to follow the Society's Facebook page (@SHPHK) and 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.


*edited by Lucilla Leung*

**Active Ingredients**
Ranolazine

**Pharmacological Properties**
Ranolazine inhibits sodium and potassium ion channel currents. It has been shown to exert weak activity on L-type calcium channels making it a weak direct vasodilator and exerts minimal direct effects on atrioventricular nodal conduction. Some additional mechanisms have been elucidated. Ranolazine exerts antagonistic activity towards the alpha 1 and beta 1 adrenergic receptors and inhibition of fatty acid oxidation

**Indications**
Add-on therapy for the symptomatic treatment of adult patients w/ stable angina pectoris who are inadequately controlled or intolerant to 1st-line antianginal therapies (e.g. β-blockers &/or Ca antagonists).

**Dosage Forms and Strengths**
Each tablets contains 375 mg ranolazine in a prolong release tablet.
Each tablets contains 500 mg ranolazine in a prolong release tablet.
Each tablets contains 750 mg ranolazine in a prolong release tablet.

**Administration**
Adult
Initially 375 mg twice daily. After 2-4 week, the dose should be titrated to 500 mg bd, and according to patient's response, further titrated to a maximum 750 mg twice daily.

**Contraindications**
Hypersensitivity.
Severe renal impairment (CrCl <30 mL/min).
Moderate or severe hepatic impairment.
Concomitant administration of potent CYP3A4 inhibitors (e.g. itraconazole, ketoconazole, voriconazole, posaconazole, HIV PIs, clarithromycin, telithromycin, nefazodone).
Concomitant administration of class Ia (e.g. quinidine) or class III (e.g. dofetilide, sotalol) antiarrhythmics other than amiodarone.

**Interactions**
Increased plasma conc w/ CYP3A4 inhibitors (e.g. itraconazole, ketoconazole, voriconazole, posaconazole, HIV PIs, clarithromycin, telithromycin, nefazodone, grapefruit, diltiazem, erythromycin, fluconazole); P-gp inhibitors (e.g. ciclosporin, verapamil); CYP2D6 inhibitors (e.g. paroxetine). Decreased steady-state conc w/ CYP3A4 inducers (e.g. rifampicin, phenytoin, phenobarb, carbamazepine, St. John's wort). Increased plasma conc of P-gp substrates; sensitive CYP3A4 substrates (e.g. simvastatin, lovastatin) & CYP3A4 substrates w/ a narrow therapeutic range (e.g. ciclosporin, tacrolimus, sirolimus, everolimus); metoprolol or other CYP2D6 substrates (e.g. propafenone & flecainide or, to a lesser extent, TCAs & antipsychotics); digoxin; atorvastatin. Increased plasma exposure of metformin (OCT2 substrate). Caution during co-administration w/ CYP2B6 substrates (e.g. bupropion, efavirenz, cyclophosphamide). Increased possible risk of ventricular arrhythmias w/ other drugs known to prolong the QTc interval e.g. certain antihistamines (e.g. terfenadine, astemizole, mizolastine), certain antiarrhythmics (e.g. quinidine, disopyramide, procainamide), erythromycin, & TCAs (e.g. imipramine, doxepin, amitriptyline).

**Adverse Reactions**
Dizziness, headache; constipation, vomiting, nausea; asthenia.

**Dosage Available**
Ranexa Prolonged-Release Tablets 375 mg in the pack of 60's.
Ranexa Prolonged-Release Tablets 500 mg in the pack of 60's.
Ranexa Prolonged-Release Tablets 750 mg in the pack of 60's.

**Forensic classification**
P1S1S3