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News & Short Communications

Overview of Health Supplement Regulations in Hong Kong: A Comparison with Drug Regulations

Review of Vaccines against Herpes Zoster: the Efficacy, Safety and Impact on Quality of Life of Shingrix® and Zostavax®
(2 CE Units)

The Activities of the Society of Hospital Pharmacists

Elunate® (HUTCHMED)

Tazverik® (HUTCHMED)

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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- Medication Safety
- Herbal Medicines & Nutraceuticals
- Society Activities
- New Products

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Navigating the Complex Landscape of Health Supplements and Vaccines

As the editor-in-chief of Hong Kong Pharmaceutical Journal, it is my privilege to present this issue, which delves into two critical aspects of public health: health supplements and vaccines. Both have a profound impact on our well-being, yet they occupy distinct regulatory landscapes and evoke different public perceptions.

The article written by Benny Lee et al., "Overview of Health Supplement Regulations in Hong Kong: A Comparison with Drug Regulations," offers a comprehensive analysis of the regulatory frameworks governing health supplements in Hong Kong. In recent years, the use of health supplements has surged in popularity, with many individuals incorporating these products into their daily routines in pursuit of improved health and well-being. As the demand for nutraceuticals continues to rise, pharmacists must have a solid understanding of the laws that regulate these products.

The article introduces the major regulations for health supplements, including safety, quality, labeling, and claims. While food and drug regulations may appear distinct, the underlying principles are fundamentally similar. By using comparison tables, the article effectively highlights the required documents for launching health supplements. Both pharmaceutical and supplement product regulations ultimately aim to safeguard safety and quality. However, the specific requirements can vary. Understanding these differences is crucial for ensuring the safe and effective use of health supplements and for promoting informed decision-making among consumers and healthcare providers.

The review article on vaccines against herpes zoster (Zostavax® and Shingrix®) by Sam Tang et al., focuses on their efficacy, safety and impact on quality of life. Zostavax® was introduced in Hong Kong in 2007, followed by the newer Shingrix® in 2020. This review provides a valuable comparison of the efficacy, safety and impact on quality of life of these vaccines. By synthesizing the latest evidence and recommendations from clinical trials and guidelines, this article serves as a valuable resource for healthcare professionals seeking to optimize their approach to preventing herpes zoster in their patient populations.

The articles in this issue offer valuable insights into two crucial areas of pharmacy practice: health supplements and vaccines against herpes zoster. From regulatory complexities to vaccine advancements, these articles provide essential knowledge for pharmacists and healthcare providers. I encourage you to explore the depth of expertise presented here. Thank you for your continued support. Your feedback is vital to the Editorial Committee as we strive to create a publication that meets your needs. Please share your ideas and suggestions for improving the Journal.

May PS Lam
Editor-in-Chief
16 September 2024

Prepared by Candice Leung & Branson Fok

Andexanet Better Controls Hematoma Expansion Than Usual Care In Patients with Intracerebral Hemorrhage who receive Factor Xa Inhibitors

Date: May 15, 2024

Patients receiving factor Xa inhibitors are at risk of acute intracerebral hemorrhage, which can lead to hematoma expansion. Andexanet alfa, a reversal agent for factor Xa inhibitors, was studied for its efficacy and safety in controlling hematoma expansion.

This randomized trial compared andexanet with usual care in patients with acute ICH with hematoma expansion volume of 0.5 to 60ml and had taken factor Xa inhibitors within 15 hours before hemorrhage onset. Patients were randomly assigned in 1:1 ratio to receive andexanet, high- or low-dose bolts over 15 to 30 minutes followed by continuous infusion over 2 hours, or usual care which could include prothrombin complex concentrate. The primary endpoint was hemostatic efficacy, defined as hematoma expansion of 35% or less at 12 hours, an increase in the score on the National Institute of Health Stroke Scale of less than 7 points (scores range from 0 to 42, with higher scores indicating worse neurologic deficit) at 12 hours, and no receipt of rescue therapy between 3 hours and 12 hours. Safety endpoints included thrombotic events and death.

A total of 530 patients were enrolled, with 263 receiving andexanet and 267 receiving usual care. Of the patients relieve usual care, 85.5% received prothrombin complex concentrate. Hemostatic efficacy was achieved in 67.0% (n=150) of the andexanet group compared to 53.1% (n=121) the usual care group (adjusted difference, 13.4 percentage points; 95% confidence interval [CI], 4.6 to 22.2; P=0.003). Thrombotic events occurred in 10.3% (n=27) of the andexanet group versus 5.6% (n=15) in the usual care group (difference, 4.6 percentage points; 95% CI, 0.1 to 9.2; P=0.048); ischemic stroke occurred in 17 patients (6.5%) and 4 patients (1.5%), respectively.

In conclusion, andexanet resulted in better control of hematoma expansion than usual care but was associated with thrombotic events, including ischemic stroke.

Source: www.nejm.org

Dupilumab Reduces Exacerbations in COPD Patients with Type 2 Inflammation

Date: May 20, 2024

Dupilumab, a fully human monoclonal antibody that is used in treating chronic obstructive pulmonary disease (COPD) with type 2 inflammation. Dupilumab targets interleukin-4 and interleukin-13, crucial drivers of this inflammation. In a previous phase 3 trial, Dupilumab was effective in reducing exacerbations and showed results in improvements of lung function and patient-reported health-related quality of life. The NOTUS study was conducted to confirm efficacy and safety findings.

In this double-blind, randomized, placebo-controlled phase 3 trial, 935 patients with COPD and elevated blood eosinophil counts (≥300 cells/μl) were enrolled. Participants received either 300 mg of dupilumab or a placebo every 2 weeks. The study aimed to evaluate the annualized rate of moderate or severe exacerbations, alongside secondary measures like lung function (FEV1) at weeks 12 and 52, and quality of life (SGRQ scores) at week 52.

Among 935 patients who underwent randomization, 470 were assigned to the Dupilumab group and 465 to the placebo group. Results revealed a significant reduction in the annualized rate of moderate or severity exacerbation for the dupilumab group (0.86, 95% confidence interval [CI], 0.70 to 1.06) compared to placebo (1.30, 95% CI, 1.05 to 1.60), with a rate ratio of 0.66 (95% CI, 0.54 to 0.82; P<0.001). Improvements in FEV1 were noted at both 12 and 52 weeks in the dupilumab group as compared to the placebo group, with a significant least-squares mean difference at week 12 of 82 ml (P<0.001) and at week 52 of 62 ml (P=0.02). No significant difference was found in SGRQ scores from baseline to 52 weeks. Adverse events were similar across both groups, consistent with the established profile of dupilumab.

In conclusion, dupilumab effectively reduced exacerbations and improved lung function in COPD patients with type 2 inflammation as indicated by elevated blood eosinophil counts.

Source: www.nejm.org

Reteplase Noninferior to Alteplase for Patients with Acute Ischemic Stroke

Date: June 14, 2024

Intravenous alteplase is the standard thrombolytic agent used for acute ischemic stroke within 4.5 hours after symptom onset. Reteplase is a recombinant plasminogen activator that is characterised by a double-bolus approach with a fixed dose regimen. The RAISE trial was conducted to study the efficacy and safety of reteplase as compared with alteplase as an alternative thrombolytic agent in patients with acute ischemic stroke.

In this phase 3, prospective, open-label, noninferiority, randomized trial conducted at 62 sites in China, patients with ischemic stroke within 4.5 hours after symptom onset were randomly assigned in a 1:1 ratio to receive intravenous reteplase (a bolus of 18mg followed by a second bolus of 18mg 30 minutes later) or intravenous alteplase (0.9mg/kg of body weight; maximum dose of 90mg). The primary efficacy outcome was an excellent functional outcome, defined as a score of 0 or 1 on the modified Rankin scale (ranges from 0 to 6) at 90 days. The primary safety outcome was symptomatic intracranial hemorrhage within 36 hours after symptom onset.

A total of 707 and 705 patients were assigned to the reteplase and alteplase group, respectively. The primary efficacy outcome occurred in 79.5% of the patients in the reteplase group and in 70.4% of the patients in the alteplase group (risk ratio, 1.13; 95% confidence interval [CI], 1.05 to 1.21; P<0.001 for noninferiority and P=0.002 for superiority). Symptomatic intracranial hemorrhage within 36 hours after disease onset was observed in 2.4% (n=17) and 2.0% (n=14) of the patients in the reteplase and alteplase group, respectively (risk ratio, 1.21; 95% CI, 0.54 to 2.75). However, the incidence of any intracranial hemorrhage at 90 days was higher with reteplase than with alteplase (7.7% vs. 4.9%; risk ratio, 1.59; 95% CI, 1.00 to 2.51), as was the incidence of adverse events (91.6% vs. 82.4%; risk ratio, 1.11; 95% CI, 1.03 to 1.20).

In conclusion, patients with acute ischemic stroke who were eligible for intravenous thrombolytic therapy within 4.5 hours after symptom onset, reteplase was superior to alteplase with respect to an excellent functional outcome at 90 days. However, patients who received reteplase was associated with a higher incidence of any intracranial hemorrhage.

Source: www.nejm.org

Regulatory Updates of Medical Gases as Pharmaceutical Products in Hong Kong

Date: June 17, 2024

The Pharmacy and Poisons Board of Hong Kong (the Board) has recently endorsed the regulation of medical gases as pharmaceutical products under the Pharmacy and Poisons Ordinance (Cap. 138) (the Ordinance) with effect from June 14, 2026.

Considering the regulatory control of medical gases in other jurisdictions and the current local situation, the Board agreed that medical gases should be regulated as pharmaceutical products in September 2023. The final decision regarding the issue was made under the overall support from the general public and relevant stakeholders, according to the Board's meeting on June 14, 2024.

A preparatory period of two years (i.e. from June 14, 2024, to June 13, 2026) is given for the trade to apply for relevant licences and product registration. In this regard, medical gases must be registered with the Board before they can be legally sold and supplied in Hong Kong when the new regulatory control comes into effect. Traders of medical gases must also obtain relevant license(s) from the Board before conducting manufacture, wholesale (including import and export) of pharmaceutical products and retail sales of pharmaceutical products containing poisons.

Under the Ordinance, illegal possession or sale of unregistered pharmaceutical products or prescription drugs, and manufacture, wholesale of pharmaceutical products and retail sales of pharmaceutical products containing poisons without relevant licences are criminal offences. The maximal penalty upon conviction is a fine of $100,000 Hong Kong dollars and two years' imprisonment for each offence.

Source: www.drugoffice.gov.hk

Weekly Subcutaneous Semaglutide Reduces the Risk of Major Kidney Events in Patients with Type 2 Diabetes and Chronic Kidney Disease

Date: July 11, 2024

Type 2 diabetes (T2DM) has been recognized as one of the common causes for chronic kidney disease that underlies various kidney and cardiovascular disease events. Renin-angiotensin system (RAS) inhibitors, sodium-glucose cotransporter 2 (SGLT2) inhibitors, and finerenone are the guideline-recommended treatment options for chronic kidney disease in patients with T2DM with proven renal and cardiovascular protective effects. Semaglutide, a glucagon-like peptide 1 (GLP-1) receptor agonist, is currently indicated for treating T2DM and providing long-term weight management whereas its effect on preserving renal function in T2DM patients is currently under investigation.

The FLOW trial was an international, double-blind, randomized, placebo-controlled trial that involved 3533 type 2 diabetes patients with defined chronic kidney disease (i.e. estimated glomerular filtration rate [eGFR] between 25 to 75 ml/min/1.73m^2). Participants were then randomized in 1:1 ratio to receive weekly subcutaneous injections of semaglutide 1mg over an 8-week dose-escalation regimen (n=1767) or placebo (n=1766). Primary outcomes of the study include the onset of major kidney disease events, sustained reduction of eGFR of ≥50% from baseline or death from kidney-related or cardiovascular causes. Safety outcome of the trial was also assessed based on data regarding serious adverse events and any events leading to treatment discontinuation.

Major kidney disease events were found less frequent in the semaglutide group than the control group (hazard ratio=0.76; 95% confidence interval [CI], 0.66-0.88; P=0.0003), and the results were consistent across prespecified patient subgroups. The risk of major related cardiovascular events was observed to be statistically lower in patients taking weekly subcutaneous semaglutide (212 vs. 254 events; hazard ratio=0.82; 95% confidence interval [CI], 0.68-0.98; P=0.029). Fewer serious adverse events related to infections or serious cardiovascular disorders were reported in the semaglutide group (49.6%) then placebo (53.8%).

Weekly subcutaneous semaglutide reduces the risk of developing clinically significant kidney and cardiovascular outcomes in patients with T2DM and chronic kidney disease based on the current findings in the FLOW trial.

Source: www.nejm.org

Insignificant Risk Reduction for Symptomatic SARS-CoV-2 Infection using Oral Nirmatrelvir-Ritonavir as Post-exposure Prophylaxis

Date: July 18, 2024

Coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 infection still remains as an ongoing threat towards the local healthcare system and the global community. Previous real-world modelling also suggested that nearly half of the disease transmission occur before symptom onset, especially with the emergence of the B.1.617.2 (delta) and B.1.1.529 (omicron) variants. Nirmatrelvir-ritonavir has been approved for treating mild-to-moderate SARS-CoV-2 infection in adult patients at high risk to progress to severe complications. Yet, its effect as post-exposure prophylaxis among household contacts of infected persons remains uncertain.

In this phase 2-3, double-blind, randomized and placebo-controlled trial, a total of 2957 adult participants with negative screening rapid antigen test for SARS-CoV-2 at baseline were randomized in 1:1:1 ratio to receive oral 300mg nirmatrelvir and 100mg ritonavir daily for 5 days (n=921), 10 days (n=917) or matching placebo (n=898). The 5-day nirmatrelvir-ritonavir group are expected to take 5-days of matching placebo upon completion of their respective 5-day nirmatrelvir-ritonavir regimen. Primary efficacy of the trial was analyzed based on the development of symptomatic SARS-CoV-2 infection to be confirmed by reverse-transcriptase-polymerase-chain-reaction (RT-PCR) or rapid antigen screening on Day 14. The safety outcomes of the prophylactic nirmatrelvir-ritonavir regimen were also assessed towards the end of the study period.

The incidence of symptomatic, confirmed SARS-CoV-2 infection by Day 14 of the trial did not demonstrate statistically significant differences between each nirmatrelvir-ritonavir group and placebo in general. Corresponding risk reductions compared with placebo were 29.8% (95% confidence interval [CI], -16.7-57.8; P=0.17) 35.5% (95% confidence interval [CI], -11.5-62.7; P=0.12) in the 5-day and 10-day treatment arm respectively. No remarkable differences in developing symptomatic COVID-19 infection were noted among participants at high risk for progression to severe complications as well. Reports of adverse reports were similar in both 5-day and 10-day treatment groups, with dysgeusia being the most frequently reported adverse event.

To summarize, post-exposure prophylactic doses of nirnatrelvir-ritonavir did not provide significant risk reduction for adult household contacts of symptomatic COVID-19 patients to develop SAR-CoV-2 infection as compared with placebo.

Source: www.nejm.org

Overview of Health Supplement Regulations in Hong Kong: A Comparison with Drug Regulations

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ABSTRACT

As the demand for health supplements rapidly grows, nutraceuticals have become a significant part of the pharmaceutical industry. Therefore, pharmacists working in the industry should have a good understanding of the laws that regulate health supplements in Hong Kong. This article introduces the major regulations for health supplements, namely safety, quality, labeling, and claims. Food and drug regulations may seem vastly different, but the underlying principles are similar. Using the format of comparison tables, this article aims to highlight the required documents for the launch of health supplements. Overall, both pharmaceutical and supplement product regulations aim to safeguard safety and quality.

Keywords: *Health supplement, Food supplement, Laws and regulations*

INTRODUCTION

An increase in the geriatric population, rising health awareness, and preventive healthcare measures have spurred demand for health supplements, and hence drive the growth of the nutraceutical industry. Starting from 2020, the annual health spending on supplements has surpassed Over-the-counter (OTC) drugs. In 2022, the global supplement market size exceeded US$ 120,000 million, and the increasing trend is expected to continue.(1) Apart from supporting normal body functions, studies have shown that supplements have a wide range of benefits to physical and mental health. However, at the same time, taking supplements could also impose health risks. Therefore, health authorities play an important role in monitoring and regulating health supplements, including their manufacturing process, quality, safety, labeling, and claims. This article will provide you with an overview of the health supplement regulations in Hong Kong.

WHAT ARE ‘HEALTH SUPPLEMENTS’?

Different regions have different terms for “health supplements.” For example, they are termed “dietary supplements” in the United States, “food supplements” in the European Union, “complementary medicine” in Australia, and “health supplements” in countries of the Association of Southeast Asian Nations (ASEAN).

In general, the definition covers the following elements:(2)

- They are marketed in dosage form and not in conventional food form, such as tablets, capsules, pills, sachets of powder, and ampoules of liquids
- They contain concentrated sources of substances, alone or in combination, such as vitamins, minerals, fish oils, herbs, microorganisms
- They are used to supplement diet and provide a health or physiological benefit

Table 1. Definition of “food” and “orally consumed products” according to Cap. 132 and Cap. 231.

Food(3)	Orally consumed products(4)
• **Including articles and substances used as ingredients in the preparation of food** • **Excluding medicine as defined by Cap. 138 and Cap. 549**	• For human consumption • Intended to be taken orally • In any of the following forms: pill, capsule, tablet, granule, powder, semi-solid, liquid

In Hong Kong, there is no legal definition for health supplements. They are classified as “food” and “orally consumed products” under Cap. 132 and Cap. 231 respectively, as shown in **Table 1**. It is also crucial to identify what is not a health supplement, based on the ingredients, intended uses, and claims **(Table 2)**.

Implications to Pharmacists

In general, health supplements are regulated as food. The laws and standards are different from those of drugs, so pharmacy law training does not cover health supplement regulations. However, many pharmaceutical companies also sell nutraceutical products. Hence, regulatory affairs (RA) officers are responsible for preparing documents, maintaining records, and ensuring legal compliance of health supplement products. Therefore, it is important that pharmacists who are interested in regulatory works to understand the regulations and standards for health supplements.

Table 2. Descriptions on what products are classified as “drugs”, “Chinese medicine”, or “conventional food products”.	
Drugs	Health supplements are **not** for treating or preventing diseases or modifying physiological functions. If a product contains ingredients from the Schedule 10 Poisons List or fulfills the definition of a pharmaceutical product under the Pharmacy and Poisons Ordinance (Cap. 138), it will be regulated as a drug. Below are scenarios when vitamin products may be considered as pharmaceutical products:(5)(6) • Vitamin A with not less than 10000 IU daily dose • Vitamin B_3 (nicotinic acid) with more than 200mg daily dose • Vitamin D with more than 1000 IU daily dose • Vitamin K, except vitamins K_1 or K_2 with 120mcg or less daily dose
Chinese medicine	If a product is composed solely of Chinese herbal substances specified in Schedule 1 and 2 of the Chinese Medicine Ordinance (Cap. 549) as active ingredients, they are regarded as proprietary Chinese medicine.(7)
Conventional food products	Meat, bread, and chewing gum are generally not regarded as health supplements.

FOOD REGULATIONS

How are Health Supplements Regulated?

In Hong Kong, health supplements, namely vitamins and glucosamine containing products, were once considered as drugs in Hong Kong. However, in December 2015, after reviewing the regulations in other countries and available scientific information, the Pharmacy and Poisons Board (PPB) decided that these supplements are no longer considered as pharmaceutical products unless certain criteria are met. Therefore, health supplements are generally regarded as food and are regulated by the Food and Environmental Hygiene Department (FEHD) under the Public Health and Municipal Services Ordinance (Cap. 132 Part V) and Undesirable Medical Advertisements Ordinance UMAO (Cap. 231). This change meant that local manufacturers, importers, and distributors should register their products with the FEHD, instead of the Drug Office under the Department of Health.(8) Unlike pharmaceutical products, health supplements are not subjected to pre-market evaluation and registration by government authorities, and hence there are no sales restrictions for health supplements. Manufacturers are responsible for evaluating product safety, quality, and efficacy, and ensuring compliance with legal requirements. In addition, the Centre for Food Safety (CFS) has a food surveillance program, which is responsible for regular inspections and sample-takings at import, wholesale, and retail levels for microbiological, chemical, and radiation testing.(9) In the following sections, more details on the different aspects of health supplement regulations will be discussed.

Food Quality and Safety Standards

Similar to pharmaceutical products, quality and safety are the top priority of food products. Therefore, there are regulations regarding ingredient restrictions, and heavy metal and microbial limits. First, all food manufacturers should have Good Manufacturing Practices (GMP) or equivalent certifications. GMP covers all aspects of food production – from the environment and the equipment to personnel and record management. Therefore, GMP certification is used as one of the guarantees that food products are manufactured under good control and are safe for consumption.

As for ingredients, unlike foreign countries, Hong Kong does not have an authoritative list of permitted or prohibited active ingredients, but there are restrictions on food additives and excipients. Products that exceed the concentration limits or contain prohibited substances are banned from sale. Related regulations are as follows:(10)

- Coloring Matter in Food Regulations (Cap. 132H)
- Sweeteners in Food Regulations (Cap. 132U)
- Preservatives in Food Regulations (Cap. 132BD)
- Pesticide Residues in Food Regulation (Cap. 132CM)
- Mineral Oil in Food Regulations (Cap. 132AR)
- Harmful Substances in Food Regulations (Cap. 132AF)(11) – Partially hydrogenated oil is prohibited in all food products. If the product contains fully hydrogenated oil, there should be a specification on the product packaging.
- Food Adulteration (Metallic Contamination) Regulations (Cap. 132V)(12) – Food groups have different heavy metal maximum limits as listed in the Schedule. If the supplement product does not fall into any food groups, CFS will continue to conduct a risk assessment to determine if the product may contain metal in a harmful amount. In such cases, suppliers can obtain a declaration from the manufacturing site to confirm that the heavy metal standard of the manufacturing country is met.

Microbial Limits (13)

Microbial	Standard
Escherichia coli	< 20 cfu/g
Listeria monocytogenes [ISO11290-2:1998/Amd1:2004]	< 10 cfu/g
Vibrio parahaemolyticus	< 20 cfu/g
Staphylococcus aureus and other coagulase-positive staphylococci	< 20 cfu/g
Clostridium perfringens	< 10 cfu/g
Bacillus cereus	< 10^3 cfu/g
Campylobactoer spp. (thermotolerant)	not detected in 25g
Escherichia coli O157 (and other Shiga toxin-producing E.Coli (STEC))	not detected in 25g
Salmonella spp.	not detected in 25g
Vibrio cholerae (O1 and O139)	not detected in 25g

Product Labeling Requirements

Under Food and Drugs (Composition and Labeling) Regulations (Cap. 132W), schedules 3 and 5 specifies the labeling requirements for all pre-packaged food.[14, 15] The information required on the label is as follows:

- Name of the food
- Ingredient list
  - Listed in descending order of weight or volume
  - Additives listed by functional class and the specific name/ identification number
  - Allergen declaration
- Nutrition label
  - Label should include energy, core nutrients (carbohydrates, sugars, total fat, saturated fat, trans fat, protein, sodium), and claimed nutrients
  - The declared value should be based on respective tolerance limits:

Energy/ Nutrient	Tolerance Limits
Energy, total fat, saturated fat, trans fat, cholesterol, sodium and sugars	< 120% declared value
Protein, polyunsaturated fat, monounsaturated fat, carbohydrates, starch, dietary fibre, soluble fibre, insoluble fibre, individual component of fibre	> 80% declared value
Vitamins and minerals (other than Vitamin A, Vitamin D and added vitamins and minerals)	> 80% declared value
Added vitamins and minerals (other than Vitamin A and Vitamin D)	> 100% declared value
Vitamin A and Vitamin D (including added ones)	80% - 180% declared value

- Indication of "use by" (此日期或之前食用) or "best before" (此日期前最佳) date
- Count, net weight, or volume of food
- Special conditions for storage or instructions for use
- Name and address of manufacturer or packer

The labeling can be in Chinese or English. However, if both languages are used in the labeling, then the name of the food ingredient list must appear in both languages. Examples of proper labeling are shown in **Figures 1** and **2**.[16]

Promotion and Nutritional Claims

No prior authority approval is needed for promotional materials like television advertisements or posters. However, companies should ensure that there are no medicinal claims, misleading claims, or violations of UMAO. Under Cap. 132W, three types of nutritional claims are permitted with specific requirements.[14, 15] Claims can only be made for nutrients included in Schedules 7 and 8.

Nutrient content claim refers to the claim that describes the energy value or the content level of a nutrient contained in a food. Common wordings include "contain", "low", "high" and "zero". Cap. 132W Schedule 8 listed the conditions for nutrient content claims for respective nutrients. Nutrients must meet the conditions to make nutrient content claims.

Nutrient comparative claim refers to the claim that compares the energy value or the content level of a nutrient in the same or similar types of food, for example, different brands of the same or similar food items. Common wordings include "less", "reduced", "extra" and "more". To make nutrient comparative claims, both the absolute and relative difference criteria should be met. Concerning the core nutrients and energy, the content should have a relative difference of at least 25%. Concerning vitamins and minerals, the content should have a relative difference of at least 10% Chinese nutrient reference value (NRV). The absolute difference should

***Figure 1 and 2**: Examples of appropriate labeling of prepackaged food.*

be greater than the figure defined as "low" or "source" in column 4 of Schedule 8. In addition, the comparison should be based on the same quantity of food and the description of food being compared should be placed close to the nutrient comparative claims.

Nutrient function claim refers to the claim that describes the physiological role of a nutrient in the growth, development, and normal functions of the body. The claims should be based on scientific evidence. Also, the content of the nutrient concerned should not be less than the minimum amount set out in column 4 of Schedule 8.

COMPARISON OF FOOD AND DRUG REGULATIONS

In Hong Kong, there are different laws and ordinances for food supplements and pharmaceutical products. Hence, there are different quality, sales, claims, and labeling requirements as shown in **Table 3**. One key difference is pre-market evaluation and approval. Pharmaceutical companies are required to submit new drug applications and dossiers, which are subjected to review by the Department of Health. In contrast, there is no pre-market approval for food products, so companies only need to prepare all the documents and conduct internal evaluations before market launch. For both, food supplements and pharmaceutical products, RA officers are involved in reviewing and ensuring legal compliance. **Table 4** shows a comparison of the required documents for new drug registration and food product launch, which highlights some similarities.

CONCLUSION

As health supplements is one of the leading trends in the healthcare industry, the aim of the article is to increase pharmacists' awareness about food regulations. In the pharmaceutical industry, it is becoming increasingly common for RA officers in pharmaceutical companies to handle the launch of food products. Since pre-market evaluation by health authorities is not required, RA officers are the final guardians before the official product launch. Thus, the role of RA officers is crucial to manage product launch, and handle inspections and enquiries. As this article provides a brief overview of health supplement regulations, more detailed guidance can be found in the technical guidelines provided on CFS websites or the Ordinance.

Table 3: General comparison of food and drug regulations

	Drug	Food
Law & Ordinance	Cap. 138, Cap. 137, Cap. 134, Cap. 231 UMAO, Cap. 60A Import Export, Cap. 132 Part V	Cap. 132 Part V Cap. 231 UMAO
Governing authority	Department of Health (DoH)	Food Hygiene and Environmental Department (FEDH)
Pre-market approval	**Yes** - Need to register and approve label - Evaluates quality, safety, efficacy - Need renewal every 5 years - Need approval for Change of Registered Particulars (CORP)	**No** - internal evaluations only - No renewal required
Sales	Regulated sales: Prescription/Pharmacy-only/ OTC	Not regulated Allow e-commerce
Promotion	No authority approval needed	No authority approval needed
Claims requirement	**UMAO** - prohibited: claims related to abortion - Schedule 1: prohibited disease and permitted purpose - Schedule 2: prohibited purpose - Schedule 4: prohibited high-risk claims and restricted claims (BG, BP, lipids), examples of allowable claims **Cap 132:** prohibited any false or misleading claims	**UMAO** **Cap 132** Additional nutrition labeling guidance (Cap. 132W): - Nutrient content claims - Nutrient comparative claims - Nutrient function claims
Labeling	Ingredient declaration for Active Pharmaceutical Ingredient (API) only Additional warning statements for some drugs	Cap 132Q: full list of ingredients, additives and their function, and potential allergen
	Nutrient claim for active nutrients	Nutrition label: Energy, core nutrients and claimed nutrients
Quality standards (microbiology & impurities)	**Harmonized standards:** Pharmacopoeia International Council for Harmonisation (ICH)/ World Health Organization (WHO) guidelines	**Separate guidelines:** Coloring Matter (Cap. 132H) Sweeteners (Cap. 132U) Harmful Substances (Cap. 132AF) Preservatives (Cap. 132BD) Pesticide Residues (Cap. 132CM) Mineral Oil in Food Regulations (Cap. 132AR) Metallic Contamination (Cap. 132V) Microbiology Guidelines for Food

Table 4: Comparison of the documents required for authority submission or internal review	
New drug registration Documents for authority submission	**New food product launch** Documents for internal review
3.2.P.1 Description and composition of the Drug Product	Master Formulation - Composition compliance - In descending order - Food additives and their functions
3.2.P.5.1 Specification derived based on pharmacopoeia	Specification derived based on importing country quality standard and risk assessment
3.2.P.5.2 Analytical Procedures	---
3.2.P.5.3 Validation of Analytical Procedures	---
3.2.P.5.4 Batch Analysis (COA)	Certificate of Analysis (COA)
3.2.P.8.3 Stability Data	Stability Data
Manufacturer licenses (Bulk, packer etc.)	Manufacturer license Manufacturer details
Certified Pharmaceutical Inspection Co-operation Scheme (PIC/S) GMP for all the above manufacturers	GMP, Hazard Analysis and Critical Control Point (HACCP) or equivalent certification
Site Master File	---
Manufacturing flow chart indicating the manufacturing process, name/address & role of the manufacturer(s) involved and proposed updates.	Manufacturing process
Final product picture (dosage form)	---
Manufacturer declaration to clarify the relationship between the Marketing Authorization (MA) holder & the manufacturer	---
Certificate of Pharmaceutical Product (CPP) (marketed) from country of Origin together with the approved labels	Free Sale Certificate from other countries (Optional)
If the country of origin is not one of the following recognized reference countries, we also need to get a CPP (marketed) from the following countries with the approved labels :- Australia, Austria, Belgium, Brazil, Bulgaria, Canada, China, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Holland, Hungary, Ireland, Italy, Japan, Latvia, Lithuania, Luxembourg, Malta, Poland, Portugal, Romania, Singapore, Slovak Republic, Slovenia, South Korea, Spain, Sweden, Switzerland, UK and USA.	---
Proposed pack sizes and labels	Labels fulfilling local labeling regulations, including - nutrition information - allergen declaration

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Review of Vaccines against Herpes Zoster: the Efficacy, Safety and Impact on Quality of Life of Shingrix® and Zostavax®

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ABSTRACT

Herpes Zoster is caused by the reactivation of latent Varicella zoster virus infection on the sensory nerve ganglion, with a significant proportion of patients developing serious complications. Zostavax and Shingrix are the two available vaccines for preventing herpes zoster. Zostavax was introduced in Hong Kong in 2007, which is followed by a newer entity Shingrix being registered in Hong Kong in 2020. This review focuses on the comparison of the efficacy, safety and the impact on quality of life of the herpes zoster vaccines.

Based on the currently available published studies, Shingrix is shown to have a higher vaccine efficacy in the age group of 50 or above while Zostavax has a significantly lower vaccine efficacy in the age group of 70 or above. Greater effectiveness in improving quality of life and durability of protection have also been reported in Shingrix recipients. Regarding safety, Injection reactions were common in both Shingrix and Zostavax but more systemic reactions were identified for Shingrix. Clinical studies, along with the recommendations from foreign public health authorities, suggest that Shingrix is superior to Zostavax. Thus, Shingrix is believed to have great potential in replacing Zostavax for preventing herpes zoster in Hong Kong.

Keywords: *Herpes Zoster Vaccine, Zostavax, Shingrix, Adjuvanted recombinant zoster vaccine, Live Zoster Vaccine, Herpes Zoster*

Abbreviations

HZ= Herpes Zoster
LZV= Live Zoster Vaccine/ Zostavax
PHN= Postherpetic Neuralgia
QoL= Quality Of Life
RZV= Recombinant Zoster Vaccine/ Shingrix
VE_{HZ}= Vaccine efficacy in reducing the incidence of Herpes Zoster

INTRODUCTION

Herpes Zoster (HZ), commonly known as shingles, refers to the reactivation of latent Varicella zoster virus (VZV) infection on the sensory nerve ganglion, characterized by painful rashes which typically resolve in 2 to 4 weeks.(1) In Hong Kong, the actual prevalence of HZ was not reported, but a survey conducted by the University of Hong Kong estimated the prevalence of HZ in Hong Kong to be 16.8%.(2)

Studies also suggested that factors such as old age and immunosuppressive diseases were significant risk factors for HZ.(3) One of the common but serious complications of HZ is postherpetic neuralgia (PHN), which is defined as a neuropathic pain syndrome associated with HZ rated 3 or more on a scale of 0 to 10 and occurs persistently or appears more than 90 days after the onset of HZ rash.(1) The same study indicated that 29.8% of HZ patients develop such serious complication, and 2% may further develop into fatal complications such as stroke and myocardial infarction.(4)

Current treatment objectives for HZ are mainly to improve quality of life (QoL) of patients and to minimize the severity of pain in patients.(5) Common treatments include the use of oral antivirals such as acyclovir within 72 hours of onset. In immunosuppressed patients or patients with high risk of serious complications associated with delayed treatment, intravenous antivirals may also be considered.(5) With the high prevalence of HZ and risk of complications, there is an urgent demand to develop prevention strategies for HZ and its associated complications.

Currently, two types of vaccines indicated for prevention of HZ are available in Hong Kong, namely live attenuated zoster vaccine (LZV, Zostavax®) and recombinant zoster vaccine (RZV, Shingrix®) which was registered in 2007 and 2020 respectively. In this article, the mechanisms, efficacy, safety and impact on QoL of Shingrix and Zostavax will be discussed.

ZOSTAVAX (LZV)[6]

Therapeutic Indication

Zostavax is indicated for the prevention of HZ and HZ-related post-herpetic neuralgia (PHN) in individuals aged 50 years and older.

Mechanism of Action

Primary infection with VZV induces specific memory T-cells production that is sufficient to keep the virus in its latent form. However, general immunosuppressed state or waning immunity associated with aging may reduce T-cells to a level that is unable to inhibit viral replication, the decline in VZV-specific immunity thereby increases the likelihood of the virus reactivation. Zostavax, which contains a lyophilized preparation of live, attenuated VZV activates specific T-cell production to boost VZV-specific immunity and avoid VZV reactivation.

Dose and Administration

Zostavax is injected subcutaneously, preferably in the deltoid region of the upper arm. It is given in one dose as a shot after reconstitution within 30 minutes.

Clinical studies

The table below **(Table 1)** summarizes the key clinical studies of LZV.

Table 1. Key clinical studies of LZV (Zostavax)

Trial	Publication year	Objective	Study summary*	Mean follow–up years	Key findings#
1.Shingles Prevention Study (SPS)[9]	2005	Evaluate the vaccine efficacy in terms of incidence of HZ, burden of illness and incidence and postherpetic neuralgia in older adults with age of 60 or above	• Randomized, placebo-controlled and double blinded clinical trial at 22 sites in the United States • n=38546	3.13 years	i) Efficacy and QoL: • Overall VE_{HZ}: 51.3% • VE_{HZ} of age ≥70: 37.6% • VE_{HZ} of age 60-69: 63.9% • Reduced incidence of PHN by 66.5% • Reduced burden of illness by 61.1% • Protection through 4 years after vaccination ii) Safety: • More adverse events were reported by the participants in the vaccinated group than that of the placebo group • Most common adverse events were injection site reactions like erythema, pain and swelling
2. ZEST[10]	2014	Evaluate the efficacy and effectiveness of Zostavax in adults with age of 50-59	• Randomized, placebo-controlled, double blinded clinical trial conducted in Europe and North America • n=22439	1.30 years	i) Efficacy: • Overall VE_{HZ}: 69.8% ii) Safety: • More participants in the vaccinated group reported adverse events than the placebo group • Most common systemic adverse event was headache
3.Short-Term Persistence Substudy (STPS)[11]	2012	Evaluate the persistence of VE for HZ burden of illness, incidence of PHN, and incidence of HZ each year through year 7	• Re-enrolled subjects from SPS with analogous methods • 12 of 22 original Shingles Prevention Study sites in the United States • n=1427	0.98 years for placebo recipients and 1.36 years for vaccine recipients	Efficacy: • Vaccine efficacy for each study outcome was lower in the STPS than in the SPS • Evidence of persistence of vaccine efficacy through year 5 post vaccination
4.Long-Term Persistence Substudy (LTPS)[1]	2015	Evaluate the persistence of vaccine efficacy for HZ burden of illness, incidence of PHN, and incidence of HZ each year from 7 to 11 years post vaccination	• Re-enrolled subjects from SPS with analogous methods • 12 STPS sites • n=6867 (SPS vaccine recipients)	3.74 years	Efficacy: • Statistically significant vaccine efficacy for incidence of HZ persisted only through year 8
5. A study on the long-term effectiveness of HZ vaccine conducted at Kaiser Permanente Southern California[12]	2016	Evaluate the long-term effectiveness of HZ vaccine in terms of overall incidence of HZ and the cumulative risk of HZ in the vaccinated and unvaccinated cohort in adults with age of 60 or above	• Conducted at Kaiser Permanente Southern California • n=704312 (176 078 vaccinated and 528 234 unvaccinated)	8.00 years	Efficacy: • Rapid decline in effectiveness of HZ prevention • Vaccines provide little protection against HZ beyond 8 years

Remark: (*): n refers to the total number of participants in the study, (#): VE refers to vaccine efficacy and VE_{HZ} refers to vaccine efficacy in reducing the incidence of HZ

Table 2. Key clinical studies of RZV (Shingrix)

Trial	Publication year	Objective	Study summary*	Mean follow–up years (Post vaccination)	Key findings#
1. ZOE-50[13]	2015	Evaluate the efficacy and safety of the subunit vaccine (Shingrix) in older adults with age of 50 or above	• Randomized, placebo-controlled, phase 3 study in 18 countries in Europe, North America, Latin America, and Asia–Australian • n=15411	3.2-3.5 years	i) Efficacy and QoL: • Overall VE_{HZ}: 97.2% • No significant difference of VE_{HZ} between age groups • significant VE in preventing postherpetic neuralgia (PHN) • Reduced the HZ burden of illness significantly ii) Safety: • More injection site reaction and systemic reaction in the vaccinated group and the symptoms are mild to moderate in intensity • Pain was the most common injection-site reaction while myalgia was the most common systemic reaction
2. ZOE-70[14]	2016	Evaluate the efficacy and safety of the subunit vaccine (Shingrix) in adults with age of 70 or above	• Same study design to ZOE-50 (randomized, placebo-controlled, phase 3 study in 18 countries in Europe, North America, Latin America, and Asia–Australia) • n=13900 in ZOE-70 • n=17531 in the pooled analysis of participants from ZOE-50 and ZOE-70	3.7-4.0 years	i) Efficacy and QoL: • Overall VE_{HZ}: 89.8% • No significant difference of VE_{HZ} between age groups • Significant VE in preventing postherpetic neuralgia (PHN) • Reduced the HZ burden of illness significantly ii) Safety: • More adverse events were reported in the vaccinated group than the placebo group • The most common injection-site reaction and systemic reaction were pain and fatigue respectively
3. NCT01295320[15]	2015	Evaluate cell-mediated and humoral immune responses to Shingrix in healthy older adults at 48, 60, and 72 months after the first dose	• Phase II, open-label, multicenter, single-group trial conducted in 4 counties • n=129	Between Month 48 and Month 72 after the first dose	Efficacy: • 6 years after vaccination, gE-specific cell-mediated immune responses and anti-gE antibody concentrations remained higher than the pre vaccination values
4. NCT02735915[16]	2020	Evaluate persistence of humoral and Cell-mediated immune response to Shingrix at months 108 and 120 after the first dose.	• Single-arm, open-label, phase IIIB, long-term follow-up study of the initial phase II trial (NCT00434577) • Conducted in 3 countries (The Czech Republic, Germany, Sweden) • n=70	Between 9 and 10 years after the first dose	Efficacy: • Immune responses persist through 20 years
5. NCT02723773[17]	2012	Evaluate the efficacy of RZV in the prevention of HZ over the total duration of the current Long Term Follow Up (LTFU) study	• Ongoing open-label, phase 3B, LTFU study of the two pivotal phase 3 clinical trials (ZOE-50 & ZOE-70) • Conducted in 18 countries • n=14648	Between 5.1 and 7.1 years post-vaccination	Efficacy: • Clinical benefit of Shingrix in older adults is preserved for at least 7 years post-vaccination
6. NCT01610414[18]	2019	Evaluate the efficacy and adverse event profile of the recombinant zoster vaccine in immunocompromised autologous Haematopoietic Stem Cell Transplant (HSCT) recipients.	• Phase 3, randomized, observer-blinded study conducted in 167 centers in 28 countries among 1846 patients aged 18 years or older who had undergone recent autologous HSCT • n=1846	29 months	i) Efficacy: • Post hoc analysis shows that efficacy for HSCT patients may not exceed 2 years ii) Safety: • Generally well tolerated, symptoms are mild and transient

Remark: (*): n refers to the total number of participants in the study, (#): VE_{HZ} refers to vaccine efficacy in reducing the incidence of HZ

SHINGRIX[7, 8]

Therapeutic Indication

Shingrix is indicated for the prevention of HZ in adults aged 50 years and older, and in adults aged 18 years and older who are or will be at increased risk of HZ due to immunodeficiency or immunosuppression caused by known disease or therapy.

Mechanism of Action

Shingrix is a recombinant vaccine, consisting of a highly specific antigen (i.e. glycoprotein E (gE)) in an adjuvant system ($AS01_B$). Glycoprotein E is the most abundant surface protein of VZV that stimulates robust and persistent VZV-specific antibody and CD4+ T cell responses the specific HZ virus. The adjuvant system enhances activation of the immune system, hence giving a stronger and sustained immune response to VZV.

Therefore, these two components together can assist the body to overcome age-related decline in immunity, which is a presiding driver of HZ.

Dose and Administration

Shingrix is provided as a 2-dose series. A first dose is at month 0, then followed by a second dose given between two to six months later. It is supplied in 2 vials, which must be reconstituted before injection. The powder (i.e. lyophilized VZV glycoprotein E (gE) antigen component) is reconstituted with the accompanying liquid solution (i.e. AS01B adjuvant suspension component). It should be administered intramuscularly and the deltoid region of the upper arm is the preferred site for injection.

Clinical studies

The table below **(Table 2)** summarizes the key clinical studies of RZV.

EFFICACY: PREVENTION OF HERPES ZOSTER(HZ)

Zostavax

Shingles Prevention Study (SPS) was conducted in 1998 to 2001 and the result was published in 2005.[9] It is a randomized, placebo-controlled trial. A total of 38546 participants with age of 60 or above were enrolled, in which there were 957 confirmed cases of HZ (315 from the vaccinated group and 642 from the placebo group) after excluding those confirmed cases within 30 days of vaccination. Hence, the incidence of Shingles was significantly reduced by 51.3% in the vaccine group when compared to the placebo group. However, another key finding is that the vaccine efficacy, measured by the incidence of having HZ (VE_{HZ}) is 37.6% among those with age of 70 or older and 63.9% in younger subjects (i.e. age of 60-69). This has indicated that LZV has a higher efficacy in adults with age of 60-69 than that of 70 or above.

With the basis of SPS, another study called the Zostavax Efficacy and Safety Trial (ZEST) was conducted in participants aged 50-59 and published in 2012.[10] ZEST is a randomized, placebo-controlled trial conducted in Europe and North America Participants received either placebo or one dose of LZV with a mean follow up of 1.3 years after vaccination. Out of 129 confirmed cases of HZ, 30 cases were from the vaccinated group and 99 cases were from placebo group. From the intention-to-treat analysis, LZV could significantly lower the incidence of HZ with an VE_{HZ} of 69.8%.

In short, SPS and ZEST are the two major studies that evaluate the VE_{HZ}. LZV has shown a VE_{HZ} of 69.8% in older adults aged 50-59 in the ZEST study. Meanwhile, in SPS, it has VE_{HZ} of 63.9% and 37.6% in the age group of 60-69 and 70 or above respectively. Even though LZV can significantly reduce the incidence of HZ, lower efficacy is reported in older adults aged 70 or above.

Shingrix

With reference to the ZOE-50 trial in 2015,[13] the efficacy and safety of RZV is studied through a randomized, placebo-controlled phase 3 clinical trial in 18 countries. The trial was conducted in adults with age of 50 or above and further stratified into 50-59, 60-69 and 70 or above. A total of around 15400 participants were evaluated, in which they received either the vaccine or placebo in two intramuscular doses two months apart. With a mean follow-up of 3.2 years, there were 216 confirmed cases of Shingles, in which 6 cases belonged to the vaccinated group and 210 cases belonged to the placebo group. As a result, the VE_{HZ} was reported to be 97.2%. Meanwhile, the VE_{HZ} were similar in all the stratified age groups, ranging from 96.6% to 97.9%.

Another trial, ZOE-70 was concurrently conducted at the same sites with an aim to investigate the safety and efficacy of the RZV in adults aged 70 or above.[14] The methodology used in ZOE-70 is similar to that of ZOE-50. A pooled analysis on the safety and efficacy of the vaccine (i.e. reducing the risk of HZ and PHN) was evaluated in adults aged 70 or above from both ZOE-50 and ZOE-70. Out of 16,600 participants in the modified vaccinated cohort, 246 cases of HZ were reported after a mean follow-up of 3.7 years. Out of these 246 cases, 23 were from those who received RZV and 223 were from those receiving placebo. Thus, a VE_{HZ} of 89.8% was reported. No significant difference was shown between the age group of 70-79 and 80 or above.

Therefore, with reference to both ZOE-50 and ZOE-70, the RZV was reported to significantly lower the risk of HZ with a higher VE_{HZ} than placebo controls in adults aged 50 or above. Same result patterns were shown in ZOE-70.

Summary of vaccine efficacy of Zostavax and Shingrix

With reference to *Table 1* and *Table 2*, the four clinical trials (ZOE-50, ZOE-70, SPS and ZEST) have assessed the VE_{HZ} in adults aged 50 or above. Note that RZV has shown no profound difference in VE_{HZ} in different age groups (i.e. older adults aged 50 or above). By contrast, LZV has shown a lower VE_{HZ} in the age group of 70 or above. Therefore, it suggests that RZV is more suitable for patients aged 70 or above due to a higher VE_{HZ}. Moreover, several trials showed that the newly invented RZV had a higher VE_{HZ} in the corresponding age groups than that of LZV.[19-21]

Both the clinical trials of RZV and LZV are funded by their manufacturer, GSK and MSD respectively. Hence, there are slight differences in terms of study design, including the countries of participants and total sample size. Yet, due to a relatively large sample size (> 14000 participants), these trials serve as a strong reference in testing the VE_{HZ} of RZV and LZV.

EFFICACY: PREVENTION OF POSTHERPETIC NEURALGIA(PHN)

Zostavax

In SPS, the incidence of PHN amongst adults aged 60 or above who received LVZ zoster vaccine was compared with that in the placebo group. The prespecified criteria for success required a reduction of 62% or more in the incidence of PHN in the vaccine group as compared with that in the placebo group.[9]

With a total of 957 cases of HZ with a median of 3.12 years of surveillance, there were 107 cases of PHN: 27 out of 315 patients in the vaccine group (0.46 case per 1000 person-years) and 80 out of 642 patients in placebo group (1.38 cases per 1000 person-years). The results met the prespecified criteria for success as the use of the vaccine reduced the incidence of PHN by 66.5%. No difference in the vaccine efficacy with respect to the incidence of PHN was observed when results were stratified according to sex and age.

The long term vaccine effectiveness against PHN was estimated in an ongoing interim analysis of a prospective observational cohort study conducted in the US integrated healthcare system database.[22] At the time of the interim analysis, 1,355,720 individuals aged 50 and above with 392,677 who received LZV were included. From the period of 2007 to 2014, there were 48,616 cases of HZ. Amongst those with incident HZ episode, 3,297 cases developed PHN (322 cases in the vaccinated cohort and 2,975 in the unvaccinated cohort). The overall effectiveness of LZV regarding the prevention of PHN during the period covered in this interim analysis in all age groups was 69%. For individuals aged 60-69, 70-79 and 80 or older at the time of vaccination, the average vaccine effectiveness against PHN over the first five years following vaccination was 72%, 69% and 61% respectively. It was concluded that the effectiveness of vaccines against HZ-induced PHN declined with age of which patients are vaccinated.[23]

Shingrix

From the pooled data of ZOE-50 and ZOE-70 (with 16596 participants), RZV vaccination reduced the incidence of PHN by 88.8% in participants of 70 years of age and above when compared with the placebo group. The effective protection could be apparently attributed to the high vaccine efficacy of 91.3% in the pooled analysis in preventing HZ. Among participants of 50 years of age or above, 91.2% of reduction in the incidence of PHN was observed, with 4 of 32 participants (0.1 case per 1000 person-years) who received 2 doses of RZV developed PHN as compared to 46 out of 477 (0.9 case per 1000 person-years) in the placebo group, given 3.8 years of mean follow-up period. This shows the high efficacy of RZV in preventing incidence of PHN.[13, 14]

Summary of prevention of PHN

From the above studies, it shows that for a period of less than 4 years post-vaccination, RZV is more efficacious in reducing the incidence of PHN than LZV. The former offers 91.2% and 88.8% of reduction in developing PHN in participants of at least 50 and 70 years of age respectively, while the latter reduced the incidence by 66.5% and 69% in individuals aged 60 or above and all age groups respectively.

EFFICACY: DURATION OF PROTECTION

Zostavax

As mentioned, the SPS trial examined the vaccine efficacy in terms of HZ-induced PHN and incidence of HZ through 4 years after vaccination. The result showed that LZV could provide protection through 4 years after vaccination.[9]

Short-Term Persistence Substudy (STPS), which was another study conducted approximately 15 months after SPS, re-enrolled 7320 vaccine and 6950 placebo recipients from the SPS population.[11] It assessed the persistence of vaccine efficacy throughout the 3.3-7.8 years after vaccination. Same as SPS, vaccine efficacy for the 3 outcome measures (i.e. HZ burden of illness, incidence of PHN and incidence of HZ) were also assessed in STPS. Compared to the SPS, it is reported that the vaccine efficacy for HZ burden of illness, incidence of PHN, and incidence of HZ, declined by 11.0%, 6.4% and 11.7% respectively. Since STPS is carried out after the completion of SPS, the aforementioned result implies that the efficacy of LZV declines overtime. In addition, when combining the data reported in SPS and STPS, the vaccine efficacy for HZ incidence and the HZ burden of illness were shown to be statistically significant at the year 5 mark. Yet, vaccine efficacy for the aforementioned two outcome measures was no longer statistically significant in year 6 and year 7 as reported in STPS. Therefore, it is concluded that the length of immunity for LZV is around 5 years, and vaccine efficacy beyond this time point is uncertain.

Following STPS, a Long-Term Persistence Substudy (LTPS) was initiated to further investigate the long-term vaccine efficacy of LZV.[1] 6867 SPS vaccine recipients were re-enrolled and were assessed for each year from 7 through 11 years. Although the vaccine efficacy was reported to decline from 46.0% in year 7 to 14.1% in year 10 for the incidence of HZ, the vaccine efficacy for incidence of HZ remained statistically significant through year 8 after vaccination, which is 3 years longer than the result obtained in STPS. Meanwhile, vaccine efficacy for reducing the incidence of PHN varied through year 7 to 11.

In another large observational study conducted in Kaiser Permanente Southern California (KPSC), which included 704,312 aged ≥ 60 years adults.[12] 176,078 individuals were vaccinated with LZV, while 528,234 were unvaccinated. The vaccine effectiveness in terms of the incidence of HZ by follow-up year after vaccination, which was estimated as 1– adjusted hazard ratios, was recorded over 8 years. Generally consistent with the results in SPS and STPS, rapid waning of protection from this live, attenuated vaccine was noted, in which the vaccine effectiveness reduced from 69% to 4% during this period. In addition, a revaccination strategy is also proposed in the same study.

From the results of these trials, it can be concluded that the efficacy of LZV in prevention of HZ diminished rapidly, even though the efficacy for prevention of PHN was partly maintained. It is also noted that most evidence supports the persistence of overall vaccine efficacy and protection through year 5 only, meanwhile, all efficacy data for incidence of HZ presented was not statistically significant 8 years after vaccination. Therefore, the evidence for protection 6 years post-vaccination remains uncertain.

Shingrix

In a phase II multicenter trial, 129 individuals who had received two doses of RZV in a pivotal trial (single-blind, randomized, controlled trial, NCT00434577) were followed up.[15] It aimed to evaluate the persistence of immune responses induced by two doses of RZV in two age cohorts (i.e. 60–69 years and ≥70 years of age) and at 3 different time points (i.e. 48, 60, and 72 months after the first dose of RZV). Results suggested that at month 72, the median gE-specific cell-mediated immunity response and anti-IgE antibody concentration were still 3.8 and 7.3-fold above the pre vaccination value, suggesting that RZV-induced immune responses persist for up to 6 years in healthy older adults.

Moreover, in a phase IIIB, long-term follow-up study of the initial phase II trial (NCT00434577), 70 adults ≥60 years of age who completed a 2-dose RZV vaccination were assessed for the immune responses through 10 years after initial vaccination.[16] Results were in line with the previous study, with additional observation showing that IgE-specific cell-mediated immunity response and anti-IgE antibody concentration remained 3.5 times and 6 times higher than the pre-vaccination levels 10 years after initial vaccination. In the same study, 3 validated models were also used for prediction, and it was proposed that immune responses could persist through 20 years.

Yet, as there is no established information regarding immunological threshold of protection against HZ, the immune response illustrated in these two studies cannot infer the clinical protection.

The other long term follow-up study indeed provided more information regarding the persistence of clinical benefit of RZV.[17] Out of the 7294 former participants of the ZOE-50/70 pivotal clinical trials, 7 and 169 shingles cases were reported in the vaccine and control group during the period ranging from a mean of approximately 5.1 to 7.1 years post-vaccination, indicating that RZV was 84.0% efficacious in preventing HZ for this period. Therefore, these findings confirmed that RZV provides clinical benefits for not less than 7 years post-vaccination for older adults.

Based on the above trials, it can be concluded that immune responses induced by RZV remain for 10 years, and potentially for 20 years. Meanwhile, clinical efficacy against HZ is confirmed to last for at least 7 years after vaccination.

Summary of protective duration

Based on the present clinical studies, it can be confirmed that the persistence of vaccine efficacy for LZV and RZV is 5 years and at least 7 years respectively. Modeling of RZV immunological results show that immune responses persist even through 20 years. Additionally, RZV's efficacy also plateaued at a very high level (i.e. 84.0%) at 5-7 years post vaccination. On the contrary, LZV not only has lower efficacy, but its effectiveness also wanes rapidly, especially by year 5 after vaccination. Such differences between 2 vaccines may be related to the adjuvant system in RZV, which enhances the immune system's response for a long lasting protection effects.

IMPACT ON QUALITY Of LIFE (QoL)

Zostavax

The impact of zoster vaccination on the HZ-related interference with activity of daily life (ADLs) and health related QoL (HRQL) were assessed in the study population of SPS. ADL and HRQL evaluations were repeated in a span of 182 days. Overall, 957 cases in which 315 belong to the vaccine group and the remaining 642 belong to the placebo group were analyzed.[24]

Zoster Brief Pain Inventory (ZBPI) was used to quantify pain and discomfort associated with HZ and measure certain activities of daily living (ADLs) and health. Participants were to rate HZ pain and discomfort in four aspects (the worst, least and average during the past 24 hours and now) as well as the interference of HZ pain and discomfort towards seven ADLs: general activity, mood, walking ability, work, relation with others, sleep and enjoyment of life on a scale of 0-10 using the 11-point Likert scale. To deduce the ZBPI ADL burden of interference, the average score of the HZ pain and discomfort regarding the seven ADLs items were taken. From day 0 to day 182 in the modified intention to treat population, LVZ was able to reduce the ZBPI ADL burden of interference by 66%.

On the other hand, the Medical Outcomes Study 12-item Short Form Survey (SF-12) was used to measure the HRQL where participants self-evaluated their general health, including limitations in daily activity, emotional problem, interference of pain with work, etc. The SF-12 is summarized into mental component summary (MCS) and physical component summary (PCS) scores. For the entire study population, LVZ reduced HZ-related decrements in PCS and MCS by 55% when compared to placebo controls. Overall, LVZ reduced the HZ-related burden of interference with daily activity by two-third and HZ-related effect on HRQL by half in the vaccinated group.

Shingrix

The QoL impact of RZV was determined in 2 trials, ZOE-50 and ZOE-70, with the following assessments: First, for patients who developed HZ after RZV vaccination (8 patients out of 7340 in ZOE-50 and 23 out of 8250 in pooled ZOE-70), the ZBPI instrument was used to assess participants' "burden of illness" and "burden of interference with ADL", as compared with 241 patients out of 7413 receiving placebo in ZOE-50 and 263 out of 8346 receiving placebo in pooled ZOE-70 respectively. Patients self-evaluated pain on 11-point Likert-type scales over a period of time. The "worst pain over the last 24 hours" category was considered clinically significant and most reliably correlated with vaccine efficacy in reducing the "burden of illness" associated with HZ pain. For "burden of interference with ADL", the extent of interference to 7 ADLs was rated based on 11-point Likert-type scales for 182 days starting from HZ rash onset.[25]

Reduction in burden of illness and burden of interference with ADLs was greater than 90% in both ZOE-50 and pooled ZOE-70. The mean worst pain scores were lower in the RZV group than the placebo group. Also, the median time to resolution of the "worst pain" was 14 days for both ZOE-50 and pooled ZOE-17, versus 17 and 22 days in the placebo groups in the respective studies.

Second, the utility loss of the HZ patients in the RZV and placebo groups in both studies over the first 28 days after rash onset was assessed with the mean EuroQol-5 Dimension (EQ-5D) utility index and compared. Patients were to grade their extent of problems on mobility, self-care, usual activities, pain or discomfort and anxiety or depression. The combination of the grades was converted to health states then into utility scores. The utility score ranged from less than 0 to 1, from the worst to best possible health state. Reduction in patients' utility loss was approximately 63.7% in ZOE-50 and 21.2% in pooled ZOE-70. In breakthrough HZ cases, estimated differences up to 0.14 in ZOE-50 study on the EQ-5D index of the HZ episode were observed, suggesting less loss of QoL in vaccinated groups.

Third, the 36-Item Short Form Survey (SF-36) was given to all patients to assess QoL with psychometric properties. Higher QoL scores were observed in RZV groups than placebo groups in both studies, but very few comparisons showed statistical significance.

Overall, RZV is shown to reduce HZ burden of illness and interference in daily activity, resulting in shorter duration of pain and increase QoL over the initial 4 weeks following rash onset. Thus, severity of HZ in vaccinated patients would decrease.

Summary of improving QoL

Both studies utilized the ZBPI to assess patients' burden of interference with ADL. The efficacy of RZV in reducing the burden of interference with ADL in patients with HZ (over 90%) appeared to be significantly higher when compared to that of the LZV (60%). However, it should be noted that there was a slight difference in the approach used to analyze the statistics. In the LZV study, the ZBPI ADL interference items were summarized into a single score for further analysis through taking the mean of the seven items, whereas the two consecutive ZBPI worst-pain scores were averaged in the RVZ study.

In terms of patient's QoL, RZV reduced patient's utility loss by approximately 63.7% in the ZOE-50 study whereas a 55% reduction in HZ-related decrements in QoL was observed after the use of LZV. As different health surveys were used (SF-12 MCS and PCS used in the RZV study vs SF-36 and EQ-5D used in the LZV study), this is a limitation for a direct comparison between the 2 vaccine studies.

SAFETY

Adverse events of LZV and RZV can be classified into local or systemic, non-serious or serious.

Zostavax

Zostavax (LZV) is generally well tolerated. In ZEST, 63.9% of the LZV recipients and 14.4% of placebo recipients aged 50 to 59 reported injection site reactions such as pain, erythema and swelling.[10] Common systemic adverse reactions reported include headache (9.4% in LZV group and 8.2% in placebo group) and pain in extremity (1.3% in LZV group and 0.8% in placebo group). On the other hand, 48% of the LZV recipients and around 17% of placebo recipients reported injection site reactions in SPS.[9] Common systemic adverse reactions (≥1%) reported include headache (1.4% in LZV group and 0.8% in placebo group). In ZEST and SPS, the number of participants reported serious adverse events within the post vaccination period of 42 days is similar in the LZV group (0.6% in ZEST and 1.4% in SPS) and placebo group (0.5% in ZEST and 1.4% in SPS). Both trials also demonstrated a similar overall incidence of death between the LZV and placebo group within the post vaccination period of 42 days. In ZEST, the mortality rate (per 1000 person per year) was 1.18 in the LZV group and 1.90 in the placebo group. In SPS, 14 and 16 cases of death were reported in the LZV group and the placebo group respectively, of which the most common cause of death was cardiovascular disease (10 in the LZV group and 8 in the placebo group).

A post-licensure retrospective study analyzed reports from the Vaccine Adverse Event Reporting System in the US and reported consistent findings as the above trials.[26] Non-serious common adverse events reported among adults ≥50 years with LZV administered included injection site redness (27%), HZ (17%), injection site swelling (17%), and rash (14%). Among the serious reports, HZ (29%), pain (18%), and rash (16%) were the most common symptoms.

Number of zoster-like rashes and varicella-like rashes within the post vaccination period of 42 days was low in the LZV and placebo groups in ZEST and SPS. Less than 0.2% of the participants in the LZV and placebo groups reported zoster-like rashes in both trials.[9, 10] On the other hand, less than 0.7% of the participants in the LZV and placebo groups reported varicella-like rashes. These rashes were generally mild. Among the rashes tested positive for varicella-zoster virus (VZV), all were associated with the wild type VZV. The Oak/Merck strain which was used in LZV was not detected.

Shingrix

Adults Aged 50 Years and Older

The safety profile of RZV in adults aged 50 or over has been evaluated in two phase III clinical trials (ZOE-50 and ZOE-70). Total of 29,305 participants over the age of 50 were involved, where 14,645 participants received at least 1 dose of RZV and 14,660 participants received placebo.[13, 14] It is noted that the mean age of these participants was 69 years old and Asian participants (18%) were included.

Among the 14,645 vaccinated participants, 1 subject reported lymphadenitis and 1 subject reported fever over 39°C. Common adverse events within 7 days after the administration of RZV (both doses combined) included injection site reactions such as pain (78%), erythema (38%), and swelling (26%). Local reactions affecting daily activities such as pain (Grade 3) were reported in 9.4% of them. Systemic adverse reactions such as myalgia (45%), fatigue (45%), headache (38%), shivering (27%), fever (21%), and gastrointestinal symptoms (17%) were reported. Around 10.8% of the vaccine recipients reported systemic reactions affecting daily activities, which was higher than that of the placebo group (2.4%). Grade 3 systemic adverse reactions were reported more frequently in participants after receiving the second dose. Generally, these common adverse events were more prevalent in adults aged between 50 and 69 than that of over 70 years old. Most of these local and systemic adverse reactions lasted for 2 to 3 days. There were no significant differences in the percentage of the participants experiencing serious adverse events between the vaccine and placebo groups. The incidence of death was similar in both RZV and placebo groups.

A post-licensure safety surveillance study reported similar findings like the aforementioned phase III clinical studies.[27] A low rate of serious adverse events was observed. Meanwhile, common adverse events like injection site reaction, swelling and pain were reported. It was also reported that adults aged between 50 and 69 had a greater chance to experience systemic reactions, whereas adults aged over 70 were more likely to have local adverse reactions.

Nonetheless, a post-marketing observational study including 849,397 RZV-vaccinated and 1,817,099 LZV-vaccinated participants aged 65 or above showed a possible increased risk of developing Guillain-Barré Syndrome (GBS), defined as an autoimmune disorder which causes nerve damages and thus lead to muscle weakness.[27] An increased risk of GBS was observed in adults aged 65 or above within 42 days after vaccination, with an estimation of 3 excess cases of GBS per million doses administered. Meanwhile, 6 excess cases of GBS per million doses administered to adults aged 65 or above within 42 days after receiving the first dose of RZV were estimated in secondary analyses. There was no increased risk observed after receiving the second dose. Some other adverse reactions, including decreased mobility of the injected arm for one or more weeks and hypersensitivity reactions, were reported during post-approval use of RZV. Yet, no causal relationship could be established between these adverse reactions and RZV due to insufficient evidence.

Immunocompromised Adults Aged 18 Years and Above

The safety profile of RZV in immunocompromised adults aged 18 or above has also been evaluated in 6 placebo-controlled clinical studies including 3116 participants from 5 different groups of immunocompromised populations, namely autologous hematopoietic stem cell transplant (auHSCT) recipients,[18, 28] renal transplant recipients,[29] those with solid tumors receiving chemotherapy[30] or hematologic malignancies[31] and HIV-infected participants.[32] Out of the total participants, 28% of the participants were aged 18 to 49 and the remaining 72% of the participants were aged over 50. Similar to the previous ZOE-50 and ZOE-70 trials, Asian population (17%) was included.

In the auHSCT study, recipients (aged 18 to 49 and ≥50 years of age) reported local adverse reactions such as pain (88% and 83%), erythema (30% and 35%), and swelling (21% and 18%) within 7 days after the administration of RZV (both doses combined).[18] Regarding systemic adverse reactions, fatigue (64% and 54%), myalgia (58% and 52%), headache (44% and 30%), gastrointestinal symptoms (21% and 28%), shivering (31% and 25%), and fever (28% and 18%) were also reported. The local and systemic adverse reactions generally lasted for 1 to 3 days among these participants. Also, within the post vaccination period of 30 days and the post vaccination period of 1 year, there was no notable difference in the percentage of participants experiencing serious adverse events between the RZV (7% and 26%) and placebo (8% and 27%) groups. The incidence of death is similar in the RZV (0.1% and 6%) and placebo (0.5 and 6%) groups. Furthermore, there was no significant difference in the new onset of potential immune-mediated diseases (pIMDs) or exacerbation of current pIMDs between the vaccine (1.3%) and placebo (1.0%) groups up to 1 year after the vaccination of the first administered dose.

Summary of Safety

Injection site reactions including erythema, pain and swelling were common after the administration of both RZV and LZV, yet more common in RZV recipients. Systemic adverse reactions were more prevalent in the RZV recipients. However, these systemic reactions are generally resolved within 2 to 3 days. On the other hand, increased risk of GBS was reported among RZV recipients.

Regarding the safety of the vaccines in immunocompromised adults, RZV is safe. Local and general adverse reactions reported by these participants were similar to those of the general population. Also, there was no significant difference in the new onset pIMDs or worsening of existing pIMDs between the vaccinated group and the placebo group. LZV contains the live and attenuated VZV, which may induce HZ infection in the immunocompromised adults. Therefore, LZV is contraindicated in this group of people while RZV is recommended for them.

APPLICATION IN HONG KONG

Having reviewed the efficacy, safety and impact on QoL of Zostavax and Shingrix, recommendations specifically for the Hong Kong population taking social context into account are drawn.

Recommendations from foreign authorities

There is a growing popularity of Shingrix worldwide. Several health authorities advise the use of Shingrix over Zostavax. Centers for Disease Control (CDC) in the United States recommends adults aged 50 or above and immunocompromised adults to receive two doses of Shingrix to prevent HZ and the related complications.[33] In addition, those vaccinated with Zostavax in the past can be revaccinated the full dose of Shingrix, supporting the effectiveness of Shingrix. Consistent with the recommendation of CDC, the Australian Technical Advisory Group on Immunization (ATAGI) in Australia also supports that Shingrix is superior over Zostavax for adults aged 50 or above in terms of its efficacy, and has recommended Shingrix as the preferred vaccine.[34]

Aging population in Hong Kong

Aging is one of the risk factors for HZ.[3] According to a report from the Census and Statistics Department, the proportion of elderly (i.e. age 65 or above) increased significantly from 13.5% in 2001 to 20.4% in 2021, and the life expectancy for both genders have generally increased in the past 50 years. Therefore, the public who is older than 70 years of age is recommended to receive Shingrix.

Public consciousness and Cost of vaccination

Although Shingrix is shown to have a higher efficacy in previous studies (i.e. ZOE50 and ZOE70), some hospitals and clinics in Hong Kong may still provide Zostavax as the only vaccination option for HZ prevention. Having both options available for the public is important as the price of Shingrix is generally higher than Zostavax. The price of Shingrix (both doses combined) is around HKD$5500, while Zostavax costs around HKD$1000-1800 in private medical providers. According to a study by HKMJ, less than 30% of respondents refused to be vaccinated due to high cost.[35] The same study also showed that up to 70% of respondents revealed interest in knowing more about prevention of HZ and would like to ask their doctors about HZ vaccination. Thus, it is important to promote and educate the public in regard to the advantages of having HZ vaccinations.

Limitations of the study

Several clinical studies were summarized in the current review article. However, the parameters used in the studies are slightly different, thus direct head-to-head comparison is not feasible. This is most notable in the comparison of the vaccines' impact on participants' QoL, which there are different approaches on selecting the data obtained from ZBPI to measure HZ-related interference with ADL in the LZV and RZV studies, as well as different survey designs used to assess the health related QoL measures. In addition, some of the significant studies were funded by pharmaceutical companies that have high financial stakes in the vaccines being evaluated. For instance, the ZOE-50, ZOE-70 trials and the ZEST study received their funding support from the same company that developed the vaccines.[10, 13, 14] These interests might potentially cause bias.

Although this article covered the safety and efficacy aspects of Zostavax and Shingrix, its efficacy in the long term and the need for revaccination are still unclear, especially for Shingrix which has only been registered in Hong Kong for less than 5 years. Further studies may be needed to determine the need and safety of revaccination.

CONCLUSION

After reviewing the efficacy, safety and impact on QoL of Zostavax and Shingrix, it can be concluded that Shingrix is superior, despite the relatively high cost. With the hope of more public education, it is anticipated that HZ vaccines will receive wide support from the local market and play a dominant role in reducing the incidence rate of HZ as well as PHN in Hong Kong. A clear guideline on the need for revaccination is helpful when discussing the pros and cons with the public or high-risk groups of patients.

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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 Vaccines against Herpes Zoster: the Efficacy, Safety and Impact on Quality of Life of Shingrix® and Zostavax®

1. ***Which of the following statements concerning vaccine administration is the most appropriate?***
   a. Zostavax is injected intravenously, preferably in a large vein
   b. Zostavax is injected intramuscularly, preferably in a deltoid region of the upper arm
   c. Shingrix is injected intramuscularly, preferably in a deltoid region of the upper arm
   d. Shingrix is injected intradermally, preferably in the lower arm

2. ***Postherpetic neuralgia (PHN) is a common adverse event associated with HZ infection. Which precaution is incorrect?***
   a. Both HZ vaccines are effective to lower the incidence of PHN
   b. Shingrix can reduce the incidence of PHN by at least 80% in clients aged 50 years old or above who completed 2 doses of vaccine
   c. Zostavax is shown to be effective to protect clients against PHN over 10 years post-vaccination
   d. The efficacy of PHN prevention by Zostavax reduces with age

3. ***The common side effects associated with Zostavax include:***
   a. Bone pain
   b. Angioedema
   c. Increased risk of fungal infections
   d. Herpes Zoster

4. ***How should an adult patient be advised in proper administration of Shingrix?***
   a. It should be given subcutaneously if there is no known allergy
   b. Pre-treatment screening is needed for those patients who have family history of hepatitis B infections
   c. It is administered as a 2-dose series with 2-6 months interval
   d. Annual live attenuated influenza vaccine is not required if clients had Shingrix in the same year

5. ***A 52-year-old Chinese male client weighs 60 kg and has no known drug allergies, who got HZ infection last year despite one dose of Zostavax 7 years ago. He is worried to have HZ infection again. Which of the following is the most appropriate option?***
   a. Have 1 dose of Shingrix, as he had 1 dose of Zostavax previously
   b. Have 2 doses of Shingrix with 2-6 months apart
   c. Have another dose of Zostavax as a booster
   d. No action is required as he got HZ infection last year

6. ***Which one of the following situations would recommend the patient to receive HZ vaccine?***
   a. COVID-19 PCR positive
   b. Hepatitis B surface antibody positive and low HBV DNA load
   c. Pregnancy test negative
   d. Scheduled renal transplant in 3 months

7. ***The key findings in ZOE-50 include the following, except:***
   a. HZ-induced burden of illness is reduced by HZ vaccine
   b. The risk of HZ-induced PHN is reduced in patients who had HZ vaccine
   c. Reduction of HZ incidence is no different in those who received HZ vaccine between age groups
   d. Rhabdomyolysis is the most common systemic reaction

8. ***The correct counselling points concerning Shingrix include:***
   a. Up to 80% of clients experience headache after vaccination
   b. Shingrix does not cause gastrointestinal symptoms
   c. Symptomatic anaemic patients should avoid Shingrix
   d. The common adverse reactions may last for 1 to 3 days

9. ***The indications of HZ vaccines do not cover:***
   a. Treatment of active HZ infections in adults aged 50 years or above
   b. Prevention of HZ-induced PHN
   c. Minimizing the risk of HZ in immunosuppressed patients aged 18 years or above
   d. Elderly who is worried about own health

10. ***Which of the following statements concerning the efficacy of Shingrix is incorrect?***
    a. The specific anti-IgE antibody is undetectable before 2 doses of vaccines are completed
    b. The efficacy of reducing HZ-induced PHN is shown in adults aged 50 years or above
    c. The duration of protection against HZ infection can last for 10 years
    d. There is no established immunological threshold of protection against HZ

Answers will be released in the next issue of HKPJ.

CE Questions Answer for 311(D&T)

Overview of the Drug Therapy of Psoriatic Arthritis

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

The Activities of the Society of Hospital Pharmacists

The Society of Hospital Pharmacists of Hong Kong (SHPHK) has recently held two press conferences to raise public awareness about the Respiratory Syncytial Virus (RSV) vaccine and the Meningococcal Group B Vaccine.

On 20th May, 2024, SHPHK president Mr. So Yiu Wah and Professor Ivan Hung Fan Ngai co-hosted a press conference where they recommended that individuals aged 60 and above should receive the RSV vaccine due to the higher risk and mortality rate among the elderly. Subsequently, on 4th August, 2024, Mr. So hosted another press conference, highlighting the global rise in meningococcal cases and advising parents to vaccinate their children before traveling or studying abroad to reduce the risk of infection.

The SHPHK conducted its 37th Annual General Meeting (AGM) on July 19, 2024, at The Mira Hong Kong. Prior to the AGM, SHPHK President Mr. So Yiu Wah presented a seminar on updates in RSV vaccination.

The general committee for 2024-2025 was elected during the meeting, comprising of 15 members (in alphabetical order):

CHU Man Wa Amy
CHUNG Wing Fai Kenneth
FUNG Crystal
KUNG Keshia
LAI Oi Lun Ellen
LAU Ka Hei Tony
NG Man Keung
NG Yi Qing Christy
SO Yiu Wah
TAM Lyanna
TSUI Hoi Tung Zoey
WONG Johnny Sze Ho
WONG Po Kwan Bryan
YIU Sui Ki Kenneth
ZHENG Sin Man Michelle

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.

NEW PRODUCTS

Elunate®
(HUTCHMED)

Active Ingredients
Fruquintinib

Pharmacological Properties
Fruquintinib is a selective inhibitor of vascular endothelial growth factor receptors (VEGFR) 1, 2 and 3, and has an inhibitory effect on VEGFR kinase activity, VEGFR 2/3 phosphorylation in cells and tissues, endothelial cell proliferation, and lumen formation, micro-angiogenesis in chick embryo chorioallantoic membrane model, and tumor angiogenesis, thereby inhibiting tumor growth.

Indication
As monotherapy is indicated for patients with metastatic colorectal cancer (mCRC) who have previously received fluoropyrimidine, oxaliplatin and irinotecan-based chemotherapy, and those who have previously received or are not suitable for receiving anti-vascular endothelial growth factor (VEGF) therapy or anti-epidermal growth factor receptor (EGFR) therapy (RAS wild-type).

Dosage Forms and Strengths
1mg and 5 mg capsules

Dosage Administration
The recommended dose is 5mg once daily, for three consecutive weeks followed by one week of drug free period (Every 4 weeks as one treatment cycle).
This product may be taken with food or on empty stomach, and it must be swallowed whole. It is recommended to take the drug at the same time each day. If the patient vomits after administering the drug, there is no need to make up for the dose; if a dose is missed, instruct the patient not to make up for the dose in the next day, but to take the next dose at its next scheduled time.

Contraindications
Hypersensitivity to the active substance or to any of the excipients of fruquintinib capsule.
Patients with severe active haemorrhage, active gastrointestinal ulcer, unhealed gastrointestinal perforation or gastrointestinal fistula are prohibited from using this product. Patients with severe hepatic impairment and renal impairment are prohibited from using this product. Pregnant, breastfeeding women are prohibited from using this product.

Adverse Reactions
The common (incidence ≥ 2%) Grade ≥3 adverse drug reactions were hypertension, hand-foot skin reaction, proteinuria, platelet count decreased, hepatic function abnormal, blood bilirubin increased, abdominal pain/ abdominal discomfort, diarrhoea, fatigue/asthenia, decreased appetite and haemorrhage.

Drug Interactions
No dose adjustment is required when used in combination with CYP3A inhibitors.
Avoid concomitant use of moderate or strong CYP3A inducers. Alternative treatment with weak CYP3A inducing properties should be considered.
No inhibitory effect was observed with fruquintinib on CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6 or CYP3A4/5 and no induction was observed with fruquintinib on CYP1A2, CYP2B6, or CYP3A4.
Monitor patients more closely when concomitant use with P-gp and BCRP substrates for any adverse reactions and make appropriate dose adjustments of the concomitant medications when necessary.
Fruquintinib can be used concomitantly with gastric acid reducing agents without any restrictions.

Dosage Available
1 mg: 7 capsules/blister pack, 3 blister packs/box
5 mg: 7 capsules/blister pack, 1 blister pack/box

Forensic classification
P1S1S3

Tazverik®
(HUTCHMED)

Active Ingredients
Tazemetostat

Pharmacological Properties
Tazemetostat is an inhibitor of the methyltransferase, enhancer of zeste homolog 2 (EZH2), and some EZH2 gain-of-function mutations including Y646X, A682G, and A692V. Tazemetostat suppressed proliferation of B-cell lymphoma cell lines in vitro and demonstrated antitumor activity in a mouse xenograft model of B-cell lymphoma with or without EZH2 gain-of-function mutations. Tazemetostat demonstrated greater effects on the inhibition of proliferation of lymphoma cell lines with mutant EZH2.

Indication
TAZVERIK is indicated for the treatment of adult patients with relapsed or refractory (R/R) follicular lymphoma (FL) whose tumors are positive for an EZH2 mutation and who have received at least 2 prior systemic therapies.

Dosage Form and Strengths
Each tablet contains 200mg tazemetostat equivalent to 228.3mg tazemetostat hydrobromide.
Tablets: 200 mg film-coated, red, round, biconvex shape and debossed with “EZM 200” on one side and plain on the other.

Dosage Administration
The recommended dosage of TAZVERIK is 800 mg orally twice daily with or without food until disease progression or unacceptable toxicity.
Swallow tablets whole. Do not cut, crush, or chew tablets.
Do not take an additional dose if a dose is missed or vomiting occurs after TAZVERIK, but continue with the next scheduled dose.

Contraindications
None

Adverse Reactions
Serious adverse reactions in ≥2% of patients who received TAZVERIK were general physical health deterioration, abdominal pain, pneumonia, sepsis, and anemia. The most common adverse reactions (≥20%) were fatigue, upper respiratory tract infection, musculoskeletal pain, nausea, and abdominal pain.

Drug Interactions
Avoid coadministration of strong or moderate CYP3A inhibitors with TAZVERIK. If coadministration of moderate CYP3A inhibitors cannot be avoided, reduce TAZVERIK dose.
Avoid coadministration of moderate and strong CYP3A inducers with TAZVERIK.
Coadministration of TAZVERIK with CYP3A substrates, including hormonal contraceptives, can result in decreased concentrations and reduced efficacy of CYP3A substrates.

Dosage Available
Bottles of 240 tablets with a desiccant.

Forensic classification
P1S1S3