Drug News
藥 物 情 報

Issue Number 69

This is a monthly digest of local and overseas drug safety news released by the Drug Office of the Department of Health in July 2015 with relevant information update before publish. For the latest news and information, please refer to public announcements or the website of the Drug Office of the Department of Health (http://www.drugoffice.gov.hk).

Safety Update

US: Codeine cough-and-cold medicines in children – the FDA evaluating potential risk of serious side effects

On 1 July 2015, the US Food and Drug Administration (FDA) was investigating the safety of using codeine-containing medicines to treat coughs and colds in children under 18 years because of the potential for serious side effects, including slowed or difficult breathing.

Codeine is a specific type of narcotic medicine called an opioid that is used to treat mild to moderate pain and also to reduce coughing. It is usually combined with other medications in prescription and over-the-counter (OTC) cough-and-cold medicines.

Children, especially those who already have breathing problems, may be more susceptible to these serious side effects. In 2013, FDA warned against using codeine in children who recently had surgery to remove their tonsils and/or adenoids. In April 2015, the European Medicines Agency (EMA) announced that codeine must not be used to treat cough and cold in children under 12 years, and that codeine is not recommended in children and adolescents between 12 and 18 years who have breathing problems, including those with asthma and other chronic breathing problems.

FDA will continue to evaluate this safety issue and will consider the EMA recommendations. Final conclusions and recommendations will be communicated when the FDA review is complete.

In Hong Kong, there are 348 registered pharmaceutical products containing codeine, which is an ingredient used to relieve pain and cough. Related news regarding the use of codeine in children has been released by various overseas drug regulatory authorities, and was reported on the Drug News Issue Nos. 44, 54 and 65. Letters to inform healthcare professionals to draw their attention to the warning were issued on 16 August 2012 and 7 June 2013. As on 24 August 2015, the Department of Health (DH) had received one adverse drug reaction (ADR) report on a codeine-containing cough and cold medicine, and it was not related to respiratory side effects. The issue was discussed in the meeting of the Pharmacy and Poisons (Registration of Pharmaceutical Products and Substances: Certification of Clinical Trial/ Medicinal Test) Committee (the Registration Committee) of the Pharmacy and Poisons Board in July 2013. The Committee concluded that codeine is not recommended for use in children less than 12 years of age, and the sales pack label and/or package insert of pharmaceutical products containing codeine should be updated to include the product should not be used in children (aged below 18 years) with conditions associated with breathing problems. The DH will remain vigilant on the US FDA review's result and any safety updates of the drug.

US: Unapproved prescription ear drop (otic) products: not FDA evaluated for safety, effectiveness and quality

On 1 July 2015, the FDA announced its intention to take enforcement action against companies that manufacture and/or distribute certain unapproved prescription ear drop products (known as otic products) labeled to relieve ear pain, infection, and inflammation. The unapproved prescription ear

drops contain active ingredients such as benzocaine and hydrocortisone, and have not been evaluated by the FDA for safety, effectiveness and quality. The labels on these products do not disclose that they lack FDA approval, and health care professionals may not be aware of their unapproved status.

Unapproved prescription otic drug products are frequently given to young children suffering from ear infections and other conditions that cause ear pain and swelling. Patients taking unapproved drugs may be at greater risk because there is no proven safety or effectiveness information. These products may be contaminated or manufactured incorrectly, which could result in patients receiving the wrong dose, even when administered according to the labeled directions for use. Unapproved prescription otic drug products containing the following ingredients are covered by this action include benzocaine; benzocaine and antipyrine; benzocaine, antipyrine, and zinc acetate; benzocaine, chloroxylenol, and hydrocortisone; chloroxylenol and pramoxine; and chloroxylenol, pramoxine, and hydrocortisone.

Consumers who believe they are using unapproved prescription ear drops should contact their healthcare provider to discuss alternatives.

In Hong Kong, all pharmaceutical products containing benzocaine and/or hydrocortisone need to be registered with the Pharmacy and Poisons Board before they can be sold, offered for sale, distributed or possessed for the purposes of sales, distribution or other use in Hong Kong. The Hong Kong registration number for a registered pharmaceutical product can be found on the sales pack in the form of "HK-xxxxx" ("x" denotes a number). Registered product can be found by searching the Drug Database (http://www.drugoffice.gov.hk/eps/productSearchOneFieldAction.do) at Drug Office website. Members of the public are strongly advised not to buy or consume any products of unknown or doubtful composition, or consume products from unknown sources including through internet. The public should consult healthcare professionals before using any medication.

Australia: Ivabradine (Coralan): risk of cardiovascular events in patients with angina

On 9 July 2015, consumers and health professionals are advised that the Therapeutic Goods Administration (TGA) has completed a safety review of ivabradine, marketed as Coralan. Subsequently, the Product Information (PI) for ivabradine has been updated to reduce the risk of cardiovascular events in patients who take the medicine for angina.

Ivabradine is a heart rate lowering agent that can be used to treat the symptoms of chronic stable angina or treatment of symptomatic chronic heart failure.

The changes to the PI, which are based on a phase III clinical study, include updated indications and contraindications and other information to reduce the risk of cardiovascular events in patients with angina. In particular, patients who take ivabradine for angina must now have a resting heart rate equal to or above 70 beats per minute (bpm) prior to treatment. This has been increased from 60 bpm.

The PI has been updated to include additional medicines that ivabradine should not be taken in combination with, including diltiazem and verapamil, which are used to treat high blood pressure or angina. An existing warning regarding a potential interaction with grapefruit juice has also been strengthened to advise that drinking grapefruit juice should be avoided (rather than 'restricted').

The TGA advises healthcare professionals that if they are treating a patient who is taking ivabradine for angina, they should review the updated indications, contraindications, precautions and interactions sections. Ivabradine must not be used in patients who have a pre-treatment resting heart rate below 70 bpm or concomitantly with potent cytochrome P450 3A4 [CYP3A4] inhibitors or moderate CYP3A4 inhibitors with heart rate reducing properties. They should educate patients regarding the signs and symptoms of the cardiovascular events identified in the PI and instruct them to seek medical attention if any are suspected.

In Hong Kong, there are two registered pharmaceutical products containing ivabradine,

namely Coralan Tab 7.5mg (HK-55438) and Coralan Tab 5mg (HK-55439). Both are prescription only medicines registered by Servier Hong Kong Ltd (Servier). Related news has been released by the the EMA, and was reported on the Drug News Issue Nos. 55 and 56. Servier has applied to the DH to include the relevant information in the package insert of the products, and the application is under evaluation. As on 24 August 2015, the DH has not received any ADR report on ivabradine. In view of the TGA's announcement on update of PI, a letter to inform the healthcare professionals was issued on the 9 July 2015. The matter will be discussed in the meeting of the Registration Committee of the Pharmacy and Poisons Board.

EU: EMA to further clarify safety profile of human papillomavirus (HPV) vaccines

On 13 July 2015, the European Medicines Agency (EMA) announced a review of HPV vaccines was started to further clarify aspects of their safety profile. These vaccines have been used in around 72 million people worldwide and their use is expected to prevent many cases of cervical cancer (cancer of the neck of the womb) and various other cancers and conditions caused by HPV. Cervical cancer is the 4th most common cause of cancer death in women worldwide, with tens of thousands of deaths in Europe each year despite the existence of screening programmes to identify the cancer early. The review does not question that the benefits of HPV vaccines outweigh their risks.

As for all licensed medicines the safety of these vaccines is monitored by the Agency's Pharmacovigilance Risk Assessment Committee (PRAC). The current review will look at available data with a focus on rare reports of two conditions: complex regional pain syndrome (CRPS, a chronic pain condition affecting the limbs) and postural orthostatic tachycardia syndrome (POTS, a condition where the heart rate increases abnormally after sitting or standing up, causing symptoms such as dizziness and fainting, as well as headache, chest pain and weakness).

Reports of these conditions in young women who have received an HPV vaccine have been previously considered during routine safety monitoring by the PRAC but a causal link between them and the vaccines was not established. Both conditions can occur in non-vaccinated individuals and it is considered important to further review if the number of cases reported with HPV vaccine is greater than would be expected. In its review the PRAC will consider the latest scientific knowledge, including any research that could help clarify the frequency of CRPS and POTS following vaccination or identify any causal link. Based on this review, the Committee would decide whether to recommend any changes to product information to better inform patients and healthcare professionals. While the review is ongoing there is no change in recommendations for the use of the vaccine.

In Hong Kong, there are three registered pharmaceutical products containing human papillomavirus, namely Gardasil Vaccine Inj (Vial) (HK-54934) and Gardasil Vaccine Inj (Pre-filled syringe) (HK-54935) which are registered by Merck Sharp & Dohme (Asia) Ltd; and Cervarix Vaccine (Pre-filled syringe) (HK-56180) which is registered by GlaxoSmithKline Limited (GSK). As on 24 August 2015, the DH has received 11 cases of ADRs on human papillomavirus vaccines, and none of them is related to CRPS and/or POTS. The DH will remain vigilant on the conclusion of the review by the EMA and safety updates by other overseas regulatory authorities for consideration of any action deemed necessary.

UK: Denosumab (Xgeva, Prolia) and intravenous bisphosphonates: osteonecrosis of the jaw - further measures to minimise risk

On 20 July 2015, the Medicines and Healthcare products Regulatory Agency (MHRA) announced 45 Yellow Card reports of osteonecrosis of the jaw (ONJ) in people taking denosumab (all doses) and 323 reports in people taking a bisphosphonate had been received. In patients treated for osteoporosis (regardless of route of administration), the risk of ONJ is small compared with that in patients treated with the higher doses used for cancer-related conditions. Other drug-specific risk factors for ONJ include drug potency (higher risk for highly potent compounds such as zoledronate, pamidronate and denosumab), route of administration (higher risk for parenteral administration) and cumulative dose. Denosumab and bisphosphonates are used to treat

osteoporosis, Paget's disease, and as part of some cancer regimens, particularly for metastatic bone cancer and multiple myeloma. Individual bisphosphonates and denosumab-containing medicines have different indications.

MHRA and other EU medicines regulators have reviewed measures to minimise the risk of ONJ in patients taking denosumab or bisphosphonates. The review recommended introducing patient reminder cards for denosumab and intravenous bisphosphonates to inform patients of the risk of ONJ and precautions to take before and during treatment. The review of ONJ and denosumab also recommended that denosumab 120 mg should be contraindicated in patients with unhealed lesions from dental or oral surgery.

Healthcare professionals are advised of the following before prescribing denosumab or intravenous bisphosphonates:

- give patients the patient reminder card for their medicine,
- explain the risk of osteonecrosis of the jaw and advise patients on precautions to take - advise patients to:
  - tell their doctor if they have any problems with their mouth or teeth before starting treatment; if they wear dentures they should make sure their dentures fit properly before starting treatment,
  - maintain good oral hygiene and get routine dental check-ups during treatment,
  - tell their doctor and dentist that they are receiving denosumab or an intravenous bisphosphonate if they need dental treatment or dental surgery,
  - tell their doctor and dentist immediately if they have any problems with their mouth or teeth during treatment (eg loose teeth, pain, swelling, non-healing sores or discharge), and
- do not prescribe denosumab 120 mg (cancer indication) to patients with unhealed lesions from dental or oral surgery.

In Hong Kong, there are 3 registered pharmaceutical products containing denosumab, and 18 registered pharmaceutical products containing intravenous bisphosphonates, including 3 products containing ibandronic acid, 4 products containing pamidronate disodium, and 11 products containing zoledronic acid. All these products are prescription only medicines. News related to denosumab and zoledronic acid (which is a bisphosphonate) had been issued by the EMA, and was reported on the Drug News Issue No. 65. A letter to inform healthcare professionals on the new risks of the products was issued on 30 March 2015. On 24 August 2015, the DH has received 3 cases of ADRs related to denosumab, including 1 case with the adverse effect of osteonecrosis. The DH has not received any ADR case related to intravenous bisphosphonates. In view of the MHRA announcement related to the new findings with denosumab 120 mg (which is now contraindicated in patients with unhealed lesions from dental or oral surgery), and with intravenous bisphosphonates, a letter to inform the healthcare professionals was issued on 21 July 2015. The matter will be discussed in the meeting of the Registration Committee of the Pharmacy and Poisons Board.

Singapore: Restrictions on the use of metoclopramide-containing products

On 23 July 2015, the Health Sciences Authority (HSA), in consultation with its Medicines Advisory Committee, would like to update healthcare professionals on the restrictions on the use of metoclopramide-containing products, following concerns raised internationally on the relationship between the use of high doses or long-term use of metoclopramide and the increased risks of neurological adverse events, such as irreversible tardive dyskinesia.

HSA's benefit-risk assessment considered the current available scientific evidence, local adverse event reports and the input of local clinical experts. It was concluded that the benefit-risk profile of metoclopramide remains favourable for restricted indications in children and adults when administered within the recommended maximum daily doses and when treatment durations beyond 12 weeks are avoided.

In Hong Kong, there are 33 registered pharmaceutical products containing metoclopramide. All products are prescription only medicines. Related news has been released by the EMA, and was reported on the Drug News Issue No. 45. A letter to inform the healthcare professionals was issued on 29 July 2013 to draw their attention to the warning. As on 24 August

2015, the DH has not received any ADR case related to metoclopramide. The matter was discussed in the meeting of the Registration Committee of the Pharmacy and Poisons Board in September 2014. The Committee decided that the sales pack label and/or package insert of metoclopramide-containing products should be updated to include the following new safety information:

For ALL dose forms:
- Metoclopramide should no longer be used in chronic conditions such as gastroparesis, dyspepsia and gastro-oesophageal reflux disease, nor as an adjunct in surgical and radiological procedures.

- In adults, metoclopramide is indicated for prevention of post-operative nausea and vomiting, radiotherapy-induced nausea and vomiting and delayed chemotherapy-induced nausea and vomiting, and for symptomatic treatment of nausea and vomiting including that associated with acute migraine.

- In children, metoclopramide is indicated as a second-line option for prevention of delayed chemotherapy-induced nausea and vomiting and treatment of established post-operative nausea and vomiting. Use is contra-indicated in children under 1 year of age.

- In order to minimise the risks of neurological and other adverse reactions, metoclopramide should only be prescribed for short-term use (up to 5 days).

- For adults and children the maximum dose in 24 hours is 0.5 mg per kg body weight; in adults, the usual dose of conventional formulations (all routes) is 10 mg up to 3 times daily. In children the recommended dose is 0.1 to 0.15 mg per kg body weight, repeated up to three times daily. A dosing table for use in children should be included in the product information.

- Given very rare reports of serious cardiovascular reactions associated with metoclopramide, particularly via the intravenous route, special care should be taken in populations likely to be at increased risk, including the elderly, patients with cardiac conduction disturbances, uncorrected electrolyte imbalance or bradycardia, and those taking other drugs known to prolong QT interval.

For injectable dose forms:
- Intravenous doses should be administered as a slow bolus over at least 3 minutes to reduce the risk of adverse effects."

US: Gadolinium-based contrast agents for magnetic resonance imaging (MRI): FDA evaluating the risk of brain deposits with repeated use

On 27 July 2015, the FDA announced that the risk of brain deposits following repeated use of gadolinium-based contrast agents (GBCAs) for magnetic resonance imaging (MRI) was being investigated. Recent publications in the medical literature have reported that deposits of GBCAs remain in the brains of some patients who undergo four or more contrast MRI scans, long after the last administration. It is unknown whether these gadolinium deposits are harmful or can lead to adverse health effects.

FDA, including its National Center for Toxicological Research (NCTR), will study this possible safety risk further. FDA is working with the research community and industry to understand the mechanism of gadolinium retention and to determine if there are any potential adverse health effects. Based on the need for additional information, at this time, FDA is not requiring manufacturers to make changes to the labels of GBCA products.

After being administered, GBCAs are mostly eliminated from the body through the kidneys. However, trace amounts of gadolinium may stay in the body long-term. Recent studies conducted in people and animals have confirmed that gadolinium can remain in the brain, even in individuals with normal kidney function. Available information does not identify any adverse health effects.

To reduce the potential for gadolinium accumulation, healthcare professionals should consider limiting GBCA use to clinical circumstances in which the additional information provided by the contrast is necessary. Healthcare professionals are also urged to reassess the necessity of repetitive GBCA MRIs in established treatment protocols.

In Hong Kong, there are nine registered pharmaceutical products which are GBCAs, and are prescription only medicines, including Magnevist Inj (HK-32608), Omniscan Inj 0.5mmol/ml (HK-43493), Gadovist Inj 1mmol/ml (HK-51750) and Gadovist Inj 1mmol/ml (Pre-filled Syringe) (HK-57330), Primovist Pre-filled Syringe Inj 0.25mmol/ml (HK-54116), Dotarem Inj 377mg/ml (Vial) (HK-41578) and Dotarem Prefilled Syringes, 377mg/ml (HK-41579), MultiHance Inj 334mg (China) (HK-55495) and MultiHance Inj 334mg (HK-57789). As on 24 August 2015, the DH has received 2 cases of ADRs related to Omniscan, and they are not related to brain deposits. The DH has not received any cases of ADR related to the other registered GBCA products. In view of the US FDA's announcement that it is unknown whether the gadolinium deposits are harmful or can lead to adverse health effects and additional information is needed to determine whether changes to the labels of GBCA products are required, the DH will remain vigilant on the conclusion by the US FDA, and safety updates by other overseas drug regulatory authorities regarding GBCA products for consideration of any action deemed necessary.

US: Brintellix (vortioxetine) and Brilinta (ticagrelor): Name Confusion

On 31 July 2015, FDA was warning healthcare professionals and patients that reports of confusion between the antidepressant Brintellix and anti-blood clotting medication Brilinta have resulted in the wrong medication being prescribed or dispensed. FDA determined that the main reason for the confusion between these two medications is the similarity of their brand (proprietary) names. None of the reports indicates that a patient ingested the wrong medication; however, reports of prescribing and dispensing errors continue.

Healthcare professionals can reduce the risk of name confusion by including the generic (established) name of the medication, in addition to the brand name, and the indication for use when prescribing these medications. Patients should check their prescriptions to ensure that the correct medication was dispensed.

In Hong Kong, Brintellix Tablets 5mg (HK-63601), 10mg (HK-63600) and 20mg (HK-63599) are pharmaceutical products registered by Lundbeck Export A/S; while Brilinta Tab 90mg (HK-61187) is a pharmaceutical product registered by AstraZeneca Hong Kong Ltd. All products are prescription only medicines. As on 24 August 2015, the DH has received one case of ADR on Brilinta, and it was not related to ingestion of the wrong medication. The DH has not received any ADR case on Brintellix. In view of the safety warning by the US FDA, a letter to inform the healthcare professionals to draw their attention was issued on 31 July 2015. The DH will remain vigilant on any safety updates of the drugs.

Canada: Gluconorm (repaglinide) - new contraindication for concomitant use with Clopidogrel

On 31 July 2015, Health Canada informed family physicians, general practitioners, nurses, nurse practitioners, pharmacists, endocrinologists and cardiovascular clinics that co-administration of repaglinide and clopidogrel (a known CYP2C8 inhibitor), may lead to a significant decrease in blood glucose levels due to a drug-drug interaction.

The concomitant use of repaglinide and clopidogrel is now contraindicated. The prescriber information for Gluconorm (repaglinide) has been updated. The prescriber information for Plavix (clopidogrel) is currently being updated. The prescriber information for the generic products will be updated.

In Hong Kong, there are 8 registered pharmaceutical products containing repaglinide and 32 registered pharmaceutical products containing clopidogrel. All are prescription only medicines. As on 24 August 2015, the DH has received one case of ADR on repaglinide and one on clopidogrel, and none of them are related to the use on the same ingredients. In view of the Health Canada's announcement, a letter to inform the healthcare professionals was issued on 3 August 2015, and the matter will be discussed in the meeting of the Registration Committee of the Pharmacy and Poisons Board. The DH will remain vigilant on any safety updates of the drug.

Batch recall of Sci-B-Vac Injection 10mcg/1ml

On 30 July 30, the DH instructed a medicine wholesaler, U.S Summit Company Limited (US Summit), to recall from consumers one batch (Batch number: B0741V1) of Sci-B-Vac injection 10mcg/1ml due to potential safety issue.

The DH received a notification from the Israeli Ministry of Health that the product's manufacturer found a cracked vial during product packaging. As a result, the manufacturer suspected microbial contamination for some of the product and decided to recall the affected batches as a precautionary measure.

Sci-B-Vac injection 10mcg/1ml is a hepatitis B vaccines manufactured in Israel. Contaminated injection could cause sepsis.

According to US Summit, about 116 vials of the affected batch has been imported for the use of particular persons. As on 24 August 2015, the DH has not received any adverse reaction report concerning the product. The DH closely monitored the recall. A notice was released on the website of the Drug Office on the same day to alert the public of the recall.

People who have used the product should consult their healthcare professional if in doubt or feeling unwell.

DH instructs recall of two batches of Vitamin D3 Tablets 1000 IU (HK-61993)

On 30 July 30, the DH instructed a licensed drug wholesaler, Julius Chen & Company (HK) Limited (Julius Chen), to recall two batches (batch numbers: 111403 and 116595) of Vitamin D3 Tablets 1000 IU with a pack size of 100 tablets from the market due to a quality issue.

Under the DH's market surveillance, samples of the said pharmaceutical product from the above two batches were collected for analysis. Upon the Government Laboratory's testing, the content of the active ingredient, colecalciferol (vitamin D3), was found to be lower than the labelled claim on the product. Since the quality defect may affect the efficacy of the product, Julius Chen was instructed to recall the two batches from the market.

The product contains vitamin D3, which is used as a nutritional supplement for bone health. It can be sold over the counter without a prescription.

The product was manufactured in the US by Nutriforce Nutrition. According to Julius Chen, 17 244 bottles from the two batches had been imported to Hong Kong since April 2014 and 3 249 of them had been supplied to local pharmacies, medicine stores and private doctors. As on 24 August 2015, the DH has not received any adverse reports in connection with the product. The DH closely monitored the recall. A notice was released on the website of the Drug Office on the same day to alert the public of the recall.

Members of the public using the above product should consult their healthcare providers for advice if in doubt.

Drug Incident

DH raids retail shop for suspected illegal sale of slimming products with undeclared controlled drug ingredients

On 29 July 2015, a retail shop in Lam Tin was raided in a joint operation by the DH and the Police where two slimming products, namely LAMI and SULAMI, suspected to contain undeclared controlled drug ingredients were sold.

During the DH's market surveillance, samples of the above two products were purchased previously from the shop for analysis. Results from the Government Laboratory revealed that LAMI and SULAMI respectively contained the Part I poisons sibutramine and spironolactone. Two women, both aged 44, were arrested by the Police for illegal sale and possession of unregistered pharmaceutical products and Part I poisons.

Sibutramine was once used as an appetite suppressant. Since November 2010, products containing sibutramine have been banned in Hong Kong because of increased cardiovascular risk. Spironolactone is a prescription drug used in the management of heart failure and should only be used under supervision of a doctor. Side-effects include headache, gastrointestinal disturbance, mental confusion, hyponatraemia (abnormally low blood sodium level) and hyperkalaemia elevated blood potassium level).

Members of the public who have purchased the above two products should stop consuming them immediately. They should consult healthcare professionals for advice if they feel unwell or are in doubt after consuming the products.

News in Brief

Xgeva® (denosumab 120mg) and Prolia® (denosumab 60mg/ml) - Clinically significant cases of hypercalcemia after cessation of treatment with denosumab in paediatric patients

On 6 July 2015, GSK Limited (GSK), a licensed drug wholesaler, informed the DH about clinically significant cases of hypercalcemia after cessation of treatment with denosumab in paediatric patients. Denosumab is marketed under the brand names of Xgeva® and Prolia® with different strengths and indications. GSK was going to issue a letter to healthcare practitioners who may be affected by this new signal, notably, oncologists, paediatric oncologists, metabolic specialists, endocrinologists, rheumatologists, orthopedic surgeons, paediatricians and pharmacists.

The information delivered by GSK is as follows:

Xgeva®
Xgeva® is indicated for the prevention of skeletal related events (pathological fracture, radiation to bone, spinal cord compression or surgery to bone) in adults with bone metastases from solid tumors, and is not indicated for the prevention of skeletal-related events in patients with multiple myeloma.

Prolia®
Prolia® is indicated for the following uses:

1) Treatment of postmenopausal women with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy. In postmenopausal women with osteoporosis, Prolia® reduces the incidence of vertebral, nonvertebral, and hip fractures.

2) Treatment to increase bone mass in men with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy.

3) Treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer. In these patients Prolia® also reduced the incidence of vertebral fractures.

4) Treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer.

GSK would like to inform healthcare practitioners of important new safety information in patients with growing skeletons being administered denosumab. Weeks to months following denosumab discontinuation in patients with growing skeletons, cases of clinically significant hypercalcemia in patients presenting with nausea and vomiting with or without acute renal failure, requiring hospitalization, have been observed as part of routine safety review by Amgen, the manufacturer of denosumab and GSK's partner in Hong Kong. The index case was seen in a skeletally mature paediatric patient who had a growing skeleton, and was being treated for giant cell tumor of the bone. Denosumab is not indicated for patients with giant cell tumor of the bone in Hong Kong. Patients with growing skeletons have received denosumab for indications that have not been approved such as osteogenesis imperfecta, fibrous dysplasia, and juvenile Paget's disease of bone.

Healthcare practitioners are advised to monitor patients with growing skeletons at the time of denosumab introduction/treatment for the development of hypercalcemia following denosumab discontinuation.

The overall benefit risk profile of denosumab remains favourable for the approved indications.

Healthcare practitioners are advised of the following:

- denosumab should not be administered for non-approved indications,
- monitor for hypercalcemia post discontinuation of denosumab in individuals with skeletons that are still growing,
- treat hypercalcemia as appropriate for symptoms of patient, and
- monitor renal function, as appropriate in cases of hypercalcemia.

In Hong Kong, there are three registered pharmaceutical products containing denosumab, namely Xgeva® Solution for Injection 120mg (HK -61163), Prolia® Solution for Injection in Pre-filled Syringe 60mg/ml (USA) (HK-60588) and Prolia® Solution for Injection in Pre-filled Syringe 60mg/ml (the Netherlands) (HK-60589). All products are registered by GSK, and are prescription only medicines. As on 24 August 2015, the DH has received one case of ADR on Xgeva® and two cases of ADRs on Prolia®, and none of them are related to hypercalcemia. Regarding the issue, GSK was going to issue a "Dear Healthcare Professional Letter" to inform the healthcare professionals. The DH maintains close contact with GSK to monitor any action deemed necessary and keep vigilant on any safety updates of the drug.

A product containing any western drug ingredient must be registered under the Pharmacy and Poisons Ordinance before it can be sold in Hong Kong. Part I poisons should be sold at registered pharmacies under the supervision of registered pharmacists. Illegal sale or possession of Part I poisons and unregistered pharmaceutical products are offences under the Pharmacy and Poisons Ordinance (Cap 138). The maximum penalty is a fine of $100,000 and two years' imprisonment for each offence. Antibiotics can only be supplied at registered pharmacies by registered pharmacists or under their supervision and upon a doctor's prescription. They should only be used under the advice of a doctor. Illegal sale or possession of antibiotics are offences under the Antibiotics Ordinance (Cap 137) and the maximum penalty is a $30,000 fine and one year's imprisonment for each offence.

All registered pharmaceutical products should carry a Hong Kong registration number on the package in the format of "HK-XXXXX". The products mentioned in the above incidents were not registered pharmaceutical products under the Ordinance in Hong Kong. Their safety, quality and efficacy cannot be guaranteed. Members of the public were exhorted not to use products of unknown or doubtful composition. They should stop using the aforementioned products immediately if they had them in their possession and to consult healthcare professionals if they felt unwell after taking the products. The products should be destroyed or disposed properly, or submitted to the Department's Drug Office during office hours.

Useful Contact

Drug Complaint:

Tel: 2572 2068

Fax: 3904 1224

E-mail: pharmgeneral@dh.gov.hk

Adverse Drug Reaction (ADR) Reporting:

Tel: 2319 2920

Fax: 2319 6319

E-mail: adr@dh.gov.hk

Link: http://www.drugoffice.gov.hk/adr.html

Post: ***Pharmacovigilance Unit,***
Drug Office, Department of Health,
Rm 1856, 18/F, Wu Chung House,
213 Queen's Road East,
Wan Chai, Hong Kong

The purpose of Drug News is to provide healthcare professionals with a summary of local and overseas drug safety news released. Healthcare professionals are advised to keep update with the information and provide corresponding advice or therapeutic measure to patients and public.