Drug News
藥 物 情 報

Issue Number 74

This is a monthly digest of local and overseas drug safety news released by the Drug Office of the Department of Health in December 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

Australia: TGA investigates proton pump inhibitors and increased cardiovascular risk

On 1 December 2015, the Therapeutic Goods Administration (TGA) announced the conclusion of a review of two recent studies linking proton pump inhibitor (PPI) use with an increased risk of myocardial infarction. The review has found that neither of the studies adequately demonstrated an increased risk that is independent of the patient population in which they are being used. As a result, no further action is required at this time.

A 2010 study by Charlot and colleagues found that PPI use in a high-risk (post-myocardial infarction) population was associated with an increased risk of adverse cardiovascular outcomes. A subsequent study in 2015 by Shah et al found that PPI use was associated with an increased risk of acute myocardial infarction in the general population.

The TGA found that neither study was designed to address the possibility that PPI use was itself a marker of increased cardiovascular risk, as information on significant baseline risk factors was not collected. Additionally, PPIs may have been used when anginal pain was mistaken for pain due to gastro-oesophageal reflux.

Because of these limitations, these two studies did not demonstrate an increased cardiovascular risk for PPIs that was independent of the patient population in which they were being used. It was determined that no further action was required at this time.

In Hong Kong, there are 179 registered pharmaceutical products containing PPI, including 20 esomeprazole products, 69 omeprazole products, 18 lansoprazole products, 2 dexlansoprazole products, 44 pantoprazole products and 26 rabeprazole products. All these products are prescription only medicines except omeprazole, which is a pharmacy only medicine. As on 15 February 2016, the Department of Health (DH) has not received any adverse drug reaction (ADR) case related to PPI. DH noted the TGA review concluded that the two studies did not demonstrate an increased cardiovascular risk for PPI that was independent of the patient population and so, determined that no further action was required at this stage. DH will continue to remain vigilant on the safety of PPI.

Australia: Potential interaction - allopurinol and 6-mercaptopurine/azathioprine

On 1 December 2015, the TGA reminded health professionals that the concomitant use of allopurinol with 6-mercaptopurine or azathioprine should be avoided because of a potentially dangerous interaction. If these medicines must be given together, the dose of 6-mercaptopurine or azathioprine should be reduced.

Allopurinol is an anti-uricaemic agent used to treat gout, uric acid nephrolithiasis and states of hyperuricaemia, including the prevention of tumour -lysis syndrome.

Azathioprine is an imidazole derivative of 6-mercaptopurine that is used as an immunosuppressant, while 6-mercaptopurine is used as a cytotoxic agent.

There are warnings regarding the potential interactions between allopurinol and 6-mercaptopurine/azathioprine in the respective Product Information (PI). Also, the Consumer Medicine Information leaflets for these medicines advise patients to tell their doctor if they are taking the other medicines linked to this interaction.

Allopurinol reduces metabolism of 6-mercaptopurine and azathioprine, significantly increasing the risk of potentially fatal bone marrow toxicities and blood dyscrasias, including leukopenia, thrombocytopenia and pancytopenia.

Health professionals are reminded that the concomitant use of allopurinol and 6-mercaptopurine/azathioprine should be avoided if possible. However, if co-administration of these medicines is necessary, the dose of 6-mercaptopurine or azathioprine should be reduced to only one quarter of the normal dose and the patient's complete blood count should be closely monitored in accordance with the PI. It is recommended that, when prescribing azathioprine or 6-mercaptopurine, health professionals should check that their patient is not being treated with allopurinol, and educate them about this medicine interaction.

In Hong Kong, there are 46 registered pharmaceutical products containing allopurinol, 2 registered products containing mercaptopurine and 10 registered products containing azathioprine. Allopurinol is a pharmacy only medicine, while mercaptopurine and azathioprine are prescription only medicines. As on 15 February 2016, DH has not received any ADR case related to interactions between allopurinol and 6-mercaptopurine/ azathioprine leading to bone marrow toxicities and blood dyscrasias. In view of the above TGA announcement, DH issued a letter to inform local healthcare professionals on 1 December 2015. The matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

Australia: Intrauterine contraceptive devices and uterine perforation

On 1 December 2015, the TGA announced that while it is known that uterine perforation is a rare adverse event associated with the use of intrauterine contraceptive devices (IUCD), a recent European study has found that risk is increased for lactating women and during the first 36 weeks postpartum.

The European Active Surveillance Study was a large prospective, comparative, non-interventional cohort study assessing users of IUCD, including levonorgestrel IUCDs and copper IUCDs, who had a primary outcome of uterine perforation. Details of the study can be found at the TGA website.

Mirena is a 20 microgram per 24 hours IUCD containing 52 mg of levonorgestrel. As Mirena contains an active pharmacological agent, it is regulated by the TGA as a medicine. Copper IUCDs are regulated by the TGA as medical devices.

While the risk of uterine perforation associated with all types of IUCDs is low, the European Active Surveillance Study identified an increased risk of uterine perforation in lactating women and during the first 36 weeks postpartum for all such devices.

The Mirena Product Information (PI) in Australia previously included information about uterine perforation and device failure as potential adverse events. However, the updated PI includes information regarding the increased uterine perforation risk for lactating women and during the first 36 weeks postpartum. Additionally, the PI now advises that there is also an increased risk for women with a fixed, retroverted uterus.

For copper IUCDs, the TT380 and LOAD 375 devices, both sponsored by Medical Industries Australia, are in the process of having their Instructions for Use updated to include the relevant information from the European study.

In Hong Kong, there is one registered pharmaceutical product which is an intrauterine system, namely Mirena Intrauterine System 52mg (HK-41251) containing levonorgestrel. It is a prescription only medicine registered by Bayer Healthcare Ltd (Bayer). Related news was previously issued by the UK MHRA, and was reported in the Drug News Issue No. 68. DH issued a letter to inform local healthcare professionals on 29 June 2015. In light of the new safety findings, Bayer has submitted an application to include the

new warnings in the package insert of the product. On 4 December 2015, the Registration Committee of the Pharmacy and Poisons Board discussed the matter, and decided that the package insert of intrauterine device or system should be updated to include the relevant warnings. As on 15 February 2016, DH has not received any ADR case related to IUCD.

Australia: Peginterferon alfa-2a and facial palsy

On 1 December 2015, the TGA advised health professionals that the Product Information (PI) for peginterferon alfa-2a has been updated to state that facial palsy has been reported during the post-marketing period for this medicine.

Peginterferon alfa-2a is a recombinant interferon alfa -2a protein conjugated with a single branched polyethylene glycol chain. It is marketed in Australia as Pegasys and in combination with ribavirin as Pegasys-RBV. It is indicated for use, under specific circumstances, in treatment of chronic hepatitis C and chronic hepatitis B.

TGA post-marketing monitoring of the Australian and international adverse event reports identified a potential link between treatment with peginterferon alfa-2a and VIIth nerve paralysis (also known as Bell's palsy).

Up to 19 August 2015, the TGA had received five reports of VIIth nerve paralysis associated with peginterferon alfa-2a, including three cases in which it was the sole suspected medicine. Based on the identified safety concern and to align with information provided for these medicines in other international jurisdictions, the TGA has worked with the sponsor to update the peginterferon alfa-2a PI to state that facial palsy has been reported during the post-marketing period. Facial palsy is also listed in the peginterferon alfa-2b PI as an adverse effect observed in the post-marketing setting.

At this stage, there have been no reports of facial palsy for Pegasys-RBV or the other six pegylated and non-pegylated interferon products available in Australia.

In Hong Kong, there are six registered pharmaceutical products containing peginterferon alfa-2a under the brand name of Pegasys. All these products are prescription only medicines. As on 15 February 2016, DH has received two ADR cases related to peginterferon alfa, but they were not related to facial palsy. In-line with other international jurisdictions, facial palsy has been included in the package inserts of the local registered Pegasys products. DH will continue to remain vigilant on the safety of peginterferon alfa-2a products.

US: SGLT2 Inhibitors - Labels to include warnings about too much acid in the blood (ketoacidosis) and serious urinary tract infections

On 4 December 2015, the US Food and Drug Adminstration (FDA) announced that a safety review has resulted in change in labels of a specific class of type 2 diabetes medicines called sodium-glucose cotransporter-2 (SGLT2) inhibitors. These changes include adding warnings to the labels about the risks of too much acid in the blood and of serious urinary tract infections, and to provide prescribing and monitoring recommendations. FDA is also requiring manufacturers of SGLT2 inhibitors to conduct a required postmarketing study. This required enhanced pharmacovigilance study requests that manufacturers perform analyses of spontaneous postmarketing reports of ketoacidosis in patients treated with SGLT2 inhibitors, including specialized follow-up to collect additional information, for a period of 5 years.

Patients should stop taking their SGLT2 inhibitor and seek medical attention immediately if they have any symptoms of ketoacidosis. Healthcare professionals should assess for ketoacidosis and urinary tract infections in patients taking SGLT2 inhibitors who present with suggestive symptoms. Ketoacidosis associated with the use of SGLT2 inhibitors can occur even if the blood sugar level is not very high. If ketoacidosis is suspected, the SGLT2 inhibitor should be discontinued and treatment instituted promptly.

In Hong Kong, there are six registered pharmaceutical products which are SGLT2 inhibitors, including two dapagliflozin products, namely Forxiga Tablets 5mg (HK-63301) and 10mg (HK-63302) which are registered by AstraZeneca HK Ltd (Astra); two canagliflozin products, namely Invokana Tablets 100mg (HK-63499) and 300mg (HK-63500) which are registered by Johnson & Johnson (HK) Ltd (J&J); and two empagliflozin products, namely Jardiance Tablets 10mg (HK-64095) and 25mg (HK-64096) which are registered by Boehringer Ingelheim (HK) Ltd (BI). All these products are prescription only medicines.

On 9 July 2015, 10 July 2015 and 14 December 2015, J&J, Astra and BI notified DH respectively that they had issued letters to inform local healthcare professionals on the risk of diabetic ketoacidosis with SGLT2 inhibitors.

News on continuing investigation on the safety of SGLT2 inhibitors to determine whether changes in the prescribing information are needed was first issued by the US FDA, and was reported in the Drug News Issue No. 67. Since then, similar safety reviews were started by various other drug regulatory authorities. As on 15 February 2016, DH has received one ADR case after taking dapagliflozin, which was related to dizziness/ fatigue/ketoacidosis/fever/urinary tract infection; while DH has not received any ADR case on canagliflozin or empagliflozin. In view of the above FDA's conclusion on the safety review, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

Canada: Information Update - Gardasil vaccine safety studies show no new risks

On 9 December 2015, Health Canada informed Canadians that the benefits of using the human papillomavirus (HPV) vaccine Gardasil continue to outweigh the risks after reviewing Canadian and international information regarding the safety of this vaccine. The overall evidence continues to demonstrate that this vaccine can be safely used and that there are no new safety risks associated with its use.

Gardasil is authorized in 133 countries around the world and is used to protect against four types of Human Papilloma Virus (HPV types 6, 11, 16, and 18), which cause 70% of cervical cancers, 90% of genital warts, and 80-90% of anal cancers.

A review of the safety of Gardasil by Health Canada was triggered by media reports of autoimmune and cardiovascular diseases. The safety review by Health Canada concluded that there is no evidence of an increased risk of autoimmune or cardiovascular diseases. Recent international reports are in line with Health Canada's findings.

Since its authorization in 2006, nearly 2 million Canadians, and more than 63 million people worldwide, have been vaccinated with Gardasil. Approximately 1800 people in Canada, which represents approximately 1 out of 1,000 Canadians, reported side effects following vaccination with Gardasil. These include light-headedness, dizziness, nausea, headache, fever, and pain, swelling or redness at the injection site. The side effects are known and described in the Canadian labelling information. The benefits of using the vaccine outweigh the risks and potential side effects.

In Hong Kong, Gardasil Vaccine Inj (Vial) (HK-54934) and Gardasil Vaccine Inj (Pre-filled syringe) (HK-54935) are prescription only medicines which are registered by Merck Sharp & Dohme (Asia) Ltd. As on 15 February 2016, the DH has received five ADR cases related to Gardasil, but none of them was related to autoimmune or cardiovascular diseases. DH noted that the Health Canada's safety review concluded that there is no evidence of increased risk of autoimmune or cardiovascular diseases, which is in -line with recent international reports. DH will continue to remain vigilant on the safety of Gardasil.

Canada: Health Canada warns of potential for serious allergic reactions to over-the-counter topical acne products

On 10 December 2015, Health Canada advised Canadians that the use of over-the-counter acne products applied to the skin containing benzoyl peroxide or salicylic acid may cause rare but serious allergic reactions. Signs and symptoms of a serious allergic reaction called hypersensitivity

reaction may include itchy hives with swelling of the face, eyes, lips, mouth or throat; difficulty breathing; throat tightness or hoarseness; and/or fainting. A type of hypersensitivity reaction called anaphylactic reaction can come on quickly and is potentially life-threatening.

Non-prescription acne products containing benzoyl peroxide or salicylic acid are applied on the skin to help treat acne. Common side effects of benzoyl peroxide and salicylic acid that are included on the labels or package information of marketed Canadian products are localized skin irritation and dryness. Signs of irritation include redness, burning, peeling and mild swelling.

Health Canada has completed a safety review which includes Canadian and foreign cases of serious hypersensitivity reactions, and has concluded that there is evidence supporting a link between the use of over-the-counter topical acne products containing either benzoyl peroxide or salicylic acid and more serious allergic reactions.

As a result of the safety review, Health Canada is updating the Health Canada Acne Therapy Monograph to include:

- Instructions for sensitivity testing to help determine whether a new user of an acne product may be sensitive or allergic to the product;
- Updated warnings relating to possible skin reactions and allergic reactions, and what consumers should do; and
- A warning that the product should not be used if someone is allergic to any of the ingredients of the product, including benzoyl peroxide or salicylic acid.

Manufacturers will be requested to revise the labelling of these acne products in Canada to include these changes.

In Hong Kong, there are 26 and 136 registered pharmaceutical products containing benzoyl peroxide and salicylic acid respectively. Related news was previously issued by the US FDA, and was reported in the Drug News Issues No. 56. On 17 February 2015, the Registration Committee of the Pharmacy and Poisons Board had considered the safety findings by the US FDA, and decided that new warnings on hypersensitivity reactions should be added to these products. DH noted that the previous US FDA announcement and the current Health Canada announcement are referring to the same safety issues related to hypersensitivity reactions with benzoyl peroxide and salicylic acid products. As on 15 February 2016, DH has not received any ADR case related to benzoyl peroxide or salicylic acid products for acne treatment. DH will continue to remain vigilant on the safety of these products.

UK: Antiretroviral medicines: updated advice on body-fat changes and lactic acidosis

On 14 December 2015, the Medicines and Healthcare products Regulatory Agency (MHRA) announced that with the exception of medicines containing zidovudine, stavudine, or didanosine, product information for antiretrovirals for HIV treatment will no longer include warnings on fat redistribution or lactic acidosis.

Warnings regarding lipodystrophy and lactic acidosis were introduced in product information for antiretrovirals for HIV treatment in the early 2000s in line with clinical findings. Class warnings for lactic acidosis applied only to nucleoside and nucleotide analogue medicines, whereas lipodystrophy warnings applied to all antiretroviral agents.

An assessment of a licence application for a new fixed-dose combination product called Triumeq (dolutegravir, abacavir, and lamivudine) identified that class warnings about lipodystrophy and lactic acidosis were being routinely applied to antiretroviral agents for HIV, but that they may not accurately reflect current scientific understanding.

An EU-wide review therefore looked at the appropriateness and applicability of the warnings to these products. The review of the risk of lipodystrophy included lipoatrophy, lipoaccumulation, and changes in weight and metabolism.

Lipoatrophy was previously considered to be associated with nucleoside reverse transcriptase inhibitors (NRTIs). The review noted that lipoatrophy was associated with reduced mitochondria levels in fat cells, and related only to substances with a high risk of mitochondrial toxicity—ie, zidovudine, stavudine, and possibly didanosine. However, lipoatrophy was not seen in regimens with other NRTI products: instead, treatment was associated with fat gain from improved HIV infection control.

As for lipoaccumulation, there was no clear evidence that disproportional body-fat redistribution was related to antiretroviral treatment.

As for blood-lipid levels (changes in weight and metabolism), warnings of increased levels of blood lipids were previously included in the product information for protease inhibitors and for nucleoside and nucleotide analogues. Protease inhibitors were also thought to be associated with a risk of hyperglycaemia. Effects on blood lipids and glucose may occur with any HIV medicine.

Consistent with current HIV treatment guidelines, product information will be amended to advise that weight gain and metabolic changes (such as lipid and glucose increases) may occur during treatment with any HIV medicine. However, these changes are partly linked to underlying disease control and lifestyle in addition to antiretroviral treatment. Warnings for lipoatrophy and lipoaccumulation will be retained only for zidovudine, stavudine, and didanosine.

As for lactic acidosis, warnings about the risk of lactic acidosis were previously applicable only to nucleoside and nucleotide analogues. The review looked at evidence from observational studies published case reports, and data from licence holders of antiretroviral medicines. The risk of lactic acidosis was considered to differ across the class, being most strongly associated with zidovudine, stavudine, and didanosine.

Therefore, in line with current evidence, warnings about lactic acidosis will be removed for nucleoside and nucleotide analogues, with the exception of products that contain zidovudine, stavudine, or didanosine. For combination medicines, any warnings still relevant to any of the active substances will remain in the medicine's product information.

Advice for healthcare professionals is as follows:

- Product information for antiretrovirals will be updated in the UK to reflect current knowledge about lipodystrophy (including lipoatrophy) and lactic acidosis, so that patients and healthcare professionals can decide on treatment based on the most up-to-date advice.
- There are no new risks or safety concerns associated with antiretrovirals. Patients can be reassured that previous information about the risk of lipodystrophy and lactic acidosis for several medicines is no longer considered relevant.

In Hong Kong, there are 15 registered pharmaceutical products containing zidovudine, 6 products containing stavudine, and 2 products containing didanosine. All these products are prescription only medicines. In view of the above MHRA announcement that warning on fat redistribution or lactic acidosis no longer applies to antiretroviral medicines for HIV treatment except zidovudine, stavudine and didanosine, DH issued a letter to inform local healthcare professionals of the update on 15 December 2015. As on 15 February 2016, DH has received two ADR cases related to stavudine, but they were not related to lipodystrophy and/or lactic acidosis. DH will continue to remain vigilant on the safety of antiretroviral medicines.

UK: Bisphosphonates: very rare reports of osteonecrosis of the external auditory canal

On 14 December 2015, the MHRA announced that osteonecrosis of the external auditory canal has been reported very rarely (fewer than 1 in 10 000 patients) with bisphosphonates, mainly in association with long-term therapy (2 years or longer).

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 have different indications. The bisphosphonates available in the UK include alendronic acid, ibandronic acid, pamidronate disodium, risedronate sodium, sodium clodronate and zoledronic acid.

Benign idiopathic osteonecrosis of the external auditory canal is a rare condition that can occur in the absence of antiresorptive therapy and is sometimes associated with local trauma.

Evidence from the clinical literature and from cases reported to medicines regulators, including one report received via the UK Yellow Card scheme, supports a causal association between bisphosphonates and osteonecrosis of the external auditory canal. Product information is being updated to include advice for healthcare professionals and patients.

A total of 29 reports indicative of osteonecrosis of the external auditory canal in association with bisphosphonates have been identified worldwide, including 11 cases reported in the clinical literature. Cases have been reported with use of both intravenous or oral bisphosphonates for both cancer-related or osteoporosis indications; there is currently insufficient evidence to determine whether there is any increased risk with higher doses used for cancer -related conditions. Most cases were associated with long-term bisphosphonate therapy for 2 years or longer, and most cases had possible risk factors including: steroid use; chemotherapy; and possible local risk factors such as infection, an ear operation, or cotton-bud use. Bilateral osteonecrosis of the external ear canal was reported in some patients, as was osteonecrosis of the jaw.

The number of cases of osteonecrosis of the external auditory canal reported in association with bisphosphonates is low compared with the number of cases reported of bisphosphonate-related osteonecrosis of the jaw, a well-established side effect of bisphosphonates.

The available data do not support a causal relation between osteonecrosis of the external auditory canal and denosumab. However, this possible risk is being kept under close review, given that denosumab is known to be associated with osteonecrosis of the jaw.

Advice for healthcare professionals is as follows:

- The possibility of osteonecrosis of the external auditory canal should be considered in patients receiving bisphosphonates who present with ear symptoms, including chronic ear infections, or in patients with suspected cholesteatoma.
- Possible risk factors include steroid use and chemotherapy, with or without local risk factors such as infection or trauma.
- Patients should be advised to report any ear pain, discharge from the ear, or an ear infection during bisphosphonate treatment.

In Hong Kong, there are 63 registered pharmaceutical products containing bisphosphonates, including 28 alendronic acid/ alendronate products, 6 ibandronic acid products, 4 pamidronate disodium products, 12 risedronate sodium products, 1 clodronate disodium product, and 12 zoledronic acid products. All these products are prescription only medicines. In view of the above MHRA announcement, DH issued a letter to inform local healthcare professionals of the warning on 15 December 2015. As on 15 February 2016, DH has received five ADR cases related to alendronic acid, but none of them was related to osteonecrosis. No ADR case has been received on other bisphosphonates. The matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

US: Rosiglitazone-containing diabetes medicines: Drug Safety Communication - FDA eliminates the Risk Evaluation and Mitigation Strategy (REMS)

On 16 December 2015, FDA announced that the Risk Evaluation and Mitigation Strategy (REMS) for rosiglitazone-containing type 2 diabetes medicines, which are approved as Avandia, Avandamet, Avandaryl, and generics would be eliminated. The REMS is no longer necessary to ensure that the benefits of rosiglitazone medicines outweigh their risks.

Safety Update

Type 2 diabetes is a disease that can lead to serious complications such as kidney failure, blindness, and premature death. Rosiglitazone can be used along with diet and exercise to control blood sugar in adults with the disease.

In 2013, FDA required removal of the prescribing and dispensing restrictions for rosiglitazone medicines after determining that data did not demonstrate an increased risk of heart attack with rosiglitazone medicines compared to the standard type 2 diabetes medicines metformin and sulfonylurea. FDA also required the drug manufacturers to provide educational training to health care professionals about the current state of knowledge regarding the heart risks of rosiglitazone medicines. Manufacturers have since fulfilled these requirements.

FDA has continued monitoring these medicines and identified no new pertinent safety information. FDA will update the public if any new information becomes available.

In Hong Kong, there are eight registered pharmaceutical products containing rosiglitazone, which are approved as Avandia (3 products) and Avandamet (5 products). All these products are prescription only medicines which are registered by GlaxoSmithKline Ltd. (GSK). Related news on cardiovascular risks of rosiglitazone was previously issued by various overseas drug regulatory authorities since 2010, and was reported in the Drug News Issue No. 7, No. 10, No. 12 and No. 20. As on 15 February 2016, DH has not received any ADR case related to rosiglitazone.

On 5 December 2012, the Registration Committee of the Pharmacy and Poisons Board (the Committee) discussed the safety and US REMS requirements for rosiglitazone, and endorsed GSK's proposed Rosiglitazone-containing Medicines Access Program (RAP) for implementation in Hong Kong (similar to the US REMS). In view of the US FDA's latest announcement to eliminate the REMS requirements, DH has contacted GSK for their latest position on the issue, and GSK is applying to remove the RAP. The matter will be discussed by the Committee.

Drug Recall

DH endorsed recall of five Advance Pharmaceutical products

On 7 December 2015, DH endorsed a licensed pharmaceutical manufacturer Advance Pharmaceutical Co Ltd (APC), to recall five products from the market, namely Harex Gripe Mixture (HK-57713), Andrex Baby Water (HK-57714), Hap Gripe Mixture 0.3% (HK-57284), Advance Gripe Mixture 0.3% (HK-58165) and Prolyter Baby Water 0.3% (HK-58168), due to quality issues.

DH was notified by APC that one batch of the above five products was found to have failed the microbial test during the ongoing stability study. As a precautionary measure, APC recalled all the above products from the market. According to APC, the affected products had been supplied to local pharmacies and medicine companies, and exported to Macau.

The above products, which all contain sodium bicarbonate, are over-the-counter medicines used for the relief of abdominal pain due to trapped wind and stomach upset in babies and young children.

Healthcare professionals and pharmacies are advised to stop supplying the affected products to patients. Members of the public who are taking the products should stop and consult their doctors for advice.

As on 15 February 2016, DH has not received any ADR case related to the affected products. DH will closely monitor the recall. A notice was released on the website of the Drug Office on the same day to alert the public of the recall.

DH endorsed recall of three veterinary products

On 15 December 2015, DH endorsed a licensed drug wholesaler, Merck Sharp & Dohme (Asia) Ltd

Drug Recall

("MSD"), to recall three veterinary products from shelf because they were considered not registered. The three products were Nobivac L vaccine (HK-42022), Nobivac DHPPi vaccine (HK-40816) and Nobivac KC vaccine (HK-48091).

The DH received notification from MSD that the particulars of three of their veterinary vaccines distributed in Hong Kong, including pack size, outer packaging and specifications, were different from the particulars registered with the Pharmacy and Poisons Board, which rendered the products unregistered. Since the supply of unregistered pharmaceutical products contravenes the Pharmacy and Poisons Regulations (Cap 138A), MSD voluntarily recalled the products from the market. The DH's investigation was continuing.

All three products are vaccines for the prevention of different diseases in dogs. All of these products are prescription only medicines. According to MSD, the affected products have been supplied to veterinary surgeons.

A notice was released on the website of the Drug Office on the same day to alert the public of the recall.

Drug Incident

DH raided a premises for suspected illegal sale of unregistered pharmaceutical product

On 4 December 2015, a premises in Mongkok was raided in a joint operation conducted by DH and the Police for suspected illegal sale of Part 1 poison and unregistered pharmaceutical product.

Following a public complaint, it was found that the above premises had been offering for sale a product called Naprogesic, which was labelled as containing a Part 1 poison, naproxen. No Hong Kong pharmaceutical product registration number was found on the product's label. A woman aged 58 was arrested by the Police for suspected illegal sale of Part 1 poison and unregistered pharmaceutical product.

Products containing naproxen are prescription only medicines which should only be used under the advice of a doctor and can only be supplied at pharmacies under the supervision of a registered pharmacist upon a doctor's prescription. Naproxen is a non-steroidal anti-inflammatory drug indicated for the relief of pain. Side-effects include gastrointestinal discomfort, nausea and peptic ulcers.

Members of the public should not use controlled medicines on their own without prior advice from a doctor. A notice was released on the website of the Drug Office on the same day to alert the public of the drug incident.

DH raided a shop for suspected illegal sale of slimming product with undeclared banned drug ingredient

On 9 December 2015, a retail shop in Sham Shui Po was raided in a joint operation conducted by DH and the Police for suspected illegal sale of a slimming product called 4C Cosmoslim, which was suspected to contain an undeclared banned drug ingredient and Part 1 poisons.

Following a public complaint, a sample of the above product was previously purchased from the above shop for analysis. The test results from the Government Laboratory revealed that the sample contained a banned ingredient, phenolphthalein, and Part 1 poisons, diclofenac and lignocaine. During the operation, a woman aged 19 was arrested by the Police for suspected illegal sale of Part 1 poison and unregistered pharmaceutical product.

Phenolphthalein was once used to treat constipation, but has been banned in Hong Kong for its cancer-causing effect. Diclofenac is a non-steroidal anti-inflammatory drug for pain relief and its side-effects include gastrointestinal discomfort, nausea and peptic ulcers. Lignocaine is a local anaesthetic and may cause hypersensitivity reactions.

Drug Incident

A notice was released on the website of the Drug Office on the same day to alert the public of the drug incident.

DH raids premises for suspected illegal sale of unregistered pharmaceutical product

On 30 December 2015, a premises in Mong Kok was raided in a joint operation by DH and the Police for suspected illegal sale of an unregistered pharmaceutical product, YI BAO, which is suspected to contain undeclared Part 1 poisons.

Acting on intelligence, a sample of the above product had been purchased previously from the premises for analysis. The test results from the Government Laboratory revealed that the sample contained Part 1 poisons, namely metformin, pioglitazone and glibenclamide. Products containing these drug ingredients are prescription only medicines which should only be used under the advice of a medical doctor and can only be supplied at pharmacies under the supervision of a registered pharmacist upon a doctor's prescription. During the operation, a woman aged 62 was arrested by the Police for suspected illegal possession of Part 1 poisons and an unregistered pharmaceutical product.

Metformin, pioglitazone and glibenclamide are used for the management of diabetes. Side effects of metformin include anorexia, nausea, vomiting, diarrhoea and lactic acidosis; pioglitazone may cause headache, dizziness and lower limb oedema; and side effects of glibenclamide include nausea and gastrointestinal upset.

A notice was released on the website of the Drug Office on the same day to alert the public of the drug incident.

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 1 poisons should be sold at registered pharmacies under the supervision of registered pharmacists. Illegal sale or possession of Part 1 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,
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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.