Drug News
藥 物 情 報

Issue Number 108

This is a monthly digest of local and overseas drug safety news released by the Drug Office of the Department of Health in October 2018 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: Inhaled or injected general anaesthetic agents and sedative medicines: possible effects on brain development in young children

On 2 October 2018, the Therapeutic Goods Administration (TGA) of Australia announced that it is working with sponsors of certain inhaled or injected general anaesthetic agents and sedative medicines to update information about the potential risk of deficits in learning and behavioural development in children, which may be associated with repeated or prolonged exposure to these products during late pregnancy or early childhood.

This concern applies to all general anaesthetic agents and sedative medicines that block N-methyl-D-aspartate (NMDA) receptors or potentiate gamma-aminobutyric acid (GABA) activity. These medicines include desflurane, isoflurane, sevoflurane, thiopentone, ketamine, midazolam, propofol, phenobarbitone injection, nitrous oxide and methoxyflurane.

The TGA has assessed the safety of certain general anaesthetic agents and sedative medicines in response to concerns raised from animal studies published in the scientific literature about possible effects on early brain development in babies and young children.

As part of its investigation, the TGA sought advice from the Advisory Committee on Medicines (ACM) at its December 2017 meeting. The ACM meeting statement can be found on the TGA website. The ACM advised that there was good evidence from animal studies that general anaesthetic agents and certain sedative medicines used during anaesthesia had effects on the developing brain, including cell death. Some evidence suggested that these changes were greatest with longer exposure (several hours of exposure to a general anaesthetic).

However, the relevance of these finding to humans is not clear. Studies that are available in humans are not conclusive. Where an association between surgery and developmental outcomes was found, this association may have been confounded by a number of factors such as complications arising from the surgery itself or the underlying illness necessitating surgery. The effect of dose and duration of anaesthesia was not clear.

There is evidence that a single, relatively brief exposure to anaesthesia in otherwise healthy children is unlikely to cause any significant long-lasting effects (clinically detectable deficits) in cognitive function or behaviour.

Consumers are advised that this potential concern only applies to unborn and young children in relation to repeated or prolonged (greater than 3 hours) use of anaesthetic agents or sedative medicines. Surgeries in young children and pregnant women should not be delayed or avoided when there is any possibility that delay may result in an adverse outcome or harm.

Healthcare professionals are advised that before using general anaesthetics and sedatives for a surgical procedure in pregnant women or young children, they should consider discussing the potential effects of these agents on neurodevelopment and learning. They should also be prepared to address questions raised by parents

and carers about this issue. These potential risks should obviously be balanced with any adverse outcomes likely to be associated with delaying or avoiding surgery. The timing of any non-urgent procedures should be discussed with patients.

The TGA is working with sponsors to update Product Information in Australia to include the following information:

- Some published studies in children have observed cognitive deficits after repeated or prolonged exposures to anaesthetic agents early in life. These studies have substantial limitations, and it is not clear if the observed effects are due to the anaesthetic/analgesic/ sedation drug administration or other factors such as the surgery or underlying illness.
- Published animal studies of some anaesthetic/ analgesic/sedation drugs have reported adverse effects on brain development in early life and late pregnancy. These studies have demonstrated that anaesthetic/analgesic and sedation drugs that block NMDA receptors and/or potentiate GABA activity during the period of rapid brain growth or synaptogenesis may result in neuronal and oligodendrocyte cell loss in the developing brain and alterations in synaptic morphology and neurogenesis when used for longer than 3 hours. These studies included anaesthetic agents from a variety of drug classes. The clinical significance of these non-clinical findings is yet to be determined.

In Hong Kong, there are 32 registered pharmaceutical products containing general anaesthetics and sedation drugs listed in the above TGA's announcement, and the previous United States (US) Food and Drug Administration's (FDA) and Health Canada's announcements on the matter, including desflurane (1 product), etomidate (1 product), isoflurane (5 products), ketamine (5 products), methoxyflurane (1 product), midazolam injection (7 products), pentobarbital (1 product), propofol (6 products), sevoflurane (4 products) and phenobarbitone injection (1 product). Desflurane, isoflurane and sevoflurane are currently over-the-counter medicines but will be up-regulated and controlled as prescription-only medicines with effect from May 2019, while the other products are prescription-only medicines.

As on 5 November 2018, the Department of Health (DH) has received 18 cases of adverse drug reaction (ADR) related to ketamine, 1 case related to lorazepam, 24 cases related to midazolam, 1 case related to propofol, 4 cases related to phenobarbital and 1 case related to thiopentone, but these cases are not related to brain development in children.

Related news was previously issued by the US FDA and Health Canada, and was reported in the Drug News Issue No. 86 and 98. The DH issued a letter to inform local healthcare professionals to draw their attention on 15 December 2016. As previously reported, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board (the Registration Committee).

EU: Fluoroquinolone and quinolone antibiotics: PRAC recommends new restrictions on use following review of disabling and potentially long-lasting side effects

On 5 October 2018, the European Medicines Agency (EMA) of the European Union (EU) announced that the EMA's Pharmacovigilance Risk Assessment Committee (PRAC) has recommended restricting the use of fluoroquinolone and quinolone antibiotics (used by mouth, injection or inhalation) following a review of disabling and potentially long-lasting side effects reported with these medicines. The review incorporated the views of patients, healthcare professionals and academics presented at the EMA's public hearing on fluoroquinolone and quinolone antibiotics in June 2018.

Very rarely, patients treated with fluoroquinolone or quinolone antibiotics have suffered long-lasting and disabling side effects, mainly involving muscles, tendons and bones and the nervous system.

Following its evaluation of these side effects, the PRAC has recommended that some medicines, including all those that contain a quinolone antibiotic, should be removed from the market. This is because they are authorised only for infections that should no longer be treated with this class of antibiotics.

The PRAC recommended that the remaining fluoroquinolone antibiotics should:

- **not** be used
  - ➢ to treat infections that might get better without treatment or are not severe (such as throat infections);
  - ➢ for preventing traveller's diarrhoea or recurring lower urinary tract infections (urine infections that do not extend beyond the bladder);
  - ➢ to treat patients who have previously had serious side effects with a fluoroquinolone or quinolone antibiotic;
  - ➢ to treat mild or moderately severe infections unless other antibacterial medicines commonly recommended for these infections cannot be used;
- be used **with caution** especially for the elderly, patients with kidney problems, patients who have had an organ transplantation or those who are being treated with a systemic corticosteroid. These patients are at higher risk of tendon injury caused by fluoroquinolone and quinolone antibiotics.

The PRAC also recommended that healthcare professionals should advise patients to stop treatment with a fluoroquinolone antibiotic at the first sign of a side effect involving muscles, tendons or bones (such as inflamed or torn tendon, muscle pain or weakness, and joint pain or swelling) or the nervous system (such as feeling pins and needles, tiredness, depression, confusion, suicidal thoughts, sleep disorders, vision and hearing problems, and altered taste and smell).

In Hong Kong, there are 190 registered pharmaceutical products for systemic administration containing fluoroquinolones and quinolones, including ciprofloxacin (81 products), levofloxacin (62 products), moxifloxacin (6 products), norfloxacin (7 products), ofloxacin (30 products), sparfloxacin (1 product), prulifloxacin (1 product), nalidixic acid (1 product) and pipemidic acid (1 product). All products are prescription-only medicines.

Related news was previously issued by overseas drug regulatory authorities and was reported in the Drug News Issue No. 46, 79, 81, 87 and 88. The DH issued letters to inform local healthcare professionals on the warnings on 16 August 2013 and 13 May 2016. In 2013, the Registration Committee discussed the safety of fluoroquinolones with peripheral neuropathy, and decided that the relevant warnings should be included in the sales packs and/or package inserts of the products. In 2016, the Registration Committee further discussed the safety of fluoroquinolones with disabling and potentially permanent side effects of the tendons, muscles, joints, nerves, and central nervous system, and subsequently decided to remain vigilant on further updates by other overseas drug regulatory authorities.

As on 5 November 2018, the DH has received 4 cases of ADR related to levofloxacin and 1 case related to moxifloxacin, of these 5 cases one of the levofloxacin case was related to tendinitis and neuropathy, other 4 cases were not related to adverse effects mentioned in the EMA's announcement. The DH has not received any case of ADR related to other fluoroquinolones and quinolones. In light of the EMA announcement in February 2017 and October 2018, the DH issued a letter to inform local healthcare professionals to draw their attention on 8 October 2018, and the matter will be further discussed by the Registration Committee. The DH will maintain vigilant on any further update from these health authorities for consideration of any action deemed necessary.

Canada: Summary Safety Review - Jakavi (ruxolitinib) - Assessing the potential risk of drug interactions with P-glycoprotein (P-gp) substrates (including rosuvastatin)

On 9 October 2018, Health Canada announced that it reviewed the potential risk of a drug interaction between ruxolitinib and rosuvastatin (a P-gp substrate) after receiving a Canadian report of a suspected interaction between these 2 drugs. The report included a description of a suspected mechanism of interaction, which prompted Health Canada to include other drugs known to utilize the same transport mechanism, known as P-gp, in the safety review. The current product information for ruxolitinib states that ruxolitinib has no effect on P-gp transporters, based on earlier laboratory studies.

At the time of the review, Health Canada had received 1 Canadian report of increased blood cholesterol due to a potential interaction between ruxolitinib and rosuvastatin. The review of this case could not conclude whether ruxolitinib interacted with rosuvastatin and/or played a role in the increased blood cholesterol observed in the patient. This is because patients with polycythemia vera may develop higher blood cholesterol levels when their disease is being treated. The review also looked at 2 articles in the published literature which did not suggest an interaction between ruxolitinib and other drugs that are known to be transported by P-gp (e.g. digoxin, dabigatran and cyclosporine). Available evidence at the time of review suggested that an interaction between ruxolitinib and rosuvastatin was unlikely because ruxolitinib did not appear to inhibit P-gp at doses typically used in patient treatment. Neither rosuvastatin nor ruxolitinib appear to directly interact with P-gp transporters.

Health Canada's review concluded that the available evidence does not suggest an interaction between ruxolinitib and rosuvastatin or other drugs that are transported by P-gp. Therefore, it is unlikely that any observed increase in blood cholesterol was due to a ruxolitinib interaction with rosuvastatin in the Canadian report. The safety information for these products is appropriate at this time.

In Hong Kong, there are 3 registered pharmaceutical products containing ruxolitinib, namely Jakavi Tab 5mg (HK-61973), Jakavi Tab 15mg (HK-61974) and Jakavi Tab 20mg (HK-61972). All products are registered by Novartis Pharmaceuticals (HK) Limited, and are prescription-only medicines. As on 5 November 2018, the DH has received 17 cases of ADR related to ruxolitinib, but these cases are not related to drug interaction. The DH will remain vigilant on safety update of the drug issued by other overseas drug regulatory authorities.

UK: Ritonavir-containing products: reports of interaction with levothyroxine leading to reduced thyroxine levels

On 11 October 2018, the Medicines and Healthcare products Regulatory Agency (MHRA) of the United Kingdom (UK) announced that reduced thyroxine levels have been reported in patients concomitantly taking ritonavir-containing products and levothyroxine.

An EU review has assessed evidence for an interaction between ritonavir and levothyroxine following a signal of reduced thyroxine concentrations and increased thyroid-stimulating hormone (TSH) plasma concentrations in patients concomitantly taking these medicines. Some of the cases reported were symptomatic, including cases of hypothyroidism.

This interaction has been added to the Summaries of Product Characteristics and Patient Information Leaflets for ritonavir-containing medicines and levothyroxine in the UK.

Levothyroxine has a narrow therapeutic index and if ritonavir is stopped, any previous modifications to levothyroxine dose may have significant consequences for thyroxine levels. Induction of metabolism (glucuronidation) of levothyroxine by ritonavir is a possible mechanism for this interaction.

Healthcare professionals are advised that TSH should be monitored in patients receiving concomitant treatment with ritonavir and levothyroxine for at least the first month after starting and ending ritonavir treatment. The duration of the monitoring proposed is based on the pharmacokinetics of the drug (the half-life of thyroxine being 6–7 days).

In Hong Kong, there are 6 registered pharmaceutical products containing ritonavir, and 9 products containing levothyroxine. All products are prescription-only medicines. As on 5 November 2018, the DH has received 35 cases of ADR related to ritonavir and 2 cases related to levothyroxine, but these cases are not related to drug interaction. In light of the above MHRA's announcement, the DH issued a letter to inform local healthcare professionals to draw their attention on 12 October 2018 and the matter will be discussed by the Registration Committee.

UK: Rivaroxaban (Xarelto ▼) after transcatheter aortic valve replacement (TAVR): increase in all-cause mortality, thromboembolic and bleeding events in a clinical trial

On 11 October 2018, the MHRA announced that preliminary analysis of a phase 3 clinical trial show risks of all-cause death and bleeding post-TAVR were approximately doubled in patients assigned to a rivaroxaban-based anticoagulation strategy compared with those assigned to receive an antiplatelet-based strategy (clopidogrel and aspirin).

Study 17938, Global Study Comparing a rivAroxaban-based Antithrombotic Strategy to an antipLatelet-based Strategy After Transcatheter aortIc vaLve rEplacement to Optimize Clinical Outcomes (GALILEO), is a randomised, open label, active-controlled, multicentre, phase 3 trial that aimed to assess clinical outcomes after successful TAVR in patients randomly assigned to receive either a rivaroxaban-based anticoagulation strategy or an antiplatelet-based strategy. The first group was assigned to receive rivaroxaban 10 mg once a day and acetylsalicylic acid (aspirin) 75–100 mg once a day for 90 days followed by maintenance with rivaroxaban 10 mg once a day. The comparator group was assigned to receive clopidogrel 75 mg and acetylsalicylic acid 75–100 mg once a day for 90 days, followed by acetylsalicylic acid alone. The primary efficacy endpoint is a composite of all-cause death, stroke, systemic embolism, myocardial infarction, pulmonary embolism, deep vein thrombosis, and symptomatic valve thrombosis. The primary safety endpoint is a composite of life-threatening or disabling (Bleeding Academic Research Consortium (BARC) types 5 and 3b/3c) and major (BARC type 3a) bleeding events. Patients with atrial fibrillation at randomisation were excluded.

The trial was stopped in August 2018, on recommendation of the independent Data Safety Monitoring Board, following a preliminary analysis of available data. The trial findings suggested an imbalance between the two study groups in all-cause mortality, thromboembolic, and bleeding events. These results are preliminary and based on incomplete data collection. The final study data will be assessed by regulatory authorities as soon as they are available, including an assessment of any implications for approved indications. The MHRA will promptly communicate any relevant updates.

Healthcare professionals are advised:

- Rivaroxaban is not authorised for thromboprophylaxis in patients with prosthetic heart valves, including patients who have undergone TAVR, and should not be used in such patients.
- Rivaroxaban treatment in patients who undergo TAVR should be stopped and switched to standard of care.
- The direct-acting oral anticoagulants apixaban and edoxaban have not been studied in patients with prosthetic heart valves and their use is also not recommended in these patients; the use of dabigatran is contraindicated in patients with prosthetic heart valves requiring anticoagulant treatment.

In Hong Kong, there are 6 registered pharmaceutical products containing rivaroxaban, namely Xarelto Tab 10mg (HK-57861), Xarelto Tab 15mg (HK-61396), Xarelto Tab 20mg (HK-61395), Xarelto Tablets 10mg (Italy) (HK-65786), Xarelto Tablets 15mg (Italy) (HK-65787) and Xarelto Tablets 20mg (Italy) (HK-65785). All products are registered by Bayer Healthcare Limited, and are prescription-only medicines.

As on 5 November 2018, the DH has received 14 cases of ADR related to rivaroxaban, and these cases include stroke and bleeding. In light of the above MHRA's announcement, the DH issued a letter to inform local healthcare professionals to draw their attention on 12 October 2018. The DH will remain vigilant on safety update of the drug, including the final results of the study, issued by the MHRA and other overseas drug regulatory authorities for consideration of any action deemed necessary.

UK: Transdermal fentanyl patches: life-threatening and fatal opioid toxicity from accidental exposure, particularly in children

On 11 October 2018, the MHRA announced that accidental exposure to transdermal fentanyl can occur if a patch is swallowed or transferred to another individual.

In 2014, following an EU review, advice on minimising risk of accidental transfer is added to Summary of Product Characteristics and the Patient Information Leaflet for transdermal fentanyl products. The MHRA continue to receive reports of preventable accidental transfer of fentanyl patches. Since July 2014 and up to October 2018, the MHRA has received 5 reports of fatal incidents specifying accidental exposure, accidental overdose, or product adhesion issue. Causes of death was not included in all reports but were understood to be related to opioid toxicity.

Healthcare professionals are advised:

- Always fully inform patients and their caregivers about directions for safe use for fentanyl patches, including the importance of:
  - not exceeding the prescribed dose;
  - following the correct frequency of patch application, avoiding touching the adhesive side of patches, and washing hands after application;
  - not cutting patches and avoiding exposure of patches to heat including via hot water (bath, shower);
  - ensuring that old patches are removed before applying a new one;
  - following instructions for safe storage and properly disposing of used patches or those which are not needed.
- Ensure that patients and caregivers are aware of the signs and symptoms of fentanyl overdose and advise them to seek medical attention immediately (by dialing 999 and requesting an ambulance) if overdose is suspected. Possible symptoms of fentanyl overdose include respiratory depression (difficulty in breathing or shallow breathing); tiredness; extreme sleepiness or sedation; inability to think, walk, or talk normally; and feeling faint, dizzy, or confused. Opioid overdose can be fatal and requires urgent medical treatment.
- In patients who experience serious adverse events, remove patches immediately and monitor for up to 24 hours after patch removal.

In Hong Kong, there are 4 registered pharmaceutical products which are transdermal patch containing fentanyl, namely Durogesic Transdermal Patch 12mcg/h (HK-53883), Durogesic Transdermal Patch 25mcg/h (HK-53755), Durogesic Transdermal Patch 50mcg/h (HK-53753) and Durogesic Transdermal Patch 100mcg/h (HK-53754). All products are registered by Johnson & Johnson (Hong Kong) Ltd., and are prescription-only medicines.

As on 5 November 2018, the DH has not received any case of ADR related to fentanyl. Related news was previously issued by various overseas drug regulatory authorities, and was reported in the Drug News Issue No. 30, 47 and 57. The DH issued a letter to inform local healthcare professionals to draw their attention on the risk of accidental exposure on 20 April 2012. In September 2014, the Registration Committee discussed the matter and decided that the package insert of fentanyl patch products should include safety information related to accidental exposure. The DH will remain vigilant on safety update of the drug issued by other overseas drug regulatory authorities.

EU: EU authorities take further action in ongoing review of sartans: Zheijiang Huahai placed under increased supervision; Aurobindo Pharma stopped from supplying irbesartan to the EU

On 15 October 2018, the EMA announced that EU authorities are placing the Chinese company Zheijiang Huahai under increased supervision following European and US inspections which revealed weaknesses in quality management at the company's Chuannan site in Linhai, China. The inspection findings included deficiencies in the way the company investigated impurities in its valsartan products and led EU authorities to issue a statement of non-compliance with good manufacturing practice (GMP), prohibiting the use of its valsartan in EU medicines. This latest action means that EU authorities will supervise the manufacture of other active substances produced by Zhejiang Huahai more closely. Authorities will monitor corrective measures being implemented by the company on a regular basis and increase the frequency of

inspections of the site. In addition, marketing authorisation holders for EU medicines will be required to perform additional tests on all active substances supplied by Zhejiang Huahai.

In July 2018, the detection of impurities – N-nitrosodimethylamine (NDMA) and N-nitrosodiethylamine (NDEA) – in valsartan from Zhejiang Huahai led to an EU-wide review of all valsartan medicines. The review was subsequently extended to other 'sartan' medicines when very low levels of NDEA were found in losartan made by Hetero Labs in India.

Both NDMA and NDEA, which have not been found in any of Zheijiang Huahai's other products, are classified as probable human carcinogens (substances that could cause cancers). A preliminary risk assessment for NDMA in valsartan indicated that the lifetime risk of cancer is low.

Low levels of NDEA have now also been found in a third sartan, irbesartan, made by another Indian company, Aurobindo Pharma. On 8 October 2018, the European Directorate for the Quality of Medicines & HealthCare (EDQM) suspended Aurobindo Pharma's certificate of suitability to the monographs of the European Pharmacopoeia (CEP) effectively stopping the supply in the EU of medicines containing irbesartan from this company. National authorities in the EU are currently considering whether to recall medicines containing Aurobindo Pharma's irbesartan from pharmacies as a precaution.

The review into the presence of impurities in sartans and their potential effects in patients is ongoing. The EMA will continue working with national authorities, international partners and EDQM and will provide updates as more information becomes available.

In Hong Kong, as on 5 November 2018, there are 253 registered pharmaceutical products containing valsartan (83 products), candesartan (19 products), irbesartan (64 products), losartan (70 products) and olmesartan (17 products). All products are prescription-only medicines.

Regarding impurities in valsartan, a public announcement was issued on 6 July 2018, and the DH issued letters to inform local healthcare professionals on 6 July 2018, 9 July 2018, 25 July 2018 and 3 August 2018. Related news for the detection of impurities in sartan-containing products was also previously issued by various overseas drug regulatory authorities, and was reported in the Drug News Issue No. 105, 106 and 107.

In summary, there are four manufacturers, namely Zhejiang Huahai, Zhejiang Tianyu and Zhuhai Rundu in China and Hetero Labs Limited in India, reported to have detection of trace amounts of NDMA in the valsartan Active Pharmaceutical Ingredient (API) by various overseas drug regulatory authorities. The DH contacted the certificate holders of all registered valsartan products to follow up on the local impact regarding valsartan API produced by the above mentioned manufacturers.

For API produced by Zhejiang Huahai, there are 5 affected products (HK-61786, HK-61787, HK-61784, HK-61785 and HK-60794) marketed in Hong Kong. The DH instructed the certificate holders to recall all the products from the market as a precautionary measure on 6 July 2018, and the DH noted that all the recalls have been completed.

For API produced by Zhejiang Tianyu, amongst the registered pharmaceutical products containing valsartan, there is only one product namely Retoni Tablets 80mg (HK-65604) registered by Swiss Pharmaceutical Co. Limited (Swiss Pharmaceutical) which has used API produced by Zhejiang Tianyu and is available in the local market. As confirmed with Swiss Pharmaceutical, the API was tested by the Taiwan Food and Drug Administration (TFDA) and the company has not received any notice from the TFDA for NDMA contamination. The DH collected samples of Retoni tablets for analysis and no NDMA was detected.

For API produced by Zhuhai Rundu and Hetero Labs Limited, the certificate holders confirmed that the valsartan products available in local market are not manufactured using API produced by Zhuhai Rundu or Hetero Labs Limited.

Regarding the announcements issued by various

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overseas drug regulatory authorities on the detection of the second impurity of NDEA in the valsartan API produced by Zhejiang Huahai, there should be no local impact as all valsartan products manufactured using API produced by Zhejiang Huahai have been recalled from the market.

Regarding the EMA's announcement on the detection of NDEA in losartan in the API produced by Hetero Labs Limited, and in irbesartan by Aurobindo Pharma in India, the DH has contacted the certificate holders of all registered candesartan, irbesartan, losartan and olmesartan products and will continue to follow up on the impact of NDEA impurities on the products available in the local market.

As on 5 November 2018, the DH has received 15 cases of ADR related to valsartan, candesartan, irbesartan, losartan and olmesartan. None of them are concluded to be related to the presence of NDMA and/or NDEA. The DH will keep vigilant on any further updates on the matter issued by overseas regulatory authorities.

Patients who are taking the above products should not stop taking the medicines, but should seek advice from their healthcare professionals as soon as possible for proper arrangement.

The DH has provided update information at Drug Office's website (www.drugoffice.gov.hk) and will remain vigilant on any safety update related to the impurities NDMA and NDEA in sartan-containing (candesartan, irbesartan, losartan, olmesartan and valsartan) products.

Drug Recall

Update on the batch recall of Ozurdex Intravitreal Implant 700mcg (HK-60336)

On 2 October 2018, the DH received a notification from the licensed drug wholesaler Allergan Hong Kong Limited (Allergan) that three more batches (E77959, E79749 and E80181) of Ozurdex Intravitreal Implant 700mcg (Ozurdex) (HK-60336) are affected by the same quality issue and would be recalled from the market further to the recall of two batches (E79233 and E80405) of Ozurdex by Allergan on 28 September 2018.

The DH received notification from Allergan that during routine testing by the manufacturer in Ireland, a silicone particle from the silicone sleeve component on the needle of the applicator was generated upon actuation of the Ozurdex unit which would give rise to the potential for the silicone particle to be injected during administration of the Ozurdex implant into the eye. Allegran recalls three more affected batches as a precautionary measure.

The above Ozurdex product, containing dexamethasone, is a prescription-only medicine used to treat macular disease. According to Allergan, the product has been supplied to Hospital Authority, private hospitals, private doctors and re-exported to Macao. Allergan has issued letter to healthcare professionals and set up a hotline (2895 9668) to answer enquiries on the above recall.

As on 5 November 2018, the DH has not received any adverse reaction reports in connection with the above batches of the product. The recall had already been completed.

Members of the public should consult healthcare professionals if in doubt or feeling unwell after using the product. Notices were posted on the Drug Office website on 28 September 2018 and 2 October 2018 to alert the public of the product recall. The recall news on 28 September 2018 was reported in the Drug News Issue No. 107.

Drug Incident

Public urged not to buy or consume virility product with doubtful composition

On 5 October 2018, the DH urged the public not to buy or consume a virility product named Hamer Candy Ginseng & Coffee as it was found to contain an undeclared and controlled substance.

Based on the DH's market surveillance, a sample of the above product was purchased from a company in Kwun Tong for analysis. The test results from the Government Laboratory confirmed that the sample contains nortadalafil, which is a Part 1 poison under the Pharmacy and Poisons Ordinance (Cap. 138) and an analogue of another Part 1 poison, tadalafil.

The DH and the Police carried out a joint operation on 5 October 2018 and raided the above company. A man aged 70 was arrested for illegal sale and possession of a Part 1 poison.

Tadalafil is used for erectile dysfunction and should only be used under the advice of a doctor. Side effects of tadalafil include low blood pressure, headache, vomiting, dizziness and transient vision disturbances. It may interact with some drugs (such as nitroglycerin for treatment of angina) and cause decrease in blood pressure to dangerous levels. Improper use of tadalafil may pose serious health risks, especially for patients with heart problems. Nortadalafil, being chemically similar to tadalafil, is expected to pose similar health risks.

The public may visit the Drug Office's webpage for the health message on sexual dysfunction and virility products and information on virility products found to contain undeclared Western medicines.

A notice was posted on the Drug Office website on 5 October 2018 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.

Under the Import and Export Ordinance (Cap. 60), pharmaceutical products must be imported or exported under and in accordnance with an import or export licence issued under the Import and Export Ordinance. Illegal import or export of pharmaceutical products are offences under the Import and Export Ordinance (Cap. 60) and the maximum penalty is a fine of $500,000 and 2 years' imprisonment.

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.

Update on Drug Office's website: You can now search the newly registered medicines in the past year at http://www.drugoffice.gov.hk/eps/drug/newsNRM60/en/healthcare_providers?pageNoRequested=1.
Details of ALL registered pharmaceutical products can still be found in the Drug Office website at http://www.drugoffice.gov.hk/eps/do/en/healthcare_providers/news_informations/reListRPP_index.html.

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,
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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.