Drug News
藥 物 情 報

Issue Number 106

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

The United States: FDA warns about increased risk of cancer relapse with long-term use of Azithromycin (Zithromax, Zmax) antibiotic after donor stem cell transplant

On 3 August 2018, the United States (US) Food and Drug Administration (FDA) issued a warning that the antibiotic azithromycin (Zithromax, Zmax) should not be given long-term to prevent a certain inflammatory lung condition in patients with cancers of the blood or lymph nodes who undergo a donor stem cell transplant. Results of a clinical trial found an increased rate of relapse in cancers affecting the blood and lymph nodes, including death, in these patients. The US FDA is reviewing additional data and will communicate their conclusions and recommendations when the review is complete.

The serious lung condition for which long-term azithromycin was being studied called bronchiolitis obliterans syndrome is caused by inflammation and scarring in the airways of the lungs, resulting in severe shortness of breath and dry cough. Cancer patients who undergo stem cell transplants from donors are at risk for bronchiolitis obliterans syndrome. The manufacturer of brand name azithromycin is providing a Dear Healthcare Provider letter on this safety issue to health care professionals who care for patients undergoing donor stem cell transplants.

Azithromycin is not approved for preventing bronchiolitis obliterans syndrome in the US. It is an FDA-approved antibiotic used to treat many types of infections affecting the lungs, sinuses, skin, and other parts of the body. It works by stopping the growth of bacteria that can cause infections.

Researchers in France identified this increased risk of cancer relapse and death while conducting a clinical trial investigating the effectiveness of long-term azithromycin to prevent bronchiolitis obliterans syndrome in patients who undergo donor, or allogenic, stem cell transplants for cancers of the blood and lymph nodes. The researchers concluded that the risks of long-term azithromycin exposure after donor stem cell transplantation may exceed the benefits. The trial could not determine why the rates of cancer relapse and death were higher with azithromycin.

The researchers stopped the ALLOZITHRO trial approximately 13 months after the study completed enrollment of 480 patients because an unexpected increase in the rate of both cancer relapses and death was observed in patients taking azithromycin. Cancer relapse was observed in 77 patients (32.9%) with azithromycin treatment compared to 48 patients (20.8%) with placebo, which is an inactive treatment. A total of 95 patients died in the

azithromycin treatment group versus 66 patients in the placebo group; thus, the 2-year survival rate was 56.6% in azithromycin-treated patients compared to 70.1% in those receiving a placebo. In the first few months of the trial, the death rate was about equal between those receiving azithromycin and placebo. However, an imbalance occurred subsequently and continued until the 2-year time point when the study was stopped.

There are no known effective antibiotic treatments for prophylaxis of bronchiolitis obliterans syndrome. Health care professionals should not prescribe long-term azithromycin for prophylaxis of bronchiolitis obliterans syndrome to patients who undergo donor stem cell transplants because of the increased potential for cancer relapse and death.

Patients who have had a stem cell transplant should not stop taking azithromycin without first consulting with health care professionals. Doing so could be harmful without health care professional's direct supervision. Talk with health care professionals if patients have any questions or concerns about taking this medicine.

In Hong Kong, there are 71 registered pharmaceutical products containing azithromycin, and all are prescription-only medicines. As on 5 September 2018, the Department of Health (DH) has received 3 cases of adverse drug reaction related to azithromycin, and these cases are not related to cancer relapse. In view of the above FDA's announcement, DH issued letters to inform local healthcare professionals to draw their attention on the above safety alert on 6 August 2018. DH will remain vigilant on the conclusion of the review by the FDA and any safety updates issued by other overseas drug regulatory authorities for consideration of any action deemed necessary.

Canada: Summary Safety Review - Oral prednisone and prednisolone (glucocorticoids) - Assessing the potential risk of a serious complication called scleroderma renal crisis in patients with systemic sclerosis

On 7 August 2018, Health Canada announced that it reviewed the potential risk of scleroderma renal crisis (SRC) with the use of oral prednisone and prednisolone products in patients with systemic sclerosis. The review was triggered after the European Medicines Agency (EMA) updated the product safety information for oral and injectable prednisone and prednisolone products on 6 July 2017 to include this risk.

Systemic sclerosis (also known as scleroderma) is a rare disease involving an abnormal response from the body's immune system. The disease causes changes in the texture and appearance of the skin, and frequently involves the internal organs. Scleroderma renal crisis is a life-threatening complication of systemic sclerosis that frequently involves severe high blood pressure and declining function of the kidneys.

Prednisone and prednisolone are available in Canada in a variety of forms and combinations. The current review focused only on prednisone and prednisolone products for oral use since this route delivers higher doses of the product throughout the body. Injectable prednisone and prednisolone are not marketed in Canada.

At the time of the review, Health Canada had received 2 Canadian reports of SRC related to the use of prednisone (none for prednisolone). In both reports, there was a possible link found between SRC and the use of prednisone. No Canadian deaths were reported. This review also looked at 6

published international reports of SRC related to the use of prednisone (1 report) and prednisolone (5 reports). In all 6 reports, there was a possible link found between SRC and the use of prednisone or prednisolone, especially at higher doses. Of the 6 international reports, 3 involved death. A possible link between death and the use of prednisolone was found in 1 of these cases. The remaining 2 cases could not be assessed as there was not enough information. Seven out of 8 possible cases of prednisone and prednisolone associated with SRC had other factors present (i.e. medical conditions, other medications) that could have caused SRC. A review of the scientific literature found 6 published studies and 3 review articles that supported an increased risk of SRC in patients with systemic sclerosis treated with prednisone or prednisolone, especially at higher doses.

Health Canada's review of the available information has concluded that there may be a link between the use of oral prednisone and prednisolone products, especially at higher doses, and SRC in patients with systemic sclerosis. Health Canada will be working with the manufacturers to update the Canadian product safety information for oral prednisone and prednisolone products to inform about this risk.

In Hong Kong, there are 4 registered pharmaceutical products containing prednisone, and all of them are oral products. There are also 45 registered oral products and 1 registered injectable product containing prednisolone. All products are prescription-only medicines. As on 5 September 2018, DH has received 5 cases of adverse drug reaction related to prednisone and 41 cases related to prednisolone, but these cases are not related to SRC. In light of the above Health Canada's announcement, DH issued letters to inform local healthcare professionals to draw their attention on the potential risk on 8 August 2018, and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

The United Kingdom: Esmya (ulipristal acetate) and risk of serious liver injury: new restrictions to use and requirements for liver function monitoring before, during, and after treatment

On 24 August 2018, Medicines and Healthcare products Regulatory Agency (MHRA) announced new restrictions to use and requirements for liver function monitoring for Esmya (ulipristal acetate). More than one treatment course is authorised only in women who are not eligible for surgery, and liver function monitoring is to be carried out in all women treated with Esmya. Before initiation, discuss with women the rare risk of liver damage and advise them to seek urgent medical attention if they develop any symptoms or signs of liver injury.

The detailed advice for healthcare professionals are as follows:

<u>Restricted indication and new contraindication</u>:

- Esmya is now indicated for:
  - the intermittent treatment of moderate to severe symptoms of uterine fibroids in women of reproductive age who are not eligible for surgery
  - one treatment course of pre-operative treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age
- Esmya treatment is to be initiated and supervised by physicians experienced in the diagnosis and treatment of uterine fibroids
- Esmya is contraindicated in women with underlying liver disorders

<u>Liver function monitoring</u>:

- before initiation of each treatment course: perform liver function tests; do not initiate Esmya in women with baseline alanine transaminase (ALT) or aspartate

aminotransferase (AST) more than 2-times the upper limit of normal (ULN)
- during the first 2 treatment courses: perform liver function tests every month
- for further treatment courses: perform liver function tests once before each new course and when clinically indicated
- at the end of each treatment course: perform liver function tests after 2-4 weeks
- stop Esmya treatment and closely monitor women with ALT or AST more than 3-times ULN; consider the need for specialist hepatology referral

Discuss the risk of liver damage with Esmya with women and report any suspected adverse drug reactions:

- before initiation of Esmya, discuss with women the rare risk of liver damage and need for liver function testing before, during, and after each treatment course
- advise women to seek urgent medical attention if they develop any symptoms or signs of liver injury (such as tiredness, yellowing of the skin, darkening of the urine, nausea and vomiting)
- pharmacists should provide the new patient card to women when dispensing Esmya; copies of this card are included in the letter sent to healthcare professionals and are available online
- report any suspected adverse drug reactions to Esmya on a Yellow Card without delay

In Hong Kong, Esmya Tablets 5mg (HK-62553) is a pharmaceutical product registered by Orient Europharma Co. Ltd, and is a prescription-only medicine. Related news was previously issued by various overseas drug regulatory authorities, and was reported in the Drug News Issue No. 98, 100 and 103. DH issued letters to inform local healthcare professionals to draw their attention on 12 February 2018. As on 5 September 2018, DH has not received any case of adverse drug reaction related to Esmya. In light of the MHRA's announcement of the new restrictions on use of Esmya, the matter together with the latest safety review by other overseas drug authorities will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

The United States: Updated: Torrent Pharmaceuticals Limited issues voluntary nationwide recall of all lots of unexpired valsartan-containing drug products, and FDA updates recall lists and releases method for the detection and quantification of NDMA in valsartan

On 24 August 2018, FDA announced that Torrent Pharmaceuticals Limited expanded its voluntary recall to all lots of unexpired valsartan-containing drug products due to the detection of N-nitrosodimethylamine (NDMA) in the active pharmaceutical ingredient (API) manufactured by Zhejiang Huahai Pharmaceuticals.

RemedyRepack, a repackager of Torrent's valsartan/amlodipine/hydrochlorothiazide (HCTZ) tablets, has also recalled.

FDA is releasing a gas chromatography-mass spectrometry (GC/MS) headspace method for manufacturers and regulators to detect and quantify NDMA in valsartan API and finished drug products. The agency is using this method to test potential NDMA-containing APIs and drug products. This method should be validated by the user if the resulting data are used to support a required quality assessment of the API or drug product, or if the results are used in a regulatory submission.

FDA has also updated the list of valsartan products under recall and the list of valsartan products not under recall.

In Hong Kong, as on 5 Spetember 2018, there are 83 registered pharmaceutical products containing valsartan, and all products are prescription-only medicines.

A public announcement was issued on 6 July 2018 on the issue, and DH issued letters to inform local healthcare professionals of the latest development, including the affected products, recommendations on drug use and possible risk on 6 July 2018, 9 July 2018, 25 July 2018 and 3 August 2018. Related news was also previously issued by various overseas drug regulatory authorities, and was reported in the Drug News Issue No. 105.

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 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 marketed in Hong Kong. DH instructed the certificate holders to recall all the products from the market as a precautionary measure on 6 July 2018, and DH noted that all the recalls have been completed. The affected products are:

Product	Hong Kong Registration Number	Registration certificate holder
Valtensin 160mg tablets	HK-61786	Actavis Hong Kong Limited
Valtensin 80mg tablets	HK-61787	Actavis Hong Kong Limited
Valtensin HCT tablets 160/12.5mg	HK-61784	Actavis Hong Kong Limited
Valtensin HCT tablets 80/12.5mg	HK-61785	Actavis Hong Kong Limited
Valsartan Stada 80mg tablets	HK-60794	Hong Kong Medical Supplies Ltd

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.

As on 5 September 2018, DH has not received any adverse reactions related to the above products affected by the recall.

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 impurity NDMA contained in valsartan products.

The United States: FDA warns about rare occurrences of a serious infection of the genital area with SGLT2 inhibitors for diabetes

On 29 August 2018, FDA warned that cases of a rare but serious infection of the genitals and area around the genitals have been reported with the

class of type 2 diabetes medicines called sodium-glucose cotransporter-2 (SGLT2) inhibitors. This serious rare infection, called necrotizing fasciitis of the perineum, is also referred to as Fournier's gangrene. FDA is requiring a new warning about this risk to be added to the prescribing information of all SGLT2 inhibitors and to the patient medication guide.

Fournier's gangrene is an extremely rare but life-threatening bacterial infection of the tissue under the skin that surrounds muscles, nerves, fat, and blood vessels of the perineum. The bacteria usually get into the body through a cut or break in the skin, where they quickly spread and destroy the tissue they infect. Having diabetes is a risk factor for developing Fournier's gangrene, however, this condition is still rare among diabetic patients. Overall published literature about the occurrence of Fournier's gangrene for men and women is very limited. Publications report that Fournier's gangrene occurs in 1.6 out of 100,000 males annually in the US, and most frequently occurs in males 50-79 years (3.3 out of 100,000). In the FDA's case series, however, FDA observed events in both women and men.

In the five years from March 2013 to May 2018, FDA identified 12 cases of Fournier's gangrene in patients taking an SGLT2 inhibitor. This number includes only reports submitted to FDA and found in the medical literature, so there may be additional cases about which FDA is unaware. In 2017, an estimated 1.7 million patients received a dispensed prescription for an SGLT2 inhibitor from US outpatient retail pharmacies. Although most cases of Fournier's gangrene have previously been reported in men, the FDA's 12 cases included 7 men and 5 women. Fournier's gangrene developed within several months of the patients starting an SGLT2 inhibitor and the drug was stopped in most cases. All 12 patients were hospitalized and required surgery. Some patients required multiple disfiguring surgeries, some developed complications, and one patient died. In comparison, only six cases of Fournier's gangrene (all in men) were identified in review of other antidiabetic drug classes over a period of more than 30 years.

Patients should seek medical attention immediately if they experience any symptoms of tenderness, redness, or swelling of the genitals or the area from the genitals back to the rectum, and have a fever above 100.4°F (equal to 38°C) or a general feeling of being unwell. These symptoms can worsen quickly, so it is important to seek treatment right away.

Healthcare professionals should assess patients for Fournier's gangrene if they present with the symptoms described above. If suspected, start treatment immediately with broad-spectrum antibiotics and surgical debridement if necessary. Discontinue the SGLT2 inhibitor, closely monitor blood glucose levels, and provide appropriate alternative therapy for glycemic control.

In Hong Kong, there are 17 registered pharmaceutical products containing SGLT2 inhibitors, including canagliflozin (2 products), dapagliflozin (5 products) and empagliflozin (10 products). All products are prescription-only medicines. As on 5 September 2018, DH has received 2 cases of adverse drug reaction related to canagliflozin, 3 cases related to dapagliflozin and 1 case related to empagliflozin, but these cases are not related to Fournier's gangrene. In light of the above FDA's announcement, DH issued letters to inform local healthcare professionals to draw their attention on 30 August 2018, and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

Safety Update

Singapore: Tecentriq® (atezolizumab) and new safety concern of immune-related nephritis

On 30 August 2018, Health Sciences Authority (HSA) announced that Roche Singapore Pte Ltd would like to inform healthcare professionals of the new safety concern of immune-related nephritis associated with Tecentriq® (atezolizumab).

Immune-related nephritis is a rare complication of checkpoint inhibitors therapy, with the most commonly reported underlying pathology being acute tubulo-interstitial nephritis. The most common presentation of immune-related nephritis includes asymptomatic increase in creatinine levels. In the absence of alternative etiologies (e.g. prerenal and postrenal causes, concomitant medications), immune-related nephritis is defined as a renal dysfunction requiring steroids treatment and/or confirmed by biopsy. Healthcare professionals are advised to monitor patients for changes in renal function and to withhold Tecentriq® for moderate (Grade 2) immune-related nephritis, and permanently discontinue Tecentriq® for severe nephritis (Grade 3 and 4). It is also recommended to administer corticosteroids and/or additional immunosuppressive agents as clinically indicated.

Roche Singapore Pte Ltd is working with HSA to update the Singapore package insert for Tecentriq® to include the risk of immune-related nephritis.

In Hong Kong, Tecentriq Concentrate For Solution For Infusion 1200mg/20ml (HK-65567) is a pharmaceutical product registered by Roche Hong Kong Limited (Roche HK), and is a prescription-only medicine. As on 5 September, 2018, DH has received 16 cases of adverse drug reaction related to atezolizumab, but these cases are not related to immune-related nephritis. Roche HK has recently submitted an application to update the package insert of the product, including the safety information on immune-related nephritis. In light of the above HSA's announcement, DH issued letters to inform local healthcare professionals of the safety concern on 31 August 2018, and DH will work with Roche HK to update the product's safety information and will remain vigilant on safety update of the product issued by other overseas drug regulatory authorities.

Drug Recall

Batches recall of Contrave Extended-Release Tablets

On 14 August 2018, DH endorsed a licensed drug wholesaler, Vantone Medical Supplies Co. Ltd (Vantone), to recall two batches of Contrave Extended-Release Tablet (batch numbers: ZCXS and ZCXT) from the market because of a potential quality issue.

The DH received notification from Vantone that the manufacturer of the product in United States advised Vantone to recall two batches of product from the market due to possible punctures in the container of the product. Vantone recalls the affected batches as a precautionary measure.

The above product, containing naltrexone and bupropion hydrocholoride, is not a registered pharmaceutical product in Hong Kong but was imported for the treatment of particular patients by registered medical practitioners. According to Vantone, 10 bottles of the affected batches have been supplied to one private hospital and one local private doctor.

A notice was posted on the website of Drug Office on 14 August 2018 to alert the public of the product recall.

Drug Incident

Public urged not to buy or consume slimming products from unknown sources or of doubtful composition

On 23 August 2018, DH appealed to the public not to buy or consume a slimming product named SUSUYA as it was found to contain an undeclared and banned drug ingredient that might be dangerous to health.

Acting upon intelligence, a sample of the above product was purchased from an Internet seller for analysis. Test results from the Government Laboratory revealed that the sample contains sibutramine and bisacodyl.

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. Bisacodyl is a laxative that may cause abdominal pain.

Weight control should be achieved through a balanced diet and appropriate exercise. The public should consult healthcare professionals before using any medication for weight control.

The public may visit the website of Drug Office of the DH for health messages on overweight problem and slimming products and information on slimming products with undeclared Western drug ingredients.

A notice was posted on the website of the Drug Office on 23 August 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,
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.

ADVERSE DRUG REACTION

Drug Office
Department of Health
Hong Kong SAR

Special Supplement to Drug News Issue No. 106

Background

The Adverse Drug Reaction Reporting System was formerly under Adverse Drug Reaction Monitoring Unit of the Pharmaceutical Service, Department of Health, from year 2005 (Trial run in year 2004). With the establishment of Drug Office in year 2011, Pharmacovigilance Unit under the Pharmacovigilance and Risk Management Division of Drug Office, Department of Health, receives the local adverse drug reaction reports concerning the use of pharmaceutical products from healthcare professionals and pharmaceutical industry.

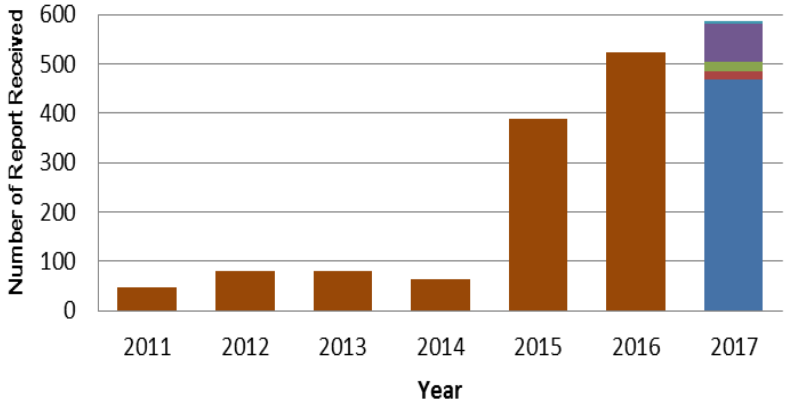
Guidance for Pharmaceutical Industry – Adverse Drug Reaction Reporting Requirements issued by Drug Office (since year 2015) sets out the requirements for reporting adverse drug reactions of all pharmaceutical products in Hong Kong by pharmaceutical industry to Drug Office, Department of Health. Pharmaceutical industry should comply with the guidance and report all serious adverse drug reactions occurring in Hong Kong to Drug Office, Department of Health as soon as possible and no later than 15 calendar days of receipt of information. A serious adverse drug reaction is any untoward medical occurrence that at any dose:

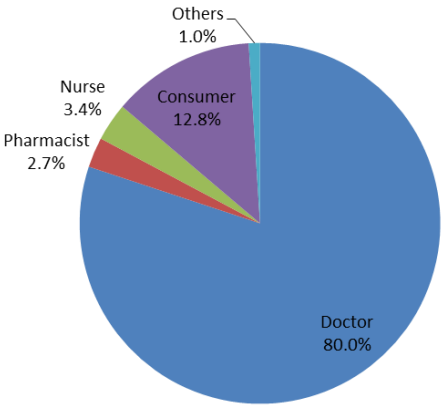
- results in death;
- is life threatening;
- requires inpatient hospitalization or results in prolongation of existing hospitalization;
- results in persistent or significant disability/incapacity;
- is a congenital anomaly/birth defect; or
- is a medically important event or reaction.

Report Analysis for 2017

A. Number of adverse drug reaction (ADR) reports and sources of reports (initial reporters)

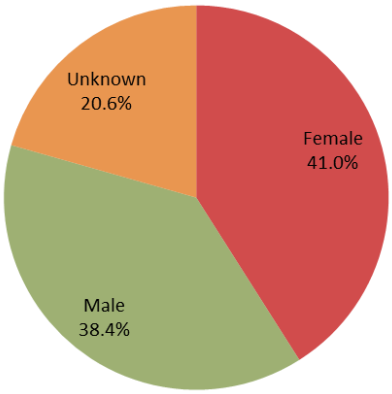
In year 2017, Drug Office received a total of 586 ADR reports (an increase of over 11% when compared with that of year 2016). From year 2004 to year 2017, Drug Office had received over 1900 ADR reports. Among the received ADR reports, Doctor as initial reporter contributed most to the number of reports.

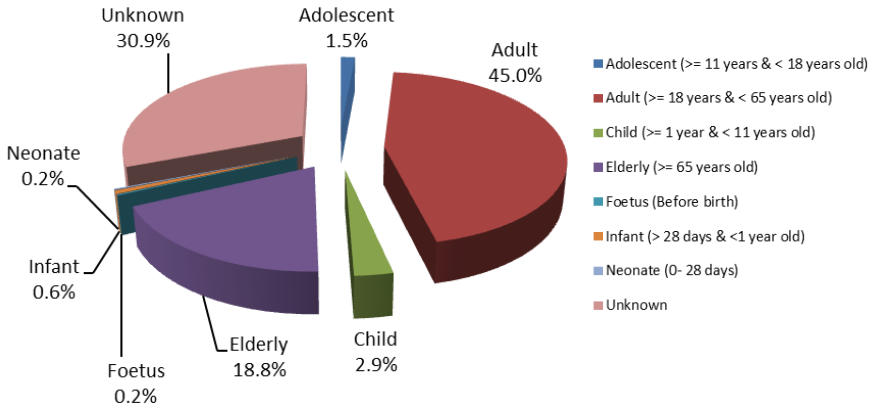




B. Demographics (Age group, Gender) of patients

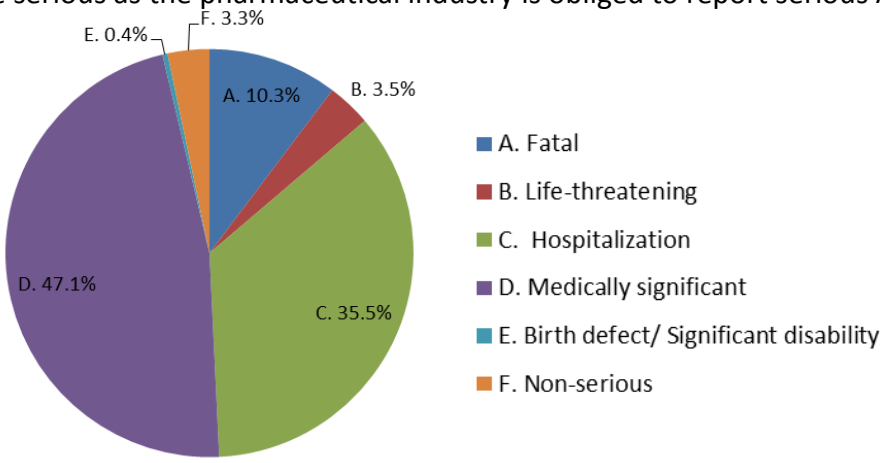
Among the ADR cases received in year 2017, there was no significant difference between the genders. Regarding the age group, 45.0% of the cases were adults. There was no age information provided in around 31% of cases.





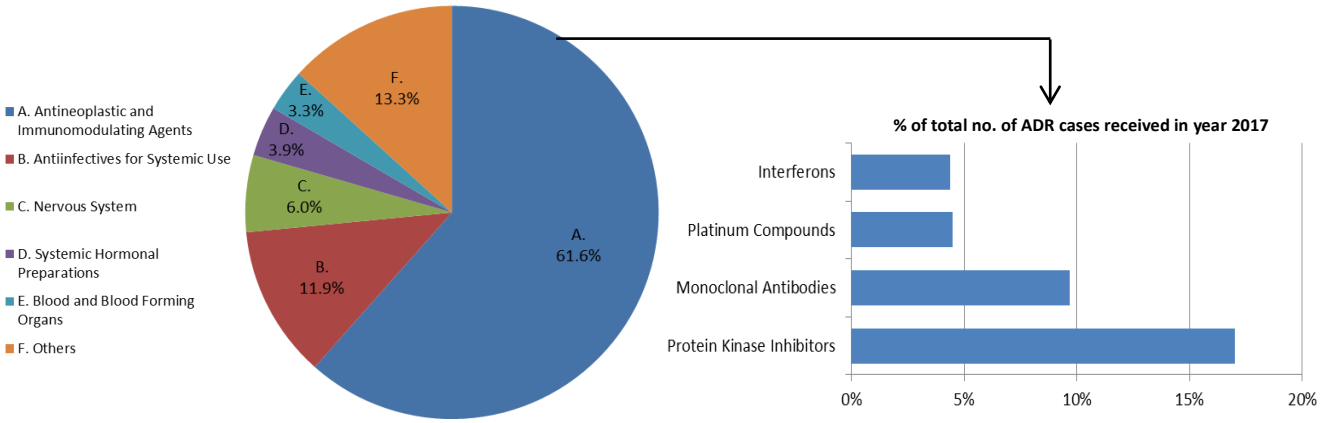
C. Seriousness

Most of the cases were serious as the pharmaceutical industry is obliged to report serious ADR cases.



D. Suspect Drugs*

The top class of suspect drugs received in ADR cases in year 2017 was Antineoplastic and Immunomodulating Agents. Among this class, protein kinase inhibitors, monoclonal antibodies, platinum compounds and interferons were the top 4 types of drugs reported.



** Suspect drugs were classified according to The Anatomical Therapeutic Chemical (ATC) classification system developed by World Health Organization (WHO)*

E. Adverse events

The top System Organ Class (SOC^) reported were General disorders and administration site conditions, followed by Investigations, Gastrointestinal disorders and Blood and lymphatic system disorders, as shown in the table below.

Ranking	System Organ Class	% of cases
1	General disorders and administration site conditions (e.g. injection site reactions, fever)	14.7
2	Investigations (eg. blood creatinine increased, ALT increased)	9.7
3	Gastrointestinal disorders (e.g. abdominal pain, vomiting)	8.7
4	Blood and lymphatic system disorders (e.g. neutropenia, anaemia)	8.6
5	Nervous system disorders (e.g. seizure, headache)	8.2

^The System Organ Class (SOC) refers to the medical terminology MedDRA (Medical Dictionary for Regulatory Authorities)

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

Disclaimers:

Information on suspected ADR should not be interpreted as meaning that the pharmaceutical product in question, or the active substance(s), generally causes the observed effect or is unsafe to use. Any robust conclusion with regard to benefits and risks of a specific pharmaceutical product always requires detailed evaluation and scientific assessment of all available data. The balance between benefit and risk of a specific pharmaceutical product also varies between individual patients. The information in these reports cannot be used to estimate the incidence (occurrence rates) of the reactions reported. If you think that you may be experiencing a side-effect from a pharmaceutical product, please seek advice from a health professional as soon as possible. Never stop or change the dose for prescription medicines without consulting your physician.