Drug News
藥 物 情 報

Issue Number 144

This is a monthly digest of local and overseas drug safety news released by the Drug Office of the Department of Health in October 2021 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

European Union: EMA starts review of meningioma risk with nomegestrol- and chlormadinone-containing medicines

On 1 October 2021, the European Medicines Agency (EMA) announced that it has started a review of medicines containing the active substance nomegestrol or chlormadinone. These medicines can be used, alone or in combination with other active substances, to treat gynaecological disorders such as amenorrhea (absence of menstrual periods) and other menstrual disorders, uterine bleeding, endometriosis (a condition in which tissue similar to the lining of the womb grows elsewhere in the body), breast tenderness, as hormone replacement therapy or as contraceptives (birth control).

The review was requested by the French medicines agency (ANSM) following new data from two epidemiological studies carried out in France in women taking these medicines to investigate the risk of meningioma, a tumour of the membranes covering the brain and spinal cord. This tumour is usually non-malignant and is not considered to be a cancer, but due to their location in and around the brain and spinal cord, meningiomas can in rare cases cause serious problems.

In light of these new data concerning the risk of meningioma, EMA's safety committee (PRAC) will now examine the available evidence and make recommendations as to whether the marketing authorisations for nomegestrol- and chlormadinone-containing medicines should be amended across the EU.

In Hong Kong, there is no registered pharmaceutical products containing nomegestrol. There is 1 registered pharmaceutical product (HK-65918) containing chlormadinone in combination with ethinyloestradiol in tablet dose form. The product is a prescription-only medicine. As of the end of October 2021, the Department of Health (DH) has not received any cases of adverse drug reaction related to chlormadinone. The DH will remain vigilant on the conclusion of the review and any safety updates issued by other overseas drug regulatory authorities for consideration of any action deemed necessary.

The United Kingdom: Chloral hydrate, cloral betaine (Welldorm): restriction of paediatric indication

On 6 October 2021, Medicines and Healthcare products Regulatory Agency (MHRA) announced that the paediatric indication for chloral hydrate (for children aged 2 years and older) and cloral (previously chloral) betaine (children aged 12 years and older) has been restricted to short-term treatment (maximum 2 weeks) of severe insomnia only when the child or adolescent has a suspected or definite neurodevelopmental disorder and when the insomnia is interfering with normal daily life. Chloral hydrate and cloral betaine should only be used when other therapies (behavioural and pharmacological) have failed.

In the United Kingdom (UK), Chloral hydrate (Welldorm Elixir) and its prodrug cloral betaine (Welldorm) are older drugs that retain some limited clinical usage. In 2009, following a national review of safety and efficacy, the authorisation for these medicines was restricted to severe insomnia that is interfering with normal daily life and where other therapies have failed, as an adjunct to non-pharmacological therapies. Chloral hydrate is licensed for use in adults and in children aged 2 years and older. Cloral betaine tablets are licensed for use in adults and adolescents aged 12 years and older.

The MHRA has conducted a further review of safety and efficacy data for these medicines and sought independent expert advice from the Commission on Human Medicines (CHM), its Neurology, Pain and Psychiatry and Paediatric Medicines Expert Advisory Groups, as well as experts in paediatric sleep disorders.

No new safety concerns were identified. However, in view of known carcinogenicity data in animals and because of concerns regarding the lack of long-term studies, a risk in humans in long-term use cannot be excluded on the basis of available data. As such, the CHM recommended that the paediatric indication of all chloral hydrate and cloral betaine products should be restricted to use only in children and adolescents with suspected or definite neurodevelopmental disorders, where the benefits of short-term use outweigh any potential risk. These changes reflect current clinical practice.

In UK, the product information is being amended to further clarify that use of chloral hydrate and cloral betaine is not recommended in children and adolescents except in these very restricted circumstances and should only be under the supervision of a specialist

Prolonged use of chloral hydrate and cloral betaine has been associated with tolerance and the risks of dependence and abuse. The maximum treatment period for these medicines in all patients has now been defined as 2 weeks in the product information.

Repeated courses are not recommended and can only be administered following medical specialist re-assessment. Following prolonged treatment, the dose should be slowly tapered before discontinuation to avoid delirium.

For the off-label use, the MHRA are aware that chloral hydrate is used for sedation in children, for example in intensive care units and before diagnostic procedures. The immature metabolism of infants and neonates results in a prolonged half-life of metabolites in these groups, with an increased risk of undesirable effects. This factor and the lack of long-term studies to demonstrate safety should be taken into account when considering prescribing in this population outside the currently licensed indication.

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In Hong Kong, there are 3 registered pharmaceutical products containing chloral hydrate, including Syrup of Chloral 1g/5mL (HK-21514), PMS-Chloral Hydrate Syrup 100mg/mL (HK-62019) and Migaphen Cap (HK-44850). All these products are prescription only medicines. There is no registered pharmaceutical product in Hong Kong for cloral betaine.

As of the end of October 2021, the Department of Health (DH) has received one case of adverse drug reaction (ADR) with chloral hydrate, which is not related to the carcinogenic risks and long-term use mentioned in the above MHRA announcement; and no ADR report has been received for cloral betaine. In light of the above MHRA announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 7 October 2021, and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board .

The United Kingdom: Tofacitinib (Xeljanz): new measures to minimise risk of major adverse cardiovascular events and malignancies

On 6 October 2021, Medicines and Healthcare products Regulatory Agency (MHRA) announced that tofacitinib should not be used in patients older than 65 years of age, people who are current or past smokers, or individuals with other cardiovascular (such as diabetes or coronary artery disease) or malignancy risk factors unless there are no suitable treatment alternatives.

Information on cardiovascular events

A clinical safety trial in patients with rheumatoid arthritis aged 50 years or older with at least one cardiovascular risk factor (Study A3921133) found that a Janus kinase (JAK) inhibitor tofacitinib was associated with an increased risk of major adverse cardiovascular events compared with TNF-alpha inhibitors (etanercept or adalimumab). The predictive risk factors identified were: age older than 65 years, current or past smoking, history of diabetes, and history of coronary artery disease (including past myocardial infarction, coronary heart disease, stable angina pectoris, or coronary artery procedures). Healthcare professionals are advised to only consider use of tofacitinib in patients with these cardiovascular risk factors, irrespective of indication, if no suitable treatment alternative is available.

Information on malignancy

The same clinical safety trial in patients with at least one cardiovascular risk factor (some of which are also malignancy risk factors) found that

tofacitinib was associated with an increased risk of malignancies (with the analysis excluding non-melanoma skin cancer [NMSC]), particularly lung cancer and lymphoma, compared with TNF-alpha inhibitors. The predictive risk factors identified were: age older than 65 years and current or past smoking. Healthcare professionals are advised to only consider use of tofacitinib in patients with these and other malignancy risk factors (current or previous history of malignancy other than successfully treated NMSC), irrespective of indication, if no suitable alternative treatment is available.

Advice for healthcare professionals to give to patients:

- tofacitinib treatment has been associated with an increased risk of heart attacks and certain cancers compared with another type of treatment (TNF-alpha inhibitors) – the incidence of these events is low and they have been linked to existing risk factors for these conditions such as older age or smoking
- patients who are already at increased risk of cardiovascular events or cancers should only be offered treatment with tofacitinib if their doctor feels there are no other suitable treatment options for their condition
- do not stop taking tofacitinib without first talking to the doctor
- read accompanied product information and communicate with the healthcare professionals for the concern about any side effects

In the United Kingdom (UK), tofacitinib (Xeljanz) is a Janus kinase (JAK) inhibitor authorised for the treatment of rheumatoid arthritis, psoriatic arthritis, and ulcerative colitis. Study ORAL Surveillance (A3921133) was a large, randomised, active-controlled, clinical safety trial to evaluate the safety of tofacitinib versus tumour necrosis factor (TNF)-alpha inhibitors. The study involved 4,362 patients with rheumatoid arthritis aged 50 years or older and with at least one additional cardiovascular risk factor. In 2018, secondary findings of this study led to new measures to minimise risks of venous thromboembolism and serious and fatal infections with tofacitinib.

The co-primary endpoints of study A3921133 were adjudicated major adverse cardiac events and adjudicated malignancies (with the analysis excluding non-melanoma skin cancer).

Doses of tofacitinib included in the study were 5mg twice-daily and 10mg twice-daily and endpoints in these groups were compared with those from patients randomised to TNF-alpha inhibitors (etanercept, 50mg once a week subcutaneously, or adalimumab, 40mg once every other week subcutaneously).

In 2021, final results from study A3921133 showed tofacitinib to be associated with an increased incidence of non-fatal myocardial infarction and malignancies, particularly lung cancer and lymphoma.

These results prompted a review into these risks of tofacitinib and how they should be minimised. Prescribers of tofacitinib were informed of the final trial results in a letter in March 2021 with a further letter with the final recommendations sent in July 2021. In the UK, the product information and educational materials for healthcare professional and patients will also be updated with this information.

In Hong Kong, there are 3 registered pharmaceutical products containing tofacitinib, namely Xeljanz Tablets 5mg (HK-63303), Xeljanz XR Extended Release Tablets 11mg (HK-66141) and Xeljanz Tablets 10mg (HK-66833) which are registered by Pfizer Corporation Hong Kong Limited. All products are prescription-only medicines. As of the end of October 2021, the Department of Health (DH) has received 8 cases of adverse drug reaction related to tofacitinib (of which one case is lung cancer and 3 cases are deep vein thrombosis).

Related news on the risk of serious heart-related problems and cancer of tofacitinib was previously issued by various overseas drug regulatory authorities, and was reported on Drug News Issues Nos. 136, 137, 138, 140 and 143. The DH issued letters to inform local healthcare professionals to draw their attention on 15 June 2021. As previously reported, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board .

Singapore: Sertraline and microscopic colitis

On 18 October 2021, Health Sciences Authority (HSA) advised healthcare professionals on the potential risk of microscopic colitis associated with the use of sertraline.

Microscopic colitis is a rare inflammatory disorder

of the colon. It presents with chronic, non-bloody diarrhoea, abdominal pain, weight loss and fatigue. It can be divided into two subtypes, namely lymphocytic colitis or collagenous colitis, which are clinically indistinguishable but have different histopathologic features. Both subtypes are typically characterised by a marked and diffuse excess of lymphocytes interspersed among the surface colonocytes and within the lamina propria. In collagenous colitis, a subepithelial collagen band can be seen in the colon on biopsy in addition to increased intraepithelial lymphocytes. The exact mechanism of microscopic colitis is poorly understood; an inflammatory mechanism triggered by environmental factors such as an infection, toxin or drugs has been suggested.

In 2013, a Spanish prospective case-control study which investigated the epidemiological risks factors in microscopic colitis found sertraline to be associated with an increased risk for lymphocytic colitis. The study included 120 patients with collagenous colitis, 70 with lymphocytic colitis and 128 controls from teaching and community hospitals across Spain from Mar 2007 to May 2010. Drug exposure before the onset of diarrhoea (for cases) or at study recruitment (for controls) was recorded for medicines taken ≥ 3 days per week for ≥ 2 weeks. Of the patients recruited, seven lymphocytic colitis cases and none of the controls took sertraline, contributing to a statistically significant association between sertraline intake and lymphocytic colitis [odds ratio 17.5 (2.0-149.2)]. These findings were similar to those from an earlier case-control study and were in line with the documented association of sertraline with high likelihood of triggering microscopic colitis.

Three case reports of microscopic colitis related to the use of sertraline described patients who presented with prolonged non-bloody diarrhoea lasting from over 20 days to three months, resulting in substantial weight loss of up to 20 kg in one report from the literature. In all three cases, microscopic colitis associated with sertraline was diagnosed based on temporal association with sertraline initiation and biopsies from the colon and/or rectum that revealed an increase in intraepithelial lymphocytes, which is characteristic of the condition. All the patients recovered upon discontinuation of sertraline.

To date, HSA has received five ADR reports of diarrhoea associated with the use of sertraline, none of which involved microscopic colitis.

Based on post-marketing experience, the association of microscopic colitis with sertraline use has been reported overseas and in published literature. HSA is working with the product registrants of sertraline-containing products to update the local package insert to include microscopic colitis as an adverse event that has been observed in the post-market setting.

While microscopic colitis related to the use of sertraline can result in severe prolonged diarrhoea and substantial weight loss, published case reports revealed that the condition resolved progressively following swift cessation of sertraline. Healthcare professionals are advised to consider the possibility of this adverse event in patients on sertraline who present with prolonged or severe diarrhoea.

In Hong Kong, there are 20 registered pharmaceutical products containing sertraline, and all products are prescription-only medicines. As of the end of October 2021, the Department of Health (DH) has received 3 cases of adverse drug reaction related to sertraline, but these cases are not related to microscopic colitis. Related news was previously issued by Australia Therapeutic Goods Administration and was reported on Drug News Issue No. 140. The DH issued letters to inform local healthcare professionals to draw their attention on 23 June 2021. As previously reported, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board .

Singapore: Anaphylaxis post-COVID 19 mRNA vaccines

On 18 October 2021, Health Sciences Authority (HSA) announced that, with the use of the two mRNA vaccines, the Pfizer-BioNTech (Pfizer) and Moderna vaccines internationally, rare reports of anaphylaxis, a severe life-threatening allergic reaction, started to be reported. Locally, HSA has received 58 adverse event (AE) reports from healthcare professionals on anaphylaxis which were adjudicated by its expert panel on hypersensitivity reactions based on the Brighton Collaboration Case Definition criteria. HSA would like to provide a brief update on these cases and the measures in place by HSA to mitigate the risk of anaphylaxis in individuals given the mRNA vaccines.

As of 31 Jul 2021, 58 local AE reports were adjudicated to be anaphylaxis. The overall incidence of anaphylaxis with the mRNA vaccines

is estimated to be 0.86 per 100,000 administered doses, which is similar to the incidence rate reported overseas. Forty-seven (81%) of these cases were reported with Pfizer vaccine and 11 with Moderna vaccine. Twenty-nine cases were assigned level 1 Brighton level of diagnostic certainty, 28 as level 2 and the remaining one as level 3. Forty (69%) cases occurred with dose 1 and 18 cases occurred with dose 2 vaccination. Forty-eight of these 58 cases (83%) involved females. The median age of the 58 patients was 42 years (range: 16 to 76 years). Forty-one (71%) patients had a known history of atopy, allergies, or allergic reactions to drugs and/or foods. For most cases (66%), the interval from vaccination to onset of symptoms were within 30 minutes. Majority of the patients were treated with epinephrine as part of the management. Twenty-seven patients were hospitalised for observation and 30 were treated in the emergency department. All of the 58 patients have since recovered.

Several measures have been introduced to mitigate the risks of anaphylaxis with mRNA vaccines. They include:

- Pre-vaccination screening prior to vaccination. Individuals with a history of allergic reaction or anaphylaxis to mRNA COVID-19 vaccine or any of its components are not recommended to receive the vaccine.
- Observing individuals closely for 30 minutes after vaccination and giving post-vaccination advice to watch out for signs and symptoms of severe allergic reaction, and to seek immediate medical attention should they experience them.
- Ensuring that all vaccination centres are medically equipped and staffed by qualified medical professionals at all times to provide medical treatment in the rare event that they are needed.
- Healthcare professionals are required to report all suspected serious adverse events associated with COVID-19 vaccines to HSA. The reports will allow better computation of the frequency of AEs in Singapore and potentially in subgroups of individuals, for the monitoring of the safety of these vaccines to ensure that their benefits continue to outweigh their risks.

In Hong Kong, the above products are not registered pharmaceutical products under the Pharmacy and Poisons Ordinance (Cap. 138). The COVID-19 vaccine by Fosun Pharma/BioNTech (i.e. Comirnaty) is authorised for emergency use in Hong Kong in accordance with the Prevention and Control of Disease (Use of Vaccines) Regulation (Cap. 599K). Safety information on the risk of anaphylaxis has already been included in the local package insert of Comirnaty. The Department of Health will remain vigilant on any safety update of the product issued by other overseas drug regulatory authorities.

Australia: Octreotide and atrioventricular block

On 25 October 2021, the Therapeutic Goods Administration (TGA) announced that atrioventricular blocks (including complete atrioventricular block) has been reported in patients receiving high doses of continuous intravenous infusion (100 micrograms/hour) of octreotide and in patients receiving bolus octreotide intravenously (50 micrograms bolus followed by 50 micrograms/hour continuous infusion) in Europe. In Australia, the approved indications for octreotide do not involve intravenous administration.

The TGA has evaluated the risk of atrioventricular blocks associated with octreotide treatment in the Australian context. In Australia, the route of administration approved for octreotide products is only subcutaneous injection for the registered indications, while the trade name Sandostatin LAR may only be administered by deep intragluteal injection.

In Europe, octreotide (but not Sandostatin LAR) is approved for use in bleeding gastro-oesophageal varices with a continuous intravenous infusion as the route of administration. The European Union Summary of Product Characteristics (SmPC) for octreotide has been updated to advise that the maximum dose of 50 micrograms/hour should not be exceeded and that patients receiving high doses of intravenous octreotide should be kept under appropriate cardiac monitoring.

In Australia, some clinical guidelines, discuss the off-label use of octreotide in bleeding oesophageal varices with a dose of 50 micrograms by intravenous injection, followed by 50 micrograms/hour by continuous intravenous infusion for up to 5 days.

With this in mind, the TGA is advising health professionals of the identified risk of atrioventricular blocks in patients receiving off-label high doses of continuous infusion (100 micrograms/hour) of octreotide and in patients

receiving bolus octreotide intravenously (50 micrograms bolus followed by 50 micrograms/hour continuous infusion).

The severity of atrioventricular block varies, with complete heart block resulting in cardiac arrest. Treatment may include pacemaker insertion. The TGA has not seen an increase of adverse events of atrioventricular block associated with octreotide.

In Hong Kong, there are 13 registered pharmaceutical products containing octreotide, and all products are prescription-only medicines. Of the 13 products, 3 products (Sandostatin LAR) may only be administered by deep intragluteal injection; the other 10 products can be administered intravenously. As of the end of October 2021, the Department of Health (DH) has received one case of adverse drug reaction related to octreotide, but this case is not related to atrioventricular block. In light of the above TGA's announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 25 October 2021, and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board .

European Union: PRAC assessing further data on risk of myocarditis and pericarditis with mRNA vaccines

On 29 October 2021, the European Medicines Agency (EMA) announced that their safety committee (PRAC) is assessing further data providing more information on the risk of myocarditis and pericarditis following vaccination with COVID-19 vaccines Comirnaty and Spikevax (previously COVID-19 Vaccine Moderna).

Myocarditis and pericarditis are inflammatory conditions of the heart. Symptoms can vary but often include breathlessness, a forceful heartbeat that may be irregular (palpitations), and chest pain.

The PRAC had previously reviewed cases of myocarditis and pericarditis spontaneously reported in the European Economic Area (EEA). The review concluded in July 2021 with a recommendation to list both conditions as side effects in the product information for these vaccines, together with a warning to raise awareness among healthcare professionals and people getting these vaccines.

The committee has now asked the companies that market these vaccines to perform an in-depth review of all published data on the association of myocarditis and pericarditis, including clinical trial data, data from the literature and data available in the public domain. EMA will continue to monitor the vaccines' safety and effectiveness and will communicate further when new information becomes available.

In Hong Kong, the above products are not registered pharmaceutical products under the Pharmacy and Poisons Ordinance (Cap. 138). The COVID-19 vaccine by Fosun Pharma/BioNTech (i.e. Comirnaty) is authorised for emergency use in Hong Kong in accordance with the Prevention and Control of Disease (Use of Vaccines) Regulation (Cap. 599K). The package insert of Comirnaty has already been updated to include myocarditis and pericarditis as its adverse reactions. Related news was previously issued by various overseas drug regulatory authorities, and was reported on Drug News Issues Nos. 140 and 141. The DH issued letters to inform local healthcare professionals to draw their attention on 28 Jun 2021. The DH will remain vigilant on any safety update of the product issued by other overseas drug regulatory authorities.

European Union: COVID-19 vaccines: PRAC finds insufficient evidence on a possible link with multisystem inflammatory syndrome

On 29 October 2021, the European Medicines Agency (EMA) announced that their safety committee (PRAC) has concluded that there is currently insufficient evidence on a possible link between COVID-19 vaccines and very rare cases of multisystem inflammatory syndrome (MIS).

MIS is a rare serious inflammatory condition affecting many parts of the body and symptoms can include tiredness, persistent severe fever, diarrhoea, vomiting, stomach pain, headache, chest pain and difficulty breathing. MIS has previously been reported following COVID-19 disease.

The committee's assessment is based on the available spontaneous reports and currently does not warrant an update of the product information.

The PRAC encourages all healthcare professionals to report any cases of MIS that may have occurred after vaccination and other adverse events in people receiving these vaccines. EMA will continue to closely monitor any new reports of the condition and take appropriate measures if necessary.

Safety Update

In Hong Kong, the above products are not registered pharmaceutical products under the Pharmacy and Poisons Ordinance (Cap. 138). The COVID-19 vaccine by Fosun Pharma/BioNTech (i.e. Comirnaty) is authorised for emergency use in Hong Kong in accordance with the Prevention and Control of Disease (Use of Vaccines) Regulation (Cap. 599K). Related news was previously issued by EMA and was reported on Drug News Issue No. 143. The Department of Health will remain vigilant on any safety update of the product issued by other overseas drug regulatory authorities.

European Union: Imbruvica: risk of sudden or cardiac death not linked to concomitant use of ACE inhibitors

On 29 October 2021, the European Medicines Agency (EMA) announced that their safety committee (PRAC) has concluded the review of a safety signal of sudden or cardiac death with Imbruvica (ibrutinib) when used in combination with angiotensin-converting enzyme (ACE) inhibitors.

Imbruvica is a medicine for treating the blood cancers mantle cell lymphoma, chronic lymphocytic leukaemia (CLL) and Waldenström's macroglobulinaemia (also known as lymphoplasmacytic lymphoma).

Interim data from a clinical trial suggested that the risk of sudden or cardiac death in patients on an ACE inhibitor when entering the study may be increased in patients randomised to ibrutinib and rituximab, compared to those randomised to fludarabine, cyclophosphamide and rituximab.

After reviewing additional analyses from different sources including other clinical trials, the PRAC has concluded that the possible association between treatment with Imbruvica with concomitant use of ACE inhibitors and the risk of sudden or cardiac death does not seem to be plausible.

Among the patients enrolled in the clinical trials sponsored by the marketing authorisation holder, there were no statistically significant differences in events of sudden or cardiac death between those treated with ACE inhibitors and Imbruvica, and those who received ACE inhibitors and a comparator.

The committee has therefore decided that although some cardiac adverse reactions are already known for Imbruvica, a further analysis of serious cardiac events is considered necessary in order to determine if these events might be linked to the use of Imbruvica alone and better characterise the risk of cardiotoxicity with the medicine, regardless of ACE inhibitor use.

The further review will be performed through a separate regulatory procedure, therefore this signal procedure is closed.

In Hong Kong, there are 4 registered pharmaceutical products containing ibrutinib, namely Imbruvica Capsules 140mg (HK-64088), Imbruvica Capsules 140mg (HK-65397), Imbruvica Tablets 140mg (HK-67062) and Imbruvica Tablets 280mg (HK-67063). The products are registered by Johnson & Johnson (Hong Kong) Ltd., and are prescription-only medicines. As of the end of October 2021, the Department of Health (DH) has received 17 cases of adverse drug reaction related to ibrutinib, but these cases are not related to sudden or cardiac death. Related news was previously issued by EMA and was reported on Drug News Issue No. 143. The DH will remain vigilant on any safety update of the drug issued by other overseas drug regulatory authorities.

Drug Recall

Recall of "Tarceva Tablet 100mg"

On 15 October 2021, the Department of Health (DH) endorsed a licensed drug wholesaler, Roche Hong Kong Limited (Roche), to recall a batch (batch number: M1026MC) of Tarceva Tablet 100mg (Hong Kong registration number: HK-57440) from the market as a precautionary measure because incorrect batch number was printed on the blister foils of the batch of product.

The DH received notification from Roche that a customer found an incorrect batch number (M1626MC) appeared on the blister foils of a recent delivery of the product. According to Roche, the product was manufactured and packed by an overseas manufacturer and has been supplied to two private hospitals and a private clinic as well as re-exported to Macao. As a precautionary measure, Roche is voluntarily recalling the batch from the market.

The above product containing erlotinib is a prescription medicine used for treatment of lung cancer and pancreatic cancer.

As of the end of October 2021, the DH has not received any adverse reaction reports in connection with the affected product. A notice was posted on the Drug Office website on 15 October 2021 to alert the public of the product recall. The DH will closely monitor the recall.

Recall of Aprovel Tablets and CoAprovel Tablets

On 21 October 2021, the Department of Health (DH) endorsed a licensed drug wholesaler, Sanofi Hong Kong Limited, to recall five batches of the following four products from the market as a precautionary measure due to the presence of an impurity in the products.

Name of product	Hong Kong registration number	Batch number
Aprovel Tablets 150mg	HK-42891	AA365
Aprovel Tablets 300mg	HK-42892	AA691
CoAprovel Tablets 150/12.5mg	HK-49777	AA557
CoAprovel Tablets 300/12.5mg	HK-49778	AA510, AA549

The DH received notification from Sanofi on 21 October 2021 of the finding by the overseas manufacturers that the active pharmaceutical ingredient of the above batches of products contains a higher than accepted level of azido impurity. As a precautionary measure, Sanofi is voluntarily recalling the above batches of the products from the market.

Azido impurity is considered a mutagen that can cause a change in the DNA of a cell and may increase the risk of cancer, but the risk of causing cancer in humans is unknown. Overseas drug regulatory authorities have been reviewing the safety impact of azido impurity found in medicinal products. The DH will closely monitor the development of the issue and any safety updates regarding the drug issued by overseas drug regulatory authorities for consideration of any necessary action.

The above products are prescription medicines used to lower blood pressure. According to Sanofi, the products have been imported into Hong Kong and supplied to Hospital Authority hospitals, clinics of the DH, private hospitals, private doctors and community pharmacies as well as re-exported to Macao.

As of the end of October 2021, the DH has not received any adverse reaction reports in connection with the affected products. A press release was posted on the Drug Office website on 21 October 2021 to alert the public of the product recall. The DH will closely monitor the recall .

Batch Recall of "Chloroquine Phosphate Tablets 250mg"

On 22 October 2021, the Department of Health (DH) endorsed a licensed drug wholesaler, Ceutical Trading Company Limited (Ceutical), to recall a batch (batch number: 20200315) of "Chloroquine Phosphate Tablets 250mg" from the market due to quality issue.

The DH received notification from Ceutical on 22 October 2021 stating that the supplier in Mainland China informed them the active ingredient content was found below the accepted limit by the National Medical Products Administration of Mainland China.

According to Ceutical, the product was manufactured by a manufacturer in Mainland China and has only been imported and supplied to hospitals of the Hospital Authority.

The above product containing chloroquine phosphate is a prescription medicine used for treatment and prevention of malaria and amebiasis. The product was unregistered but imported for the treatment of particular patients by the Hospital Authority.

As of the end of October 2021, the DH has not received any adverse reaction reports in connection with the affected product. A notice was posted on the Drug Office website on 22 October 2021 to alert the public of the product recall. The DH noted that the recall was completed.

Batch Recall of "Orphenadrine Citrate Extended Release Tablets 100mg"

On 29 October 2021, the Department of Health (DH) endorsed a licensed drug wholesaler, Trackcircle.com Limited (Trackcircle), to recall a batch (batch number: JY6254) of Orphenadrine Citrate Extended Release Tablets 100mg from the

Drug Recall

market due to the presence of an impurity in the product.

The DH received notification from Trackcircle on 29 October 2021 stating that the overseas manufacturer informed them that the above batch of product contains a nitrosamine impurity, namely N-methyl-N-nitroso-2-[(2 methylphenyl) phenylmethoxy]ethanamine, exceeding the accepted level. As a precautionary measure, Trackcircle is voluntarily recalling the above batch from the market.

Some nitrosamine impurities are classified as probable or possible human carcinogens, based on laboratory tests such as rodent carcinogenicity studies. Overseas drug regulatory authorities have been reviewing the safety impact of nitrosamine impurities found in medicinal products. The DH will closely monitor the development of the issue and any safety updates issued by drug regulatory authorities for consideration of any necessary follow-up action.

The above product contains the active ingredient orphenadrine citrate and is a prescription medicine used for the treatment of muscle spasms. The product was unregistered but imported for the treatment of particular patients by the Hospital Authority.

As of the end of October 2021, the DH has not received any adverse reaction reports in connection with the above batch of product. A notice was posted on the Drug Office website on 29 October 2021 to alert the public of the product recall. The DH will closely monitor the recall.

Drug Incident

Woman arrested for suspected illegal sale of slimming product with undeclared banned drug ingredient

On 21 October 2021, the Department of Health (DH) conducted an operation against the sale of a slimming product, which was found to contain an undeclared and banned drug ingredient. During the operation, a 46-year-old woman was arrested by the Police for the suspected illegal sale of a Part 1 poison and an unregistered pharmaceutical product.

Acting upon intelligence, a sample of the above suspected unregistered pharmaceutical product was purchased via a social media platform for analysis. Test results from the Government Laboratory revealed that the oral tablets included in the sample contained sibutramine, which is a banned ingredient. The DH's investigation is continuing.

Sibutramine is a Part 1 poison under the Pharmacy and Poisons Ordinance (Cap. 138) that was once used as an appetite suppressant. Since November 2010, pharmaceutical products containing sibutramine have been banned in Hong Kong because of an increased cardiovascular risk.

Press release was posted on the Drug Office website on 21 October 2021 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 $50,000 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 accordance 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.

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: Adverse Drug Reaction and Adverse Event Following Immunization Unit,
Drug Office, Department of Health,
Room 1856, 18/F, Wu Chung House,
213 Queen's Road East,
Wanchai, 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.