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Dear Healthcare Professionals,

Update to information on psychiatric disorders for chloroquine and hydroxychloroquine

Your attention is drawn to the European Medicines Agency's (EMA) safety committee Pharmacovigilance Risk Assessment Committee (PRAC) is recommending to update the product information for all chloroquine or hydroxychloroquine-containing medicines following a review of all available data that confirmed a link between the use of these medicines and the risk of psychiatric disorders and suicidal behaviour.

The review was initiated in May 2020 after EMA had been informed by the Spanish Medicines Agency AEMPS of six cases of psychiatric disorders in patients with COVID-19 who were given higher than authorised doses of hydroxychloroquine. Chloroquine and hydroxychloroquine are authorised in the EU for the treatment of certain autoimmune diseases, such as rheumatoid arthritis and lupus, as well as for prophylaxis and treatment of malaria. They are not authorised for the treatment of COVID-19, but both medicines have been used as off-label treatment in patients with the disease. However, chloroquine and hydroxychloroquine have not shown any beneficial effects in treating COVID-19 in large randomised clinical trials.

In view of their use during the COVID-19 pandemic, EMA had reminded healthcare professionals of the risks of these medicines in April and in May 2020. It is already known that chloroquine and hydroxychloroquine, even used in approved doses for authorised indications, can cause a wide spectrum of psychiatric disorders. Psychotic disorders and suicidal behaviour are listed in the product information of some chloroquine or hydroxychloroquine-containing medicines as rare side effects or side effects occurring at an unknown frequency.

The review confirmed that psychiatric disorders have occurred and may sometimes be serious, both in patients with and without prior mental health problems. Based on the available data, the review showed that, for hydroxychloroquine, the side effects may occur in the first month after the start of treatment. For chloroquine, there was not sufficient data to establish a clear timeframe.

The PRAC recommends updating the product information for these medicines to provide better information to healthcare professionals and patients on the risk of suicidal behaviour and psychiatric disorders.

Patients using chloroquine or hydroxychloroquine medicines who experience mental health problems (e.g. irrational thoughts, anxiety, hallucinations, feeling confused or feeling depressed, including thoughts of self-harm or suicide), or others around them who notice these side effects, should contact a doctor straight away.

Please refer to the following website in EMA for details:
https://www.ema.europa.eu/en/news/meeting-highlights-pharmacovigilance-risk-assessment-committee-prac-23-26-november-2020

In Hong Kong, there are 5 registered pharmaceutical products containing hydroxychloroquine, and all products are prescription-only medicines. There is no registered pharmaceutical product containing chloroquine. So far, the Department of Health (DH) has received 4 cases of adverse drug reaction related to hydroxychloroquine, but these cases are not related to suicidal behaviour or psychiatric disorders. The DH has not received any case of adverse drug reaction related to chloroquine.

Rare adverse effects of chloroquine and hydroxychloroquine about mental changes including psychotic episodes and hallucinations, delirium, anxiety, and agitation, insomnia, depression, and personality changes are documented in overseas reputable drug references such as the "Martindale: The Complete Drug Reference". In light of the above EMA's announcement, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board. Healthcare professionals are advised to balance the risk of possible adverse effects against the benefit of treatment.

Please report any adverse events caused by drugs to the Undesirable Medical Advertisements and Adverse Drug Reaction Unit of the DH (tel. no.: 2319 2920, fax: 2319 6319 or email: adr@dh.gov.hk). For details, please refer to the website at Drug Office under "ADR Reporting": http://www.drugoffice.gov.hk/adr.html. You may wish to visit the Drug Office's website for subscription and browsing of "Drug News" which is a monthly digest of drug safety news and information issued by Drug Office.

Yours faithfully,

(Joseph LEE)
for Assistant Director (Drug)