MedWatch The FDA Safety Information and Adverse Event Reporting Program

Direct-Acting Antivirals for Hepatitis C: Drug Safety Communication – Risk of Hepatitis B Reactivating

[Posted 10/04/2016]

FDA 發布一則安全簡訊，C 型肝炎治療用藥 Direct-Acting Antiviral (DAA) 有誘發 B 型肝炎病毒再活化的風險。根據通報至 FDA 的不良反應，其中有少數案例導致嚴重的肝臟問題或者是死亡。而 B 型肝炎病毒再活化的發生時間通常在使用 Direct-Acting Antiviral (DAA)的 4-8 週內。
FDA 要求 Direct-Acting Antiviral (DAA)藥物於仿單的黑框警語新增有 B 型肝炎再復發的風險，同時也提醒醫療人員做 B 肝病毒的監測。警語也會一併新增於病患用藥資訊與用藥指南。

建議：
醫療人員在病患開始使用 Direct-Acting Antiviral (DAA)前，應該先篩檢病人是否感染 B 型肝炎，並在治療過程與結束後，檢驗追蹤 B 型肝炎是否再復發。

病患在治療 C 型肝炎前如果有 B 型肝炎病史或其他肝臟疾病應先告知醫療人員。在開始使用 Direct-Acting Antiviral (DAA)後，不應該在沒有告知醫療人員的情況下自行停用藥物，因為可能會使藥物對病毒的反應效果變差。病患也應詳讀每次新處方開立的藥品使用資訊。服用藥品後如果有疲倦、虛弱、食慾不振、噁心、嘔吐，眼睛或皮膚變黃、糞便顏色變淡等肝臟疾病的症狀時請立即連絡醫療人員。

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AUDIENCE: Infectious Disease, Gastroenterology, Patient

ISSUE: The FDA is warning about the risk of hepatitis B virus (HBV) becoming an active infection again in any patient who has a current or previous infection with HBV and is treated with certain direct-acting antiviral (DAA) medicines for hepatitis C virus. In a few cases, HBV reactivation in patients treated with DAA medicines resulted in serious liver problems or death. HBV reactivation usually occurred within 4-8 weeks.

As a result, FDA is requiring a Boxed Warning, our most prominent warning, about the risk of HBV reactivation to be added to the drug labels of these DAAs directing health care professionals to screen and monitor for HBV in all patients receiving DAA treatment. This warning will also be included in the patient information leaflet or Medication Guides for these medicines.

BACKGROUND: Direct-acting antiviral medicines are used to treat chronic hepatitis C virus (HCV)

infection, an infection that can last a lifetime. These medicines reduce the amount of HCV in the body by preventing HCV from multiplying, and in most cases, they cure HCV. Without treatment, HCV can lead to serious liver problems including cirrhosis, liver cancer, and death (see List of Direct-Acting Antivirals in the FDA Drug Safety Communication).

FDA identified 24 cases of HBV reactivation reported to FDA and from the published literature in HCV/HBV co-infected patients treated with DAAs during the 31 months from November 22, 2013 to July 18, 2016. This number includes only cases submitted to FDA, so there are likely additional cases about which FDA is unaware. Of the cases reported, two patients died and one required a liver transplant. HBV reactivation was not reported as an adverse event in the clinical trials submitted for the DAA approvals because patients with HBV co-infection were excluded from the trials. See the data summary section in the Drug Safety Communication for more detailed information.

RECOMMENDATION: Health care professionals should screen all patients for evidence of current or prior HBV infection before starting treatment with DAAs, and monitor patients using blood tests for HBV flare-ups or reactivation during treatment and post-treatment follow-up.

Patients should tell your health care professional if you have a history of hepatitis B infection or other liver problems before being treated for hepatitis C. Do not stop taking your DAA medicine without first talking to your health care professional. Stopping treatment early could result in your virus becoming less responsive to certain hepatitis C medicines. Read the patient information leaflet or Medication Guide that comes with each new prescription because the information may have changed. Contact your health care professional immediately if you develop fatigue, weakness, loss of appetite, nausea and vomiting, yellow eyes or skin, or light-colored stools, as these may be signs of serious liver problems.

List of Direct-Acting Antivirals (DAAs)		
Brand name	**Active ingredient(s)**	**Drug Manufacturer**
Daklinza	daclatasvir	Bristol-Myers Squibb
Epclusa	sofosbuvir and velpatasvir	Gilead Sciences
Harvoni	ledipasvir and sofosbuvir	Gilead Sciences
Olysio	simeprevir	Janssen
Sovaldi	sofosbuvir	Gilead Sciences
Technivie	ombitasvir and paritaprevir and ritonavir	Abbvie
Viekira Pak	dasabuvir and ombitasvir and paritaprevir and ritonavir	Abbvie
Viekira Pak XR	dasabuvir and ombitasvir and paritaprevir and ritonavir	Abbvie
Zepatier	elbasvir and grazoprevir	Merck Sharp Dohme