



EUROPEAN MEDICINES AGENCY
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PRAC warns of risk of hepatitis B re-activation with direct-acting antivirals for hepatitis C

Review of liver cancer risk not conclusive and further studies are needed

EMA's Pharmacovigilance Risk Assessment Committee (PRAC) has confirmed that patients treated with medicines known as direct-acting antivirals for hepatitis C may be at risk of hepatitis B re-activation. As a result of this review, the PRAC has recommended that, before starting treatment, all patients should be screened for hepatitis B virus; those patients co-infected with hepatitis B and C viruses must then be monitored and managed according to current clinical guidelines.

Direct-acting antivirals (marketed in the EU as Daklinza, Exviera, Harvoni, Olysio, Sovaldi and Viekirax)¹ are important medicines for the treatment of chronic (long term) hepatitis C, an infectious disease that affects the liver caused by the hepatitis C virus.

Cases of the return of previously inactive hepatitis B infection (re-activation), which can be fatal, have been reported in patients treated with direct-acting antivirals who were infected with hepatitis B and C viruses. This is thought to be the consequence of the rapid treatment-induced reduction in hepatitis C virus, which is known to suppress the hepatitis B virus, and the lack of activity against hepatitis B virus of direct-acting antivirals.

Although the frequency of hepatitis B re-activation appears low,² the PRAC recommended that a warning be included in the prescribing information for these medicines.

The PRAC also reviewed the available data on liver cancer (hepatocellular carcinoma) in patients treated with direct-acting antivirals and concluded that further studies should be carried out before firm conclusions can be drawn. The Committee will continuously review any other new data as they become available.

The PRAC recommendation will now be forwarded to the Committee for Medicinal Products for Human Use (CHMP) for the adoption of the Agency's final opinion. Further detailed advice for patients and healthcare professionals will be published at the time of the CHMP opinion.

¹ Since the start of this review, two other direct-acting antivirals, Eplclusa (sofosbuvir / velpatasvir) and Zepatier (elbasvir / grazoprevir), have been authorised in the EU.

² Around 30 cases of hepatitis B re-activation have been reported to date among the many thousands of patients treated.



More about the medicines

The review covers the following direct-acting antivirals for treating chronic hepatitis C: Daklinza (daclatasvir), Exviera (dasabuvir), Harvoni (sofosbuvir / ledipasvir), Olysio (simeprevir), Sovaldi (sofosbuvir) and Viekirax (ombitasvir / paritaprevir / ritonavir). Since the start of this review, two other direct-acting antivirals, Epclusa (sofosbuvir / velpatasvir) and Zepatier (elbasvir / grazoprevir), have been authorised in the EU.

Direct-acting antivirals work by blocking the action of proteins in the hepatitis C virus which are essential for it to make new viruses.

More information on these medicines can be found on EMA's website: ema.europa.eu/Find/medicine/Human_medicines/European_public_assessment_reports.

More about the procedure

The review of direct-acting antivirals for the treatment of hepatitis C was initiated on 17 March 2016 at the request of the European Commission, under Article 20 of Regulation (EC) No 726/2004. On 14 April 2016 the scope of the review was extended to include the risk of liver cancer, in addition to the potential risk of hepatitis B re-activation.

The review has been carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the committee responsible for the evaluation of safety issues for human medicines, which has made a set of recommendations.

The PRAC recommendations will now be sent to the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which will adopt the Agency's opinion. The final stage of the review procedure is the adoption by the European Commission of a legally binding decision applicable in all EU Member States.

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