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Updated advice on body fat changes and lactic acidosis with HIV medicines

EMA recommends removal of class warnings for several medicines

The European Medicines Agency (EMA) has updated the advice on the risk of body fat changes and lactic acidosis with medicines for the treatment of human immunodeficiency virus (HIV) infection. As a result, HIV medicines will no longer require a warning concerning fat redistribution in their product information, and a number of medicines of the class 'nucleoside and nucleotide analogues' will no longer require a warning about lactic acidosis.

Body fat changes

The warning about body fat changes (lipodystrophy) was introduced in the early 2000s in the light of clinical findings in patients taking combinations of medicines available at the time. The term 'lipodystrophy' in this context refers to changes in the amount of body fat as well as the distribution of fat in the body. More recent analyses suggest that only some medicines cause fat changes (zidovudine, stavudine and, probably, didanosine), and that these fat changes concern the loss of subcutaneous fat (lipoatrophy). There is no clear evidence that HIV medicines cause fat accumulation.

In line with current evidence:

- the general warning about lipodystrophy is therefore being removed for HIV medicines;
- a specific warning related to loss of subcutaneous fat will remain for medicines containing zidovudine, stavudine, and didanosine.

Lactic acidosis

Similarly, a warning about lactic acidosis, a harmful build-up of lactic acid in the body, was introduced in the early 2000s for nucleoside and nucleotide analogues. However, an analysis of studies, case reports and published literature now shows that the risk of lactic acidosis differs substantially between medicines in the class.

In line with current evidence, the class warning about lactic acidosis is being removed for nucleoside and nucleotide analogue medicines, with exception of products containing zidovudine, stavudine and didanosine.

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Companies affected by these recommendations will now start regulatory procedures to update the product information of their medicines accordingly.

Information for patients and healthcare professionals

- The product information of HIV medicines are being updated to reflect current knowledge about body fat changes and lactic acidosis, so that patients and healthcare professionals can decide on treatment using up to date advice.
- This review raised no new risks or concerns; patients can be reassured that for several medicines, previous information on the risk of body fat changes and lactic acidosis is no longer considered relevant.
- Patients should continue to take their medicines as prescribed.
- Patients who have any questions should discuss them with their healthcare professional.

More about the medicines

EMA's review covered centrally authorised HIV medicines. The following centrally authorised medicines no longer require a warning concerning fat redistribution: Aptivus, Atripla, Combivir, Crixivan, Edurant, Emtriva, Epivir, Eviplera, Evotaz, Intelence, Invirase, Kaletra, Kivexa, Lamivudine ViiV, Norvir, Prezista, Reyataz, Rezolsta, Stribild, Sustiva, Telzir, Triumeq, Trizivir, Truvada, Viramune, Viread, Zerit and Ziagen.

For lactic acidosis, the following medicines no longer require a class warning: Atripla, Emtriva, Epivir, Eviplera, Kivexa, Lamivudine ViiV, Stribild, Triumeq, Truvada, Viread and Ziagen.

Combivir, Trizivir and Zerit will now have a warning about fat loss (lipoatrophy) and will also retain the lactic acidosis warning.

The product information for nationally authorised medicines will also be updated in line with the latest advice.

More about the procedure

The purpose of the review (part of a procedure known as a legally binding measure, or LEG) was to determine if the advice about body fat changes and lactic acidosis adequately reflected current knowledge and to make recommendations on amendments to the product information for HIV medicines.

EMA's Pharmacovigilance Risk Assessment Committee (PRAC) conducted the initial review, taking advice from a scientific advisory group (SAG) on HIV. The Committee for Medicinal Products for Human Use (CHMP) then adopted PRAC's recommendations as the Agency's final opinion.

Marketing authorisation holders will now start regulatory procedures known as variations to update the product information of the affected medicines.

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