Updated advice on HIV medicines

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Information on antiretroviral medicinal products

- Antiretroviral medicinal products are authorised in the European Union as treatment for patients with viral diseases such as HIV(AIDS). Six classes of antiretroviral products currently exist:
    - Nucleoside reverse transcriptase inhibitors (NRTIs)
    - Non-nucleoside reverse transcriptase inhibitors (NNRTIs)
    - Protease inhibitors (PIs)
    - Integrase inhibitors (INSTIs)
    - Fusion inhibitors (FIs)
    - Chemokine receptor antagonists (CCR5 antagonists)

- Each class targets a different step in the viral life cycle.
- The use of these medicinal products in clinical practice is largely dictated by their ease or complexity of use, expected efficacy in a patient, whether a patient is treatment experienced or naïve and the side-effect profile.

Information from the European Medicines Agency about the review

The EMA reviewed all centrally authorised antiretroviral medicinal products with a view to determine if the advice about body fat redistribution (lipodystrophy) and lactic acidosis adequately reflected current knowledge. The adverse events lipodystrophy and lactic acidosis were included in the product information in the early 2000 in the light of clinical findings in patients taking combinations of medicines available at the time.

Regarding lipodystrophy more recent analyses suggest that only some medicines cause fat redistribution 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.

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.

Medicines Authority
203 Level 3, Rue D'Argens, Gzira, GZR 1368 – Malta.
Tel. (+356) 23439000 Fax. (+356) 23439161 www.medicinesauthority.gov.mt

Similarly, regarding the warning about lactic acidosis, a (harmful build-up of lactic acid in the body), an analysis of studies, case reports and published literature now shows that the risk 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. 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.

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

In Malta

Information to healthcare professionals and patients

- The product information of antiretroviral medicines are being updated to reflect current knowledge about lipodystrophy and lactic acidosis.
- 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.

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance on antiretroviral medicines. Suspected Adverse Drug Reactions (side effects) or medication errors may be reported using the Medicines Authority ADR reporting form or online at **http://www.medicinesauthority.gov.mt/adrportal** or to the marketing authorisation holder or their local representatives.

Prof. John J Borg PhD (Bristol)
Post-licensing Director

Healthcare professionals and patients are encouraged to regularly check the Medicine Authority website for product safety updates as these are issued on an ongoing basis.

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