



European Medicines Agency
Post-authorisation Evaluation of Medicines for Human Use

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Direct Line (44-20) 7418 8592

TRT-5
Groupe Interassociatif Traitement & Recherche Thérapeutique
Tour Essor, 14 Rue Scandicci
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France

Re: Viracept and the contamination of the active substance nelfinavir mesilate with ethyl mesilate (EMS).

Dear Sirs,

Thank you for your letter, received on 23 July 2007, in which you address a number of questions to the EMEA in relation to Viracept, following the product's recall due to the detection of high levels of ethyl mesilate (EMS) in its active substance.

The EMEA fully appreciates your concerns and is committed to resolve the issue and to inform patients and healthcare professionals about all of the steps being taken to avoid similar problems from happening again. The recall of Viracept began on 6 June 2007, and our first priority was to minimise the hazard to patients resulting from the contaminated product having been distributed, and to inform them and healthcare professionals within 24 hours, so that the impact on continued treatment could be rapidly addressed. A detailed and thorough investigation and scientific assessment of the reasons for the contamination and its consequences have been underway since that time. Until this investigation and assessment have finished, the Agency is limited in terms of the level of information it can provide. However, the Agency is committed to making a detailed explanatory report publicly available once this process is complete. At this point in time we would like to answer your questions as fully as possible, given that the above process is still ongoing.

I Guarantee of quality and safety, and transparency of the checks planned before and after the marketing authorisation of a medicinal product

During the manufacture of any medicinal product, certain clearly defined quality steps are put in place to ensure that the finished product is of an acceptable quality, as described in the good manufacturing practice (GMP) guidelines (available on the European Commission website at <http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/homev4.htm>).

The responsibility for the quality of the medicinal product that is released onto the market lies with a qualified person, or QP, a specialised member of staff within the pharmaceutical company. The QP personally has to check that the production of the product, and all necessary quality measures, have been carried out in compliance with GMP. All relevant sites of manufacture undergo regular GMP inspections by the relevant competent authority, and records are inspected to verify that the company complies with its duties.

In the case of Viracept, the manufacturer and all Authorities involved are currently carrying out investigations to understand as fully as possible how the contamination occurred in spite of the quality systems that were in place. As stated above, while the investigation is ongoing, we are limited in the amount of information we can provide. More details regarding what caused the contamination, how it was detected, the levels of EMS that were found, and future quality assurance measures introduced to avoid such contamination happening again, will be made available in the report, as stated above.

II Action plan to follow-up patients – communication to patients

The recall of Viracept was required to be done for safety reasons at patient level. This means that the issue was of such importance that it was necessary for patients to be informed immediately that they had to stop taking the medicine and seek their doctor's advice regarding switching to alternative treatment options.

The Agency operates in a complex network of 27 EU Member States, and has to balance the need for fast provision of information to patients and healthcare professionals in the EU against the need for tailored information adapted to each country's specific network for communication. In this instance, we chose to act speedily, but our communication was still shared in advance with all the EU National Competent Authorities, the European Commission as well as the World Health Organization (WHO). In addition, a patient expert (nominated by EATG, a patients' organisation eligible to work with the EMEA¹) provided input into the drafting of this communication to ensure that both the content and style of the communication took the needs of patients into account.

We always consider, when releasing information, the time needed for our partners within the EU Regulatory System network to adapt it to their needs. However, we acknowledge your concerns, and will take them into account during our ongoing review of existing risk communication procedures within the EU Regulatory System network.

The safety issue with EMS and Viracept is complex. There has been an evolving assessment as new information was becoming available (e.g. on the toxicity of EMS). We have updated our initial communication twice since the start of the recall and, in both instances, included in the question-and-answer (Q&A) document all new information that is of relevance. In particular, the latest version of the Q&A document, published on 26 July 2007, gives more details on the patient registries to be established by Roche. In the meantime, Roche has also communicated on the subject of the registries directly to healthcare professionals. The establishment of the registries is also a complex task, requiring close cooperation between all concerned parties, including the company, the EMEA and its experts, and Health Authorities in the Member States.

III Problems linked to the replacement of Viracept

We share your concerns with regard to the replacement of Viracept in those patients who may not easily be switched to alternative antiretroviral therapies. Indeed, the Agency's Committee for Medicinal Products for Human Use (CHMP) is ready to rapidly evaluate new data being generated by Roche to address the conditions for lifting the suspension of the marketing authorisation, so as to resume supply to the affected patients as quickly as possible. In the interim, the possibility does exist in Member States for healthcare professionals to initiate the import of Viracept manufactured by Pfizer on a named-patient basis, according to national legislation. Because Pfizer does not hold a marketing authorisation for Viracept in the EU, there is no possibility within the existing legal framework to allow for a general import into the EU.

The Agency is well aware of the impact of the Viracept recall on countries outside the EU that rely on the EU authorisation to allow medicinal products on their markets, and these include countries in Africa. For this reason, the EMEA has maintained regular contact with WHO since the initial product

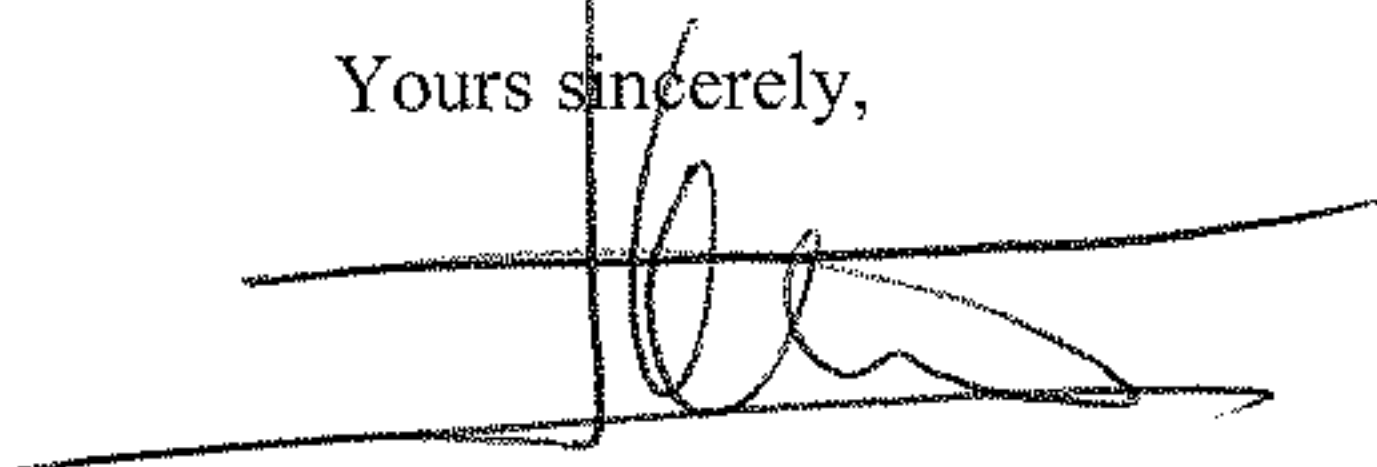
¹ Patients' organisations eligible to work with the EMEA need to fulfil criteria regarding their not-for-profit status, and their involvement at EU level. For further information see: <http://www.emea.europa.eu/Patients/organisations.htm>

recall to keep them informed of the steps taken by Roche to address the manufacturing deficiencies and to resume product supply. In particular, WHO attended the recent meeting called by the EMEA where Roche reported on the progress made with their plan of action.

Whilst progressing towards the full resolution of the contamination of Viracept, the EMEA remains committed to informing all interested parties, including patient organisations such as yourselves, and to update our existing communications as appropriate.

We thank you again for your constructive comments.

Yours sincerely,

A handwritten signature in black ink, appearing to be 'Noël Wathion', written over a horizontal line.

Noël Wathion
Head of Unit
Post-authorisation Evaluation of Medicines for Human Use

CC Mr Eric Abadie, Chairman of the Committee for Medicinal Products for Human Use, EMEA
Mr Jean Marimbert, Executive Director, AFSSAPS
Mr Markos Kyprianou, Commissioner for Health
Mr Günter Verheugen, Vice-President of the European Commission in charge of Enterprise and Industry