22 September 2016
EMA/633693/2016

EMA recommends suspension of medicines over flawed studies at Semler Research Centre

Bioequivalence studies performed at the site cannot be used to support medicines approval in the EU

On 21 July 2016, the European Medicines Agency (EMA) recommended suspending a number of nationally approved medicines for which bioequivalence studies were conducted at Semler Research Centre Private Ltd, Bangalore, India. The Agency also recommended that medicines being evaluated for authorisation and which rely only on bioequivalence studies from this site should not be authorised until bioequivalence is demonstrated using alternative data. Bioequivalence studies usually form the basis for approval of generic medicines.

The list of medicines recommended for suspension can be found here.

EMA's review followed an FDA inspection[1] that identified several issues at Semler's bioanalytical site, including the substitution and manipulation of subjects' clinical samples. The World Health Organization (WHO) also raised serious concerns[2] regarding data integrity and manipulation of study samples following its own inspections of Semler's bioanalytical and clinical sites.

The findings from FDA and WHO inspections called into question the quality management system in place at Semler, and thus the reliability of the data of all bioequivalence studies, including those used to support marketing authorisation applications in the EU. EMA's Committee for Medicinal Products for Human Use (CHMP) concluded that the studies conducted at Semler cannot be accepted in marketing authorisation applications in the EU. Thus, no medicines can be approved on the basis of these studies.

During the evaluation, alternative studies were provided for some of these medicines. These studies show bioequivalence, and therefore, the CHMP recommended that these medicines can remain on the market. The list of medicines recommended to remain on the market can be found here.

Some of the medicines which have been recommended for suspension may be of critical importance (e.g. due to lack of available alternatives) in a given EU Member State. Therefore national authorities can temporarily postpone the suspension in the interest of patients. Member States should also decide whether recalls of the affected medicines are needed in their territories.

[1] http://www.fda.gov/Drugs/DrugSafety/ucm495778.htm

[2] http://apps.who.int/prequal/info_applicants/NOC/2016/NOC_Semler12April2016.pdf

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The CHMP's recommendation concerning these medicines was sent to the European Commission for a legally binding decision valid throughout the EU.

Information for patients and healthcare professionals

- A number of medicines for use in the EU rely on studies carried out at the Semler site in India. The studies, called 'bioequivalence' studies, are usually the basis for approving generic medicines.
- The bioequivalence studies performed at the Semler site have been found to be flawed, so they cannot be relied on. As a result, several medicines approved in the EU have been suspended.
- The list of medicines recommended for suspension can be found here.
- National authorities in the EU will consider how critical individual medicines are in their countries and make final decisions on whether to suspend or allow them to remain available, while new data are generated.
- There is currently no evidence of unexpected harm or lack of effectiveness with any medicine approved on the basis of studies conducted at Semler.
- Generic medicines containing abacavir/lamivudine (used to treat HIV), which were approved on the basis of studies conducted at Semler, can remain on the market in the EU. This is because during this review, alternative studies from different sources were provided that show bioequivalence.
- Medicines still under evaluation cannot be granted authorisation in the EU on the basis of studies conducted at Semler; further data would have to be provided to support authorisation.
- Medicines that have been suspended can have their suspension lifted if the companies provide alternative data demonstrating bioequivalence.
- Patients should continue to take their medicines as prescribed and contact their doctors in case of questions or concerns.

More about the medicines covered by this review

The review covered medicines authorised via national procedures in individual EU Member States, whose marketing authorisation applications included data from Semler's bioanalytical site (Semler Research Center Private Ltd, 75A, 15th Cross, 1st Phase, JP Nagar, Bangalore 560 078, Karnataka, India) and from Semler's clinical site (PA Arcade, #21, 22, 23, Kodigehali Main Road, Sahakaranagar Post, Bangalore 560 092, Karnataka, India).

It also included ongoing marketing authorisation applications for medicines which use study data from these sites. No generic medicine authorised centrally via EMA was tested in these sites.

More about Semler

Semler is a contract research organisation (CRO) with an analytical and a clinical site located in Bangalore, India. These sites conduct the analytical and clinical parts of bioequivalence studies, some of which are used to support marketing authorisation applications of medicines in the EU. The Semler

site also performs bioequivalence studies for some medicines authorised in the US and medicines included in the WHO prequalification programme[3].

More about the procedure

The review of Semler was initiated on 28 April 2016 at the request of Denmark, Germany, the Netherlands, Spain and the United Kingdom under Article 31 of Directive 2001/83/EC.

The review was carried out by the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which has adopted the Agency's opinion. The CHMP opinion was forwarded to the European Commission, which issued a final legally binding decision applicable in all EU Member States on 22 September 2016.

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[3] http://www.who.int/prequal