Berlin, 26. Febr. 85

Application for registration of
FLUCTIN® (formerly Fluoxetin, Lilly) 20/40/60 capsules

Ladies and Gentlemen,

after the commission according to § 25 par. 6 AMG was heard, we intend to refuse the registration of the above mentioned drugs for the following reasons.

1. The drugs concerned are not sufficently tested according to the secured state of scientific knowledge and the therapeutic efficacy, which is claimed for them, is insufficiently substantiated (§ 25 par. 2 No. 2 and 4 AMG).

1.1. Fluoxetin's profile of action was insuffiently characterized. A definite judgement on the efficacy is not possible because of methodical problems at the carrying-out of the studies (to short wash-out period, concomitant treatment with other psychotropic drugs, choice of control drug).

Evidence in hospitalized and out-patients from the Federal Republic of Germany or another EC-country is missing. Studies of the required kind would have to be done using internationally accepted evaluation criteria. This was not done in the case at hand.

Amitriptylin should more frequently be used as control drug.

1.2. The completed studies do not allow a judgement on efficacy and safety in long-term use. A statistical comparative evaluation of long-term use of fluoxetine versus a control drug was not submitted.

2. For the drugs concerned there is according to their specific profile of adverse effects, the justified suspicion, that they have unacceptable damaging effects (§ 25 par. 2 No. 3 AMG).

2.1. The use of the preparations seems objectionable, as the increase in agitating effect occurs earlier than the mood elevating effect and therefore an increased risk of suicide exists.

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2.2. During treatment with the drugs some symptoms of the underlying disease (anxiety, insomnia, agitation) increase, which as adverse effects exceed those which are considered acceptable by medical standards.

2.3.

According to § 25 par. 4 AMG we herewith give you the opportunity to amend the before mentioned deficiencies within three month of the receipt of this letter. In case you should not amend the before-mentioned deficiencies within the given time, the registration of the drug concerned has to be rejected. Alternatively you can withdraw the present applications and submit new applications, when you have amended the mentioned deficiencies.

If the reasons, which make a rejection necessary, are no longer applicable, the following additional statements have to be included in the package-insert (conditions for approval):

Kind regards

Dr. U. Schmidt

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