Information about Case Reports of Acemap (Penfluridol)

Background

This report has been sent to the MEB previously as a separate report and has been added to this Quarterly Report for the sake of completeness.

The drug penfluridol has been having delivery problems for years. In 2009 Janssen-Cilag suspended marketing authorization for the specialty Semap due to its small area of distribution. Psychiatrists responded to this due to clinical necessities. Penfluridol is the only antipsychotic drug available in tablet formulation that can be administered once weekly; the alternative, pimozide tablets must be administered three times a week. Furthermore, the only antipsychotic drugs available for prolonged release are administered as injections. Psychiatrists especially prescribe penfluridol to patients with psychosis who avoid psychiatric care and reject antipsychotic drug injections.

In 2010, the firm Alkopharm from Luxemburg, took over the marketing authorization of Semap from Janssen-Cilag and a French firm was in charge of production and distribution. However, due to the increase in demand and slowdown in the production process, in April of that year, Alkopharm sent a letter to physicians reporting that it was out of stock. Semap was then imported from Belgium and Denmark where it was still in supply. In June, the Netherlands Association for Psychiatry (NVvP) advised physicians to prescribe alternatives for Semap.

In the beginning of 2012 the French authorities informed that there were problems with the availability of Semap (penfluridol) and that Alkopharm (the producer) was denied permission to start or continue the production of Semap.

Acemap (penfluridol) does not have a marketing authorization and is dispensed under **Article 3.17** of the Dutch Medicines Act (compassionate use programme). This drug is also reimbursed. Acemap is produced by ACE Pharmaceuticals B.V., Zeewolde, Netherlands. This firm specializes in producing medicines for medical necessity which do not or no longer have a marketing authorization and medicines for research. Acemap is dispensed via ACE Pharmacy in Zeewolde.

Reports

The Netherlands Pharmacovigilance Centre has received a number of reports concerning an aggravation of psychosis in patients in which Semap was substituted for Acemap (table 1)

Table 1. Reports of aggravation of psychosis after Semap was substituted for Acemap

Patient, Sex, Age, Source	Drug,daily dose Indication for use	Concomitant medication	Suspected adverse drug reaction	Time to onset, Action with drug outcome
A 1492356 M, 21-30 years Specialist doctor	acemap tablet 20mg Schizophrenia		Schizophrenia relapse, therapeutic response unexpected with drug substitution	5 weeks dose increased not yet recovered

Patient, Sex, Age, Source	Drug,daily dose Indication for use	Concomitant medication	Suspected adverse drug reaction	Time to onset, Action with drug outcome
B 149237 F, 51-60 years Specialist doctor	acemap tablet 20mg Schizophrenia	movicolon, coughing syrup, ferogradumet	Schizophrenia relapse, therapeutic response unexpected with drug substitution	5 weeks dose increased not yet recovered
C 149328 M, 21-30 years Specialist doctor	acemap tablet 20mg Schizophrenia	calcium carbonate/Vit D	Schizophrenia relapse, therapeutic response unexpected with drug substitution	5 weeks dose increased not yet recovered
D 149329 M, 31-40 years Specialist doctor	acemap tablet 20mg Schizophrenia		Schizophrenia relapse, therapeutic response unexpected with drug substitution	5 weeks dose increased not yet recovered
E 149408 M, 41-50 years Specialist doctor	acemap tablet 20mg Schizophrenia		Schizophrenia relapse, therapeutic response unexpected with drug substitution	5 weeks dose increased not yet recovered
F 149408 F, 31-40 years Specialist doctor	acemap tablet 20mg psychosis	floxapen, augmentin	psychosis aggravated, therapeutic response unexpected with drug substitution	3 months no change not yet recovered

Patients A-E are from the same reporter. Five out of the seven patients treated by this psychiatrist have had a relapse after substitution of Semap for Acemap. This occurred in October 2012.

Patient F was hospitalized due to a psychosis for 4 weeks. The patient was treated with antipsychotic drugs. Between September and December 3rd the patient had three antibiotic treatments: Floxapen for a throat infection, nitrofurantoin for a urinary tract infection and Augmentin for a skin infection. There was no septicemia. Additional information: end of August Semap was substituted for Acemap. The patient claims to have been compliant while using Acemap, and was stable on Semap. Therapeutic plasma concentrations, despite being requested, were not determined. It is suspected that the bioavailability of Acemap is less than that of Semap.

Even though there are only six reports of which the majority are from the same reporter, it is exceptional that these patients all experienced a relapse after switching from Semap to Acemap. A possible cause for this is due to differences in bioavailability.

This signal has been raised on 31 October 2013. It is possible that in the meantime other information became available. For the latest information please refer to the website of the MEB www.cbgmeb.nl/cbg/en/default.htm or the responsible marketing authorization holder(s).