Agence nationale de sécurité du médicament et des produits de santé

# Summary of conclusions

## 16 February 2016

The Temporary Specialist Scientific Committee on inhibitors of the FAAH (Fatty Acid Amide Hydrolase) met on 15 February 2016 at ANSM.

The Committee examined data on the molecule in question, the endocannabinoid system on which it is supposed to act, the conduct of the trial and its follow-up, the toxicological and pharmacological analyses and the pathophysiology of the accidents.

The Committee concluded that, on the basis of a detailed analysis of the toxicological data available, the results of the studies carried out on animals met the necessary prerequisites and, as a result, allowed testing on humans to begin. Furthermore, the pharmaceutical quality of the product also met the expected requirements for a clinical trial.

The following was noted among volunteers presenting negative adverse events (50mg per day cohort), one with fatal progression: a purely cerebral neurological symptomology with very fast appearance, relatively consistent among volunteers but with great variability in severity and progression. Anomalies found under radiology imaging (MRI) show micro cerebral tissue damage of varying severity with very unusual topography but, like with the clinical symptomology, consistent among volunteers.

No warning signs were identified among the other trial volunteers, be it those who received daily administrated doses under 50 mg or those who received doses up to 100 mg in a single dose.

The appearance of serious negative adverse events after 5 or 6 daily doses of 50 mg therefore demonstrates a threshold effect, between 20 mg and 50 mg. Among the various hypothesis put forward, two held preference:

- an effect of the molecule which exceeds the only inhibition of the FAAH;
- the effect of a metabolite[1] from the tested product.

As a result, the Committee has decided to continue its work. Additional data will be gathered in the next few days, to shed light on these avenues of research. They will come under analysis by the members of the Committee, which will meet again before the end of March.

[1] a metabolite is a drug degradation product after absorption.