Impending approval of a dangerous amphetamine drug for use in weight control? An unacceptable EMA recommendation that must be overturned

PRESS RELEASE – Paris, 19 December 2014. Today, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has announced its decision to recommend that marketing authorisation be granted for the combination ***naltrexone* + *amfebutamone*** (also known as *bupropion*) for use in weight control **(MYSIMBA°** in the EU/**CONTRAVE°** in other parts of the world), despite "*uncertainties with regard to cardiovascular outcomes in the longer term*" (1).

A major regression for European patients' safety. *Amfebutamone* is an amphetamine drug, as is *amfepramone*. In 2000, the EMA withdrew the marketing authorisation of several appetite suppressants with a similar mechanism of action to that of *amfepramone* (*clobenzorex*, *dexfenfluramine*, *fenfluramine*, *fenproporex*, etc.), in order to protect public health (2). In 2009, *sibutramine* (Sibutral°), an appetite suppressant structurally related to amphetamines, was also withdrawn by the EMA due to disproportionate and serious adverse drug reactions (3). And *benfluorex* (Mediator°) was also withdrawn from the whole European Union market in 2010 (4).

In addition, in 2013, the EMA rightly refused to authorise the dangerous fixed-dose combination *phentermine* + *topiramate* on safety grounds, and the application for the drug *lorcaserin* (Belviq°) was withdrawn by the company following the CHMP's "*provisional opinion that Belviq could not have been approved for weight control in obese and overweight patients*" (5,6). How is it possible that the CHMP now takes an incongruent decision on the fixed-dose weight-control combination *naltrexone* + *amfebutamone* (also known as *bupropion*) (CONTRAVE°/MYSIMBA°)?

Health authorities should learn from past public health disasters. A weight loss of a few kilograms achieved through drug therapy cannot in itself justify exposing obese or simply overweight patients to a disproportionate risk of adverse drug reactions, especially since the weight lost is very often regained within months of discontinuing treatment (**a**).

Health authorities should learn the lessons from past public health disasters, notably those due to several appetite suppressants subsequently withdrawn from the EU market for disproportionate and serious adverse drug reactions (*sibutramine* (Sibutral°), *benfluorex* (Mediator°), *rimonabant* (Acomplia°)) (3,4,7).

***Prescrire* urges national Drug Regulatory Agencies' representatives with a seat at the CHMP and who voted against the recommendation on *naltrexone* + *amfebutamone* (CONTRAVE°/MYSIMBA°) to insist that patients' safety be defended.** Member States opposing the recommendation still can and should require arbitration by the European Commission and convene a standing Committee meeting. The EU Commission, as last gatekeeper, also has the possibility of deciding not to follow the CHMP's recommendation.

In 2015, weight-control medicines that do more harm than good should no longer be authorised in the European Union.

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a- In its response to the EMA public consultation on the revision of its Guideline on medicinal products used in weight control (EMA/CHMP/311805/2014), *Prescrire* insisted on the need to use morbidity and mortality endpoints to evaluate whether or not the effects on weight translate into improved prognosis, and on the need for proactive, intensive monitoring of adverse drug reactions (ref. 8). As of 2014 there are several weight-control medicines in the pipeline, some at a very advanced stage of development, such as *liraglutide* (Saxenda°). These circumstances require an urgent revision of the guideline, so that the CHMP can produce robust recommendations to protect patients from dangerous medicinal products.

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2- European Commission – DG Health "Human referrals" http://ec.europa.eu/health/documents/community-register/html/refh_others.htm

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