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TESOFENSINE CAN PRODUCE WEIGHT LOSS DOUBLE THAT OF CURRENTLY APPROVED OBESITY DRUGS

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Issued by Tony Kirby, Press Officer, *The Lancet*

Tesofensine can produce weight loss double that of currently approved obesity drugs, and should be studied in phase III trials. These are the conclusions of an **Article** published early **Online** and in an upcoming edition of *The Lancet*, written by Professor Arne Astrup*, Department of Human Nutrition, Faculty of Life Sciences, University of Copenhagen, Denmark, and colleagues.

Increased obesity prevalence worldwide, in both developed and developing countries, results in more people with cardiovascular disease, diabetes, musculoskeletal disorders, and cancer. Whilst gastric bypass surgery substantially reduces bodyweight and obesity-related disease, the researchers believe a treatment gap exists between the effectiveness of currently marketed obesity drugs and gastric-bypass surgery. Tesofensine—which inhibits the presynaptic uptake of the neurotransmitters noradrenaline, dopamine, and serotonin in the brain—has been shown to be safe and effective in animal models. It also caused unintended weight loss when it was given obese patients with Parkinson's or Alzheimer's disease when it was researched for those conditions. The drug works by suppressing hunger, leading to an energy deficit which burns off excess body fat.

This randomised, placebo-controlled phase II study was done in five Danish obesity management centres, and involved 203 obese patients (body mass index 30–40 kg/m^2), weighing a mean of just over 100 kg. They were prescribed a limited-energy diet and assigned to tesofensine 0·25mg (52 patients), 0·5 mg (50), 1·0 mg (49), or placebo (52), all once daily for 24 weeks. The primary outcome was percentage change in bodyweight. A total of 161 patients completed the study, and mean weight loss recorded for placebo and diet was 2·2 kg; and for tesofensine 0·25 mg, 0·5 mg and 1·0 mg was 6·7 kg, 11·3 kg, and 12·8 kg respectively. For the 0·5 mg and 1·0 mg doses, this represented a weight loss around twice that attained using sibutramine** or rimonabant, the currently-approved therapies in Europe. Tesofensine increased blood pressure in the 1·0 mg group; the most common side-effects

caused by tesofensine were dry mouth, nausea, constipation, hard stools, diarrhoea, and insomnia.

The authors conclude that the 0·5 mg dose of tesofensine is more promising than the 1·0 mg dose because it produces a similar weight loss with fewer side-effects. They say: "We conclude that tesofensine 0·5 mg, once daily for 6 months, has the potential to produce twice the weight loss as currently approved drugs; however, larger phase III studies are needed to substantiate our findings."

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Notes to editors

*Conflict of interest statement from the authors: Arne Astrup receives an honorarium as a consultant and for membership of the Tesofensine Advisory Board for Neurosearch. Arne Astrup and Thomas Jensen own shares in Neurosearch A/S purchased on the stock exchange. Thomas Meinert Larsen has received one travel grant from Neurosearch A/S. Jens Peter Kroustrup, Leif Breum, and Sten Madsbad declare that they have no conflict of interest.

** Sibutramine has the trade name Meridia in the U.S. and Canada, Reductil in Europe and most other countries. Rimonabant is licensed in Europe and other countries as Acomplia.