Off-label drugs for obesity

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LETTERS

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We do not believe the article 'Medicines for long-term obesity management'[1] is consistent with the NPS MedicineWise philosophy, to provide independent and evidence-based advice to health professionals.

The concluding statement 'They [weight-loss drugs] are useful during the weight loss phase, but are essential in the maintenance phase' is contentious but presented as fact. Despite these drugs being used for decades, there are still no trials reporting their benefit on end points, such as cardiovascular events and death. A Cochrane review of their long-term effects in people with hypertension found only one randomised trial reporting cardiovascular outcomes. This showed no differences in all-cause mortality or cardiovascular mortality or morbidity.[2]

Some drugs, such as topiramate, are not approved in Australia for weight loss, but this was glossed over. Saying that 'no one has applied to register it for treating obesity' is insufficient justification for off-label use. The article seems to only consider positive news on drugs. For example, it says semaglutide 'is under consideration by European authorities for the treatment of obesity', but does not mention that marketing authorisation was refused for phentermine/topiramate due to safety concerns.

Despite the author acknowledging that there is no evidence base to support using a combination of drugs, several potential combination regimens are suggested on theoretical grounds. This is not in line with the evidence-based philosophy that underpins the work of NPS MedicineWise.

Conflicts of interest also call into question the independence of some recommendations. It is now recognised that pharmaceutical sponsorship may influence the reporting of trial results and recommendations made about medicines.[3]

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Joseph Proietto AM, the author of the article, comments:

The need for medicines to maintain weight loss is based on the fact that nearly everyone regains weight after weight loss. I agree that there is a need to test these drugs for long-term safety. The problem is that regulatory authorities mandate that to register a drug to treat obesity it must show 5% weight loss. In fact, they should mandate safety studies with long-term use.

So far, we have a 3.8-year safety study showing that liraglutide improves cardiovascular outcomes in patients with type 2 diabetes.[1] A two-year study of patients with diabetes and established cardiovascular disease showed that semaglutide once weekly reduced cardiovascular events.[2] Another two-year study concluded that a combination of phentermine and topiramate maintained weight loss and improved cardiovascular and metabolic variables and decreased rates of incident diabetes compared to placebo.[3] A study to assess cardiovascular safety for naltrexone/bupropion was terminated early following an interim analysis after 25% and 50% of expected cardiovascular events had occurred. More research is needed, however the 25% and 50% data showed a mild reduction in events in the treatment group. Topiramate was mentioned because it is the only obesity drug that is cheap and thus affordable for most, and it was approved by the US Food and Drug Administration in combination with phentermine.

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