

BODY WEIGHT CHANGES DURING ATOGEPANT THERAPY: A CASE REPORT AND NARRATIVE REVIEW OF THE METABOLIC ROLE OF CGRP

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Background. Calcitonin gene-related peptide (CGRP) receptor antagonists (gepants) have expanded therapeutic options for migraine prevention. Although randomized clinical trials have demonstrated favorable efficacy and safety, emerging evidence suggests that atogepant may be associated with modest weight loss.

Methods. We report the case of a woman with resistent chronic migraine and medication-overuse headache who experienced body weight changes during preventive treatment with atogepant. Clinical features, anthropometric data, headache outcomes and concomitant medications potentially affecting body weight were reviewed. A narrative review of randomized clinical trials, pooled analyses, long term extension studies and experimental evidence on the metabolic effects of CGRP receptor antagonism was also performed.

Results. Before atogepant, the patient had approximately 20 monthly migraine attacks (NRS 9/10), poorly responsive to NSAIDs, bronchial asthma and gastroesophageal reflux disease. Topiramate was discontinued due to paresthesias, memory impairment, limited efficacy and worsening of mood, while pregabalin was discontinued following a 5-kg weight gain over three months and insufficient therapeutic response; duloxetine was subsequently added to the treatment regimen for concomitant anxiety and depressive symptoms. Atogepant was introduced in July 2024, with eletriptan as acute treatment. Headache frequency improved to 6–7 monthly attacks (NRS 6–7/10), no longer associated with photophobia or phonophobia, with only mild nausea and consistent response to eletriptan. Body weight was 72 kg (BMI 28.1 kg/m^2) at baseline, decreased to 70 kg (BMI 27.3 kg/m^2) after 12 months and increased to 74 kg (BMI 28.9 kg/m^2) after 24 months.

Conclusions. Pregabalin is commonly associated with weight gain and long-term duloxetine treatment may also contribute to modest weight increase, so these concomitant factors should be considered when interpreting weight changes. Nevertheless, available evidence suggests that rimegepant and ubrogepant are weight neutral, whereas atogepant is associated with a modest, dose- and duration-dependent reduction in body weight (approximately 1.5–2 kg after 52 weeks). The mechanisms underlying this differential effect on body weight between gepants remain unclear, although a specific metabolic effect cannot be excluded. This case highlights the complexity of interpreting body weight changes during long-term atogepant treatment in the presence of potential confounding medications. Nevertheless, the transient weight reduction observed after one year is consistent with published evidence and supports prospective monitoring of body weight during atogepant therapy. Further studies are needed to clarify the metabolic effects of CGRP receptor antagonism. References of 1. Peterlin BL, Bond DS, Ailani J, et al. Weight loss with atogepant during the preventive treatment migraine: A pooled analysis. Cephalalgia. 2024;44(12). doi:10.1177/03331024241299753 2. Bond DS, Smith JH, Sinclair A, et al. Weight loss with atogepant in the long-term treatment of migraine: An interim analysis of a safety endpoint from a phase 3, multicenter, open-label, 156-week extension study. Headache. Published online July 3, 2026. doi:10.1111/head.70162 3. Rizzoli P, Marmura MJ, Robblee J, et al. Safety and tolerability of atogepant for the preventive treatment of migraine: a post hoc analysis of pooled data from four clinical trials. J Headache Pain. 2024;25(1):35. Published 2024 Mar 11. doi:10.1186/s10194-024-01736-z