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Concomitant Use of CGRP Antagonists

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The evidence to support concomitant use of CGRP antagonists is very limited with no published studies that establish a synergistic effect in terms of efficacy. Therefore, at this time, clinical criteria prohibit concomitant CGRP use. Formulary status of CGRPs and applicable criteria are reviewed and approved by the Pharmacy & Therapeutics (P&T) Committee at least once per year. PerformRx also reviews the available published data regarding concomitant CGRP use at least once per year to assess clinical appropriateness and any changes that may be warranted.

While the FDA labeling for CGRP antagonists do not outright prohibit concurrent use, there are zero published randomized clinical trials studying concurrent use. It is theoretically possible for concomitant use of preventative and acute migraine CGRPs to have some synergistic effect that could lead to improved efficacy, as the monoclonal antibodies (-mabs) act peripherally, while the oral small molecules (-gepants) can act centrally due to their ability to cross the blood brain barrier. Current evidence is limited to case reports and studies that focus on tolerability and safety. Both existing studies, including one substudy[1] with only 13 patients, and one retrospective study/claims analysis[2] with 516 patients, have demonstrated no major safety issues with concurrent use. The search was conducted utilizing the PubMed database using the following search terms: concurrent CGRP, concomitant CGRP, combining CGRP, acute and preventative CGRP combination, gepants and monoclonal antibodies, combination of gepants and monoclonal antibodies, as well as concomitant use of gepants and monoclonal antibodies.

There are two applicable CGRP-related criteria. The first criteria, “Acute Migraine Treatments,” checks for age, prescriber specialist, migraine diagnosis, FDA approved dose, trial/failure of two formulary triptans, and that the medication will not be used in combination with another CGRP inhibitor. For Nurtec ODT, members must trial/fail Ubrelvy and an analgesic medication. Reauthorization criteria requires documentation of improvement in pain and symptoms, and that the medication will not be used in combination with another CGRP inhibitor. The second criteria, “Calcitonin Gene-Related Peptide (CGRP) Antagonists for Headache Prevention,” excludes use for chronic cluster headaches or

concomitant use of botulinum toxin and a CGRP for chronic migraine prevention. The migraine-specific criteria checks for age, diagnosis, number of headache days per month, FDA approved dose, trial/failure of two formulary agents (e.g., beta blockers, topiramate/divalproex, amitriptyline/venlafaxine, etc), and that the medication will not be used in combination with another CGRP inhibitor. Reauthorization criteria for migraines requires documentation of at least 50% reduction in number of headache days per month relative to baseline, number of headache days per month, and that the medication will not be used in combination with another CGRP inhibitor.

References:

1. Berman G, Croop R, Kudrow D, et al. Safety of Rimegepant, an Oral CGRP Receptor Antagonist, Plus CGRP Monoclonal Antibodies for Migraine. Headache. 2020;60(8):1734-1742. doi:10.1111/head.13930
2. Alsaadi T, Suliman R, Santos V, et al. Safety and Tolerability of Combining CGRP Monoclonal Antibodies with Gepants in Patients with Migraine: A Retrospective Study. Neurol Ther. 2024;13(2):465-473. doi:10.1007/s40120-024-00586-w

Questions:

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