Nurtec™ ODT Executive Summary

Migraine is characterized as a chronic neurologic disease with unpredictable and disabling attacks lasting from 4 to 72 hours.[1-3] Regardless of frequency, severity, or use of preventive medications, all migraine patients require effective acute treatment for their migraine attacks to alleviate pain and associated symptoms.[3] In the United States, migraine affects more than 38 million people with three quarters being women.[4] Migraine is the most disabling of all health conditions in those younger than 50[5] and is associated with a substantial decline in quality of life due to migraine-related disruptions in professional, academic, and social activities.[4] Nearly 160 million workdays are lost each year in the U.S.[4] as a result of migraine and associated symptoms, and the annual cost of healthcare and lost productivity is estimated at over $35 billion.[4]

Migraine patients report high abandonment and low satisfaction with current acute treatments[7] and are twice as likely to use opioids.[6] Triptans, the first of which was approved in the 1990s as the first migraine-specific treatment, are considered the standard of care for the acute treatment of migraine.[8] However, one-third of the patients who receive a triptan discontinue use within a year because of lack of efficacy and/or intolerable side effects.[6,8] Triptans are contraindicated in patients with cardiovascular conditions[9] and are also among the most common causes of medication overuse headache.[8]There remains an unmet need for patients with migraine for whom triptans are not effective, not tolerated, or are contraindicated, which represents about 24% of the migraine patient population.[11]

Rimegepant, the active ingredient in Nurtec™ ODT is an antagonist of the receptor for calcitonin gene related peptide (CGRP), which represents a novel mechanism of action that directly targets the underlying pathophysiology of migraine. Rimegepant is believed to relieve migraine through three mechanisms: decreasing artery dilation, blocking neuroinflammation, and inhibiting exaggerated pain transmission.[12,13] Importantly, rimegepant treats migraine without the vasoconstrictive effects of triptans, and this mechanism of action is not associated with addiction potential or medication overuse headache.[14]

Unlike the injectable CGRP monoclonal antibodies indicated for the preventive treatment of migraine, Nurtec™ ODT is approved for the acute treatment of migraine with or without aura in adults and is available in a blister pack of eight orally disintegrating tablets (ODT). This ODT formulation dissolves rapidly within seconds on or under the tongue without the need for water and has a half-life of approximately 11 hours.[15] The safety and efficacy profile of rimegepant for the acute treatment of migraine has been established across three pivotal Phase 3 trials[16,17] and a one-year long-term safety study.[18] To-date, over 3100 patients have been treated with rimegepant and over 113,000 doses have been administered. [16-19]

In a Phase 3 study with Nurtec™ ODT, a single dose of 75mg rimegepant demonstrated superiority over placebo on the co-primary endpoints of freedom from pain and freedom from most bothersome symptom at two hours post-dose as well as 19 of 21 total consecutive, pre-specified, hierarchically tested secondary endpoints. Patients achieved rapid pain relief and return to normal function beginning at 15 minutes with statistical significance achieved at 60 minutes. Efficacy was sustained through 48 hours with a single dose of Nurtec™ ODT, including pain relief, pain freedom, return to normal function, and freedom from most bothersome symptom. Sixty-three percent of patients who experienced pain freedom at 2 hours remained pain free through 48 hours without relapse. Eighty-six percent of patients in this trial did not use rescue medication after 2 hours; only NSAIDs, acetaminophen, baclofen and/or anti-emetics were permitted as rescue medications. The most common adverse reaction was nausea, which occurred in 2% of Nurtec™ ODT-treated patients compared to 0.4% on placebo.[17]

The safety and tolerability profile was maintained in a long-term, open-label study in which nearly 1800 patients were treated with rimegepant as-needed up to once daily for 52 weeks. Overall, 2.7% of patients discontinued due to an adverse event, no serious adverse events were considered to be related to rimegepant, and no clinically relevant laboratory abnormalities were observed. Patients in this study were allowed to take rimegepant as needed up to once daily. Despite a historical frequency of up to 14 migraines per month, the median usage was less than 8 pills per month, supporting the 48-hour long-term effects observed in the Phase 3 study without the need for redose. Treatment with 75mg rimegepant as-needed up to once daily in this study reduced lost productivity time by approximately 44% and significant improvements were demonstrated in migraine-related disability.[18,20,21]

In summary, Nurtec™ ODT addresses the unmet needs for the acute treatment of migraine and is consistent with the goals of acute treatment outlined by the American Headache Society[3], including:

- Rapid and consistent freedom from pain and associated symptoms without recurrence
- Restored ability to function
- Minimal need for rescue medications
- Minimal or no adverse events

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