Safety and Tolerability of Once-Daily Hydromorphone ER in Adults With Moderate to Severe Chronic Noncancer and Cancer Pain: Pooled Analysis of 13 Clinical Trials

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Purpose

This analysis was designed to assess the safety and tolerability of once-daily hydromorphone extended-release (ER) in patients with chronic pain secondary to cancer and noncancer etiology.

Method

Safety results for once-daily hydromorphone ER were pooled from 13 controlled and uncontrolled clinical trials including two 12-week, double-blind, placebo-controlled trials, 4 active-controlled studies, and 7 uncontrolled studies. Total study durations ranged from approximately 3 weeks to 52 weeks. Patients were included in the safety population if they took at least 1 dose of study medication. The following types of data were integrated and analyzed for the controlled and uncontrolled study pool: patient disposition, demographics and baseline characteristics, medical history, physical examination findings, use of rescue medication, and adverse events.

Results

Of the 3075 patients in the pooled population, 2335 (76%) received at least 1 dose of once-daily hydromorphone ER, with a duration of dosing of up to 1.5 years; 420 patients were treated with once-daily hydromorphone ER for at least 6 months and 141 for more than 1 year. Enrolled patients who received once-daily hydromorphone ER (n=2335) were predominantly white (90.9%), and a majority were female (55.5%). Geriatric representation in this analysis (patients aged ≥65 years) was 21.9% of once-daily hydromorphone ER-treated patients (n=511). Overall incidence of adverse events with once-daily hydromorphone ER treatment was 80.5% (n=1880); in the 466 patients receiving placebo, incidence of adverse events was 61.2% (n=285). The most common adverse events overall were constipation (30.1%, 702 patients), nausea (27.5%, 642 patients), vomiting (13.8%, 322 patients), somnolence (13.8%, 322 patients), headache (12.8%, 300 patients), and dizziness (10.6%, 247 patients). The incidence of adverse events was generally higher in patients aged 65 years or older, in women, and in opioid-naïve patients. AEs were the cause of discontinuation from once-daily hydromorphone ER treatment due to AEs was 23.0% (n=538). The tolerability profile was similar in the short-term and long-term trials.

Conclusions

These data demonstrate a consistent safety and tolerability profile of once-daily hydromorphone ER with both short-term and long-term therapy, comparable with that observed for other opioid analgesics.