

## Opioid Use Among Patients with Chronic Nonmalignant Pain Receiving Methylnaltrexone for Opioid-Induced Constipation

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### Purpose

Methylnaltrexone is a peripheral  $\mu$ -opioid receptor antagonist that significantly decreases opioid-induced constipation (OIC) without affecting centrally mediated analgesia. This study evaluates opioid use among patients with chronic pain and OIC who received subcutaneous methylnaltrexone 12 mg.

### Method

Patients taking opioids daily for nonmalignant pain were randomized to receive subcutaneous methylnaltrexone 12 mg once daily (QD) or once every other day (QOD) or daily placebo for 4 weeks. Patients completing the double-blind (DB) phase entered an 8-week open-label (OL) phase where they received methylnaltrexone 12 mg QD as needed. All patients took opioid medications daily for  $\geq 2$  weeks before the start of the study. Opioid use was assessed weekly during the 4-week DB phase and once every other week during the 8-week OL phase. Opioid use was reported as daily oral morphine equivalents.

### Results

A total of 460 patients were included in the DB phase (methylnaltrexone QD n=150; methylnaltrexone QOD n=148; placebo n=162). Of these, 364 patients entered the OL phase. Median baseline opioid doses were 161.0 mg/day for the QD group (range 45.5 - 831.2 mg/day), 154.8 mg/day for QOD (range 7.2 - 1334.3 mg/day), and 160.8 mg/day for placebo (range 13.6 - 1286.5 mg/day). The most commonly prescribed opioids in each group were oxycodone (20%), methadone (19%), and hydrocodone (14%). During the DB phase, mean daily opioid use changed only slightly from baseline in all treatment groups (-3.1 mg QD methylnaltrexone; -5.2 mg QOD methylnaltrexone; 1.3 mg placebo). At week 1 of DB treatment, mean opioid use decreased from baseline more for patients receiving methylnaltrexone compared with placebo (-8.0 mg QOD,  $p=0.005$ ; -4.8 mg QD,  $p=0.054$ ; 1.8 mg placebo) but not at weeks 2 through 4. During the OL phase, the median weekly opioid dose remained stable regardless of the initial treatment received during the DB phase (DB methylnaltrexone QD: median dose 180 mg/day; DB methylnaltrexone QOD: median dose 160 mg/day; DB placebo: median dose 180 mg/day).

### Conclusions

In this study, subcutaneous methylnaltrexone for OIC in patients with chronic nonmalignant pain did not result in clinically significant changes in the morphine equivalent dose used during the DB period. During the OL phase, opioid use remained stable. These findings support the peripheral mechanism of action of methylnaltrexone.