Galer BA, Lee D, et al. MorphiDex (morphine sulfate/dextromethorphan hydrobromide combination) in the treatment of chronic pain: Three multicenter, randomized, double-blind, controlled clinical trials fail to demonstrate enhanced opioid analgesia or reduction in tolerance. Pain 2005;115:284-295.

Design: Three randomized clinical trials

Brief summary of results:

- Three separate multicenter trials of morphine sulfate (MS) and MS plus dextromethorphan (DM) were done as Phase 3 drug registration trials
- Study A enrolled adults with chronic, non-malignant, non-neuropathic pain for at least 3 months, requiring analgesic medication for at least 1 month prior to entry
- Study B enrolled adults with chronic pain due to osteoarthritis of the hip and knee, requiring analgesic medication for at least 3 months
- Study C enrolled adults with chronic, non-malignant, non-neuropathic pain for at least 6 months, requiring daily, around-the-clock opioid medication for at least 1 month
- All 3 studies involved a run-in titration phase of 7-21 days, followed by randomization in a double-blind phase for 90 days
- All studies compared MS/DM with MS during the randomized double-blind phase
- The primary outcome for Study A was the mean change in average daily pain intensity from baseline (end of the 7-21 day titration period) to the end of the study
- The primary outcomes for Studies B and C was the change in average daily MS use during the last 30 days of the randomized treatment period
- Study A found that average daily pain intensity was similar for MS and MS/DM
- Study B found that average daily MS doses were comparable for patients taking MS and patients taking the combination MS/DM
- Study C found that the average daily MS dose in the MS/DM group was slightly higher than for the MS group

Authors' conclusions:

- DM does not enhance analgesia when combined with MS
- DM does not decrease MS dosage for equivalent amounts of pain relief

Comments:

- These Phase 3 studies were done to secure FDA approval for the MS/DM combination, but the combination was not approved
- The studies appear to have been adequately done

Assessment: Adequate for evidence that DM does not enhance analgesia from MS and does not decrease the dose of MS needed for pain relief