

## **Dose Linearity, Consistency, and Predictability with BioErodible MucoAdhesive (BEMA™) Fentanyl**

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**Introduction:** The BEMA™ (BioErodible MucoAdhesive) drug delivery system is a small, bilayered, buccal-soluble film designed to provide oral transmucosal dosing reliability, tolerability, and patient acceptance. BEMA™ Fentanyl is formulated with the opioid fentanyl for buccal administration.

**Methods:** Three Phase 1 studies were conducted in healthy volunteers to assess: 1) dose-linearity across a range of doses; 2) consistency of repeat-dose administration; and 3) predictability when dosing with a single-unit (1x800µg) or multiple-unit (4x200µg) regimen. All study protocols and informed consents were approved by a regional IRB.

**Results:** Study 1 (Linearity): Mean  $C_{max}$  values for BEMA™ Fentanyl doses of 200, 600, and 1200µg were 0.38, 1.16, and 2.19ng/mL, and corresponding values for mean  $AUC_{inf}$  were 3.46, 11.72, and 20.43ng•hr/mL, respectively. Study 2 (Consistency): Two single 600µg doses of BEMA™ Fentanyl administered 3 days apart in Periods 1 and 2 produced nearly identical mean  $C_{max}$  (1.08 and 1.01ng/mL) and  $AUC_{0-12}$  (6.3 and 6.2ng•hr/mL). Three days later, application of three 600µg doses of BEMA™ Fentanyl at 1-hour intervals in Period 3 produced a proportional increase in peak plasma concentration and exposure compared to a single dose (Period 3, 1800µg [3x600µg]: mean  $C_{max}$  3.31ng/mL,  $AUC_{inf}$  30.31ng•hr/mL vs. Period 1, 600µg: mean  $C_{max}$  1.08ng/mL,  $AUC_{inf}$  9.143ng•hr/mL). Study 3 (Predictability): Application of one 800µg dose unit compared to four 200µg dose units produced identical  $C_{max}$  (1.33ng/mL) and nearly identical  $AUC_{last}$  (11.4 vs. 11.7ng•hr/mL).

**Conclusions:** Fentanyl plasma concentrations and exposure across the 200-1200µg BEMA™ Fentanyl dose range were linear. Fentanyl exposure from BEMA™ Fentanyl was also highly consistent from dose to dose. Fentanyl  $C_{max}$  and AUC following 1x800µg and 4x200µg dose units were bioequivalent, which supports the recommended titration process for BEMA™ Fentanyl. The predictability and consistency of dosing with BEMA™ Fentanyl can be attributed to the proportional relationship between the fentanyl dose and the film's surface area.

### **References:**

- Blum D, Breithaupt I, Hackett S, Kapoor R, Finn A. The safety of BEMA (BioErodible MucoAdhesive) Fentanyl for breakthrough pain (BTP) in cancer patients. *J Clin Oncol.* 2008;26(15S):Abstr 20586.
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