Comparison Of Sustained Release Buprenorphine and Transmucosal Buprenorphine In Cats

This study was conducted to compare blood levels produced by a subcutaneous administration of a novel sustained release formulation of buprenorphine HCl with the common transmucosal administration of buprenorphine HCl.

The primary study objective was to determine if this new subcutaneously administered Buprenorphine SR™ [sustained release] formulation is equivalent to repeated doses of transmucosal administration of the commercial preparation Buprenex™ over a period of 72 hours in domestic cats.

Test Animals: 8 adult female cats

Identification:
Each animal was assigned a test animal number unique within the population making up the study for accurate logging of raw data records and specimens.

Housing:
Animals were singly housed in stainless steel cat cages and kept in one room during the study*. All animals assigned to test groups were.

Environmental Conditions:
Temperature: 64 – 84 °F (20-24°C)
Humidity: 30 – 70%, Light: 12 hours light/12 hours dark.

Feed/Water:
All cats were fed Purina® Cat Chow®, ad libitum for the duration of the study. Fresh tap water was offered from secured bowls. Treatment of the animals was in accordance with standard laboratory animal use guidelines*.

Acclimation, Prestudy Health Screen and Selection Criteria:
Prior to treatment, the animals were acclimated for a three-day period to assure their suitability as test animals. During acclimation the animals were observed and evaluated daily in accordance with accepted veterinary practice. Only animals considered acceptable for use in this study were released from acclimation.

Assignment to Study Groups:
Animals used in this study were those that met the selection criteria and were accessible for administration of the test articles.

Treatment Levels and Number of Animals: Eight female animals were used for test purposes. A description of the treatment groups is found in the table below:

<table>
<thead>
<tr>
<th>Treatment Groups</th>
<th># Animals</th>
<th>Test Article</th>
<th>Dose</th>
<th>Route of Administration</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6 Female</td>
<td>Test Article A Buprenorphine HCl SR</td>
<td>120 micrograms/kg</td>
<td>Subcutaneous (dorsal, mid-scapula)</td>
<td>Single injection</td>
</tr>
<tr>
<td>2</td>
<td>2 Female</td>
<td>Test article B Buprenorphine HCl</td>
<td>20 micrograms/kg</td>
<td>Cheek Pouch</td>
<td>Every 12 hours for 72 hours</td>
</tr>
</tbody>
</table>

*as described in the Guide for the Care and Use of Laboratory Animals National Academy Press, Washington DC, 1996
Buprenex™ is a registered trademark of Reckitt Benckiser Pharmaceuticals, Inc.
Buprenorphine SR™ is a registered trademark of SR Veterinary Technologies, LLC
Purina® Cat Chow® is a registered trademark of Société des Produits Nestlé S.A., Vevey, Switzerland
Treatments: [Test Articles] were administered according to the table above.

- **Buprenorphine HCl SR™** [sustained release] formulation was administered to Treatment Group 1 animals by subcutaneous injection (dorsal, mid scapula)
- **Buprenex™ HCl** was administered to Treatment Group 2 animals every 12 hours for 72 hours by dispensation into the cheek pouch (transmucosal)

Animal Weights:
The animals ranged in weight from 2.28 to 4.62 kg. [determined just prior to dosing on day 1]

Blood Samples: Blood samples were obtained by jugular venipuncture.
- A sample from each animal was obtained just prior to dosing at time 0
- Treatment Group 1 and Treatment Group 2 also had samples obtained at 1, 4, 8, 12, 18, 24, 36, 48 and 72 hours
- Treatment Group 2 blood samples were obtained just prior to repeat dosing at 12, 24, 36, and 48 hours

Sample processing: Blood samples were collected into 500 Hl K₂EDTA tubes. Following the completion of sample collection at each timepoint, samples were centrifuged and a minimum of 200 Hl of plasma was transferred to polypropylene storage tubes using sterile transfer pipettes and stored at ≤ -76° C.

Significant Findings:
- Buprenorphine SR maintained blood levels for 72 hours
- No visible injection site irritation
- No clinical side effects reported

**NOTE:** Salivation reported immediately following dosing at 48 and 60-hour timepoints for one Cat in Treatment Group 2