Figure Legend: Figure 1 Oral mucosa - Ulcer in a female F344/N rat from a chronic study. A portion of the hard palate mucosa is absent (arrow), exposing the underlying connective tissue. Figure 2 Oral mucosa - Ulcer in a female F344/N rat from a chronic study (higher magnification of Figure 1). A portion of the hard palate mucosa is absent, exposing the underlying connective tissue. Figure 3 Oral mucosa - Ulcer in a female F344/N rat from a chronic study. A portion of the hard palate mucosa is absent (arrow), exposing the inflamed underlying connective tissue. Figure 4 Oral mucosa - Ulcer in a female F344/N rat from a chronic study (higher magnification of Figure 3). A portion of the hard palate mucosa is absent (arrow), exposing the inflamed underlying connective tissue.

Comment: As with mucosal necrosis, mucosal ulceration in the oral cavity (Figure 1, Figure 2, Figure 3, and Figure 4) can be a treatment-related effect but is more commonly caused by trauma due to the
gavage procedure and/or the presence of foreign bodies (hair shafts, food material). Areas of ulceration can be accompanied by chronic active inflammation (Figure 3, Figure 4) and granulation tissue. However, because of the proliferative capacity of the oral epithelium, minor traumatic lesions are usually healed in a few days. Keratinization of the squamous epithelium in the rodent oral cavity generally makes it less susceptible to direct toxicity from xenobiotics than the human oral cavity, which is lined primarily by a nonkeratinizing epithelium.

**Recommendation**: Ulcers should be diagnosed and graded based on the extent and number of lesions. Inflammation and epithelial hyperplasia associated with ulcers is usually not diagnosed separately unless it is a significant component of the lesion. If epithelial cells are missing from the mucosa but the basal layers are still present and covering the submucosa, then erosion may be diagnosed. Ulcers are diagnosed when a portion of the epithelium is absent or not attached to the submucosa. If the epithelium is necrotic but is still present and attached to the submucosa, then necrosis is diagnosed.

**References:**

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