Dermatologic and Ophthalmic Drugs Advisory Committee Meeting
March 9, 2015
Concerning deoxycholic acid (DCA) for lipolysis of submental fat

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I have no financial conflict of interest

Main Safety Concerns

- Significantly increased mandibular nerve damage without an adequate causal explanation or data comparing its frequency to that seen with submental surgical procedures

- Significantly increased dysphagia, lasting as long as 81 days, without evidence that nerve damage is not also a causative factor, along with local induration, edema, etc.

Mandibular Nerve Injury

“In the pivotal Phase 3 trials, twenty subjects (4%) treated with DCA and one subject (<1%) treated with placebo experienced mandibular nerve injury, described as asymmetry of the lower lip on the affected side (paresis of lip depressors). The duration of the paresis ranged from 1 day to 298 days. Dosing was interrupted for four subjects. All nerve injuries resolved completely and without treatment. [p =<.0001]”

“[Marginal mandibular nerve] injury is a well-recognized complication of surgical interventions involving the face and neck.”

FDA Briefing Document page 12

Kythera Explanation for mandibular nerve damage
(briefing document page 101)

"Of note, motor nerve injury and ulceration were identified as special interest AEs **likely to be related to incorrect injection procedure or technique; either injection placement outside of the submental region or failure to inject midlevel into SC fat." (emphasis added)**

Dysphagia

"Difficulty swallowing occurred in the context of administration site reactions, e.g., pain, swelling, and induration of the submental area and **not as result of** esophageal or **nerve injury**." (Emphasis added)

"A total of 11 subjects experienced dysphagia in pivotal Phase 3 trials, and all but one were in the DCA group. Two subjects discontinued treatment because of dysphagia, one of whom had not recovered at the time of trial discontinuation. The duration of dysphagia ranged from 1-81 days.

[p =.011]"

FDA Briefing document page 13

Conclusions

- For the proposed use, the sponsor has failed to demonstrate that the benefits of DCA outweigh its risks.
- There inevitably will be significant off-label use of DCA injections, thereby endangering nerves in other parts of the body.
- Before approval, it is essential that adequate pre-clinical investigations be done to determine the exact mechanism of the neurotoxicity and whether its occurrence, during likely, off-label use, might cause even more serious medical problems.