Jelmyto™ (mitomycin) – New orphan drug approval

- On April 15, 2020, the FDA announced the approval of UroGen Pharma's Jelmyto (mitomycin), for the treatment of adult patients with low-grade upper tract urothelial cancer (LG-UTUC).

- Upper tract urothelial cancer (UTUC) corresponds to a subset of urothelial cancers that arise in the lining of the kidney or the ureter. UTUC can block the ureter or kidney, leading to swelling, infections, and impairment of kidney functions. UTUCs can develop as low-grade or high-grade tumors.

    - In general, LG-UTUC is not invasive and very rarely spreads from the kidney or ureter. However, they often recur, and management involves treating visible tumors and trying to preserve the urinary tract. LG-UTUC is rare, but affects 6,000 to 8,000 new or recurrent patients in the U.S. each year.

- Jelmyto is an alkylating drug that inhibits the transcription of DNA into RNA, interfering with protein synthesis and cell replication of tumor cells.

- The efficacy of Jelmyto was established in an open-label, single-arm study in 71 patients with LG-UTUC. Patients were administered Jelmyto via ureteral catheter or nephrostomy tube once a week for six weeks, and if assessed as a complete response (CR), monthly for up to 11 additional months. The primary endpoint of the study was CR at three months following initiation of therapy. A secondary endpoint was the proportion of patients with a complete response who achieved a duration of response (DOR) lasting at least 12 months.

    - CR was achieved in 58% (95% CI: 45, 69) of the patients following six treatments of Jelmyto administered weekly.
    - In patients with a CR, 46% had a DOR lasting at least 12 months.

- Jelmyto is contraindicated in patients with perforation of the bladder or upper urinary tract.

- Warnings and precautions for Jelmyto include ureteric obstruction, bone marrow suppression, and embryo-fetal toxicity.

- The most common adverse reactions (≥ 20%) with Jelmyto use were ureteric obstruction, flank pain, urinary tract infection, hematuria, renal dysfunction, fatigue, nausea, abdominal pain, dysuria, and vomiting.

- The recommended dose of Jelmyto is 4 mg per mL via ureteral catheter or nephrostomy tube, with total instillation volume based on volumetric measurements using pyelography, not to exceed 15 mL (60 mg of mitomycin). Jelmyto is for pyelocalyceal use only.

    - Jelmyto should be administered once weekly for six weekly. For patients with a CR three months after initiation, Jelmyto may be administered once a month for a maximum of 11 additional instillations.
    - Prior to every instillation, patients should be instructed to take 1.3 g of sodium bicarbonate orally the evening prior to, the morning of, and 30 minutes prior to the instillation procedure (total of 3.9 g).
    - Jelmyto is not for intravenous use, topical use, or oral administration.

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- UroGen Pharma plans to launch Jelmyto on June 1, 2020. Jelmyto will be available in a single-dose carton containing two vials of 40 mg lyophilized powder of mitomycin and one vial of 20 mL of sterile hydrogel for reconstitution.