Vyxeos™ (daunorubicin/cytarabine) – New orphan drug approval

- On August 3, 2017, the FDA announced the approval of Jazz Pharmaceuticals' Vyxeos (daunorubicin/cytarabine) for the treatment of adults with newly-diagnosed therapy-related acute myeloid leukemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC).

- AML is a rapidly progressing cancer that forms in the bone marrow and results in an increased number of abnormal white blood cells in the bloodstream and bone marrow. The National Cancer Institute estimates that approximately 21,380 Americans will be diagnosed with AML and 10,590 patients will die of the disease this year.

    - T-AML occurs as a complication of chemotherapy or radiation in approximately 8 -10% of all patients treated for cancer within an average of 5 years after treatment.
    - AML-MRC is characterized by a history of certain blood disorders and other significant mutations within cancer cells.
    - Patients with t-AML or AML-MRC have very low life expectancies.

- Vyxeos is a liposomal formulation that delivers a fixed-ratio of daunorubicin and cytarabine to the bone marrow that has been shown to have synergistic effects at killing leukemia cells *in vitro* and in animal models.

- The safety and efficacy of Vyxeos were based on an open-label study of 309 patients with newly diagnosed t-AML or AML-MRC who were randomized to receive Vyxeos or separately administered treatments of daunorubicin and cytarabine. Efficacy was established on the basis of overall survival (OS).

    - OS was 9.6 months in the Vyxeos arm vs. 5.9 months in the daunorubicin/cytarabine arm (Hazard ratio = 0.69 [95% CI: 0.52, 0.90]; $p < 0.005$).

- Vyxeos carries a boxed warning stating that it should not be interchanged with other daunorubicin- and/or cytarabine-containing products.

- Other warnings and precautions of Vyxeos include hemorrhage, cardiotoxicity, hypersensitivity reactions, copper overload, tissue necrosis, and embryo-fetal toxicity.

- The most common adverse reactions (≥ 25%) with Vyxeos use were hemorrhagic events, febrile neutropenia, rash, edema, nausea, mucositis, diarrhea, constipation, musculoskeletal pain, fatigue, abdominal pain, dyspnea, headache, cough, decreased appetite, arrhythmia, pneumonia, bacteremia, chills, sleep disorders, and vomiting.

- The recommended dosage of Vyxeos consists of 1 - 2 cycles of induction and up to 2 cycles of consolidation administered via intravenous infusion over 90 minutes as follows:

Cycle	Vyxeos Dose and Schedule
First induction	(daunorubicin 44 mg/m^2 and cytarabine 100 mg/m^2) liposome days 1, 3 and 5
Second induction*	(daunorubicin 44 mg/m^2 and cytarabine 100 mg/m^2) liposome days 1 and 3
Consolidation	(daunorubicin 29 mg/m^2 and cytarabine 65 mg/m^2) liposome days 1 and 3

* Only for patients failing to achieve a response with the first induction cycle.

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- The second induction cycle, if needed, should be administered 2 - 5 weeks after the first induction cycle.
- The first consolidation cycle should be administered 5 - 8 weeks after the start of the last induction.

- Jazz Pharmaceuticals plans to launch Vyxeos within one week. Vyxeos will be available as a single dose vial for reconstitution containing 44 mg daunorubicin and 100 mg cytarabine encapsulated in liposomes as a lyophilized cake.