Maryland
DEPARTMENT OF HEALTH

Continuing Medical Education (CME) &
Pharmacy Continuing Education (ACPE) Seminar

THE MOST EXPENSIVE DRUGS APPROVED IN 2023: HOW DID WE GET HERE AND WHAT TO EXPECT NEXT?

Saturday, October 21, 2023

Presented by:
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Q&A

1. **Given the evolving landscape of gene therapies for which beneficiaries include those with rare diseases [often genetic in nature] and not common diseases, do you think as this technology matures in development, is it likely advances will reduce cost of production and costs to patient?**

   Yes, I think there is likely going to be *some* economy of scale within the cell and gene therapy space. The more of these treatments we have on the market, the better that manufacturers will be at making them, and potentially the easier and less expensive it will be. The more experience the industry gains in this space the better. However, I think this economy of scale and price reduction with increased expertise will likely be somewhat limited due to the very heterogenous and often patient-specific nature of many cell and gene therapies.

2. **What is the impact of the Inflation Reduction Act on rare disease patients to receive affordable, equitable access to these transformative and potentially curing gene therapies and/or expensive novel therapies?**

- Do I think the IRA will affect patients living with rare diseases in terms of their ability to access affordable, equitably priced treatments like gene therapies? It's possible. I think we are a long way from understanding how the IRA will affect gene therapies specifically, but I think any amount of money we can save through lower drug prices helps increase the chance we have funds available to pay for innovative cell and gene therapies when they are needed. If we are talking about drugs to treat rare diseases outside of the cell and gene therapy categories, the IRA has specific language that details how drugs for rare diseases will qualify for or be exempt from Medicare price negotiation. There are some who say that the IRA disincentivizes drug developers from studying such drugs for more than one rare disease indication – but I think we need to wait and see how this plays out over time.

3. **Any ideas if additional studies will be done on potential side effects for Semaglutide with label expansion?**
   Semaglutide is currently being evaluated in a number of ongoing trials – both for weight loss, diabetes, and other potential indications. It's being studied as a subcutaneous injection and as an oral medication. I'm not aware if any of these trials are specifically looking at safety alone, but it's likely that our overall understanding of this agent's safety will continue to evolve as more data from these trials emerge and as we gather data in real-world populations.

4. **Do you have any idea what the primary cause of obesity is in this country. Also, is it possible that Wegovy etc. is being used for those who want to lose weight making it impossible for those using it for diabetes to get this drug?**

   This is such a great question and not one I have the answer for. But it certainly feels like it needs to be part of the larger conversation we are having about weight management and health outcomes in this country. Semaglutide and other GLP products can certainly help improve outcomes for patients with obesity, but they don't get at what might be causing rates of obesity to climb overall in this country.

5. **Can you give your opinion as to the cost benefit of therapies such as gene therapy versus much cheaper meds with wider applications. As an example, some jurisdictions or countries simply cannot afford all therapeutic options.**

   If I'm understanding this question correctly, it's a really tough one. It's hard to speak to the relative cost-effectiveness of gene therapies for a small/niche patient population vs a more broadly helpful "traditional" drug. However, you're exactly right that there are tradeoffs inherent in trying to pay for healthcare these days: every dollar spent is a dollar that is no longer available to spend on another healthcare intervention. This tension is growing with the increase in multi-million dollar gene therapies approved.

Zurzuvae® Zuranolone Follow-up Questions

6. **How does the effect of this agent compare to paroxetine for post-partum depression?**

   Zuranolone was not compared head-to-head with paroxetine in any of the studies used to support FDA approval for post-partum depression, so any comparison to the effects of paroxetine or other antidepressants would be limited (as cross trial comparisons are).

   It's worth noting that while SSRIs may be used and have been studied in post-partum depression, prior to the approval of Zurzuvae® (Zuranolone), the only FDA-approved treatment specific for post-partum depression was Zulresso® (brexanolone). It will be important to see if/how post-partum depression treatment guidelines evolve now that there is a new entrant into this space. The role of Zuranolone vs lower-cost, generic SSRIs will likely be a topic of discussion among providers and payers in the months/years to come.

7. **How soon could patients repeat dosing?**

The use of repeat courses of Zuranolone was not included in the post-partum studies, and the approved prescribing information states "The safety and effectiveness of ZURZUVAE use beyond 14 days in a single treatment course have not been established."

But two of the studies in the major depressive disorder population looked at more than one course of treatment:

- **SHORELINE** (NCT03864614)
  - Interim results from this trial were shared in a press release on 9/16/2022 and presented at the 2022 Psych Congress.
  - These findings state
    - "An analysis from the ongoing open-label, longitudinal SHORELINE Study in MDD (30 mg cohort n=725, 50 mg cohort n=199) found the median time to the first repeat treatment course for those patients who responded to the initial 14-day treatment course was 135 days for the completed 30 mg cohort (n=489) and 249 days for the ongoing 50 mg cohort (n=146). These data further support zuranolone as a potential episodic treatment for people with MDD." (Full press release available here)

- **REDWOOD** (NCT04007367)
  - Will also be assessing repeat dosing, but no results are available yet

Breastfeeding data

According to the prescribing information approved on 8/4/2023,

- "**Risk Summary**" Available data from a clinical lactation study in 14 women indicate that zuranolone is present in low levels in human milk (see Data). There are no data on the effects of zuranolone on a breastfed infant and limited data on the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ZURZUVAE and any potential adverse effects on the breastfed child from ZURZUVAE or from the underlying maternal condition.

  - **Data**: A steady-state milk study was conducted in 14 healthy lactating women treated with daily oral administration of 30 mg of ZURZUVAE for 5 days. At steady state (Day 5), the calculated maximum relative infant dose for ZURZUVAE was < 1%. The daily infant dose was low (approximately 0.0013 mg/kg/day), reflecting a mean relative infant dose of 0.357% compared to the maternal dose. Concentrations of ZURZUVAE in breastmilk were below the level of quantification limit (BQL) by 4-6 days after the last dose."
  - Full prescribing information