A TRILOGY OF PHARMA TOPICS

INVESTMENT FORUM

OCTOBER 18, 2023

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THREE TOPICS FOR DISCUSSION TODAY

- Has the coverage of "weight loss" drugs become irrationally exuberant?
- Compounding pharmacies are a piece of the puzzle.
- Getting comfortable with turbulence – Inflation Reduction Act ("IRA") and pharma.

TOPIC NUMBER 1: DON'T' GET LOST WITH "WEIGHT LOSS" DRUGS

- For any drug, keep in mind a helpful three-part "rule of thumb:"
  - Most drugs are xenobiotics – not naturally produced or expected to be present.
  - Drugs are unavoidably dangerous – role of the prescribing physician.
  - Risk is always part of the balancing test for approval by FDA.
- Get a roadmap for the various "weight loss" drugs (GLP-1 agonists class – there are others).

Drug	Manufacturer	How Taken	Indication
Dulaglutide (Trulicity®)	Eli Lilly	Weekly Injection	Treatment of Type 2 Diabetes
Exenatide extended release (Bydureon®)	AstraZeneca	Weekly Injection	Treatment of Type 2 Diabetes
Exenatide (Byetta®)	Eli Lilly	Twice daily injection	Treatment of Type 2 Diabetes
Semaglutide (Ozempic®)	Novo Nordisk	Weekly injection	Treatment of Type 2 Diabetes
Semaglutide (Wegovy®)	Novo Nordisk	Weekly injection	Treatment of Type 2 Diabetes
Liraglutide (Victoza®, Saxenda®) (daily)	Novo Nordisk	Daily injection	Treatment of Type 2 Diabetes ***and Obesity***
Lixisenatide (Adlyxin®)	Sanofi-Aventis	Weekly injection	Treatment of Type 2 Diabetes
Semaglutide (Rybelsus®)	Novo Nordisk	Daily orally (tablet)	Treatment of Type 2 Diabetes

TOPIC NUMBER 1: DON'T' GET LOST WITH "WEIGHT LOSS" DRUGS (2)

- Some issues to consider:
  - What will the safety database for these drugs look like with much wider off-label use than the composition of the clinical trials?
  - Additional, confirmatory or contradictory clinical trials and meta-analyses by third parties.
  - Labeling changes – positive (new indication) or negative (additional warnings).
  - What are the behavioral aspects when the weight loss is temporary without chronic dosing and compliance?
  - Costs – formulary review, reimbursement and co-pays, out-of-pocket.
  - Even though FDA has limited ability to police off-label promotion, there is a "shadow" regulatory scheme – the plaintiff's bar. And it has started.
  - How will costs be managed for these drugs, including current and future government pricing and reimbursement and eligibility. Consider the recent experience of Biogen with Aduhelm®.
  - Supply chain hiccups and extended shortages – Novo Nordisk CEO.
  - Generic manufacturers are putting pieces into place (A dozen or so Drug Master Files submitted to FDA already for semaglutide).

TOPIC NUMBER 2: CAN MY PHARMACIST MAKE THESE DRUGS?

- Here's the answer – maybe (classic lawyer response that aggravates clients).
- Pharmacy compounding is an intricate mix of state and federal law – tempestuous and vexatious relationships between States and FDA.
- Federal law defines two types of compounding pharmacies.
- Each type has some different rules about what drugs it can compound with special attention to the active ingredient for a drug and the written prescription.
- The FDA drug shortage lists affects those rules – source of recent press, consternation, commercial opportunity and shenanigans.
- Compounding pharmacies can act to fill gaps in the supply chain – COVID19 critical drugs for example. And "weight loss" drugs too.
- Deluge of litigation by commercial manufacturers against compounders - preemption defenses have been successful and questions about patent infringement as well.

TOPIC NUMBER 3: HOW WILL THE "IRA" SAGA PLAY OUT?

- New and complex piece of legislation – significant litigation has started (at least 8 cases pending with various Constitutional and Administrative Procedures Act issues).
- Interpretation and implementation will take years if not longer (shades of the Affordable Care Act).
- Let's presume that the law is not significantly changed, and implementation begins in 2026.
- Some modeling suggests that prices set below the statutory maximum will result in significant revenue erosion, particularly for small molecule drugs (biologics are favored in the legislation).
- The pressure from falling reimbursement rates could result in Medicare prices acting as the market prices.
- Drugs in development today face the future risk of "negotiated" Medicare prices.
- Health care plans have increased responsibility and likely tighten drug utilization review and shrink formulary choices.

TOPIC NUMBER 3: HOW WILL THE "IRA" SAGA PLAY OUT? (2)

- New drugs might have difficulty with gaining access to Medicare coverage.
- There was legislation drafted that was more aggressive than the "IRA" – there is the potential that the "IRA" is just one step in a larger effort for more drugs to be subject to price controls.
- Manufacturers may resort to higher prices at the time a new drug launches – diabetes and inflammation could be examples of markets where these price increases could offset the "negotiated" prices mandated by the "IRA."
- There is the risk of price control creep earlier in a new drug's lifecycle.
- The pharma industry has warned about lack of incentives for R&D and penalties for using federal funding for R&D (for example, technology transfer from NIH).
- There is also an impact on patent protection – single sourced high-cost drugs with no generic version are at higher risk for price "negotiation." Adjust patent infringement strategies.
- Remain vigilant with analyst sentiment of limited impact on pharma and the CBO report of only 1% reduction in new drugs.