PLENARY 1

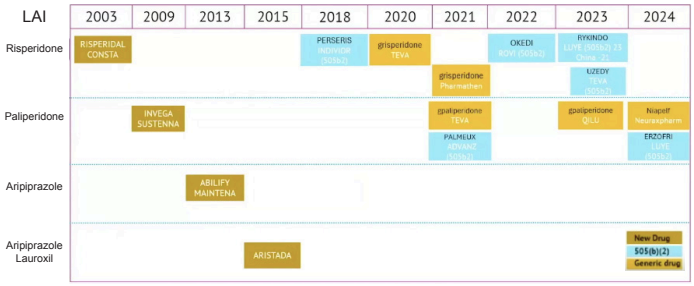
Parag Nimbolkar Medicines Patent Pool (MPP)

"Landscape analysis of approvals and market update of generic or equivalent formulations for CNS LAI medicines"

"[CNS-focused LAIs] are more commercially successful ... the idea is to collaborate and understand their journey of development"

Market analysis of CNS-focused products

Summary of EMA/FDA approvals of LAI products.



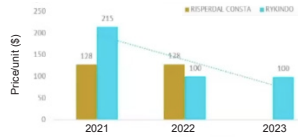
Takeaways.

- Huge delays from brand to generic and 505(b)(2) product approvals.
  - ◊ Risperidone LAI.
    - * 15 years to first 505(b)(2) product approval: Perseris (Indivior).
    - * Nearly 20 years to first generic product approval: grisperidone (TEVA).
  - ◊ Paliperidone LAI.
    - * 12 years to first 505(b)(2) and generic product approvals.
- Few therapeutically equivalent products vs 505(b)(2) products.
- Recent uptick in generic development and approvals due to improved clarity of regulatory guidance.
  - ◊ More companies are devoting resources to creating their own technology platform, "cracking" formulation complexity, and developing a therapeutically equivalent product.
  - ◊ Risperidone LAI. Generic developers have made huge strides in recent years.
  - ◊ Paliperidone palmitate LAI. At least five generic companies with tentative approvals.
- Most generic products are not present in LMICs.
  - ◊ Generics are in Australia, Canada, Europe, Japan, and US.

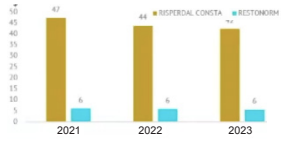
Impact of generic entry. Generally, prices decrease with benefit to the consumer.

- Risperidone LAI pricing analysis. Generic (Yellow)/alternative product (Blue) launch impacts pricing and innovator (Gold) sales; Degree of impact varies by territory.

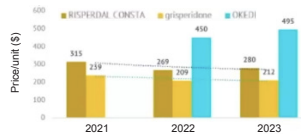
China – Generic launched at a huge discount.



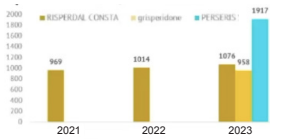
India – Huge difference in price between the innovator (Gold) and branded generic (Blue).



Germany – Generic (Yellow) priced 30% lower than the innovator (Gold).



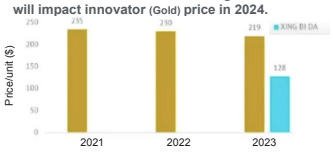
US – Generics (yellow) recently approved; The impact on price is not yet visible.



- ◊ Generics are capturing the market very fast, at least starting with high-income countries.
  - * Innovator market share decreased from 91% in 2021 to 74% by the end of 2023.

- Paliperidone palmitate pricing analysis. Impact of generic/alternative product launch on pricing will be visible in a few years.
  - ◊ Generics have only recently been launched.

China – Generic launched at a huge discount & will impact innovator (Gold) price in 2024.



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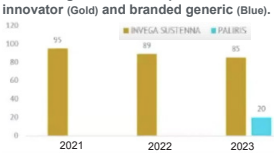
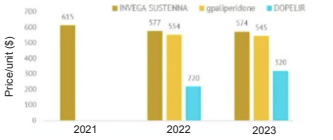
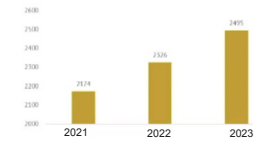


Germany – Generics (Yellow) may not impact price, but will greatly impact innovator (Gold) sales.



US – Generics are not commercially available due to patent protection.



Noteworthy success stories

Aristada (Aripiprazole lauroxil) IM ER suspension.

- **Submission type.** Type 1 new molecular entity.
  - ◊ Technology: Nanocrystal technology.
  - ◊ RLD: Abilify tablets.
- **Clinical path.** Alkermes submitted P3 (safety and efficacy) and SD/MD P1 PK studies.
  - ◊ Prior agency finding of safety and efficacy for oral aripiprazole was considered.
- **Value addition.** First LA atypical antipsychotic with QM and Q6W dosing options.
- **Commercial performance.** Doing well against the innovator.
  - ◊ $444M in sales vs Innovator $1.2B (2023).

Rytary (Carbidopa and Levodopa) ER capsule.

- **Submission type.** Type 5 new formulation or new manufacturer.
  - ◊ Technology: IR and ER beads designed for different release rates in GI tract.
  - ◊ RLD: Sinemet tablet, Sinemet CR tablet, and Stalevo tablet.
- **Clinical path.** Impax submitted two randomized P3 studies and six additional studies (i.e., PK, food effect, BA).
- **Value addition.**
  - ◊ Consistent PK profile to reduce motor fluctuations and dosing frequency.
  - ◊ Reduced time interval where patient symptoms are inadequately controlled.
  - ◊ ER formulation improves "off time" by over one hour each day.
- **Commercial performance.** Captured the market.
  - ◊ $298M in sales vs Innovator NA (2023).

Cinvanti (Aprepitant) IV emulsion.

- **Submission type.** Type 3 new dosage form.
  - ◊ Technology. Oil-in-water emulsion with improved aprepitant solubility.
  - ◊ RLD: Emend (fosaprepitant) injection.
- **Clinical Path.** Heron Therapeutics submitted two BA studies.
- **Value addition.**
  - ◊ Unique synthetic, surfactant-free formulation administered as IV push or infusion.
  - ◊ IV push saves $1.99 per push and 33 min vs 30-min IV infusion.
- **Commercial performance.** Captured the market;
  - ◊ $187M in sales vs Innovator $9M (2023).

Sublocade (Buprenorphine) SC ER injection.

- **Submission type.** Type 3 new dosage form.
  - ◊ Technology. Atrigel technology (in situ-forming gel/depot for SR over one month).
  - ◊ RLD: Subutex SL tablet
- **Clinical Path.** Indivior submitted one inpatient opioid blockade study and one RCT for safety and efficacy.
- **Value addition.**
  - ◊ Sustains therapeutic plasma concentrations for one month.
  - ◊ Blocks rewarding affects of opioids.
- **Commercial performance.** Captured the market.
  - ◊ $192M in sales vs Innovator withdrawn (2023).