SCYNEXIS

LPAD

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LPAD Applied to Antifungal Products

- Serious or life-threatening fungal infections (mortality)
  - *C. auris* infection (up to 60%)[a]
  - Azole-resistant invasive aspergillosis (~50%)[b]
  - Serious fungal disease failing or intolerant to existing therapies (~30%)[c]
  - Rare fungal infections (Scedosporiosis, Fusariosis, >50%)[d]

- These infections occur in a limited population of patients that are clinically relevant to health care providers

- There are unmet medical needs:
  - Only 3 main classes of antifungals – echinocandins, azoles, polyenes
    - only one is oral,
    - one has significant DDI concerns,
    - one has significant nephrotoxicity concerns.

[a] https://www.cdc.gov/fungal/candida-auris/candida-auris-qanda.html

[b] Verweij P. et al. Clin Infect Dis 2016; [c] Kullberg BJ. et al, Clin Infect Dis 2019; [d] Seidel D. et al, Crit Rev Microbiol 2019

Example of Product Eligible for LPAD

- DRUG-X is indicated in adults who have limited or no alternative treatment options, for the treatment of documented *invasive fungal* infections refractory to one or more treatments, or caused by pathogens known to be resistant to, or in whom the treatment is not tolerated.
  - Refractory: Defined by an independent committee
    - Example: invasive candidiasis with lack of clinical improvement and persistent positive cultures at a defined timepoint after initiation of approved therapy
  - Resistant:
    - Infection caused by a pathogen with known resistance (*e.g.*, azole-resistant *C. glabrata*, MDR *C. auris*, azole-resistant *Aspergillus*, rare molds)
  - Intolerant:
    - Toxicity associated with administrative of approved therapies or potential interactions with other drugs

Example of Product Eligible for LPAD

- This scenario is consistent with LPAD pathway
  - By definition a limited population because of lack of alternative therapy
  - The population is a defined subset of a broader population of patients for whom the drug could potentially be effective
  - The labeling defines the population in a way that a health care provider can identify the patient in a clinical setting
  - The indication represents an unmet medical need

Example of Product Eligible for LPAD

- DRUG-X can be approved when substantial effectiveness is based on the weight of evidence:
  - A single arm study
    - Placebo or ineffective active control or unsafe drug is unethical
    - Population is limited, size will need to be small (N=<100)
  - Historical data can serve as the control group
  - *In vitro, in vivo* and PK/PD studies support the activity of the drug against the target pathogen
  - Supportive clinical studies with related pathogens
  - The drug has shown clinical evidence of safety in a sufficiently large population
  - Limited Population labeling provides adequate controls on use to justify benefit to risk

Other Examples of LPAD pathway in Antifungal Development

- Novel therapeutic strategies for invasive fungal disease with poor outcomes
  - Combination therapy for fungal infections in which single agents are ineffective or infections with sub-optimal outcomes (high mortality) with currently available options
- Novel therapeutic strategies for invasive fungal disease with other significant unmet needs
  - Osteo-articular infection due to azole-resistant *Candida* spp. or intolerant to azole therapy.
    - Treatment guidelines requires 6-12 months of therapy
    - Only IV alternative options – significant unmet need for oral alternatives