Neglected populations: Developing child-friendly medicines

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Paediatric needs: Beginning with the end in mind

Key Elements:

✔ Children are different from adults
✔ Driven by the needs of children and caregivers
✔ Strong epidemiological data
✔ Clear Target Product Profile
✔ Early involvement of regulatory authorities/WHO
Children are different from adults
Need for pharmacokinetics studies

Children and adults differ in:

- Absorption
- Distribution
- Renal function (excretion)
- Hepatic function (metabolism)
- Pharmacodynamics:
  - therapeutic response
  - adverse reactions
  - mechanisms of disease
# DNDi R&D Portfolio December 2017

7 new treatments available and up to 20 new chemical entities in the pipeline

**Screen**

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<td>Two ‘4-in-1’ LPVr/ABC/3TC</td>
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<td>LPVr pellets with dual NRTI</td>
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**New Chemical Entity (NCE); Fexinidazole (for HAT and Chagas disease) = 1 NCE; Fosravuconazole = 1NCE**

**Development**

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<td>NECT Nifurtimox-Eflornithine Combination Therapy</td>
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<td>Superbooster Therapy Paediatric HIV/TB</td>
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Malaria: Clear target drug profile
Well-designed product & adapted packaging = IMPACT
Visceral Leishmaniasis
50% of cases are below the age of 12

Allometric dosage of Miltefosine for children in E Africa:

- DNDi and LEAP clinical trial in Sudan and Kenya, completed 2012
- Safety, efficacy and pharmacokinetic data

Age distribution of leishmaniasis patients

- 1939, 6%
- 11484, 38%
- 12647, 41%
- 4637, 15%

<2 years  2-11 years  12-17 years  ≥18 years

Chagas disease: no paed dose prior to 2011

High risk of delivering improper dosages (40-160% of target BZ content)

15 years ago

Benznidazole Nifurtimox

Treatment limitations
- Toxic
- Limited efficacy
- Lack of availability
- No paediatric formulation

2011

Paediatric dosage form of benznidazole:
- age-adapted
- easy-to-use
- affordable

Aim: improve existing treatments and strong effort in drug discovery
Paediatric HIV: children and caregivers’ needs-driven

160,000 new infant infections still occur each year
2.1 million children have HIV/AIDS: 88% in sub-Saharan Africa

> 430 new paediatric HIV infections daily
> 320 deaths in HIV+ children daily

Half of HIV+ babies will die before 2 yrs of age
Children <3 yrs still get ill-adapted treatments

Limitations of LPV/r

• Solution contains over 40% alcohol
• Unstable in tropical climates (not heat-stable)
• Horrible taste
• Up to 50% of children co-infected with TB, and need anti-TB therapy – with major negative DDI with LPV/r
• Liquid formulations (not just of LPV/r) extremely complex for caregivers to administer
Clear Target Product Profile:
Paediatric HIV: the right dose, the right taste

- 4 products in 1: granules (FDC)
- Simply open and use with water, milk, food
- No taste
- No cold chain
- Suitable for infants (< 2 mos-3 yrs)
- TB-treatment compatible
- Affordable

Modular format allows flexibility to replace drug in the combination

To be added during HIV/TB therapy

4-in-1 granules in Fixed-Dose Combinations

CIPLA / DNDi project supported by UNITAID
GARDP’s focus and priorities

Focus
• drug-resistant bacterial infections for which adequate treatment is not available
• address global health priorities that reflect the realities of clinical practice

Programmes prioritised to consider the intersection between priority pathogens; specific populations’ health needs; and individual diseases and broader syndromes.

Neonatal sepsis programme:
• One empiric treatment in place of ampicillin/gentamicin in settings of high extended spectrum beta-lactamase
• One treatment for neonates with confirmed Gram-negative carbapenem resistance

Paediatric antibiotics programme:
• Expedite development of late-stage pipeline antibiotics for use in paed populations
• Extend the use of existing classes of antibiotics
• Develop, with existing networks, a paed clinical trial platform that includes high, mid and low income countries
Regulatory environment for paediatric medicines

Example: EU

Paediatric Investigation Plan (PIP)


A development plan to support use of the medicine in children

Note: requirements do not apply to Article 58 applications (*EMA opinions in cooperation with WHO; Regulation (EC) No 726/2004*) for medicines for use outside EU, however scientific advice is encouraged to discuss products development in the paediatric population.
Conclusions: lessons learned
Beginning with the end in mind

- Poverty-related diseases bear a heavy paediatric burden
- Children are a neglected population for R&D
- Paediatric formulations for many diseases remain insufficient – children are at higher risk of dying
- Any development requires specific paediatric R&D efforts, including diagnostics
- Early consultation with end-users and regulators will facilitate regulatory and field adoption
- WHO EML for children supports adapted guidelines at country level