Access to Tranexamic Acid (TXA)
Lester Chinery (Petra Procter presenting on his behalf)
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Product Introduction: Insights from Market Research and Local Leadership - Parallel Session
Access to tranexamic acid (TXA), introduction

- Developed early 1960’s TXA is an antifibrinolytic agent that is indicated in multiple situations to prevent or treat bleeding (e.g., accident and trauma, surgery, dentistry etc.).

- TXA is an essential drug for reducing many forms of bleeding; it is inexpensive, not difficult to manufacture, comprising TXA API and water for injection, does not require cold chain storage and is relatively easy to administer by IV infusion.

- In 2017, following the publication of the WOMAN trial results in The Lancet, WHO recommended intravenous TXA administration for PPH treatment, in addition to oxytocin and other standard treatment options.

- While TXA has been in the market for many years for other indications, this was the first time its use became a strong recommendation for PPH treatment. Subsequently, TXA was included in the WHO Essential Medicines List and an expression of interest to manufacturers for WHO prequalification was issued.

- TXA not labelled for obstetric indications. Use for PPH treatment is off-label.
Quality of oxytocin and tranexamic acid for the prevention and treatment of postpartum hemorrhage in Kenya, Nigeria, South Africa, and Tanzania


Challenges in updating national guidelines and essential medicines lists in Sub-Saharan African countries to include WHO-recommended postpartum hemorrhage medicines

Joyce Ng’ang’a, Tabeth Chitimbe, Rosemary Mburu, Sara Rushwan, David Ntirushwa, Lester Chinery, and A. Metin Gülmezoglu

The compatibility of oxytocin and tranexamic acid injection products when mixed for co-administration by infusion for the treatment of postpartum haemorrhage: an in vitro investigation

Peter Lambert, Alessandra Tomazzini, Philip Wright, Claire McEvoy, Ioannis Gallos, Anne Ammerdorffer, Lester Chinery, Arri Coomarasamy, Ahmet Gülmezoglu
Understanding TXA Quality, Interactions & Regulatory Pathways

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Objectives

I. Assessing the compatibility of oxytocin-TXA & heat-stable carbetocin-TXA co-administration
   ➢ Expanded confirmatory study of compatibility between TXA and uterotonics and root cause analysis from observed negative interactions

II. Establishing the pathway for LMIC availability of quality assured TXA products for obstetric use
   ➢ Global mapping of TXA manufacturing to identify shortlist of candidate companies for forward engagement
   ➢ Identify current TXA registration status in 21 high-burden LMIC/mapping to MMR.
   ➢ Detail TXA regulatory requirements in target countries
   ➢ Develop forward strategies for TXA innovations

III. Identify and define potential implications of the investment activities - strategic analysis of TXA health systems pathways to scale and market shaping intervention options.
Global mapping of TXA manufacturing

Outcomes
- 172 distinct TXA manufacturers,
- Producing and marketing
- 226 TXA products (some manufacturers producing multiple brands)
- Further 60 identifiable injectable TXA products*
- Total of 286 identifiable products in global markets
- Majority - 75% not QA!

*Where the marketing authorization holder and country registration/availability is known, but where the specific manufacturing company/site could not be identified and/or verified.
Global mapping of TXA manufacturing

- Manufacturing across 35 different countries
- 114 located in Asia, overwhelmingly India (78) and Pakistan (34)
- Europe 31
- Americas 18
- Only 2 manufacturers were identified in Africa
### Availability vs. Need in 21 SSA countries

<table>
<thead>
<tr>
<th>Country</th>
<th>MMR Category</th>
<th>Registered Injectable TXA Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chad</td>
<td>Extremely High (&gt;1000)</td>
<td>1</td>
</tr>
<tr>
<td>Nigeria</td>
<td>Extremely High (&gt;1000)</td>
<td>2</td>
</tr>
<tr>
<td>Central African Republic</td>
<td>Very High (500-999)</td>
<td>0</td>
</tr>
<tr>
<td>Guinea</td>
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</tr>
<tr>
<td>Kenya</td>
<td>Very High (500-999)</td>
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<tr>
<td>Benin</td>
<td>Very High (500-999)</td>
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<td>Burundi</td>
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<tr>
<td>Côte d’Ivoire</td>
<td>High (300-499)</td>
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<td>Mauritania</td>
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<td>Sierra Leone</td>
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<tr>
<td>Niger</td>
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<td>0</td>
</tr>
<tr>
<td>Mali</td>
<td>High (300-499)</td>
<td>1</td>
</tr>
</tbody>
</table>

- No active registrations
- 1-2 registrations
- 3-5 registrations
- 5+ registrations

+ 95% of registered products not quality assured
Market Characterization

Significant global manufacturing
• 172 companies across 35 countries
• Countries + 286 products
• 75% NOT quality-assured

Identified quality concerns
- CF past studies
• Post marketing
• Compatibility with oxytocin

Limited availability where most needed
• Registration insufficient in
• 81% target countries
• No WHO-PQ TXA products

Evidence of uptake and use of oral TXA in response to recommendations
• Nigeria

Strategic analysis of TXA health systems pathways to scale and market shaping intervention options.
Towards a healthy market

Step 1 - developing the business case for TXA manufacturers.

Step 2 - expand engagement with candidate manufacturers who currently have products approved by an SRA - to facilitate and support fast-track registration in high-burden SSA.

Step 3 - provision of technical manufacturing support to selected candidates to achieve WHO compliant GMP, followed by regulatory support for submission to WHO-PQP until prequalified - support fast-track registration in SSA.

Step 4 - continued collaboration with TXA innovators, providing technical advice on forward clinical study requirements, batch manufacturing and scale-up, engagement with regulators.
TXA Candidate selection - steps 2 and 3

- Long list of 172 companies
- Reduced to +/- 30 based upon criteria
- Expression of interest + technical questionnaire

6 companies willing to participate
- 4 with existing SRA TXA registrations
- 1 manufacturing TXA with other products prequalified by WHO
- 1 African manufacturer
TXA Market Shaping

STRATEGY OVERVIEW

Step 1: Establish TXA business case

Step 2: Territory scope, Regulatory strategy/dossier amendment, Dossier submission - target LMIC, Registration

Step 3: Tech support, PQ dossier submission, Clinical data package, Dossier submission WHO PQP

Step 4: Support pre-clinical, Establish clinical/reg pathway, Batch manufacturing/scale-up, Clinical trials

Advocacy, demand creation
For further information on our TXA initiatives, contact Alessandra Fleurent a.fleurent@conceptfoundation.org