Challenges in commercialization of Combination pills for Cardiovascular disease

Dr. Sandeep Bhattacharyya, Chief Innovation & Strategy Officer, Merck & Co., Inc. / MSD - Asia Pacific

Disclaimer: The opinions expressed in this presentation are the personal opinions of the speaker & do not necessarily reflect the position of Merck & Co., Inc / MSD
The Burden of Cardiovascular disease is in Developing Countries

Total number of deaths due to cardiovascular diseases in the world: 17 327 000

Europe
4 584 000

East Med.
1 195 000

The Americas
1 944 000

Africa
1 254 000

South-East Asia
3 616 000

Western Pacific
4 735 000

CV mortality ~1% per annum puts CV risk population at 1.7 Billion globally
The Burden of Cardiovascular disease in Developing Countries

Usage of secondary prevention drugs - PURE study

- Antiplatelet
- ACE - I / ARB
- Beta-blockers
- Statins
- Diuretics


Affordability  Accessibility  Acceptability
Secondary prevention (“Low Hanging Fruit”) - Improved delivery of care:

* Avoiding complex algorithms to identify individuals
  * for therapy (e.g. diabetes or established CHD),
* Increasing the ease of prescribing,
  * potentially allowing task sharing & task shifting to nurse practitioners
  * Avoiding multiple steps for dose titration of each drug
* More at-risk individuals could be treated

Primary Prevention (“The Holy Grail”)

* The Individualized therapy approach - based on “identification of high risk patients”
  * High cost of screening - beyond the scope of less developed countries with large populations at risk and low doctor: population ratios
* The Population Risk approach - using the risk clustering for screening
  * Patients above a certain age threshold (e.g. > 55 years) with one additional risk factor (e.g. hypertension)
Acceptability

Clinical inertia

“the primary care providers generally “failed to apply . . . guidelines in the very high-risk population, even when prompted”


Patient adherence
Accessibility

Guideline challenges

- More support in secondary prevention than in primary prevention
- Individualization of therapy
- Start low-Go slow

Regulatory challenges

- Convenience of FDCs & improved adherence not “adequate”
- Demonstration of value of each component - “synergy”
- Bioequivalence in a multi-component formulation
An alternative approach?
Treat the solution as that for a public health problem?

....... a trade-off between perfect therapy and broad population coverage.......
FDA position on Combination vaccines
Accepting “convenience” and not expecting “synergy”

FDA position on “small molecule” FDCs
* Two or more drugs may be combined in a single dosage form when:
  * each component makes a contribution to the claimed effects and
  * the dosage of each component (amount, frequency, duration) is such that the combination is safe and effective
  * for a significant patient population requiring such concurrent therapy as defined in the labelling for the drug.

Regulatory approval through WHO pre-qualification process

Will strong outcomes data open regulatory doors?
Focused on the impact of the intervention on population risk as in the case of vaccines, not just individual risk factors in individual patients.
## Affordability

### Generic prices
- Aspirin
- Atenolol
- Simvastatin
- Ramipril
- HCT

$90 per annum

$0.25 at current market prices in India

## Accessibility

- Clinician education to overcome clinical inertia
- Health worker counseling to overcome patient adherence at grass root level

With investments required for clinician education & overcoming patient adherence, can industry meet the burden of payment aspirations of governments in a commercially viable manner?
Conclusions

* The Burden of CV Disease & huge treatment gap warrants immediate action from stakeholders (Governments, payers, etc.) to arrest this public health NCD pandemic, especially in Developing Countries.

* Current Regulatory agencies and major society guidelines not fully aligned with seeking a solution to cut population risk - focusing rather on individualization of care.

* With strong outcomes data using combination pills (TIPS 3, HOPE 4) and epidemiological data from large cohort studies on clustering of risk, there could be a significant change in the position of regulators, perhaps under the guidance of bodies like WHO through their NCD programs.

* Cost-efficient supply chain models will be needed to make this public health solution designed for wide patient access also commercially viable.