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Benefit- Risk assessment and communication

Eric Abadie, MD, MBA
AFSSAPS, CHMP chair

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Current Role of Regulatory Agencies

- to assess contents of a MA dossier
- draw "scientific" conclusions
- take decisions based on an overall Benefit- Risk assessment (Article 26, Directive 2001/83)

on behalf of other stakeholders such as patients, doctors, other health care providers etc.

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Will a drug having being granted a favourable opinion by CHMP be prescribed ?

It will depend on:

- Reimbursement
- National treatment recommendations
- Local drug committees
- Doctors
- Patients
- Media attention, etc…

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Benefit – risk assessment

- Regulators take decisions on behalf of patients and prescribers.
- It is a subjective process, influenced by e.g. experience and distance.
- Regulators are more and more challenged by patients, patient organisations, health care professional and industry…. but also medias and politics

A B/R assessment is

- valid at a given point in time, but may be different later on
- often relative to other products, although not explicit in the legislation (should we approve B, inferior to A already on the market)
- what is a "clinically significant effect"? Difference between mean and responders (Example of anti diabetics, or antidepressants)

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Balancing B and R is complex

- Uncertainty
- Multiple objectives
- Differences in perspective
- Difficulty of trading off effect of different importance
- Lack of agreement of what valuation criteria to use
- Heterogeneity of effects across patient population

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CHMP WG (May 2006)

- To meet challenges coming from outside world: consistency, transparency, and objectivity in assessment B/R balance (translated in EPAR)
- Transparent: to explain to the outside world how we assess B/R, currently « implicit » more than « explicit » (impact on EPAR)
- Consistent: to use the same methodology across different products
- Communication: clear and explicit

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Recommendations to the CHMP

- To use a stepwise approach

  1) To revise the current B/R assessment section of CHMP assessment report template

  2) To explore further development in methodologies for quantitative B/R assessment

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1) To revise the current B/R assessment section of CHMP AR (EPAR) (June 2009)

- Benefits
  - Beneficial effects
  - Uncertainty
- Risks
  - Unfavourable effects
  - Uncertainty
- Benefit-Risk balance
  - Assign values, most important effects (trade-offs)
  - Assess the benefit-risk balance (trade-offs)
  - Discuss
  - Conclude

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2) To explore further development in methodologies for B/R assessment

- Proposal based on the FP 7 model
- Five work packages (Current practice, applicability of current tools and processes, field tests, development of B/R tools and process, training package)
- Necessity of collaboration with NCA's

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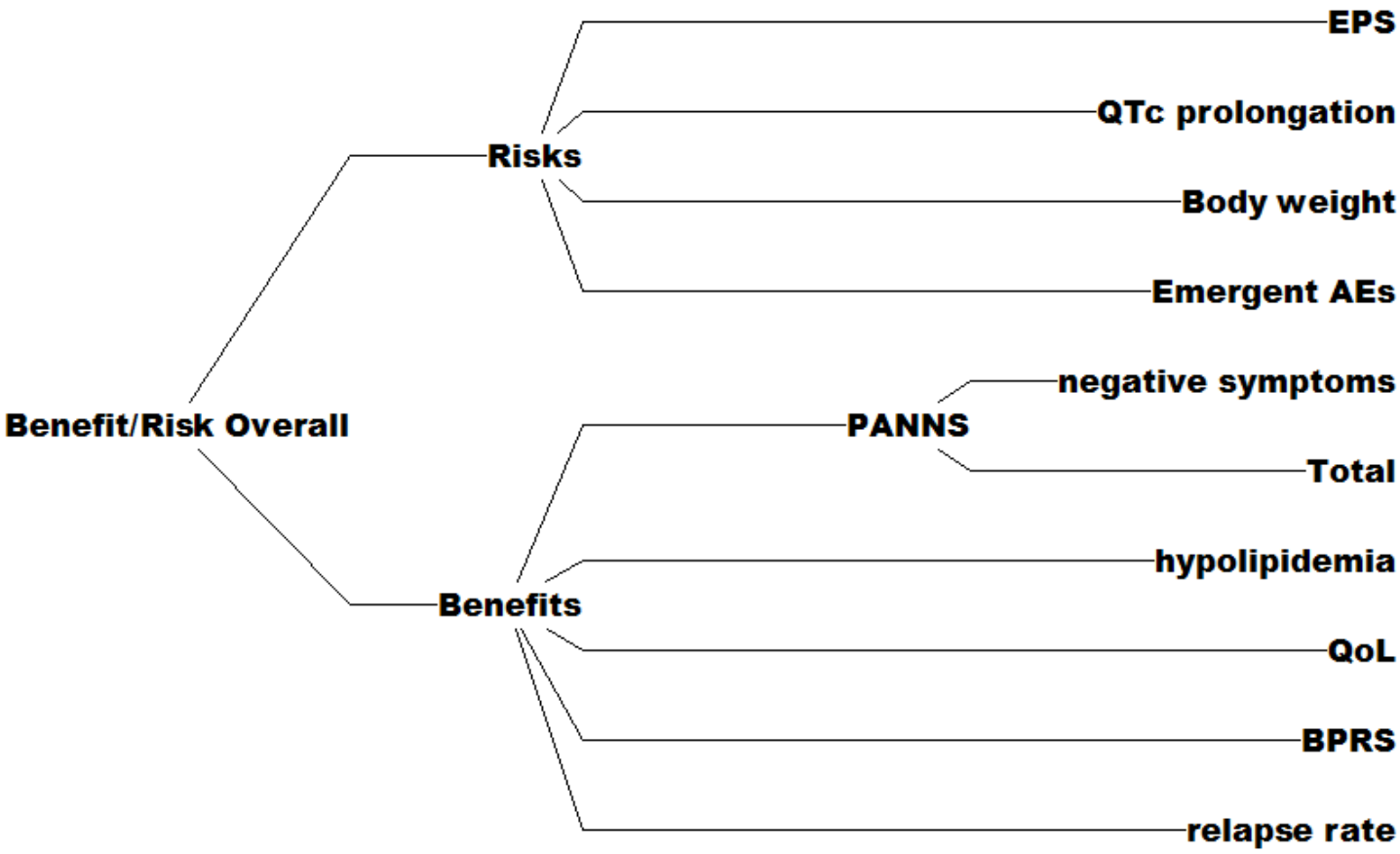
MCDA: an example of value tree



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Obstacles to overcome and opportunities for further research

- The assymetry between B and R in clinical trials and in post marketing
- The metric (same unit for B and R)
- The weight incorporation (including the perspective)
- The global issue

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Conclusion

- Quantitative models complex, time consuming, need of software….but could be (potentially) useful for regulators (major question: when ?)
- Advantage: may involve patients and HCP in weighting, may enhance transparency, consistency and objectivity of decisions
- Today « mood » is more on qualitative methodology (clearly express the contents of benefit and risk in approval documents)…