The Patient’s Perspectives on Significant Benefit

Yann Le Cam, Chief Executive Officer, EURORDIS
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SIGNIFICANT BENEFIT IS FOR PATIENTS

• To stimulate the development of new orphan drugs providing a medical benefit meaningful to patients, «a relevant advantage» or «major contribution to patient care» for rare conditions over existing methods of treatment (or prevention or diagnostic).

• SB is unique in Europe, it does not exist in the USA.

• We observe that SB has an impact on:

  a) competitive environment
  b) investors decision and strategy of development and market introduction
  c) payers perception
SIGNIFICANT BENEFIT IS IMPORTANT

• Significant Benefit creates value:
  
  ➢ A measure to incentivise and channel investment into unmet medical needs by developing products bringing value to society

  ➢ A virtuous circle for the development of ODs

• But the way to assess SB has been questioned over the past years: what is the right trade-off between sufficient evidence and too high requirements for evidence? Do we recognise that medical improvements are incremental in rare diseases as for frequent diseases e.g. cancers?
EURORDIS advocated for SB

• EURORDIS and Patients’ organisations advocated in 1996-1999 for Significant Benefit (SB) to be included in the Regulation (EC) N°141 /2000, and contributed to its wording

• From first 2 COMP mandate to current COMP mandate

• As patient representatives, EURORDIS has contributed to make SB more than a formality: from « Potential SB still holds » to « Demonstration of SB based on evidence »
Time & Context!

- The concept of SB is unique, it doesn’t exist elsewhere.
- The SB was conceived between 1996 and 1999.
- Since then..... HTA has emerged! Effectiveness and Relative Effectiveness have been clarified in EU several years later.
- How would we call SB today?
- We are doing contortion to position SB within the value determination, because it is there in the EU Regulation.
- Also, it is time to reconsider this concept in light of the current move towards adaptive pathways, regulatory flexibility and seamless approaches...continuum of evidence generation.
4 MAIN ISSUES

1. Continuum of evidence generation
2. Which data?
3. Assessment process
4. Re-use of assessment and public information
1. Continuum of evidence generation

• First, potential SB is assessed by COMP, at the time of orphan designation and secondly, re-assessed at the time of MA for maintenance (or not) of the orphan status

• New paradigm: Adaptive pathways: need of evidence generation all along the life cycle of a product

• With the aim of convincing the different stakeholders: regulators, HTA bodies and payers

• When meaningful data to assess significant benefit are lacking (early approval, conditional approval), need of post-marketing data collection

• Need for post- marketing re-assessment of SB when more evidence are available
1. Continuum of evidence generation (2)

• A mechanism of post-marketing re-assessment of the SB, not foreseen in the regulation, is needed and would allow more flexibility without hampering the value of the orphan status

• In the context of a conditional approval -> we could have a conditional SB and then a full SB assessment at the time of the full marketing authorisation

• When companies seek Scientific Advice /Protocol Assistance or Parallel HTA /SA –> the SAWP should pro-actively raise the questions on SB and evidence generation

• Find ways to promote more the early dialogues between companies, regulators, HTA bodies and payers, when the product has to show SB
2. Which data?

- Patient Relevant Outcomes Measures & Patient Reported Outcomes: Importance for the benefit/risk assessment at CHMP, but also when supporting the claim for Major Contribution to Patient Care / SB at COMP. Highly relevant for HTA bodies and payers → to be anticipated in Scientific Advice(s) / Protocol Assistance

- Real World Evidence: data from clinical use, observational studies. These data need to be collected after MA to assess the real value of the product in a real life setting → heterogeneity of patients for a given rare condition compared to patients involved in a clinical trial. → would inform the post-marketing re-assessment of SB
3. Assessment process

- The SB assessment has to be made within the context of appropriate skills and resources

- COMP needs to invite (F2F or TC) more medical/clinical experts and concerned patient experts when assessing Significant Benefit

- A minimum of two expert patients should be involved systematically in each SB discussion at the time of MA

- The burden of assessment of SB by COMP members is increasing and should be better rewarded – as there are no fees for the NCA (additional support/daily rate to assessors in view to better help them perform their tasks)
3. Assessment process (2)

- COMP has established a **Working Group on Significant Benefit** -> *should this WG become a sustainable body so to provide oversight to maintain quality and strategic improvement of the overall process?*

- EMA / COMP should establish a **collaboration with EUNetHTA** at two levels:
  -> *work together on SB Assessment Reports as CHMP did for EPARs*
  -> *have a permanent EUnetHTA representative/expert at COMP for SB Assessments, or, have ad hoc representativity from EUnetHTA for each SB Assessment*

- The administrative burden and the reimbursement issues are a bottleneck to take into account to **involve experts** (clinical experts, EUNetHTA reps. and patient experts)
4. Re-use of assessment report and public information

• The SB reports’ content and format could benefit from input not only of EunetHTA, but also of NCAPR -> through MoCA experts

• The reports of SB assessment should and could be available to inform other stakeholders

• Public Summary of Opinions (PSOs) on orphan designation and European Public Assessment Reports (EPARs) are made public and therefore intended to be easily understood by non scientists

• The document ‘Recommendation for maintenance of orphan designation at the time of marketing authorisation’ -> could be added in annex to PSO and EPAR.
CONCLUSIONS

• The spirit of the Orphan Regulation is to provide an attractive ecosystem for the development of rare disease therapies fostering investment in this area of unmet medical needs

• We need to keep this spirit alive for the benefit of patients

• We need to recognise that Significant Benefit was the precursor of comparative efficacy, comparative / relative effectiveness + major contribution to patient care (also considered in HTA)

• Over last 10 years, relative effectiveness has become more adaptive, flexible, and looking at post-MA data ageneration

• Significant benefit can still be an asset of the EU Orphan Legislation if positioned clearly in the new context of HTA and adaptive pathways => Alignment + Flexibility
CONCLUSIONS

• We need to keep the right trade-off between the need for evidence to perform SB assessment and the flexibility needed to give time to generate these evidences post-MA.

• Risk are real to create a new silo of “disconnected rational decisions” and we will defer the submission of MAA as sponsors will wait to collect sufficient evidence for SB.

• There are only 3 scenarios: a) Require higher level evidence, create uncertainties on orphan status maintenance, des-incentivize investment in OMP, go against the adaptiveness and seamless approach, defer submission of MAA; b) Push the potentials of the EU Reg OMPs and create possibility to conditional SB or SB re-assessment; c) Reduce requirements, back to “Potential SB still holds”, leave it to HTA, align with US.
THANK YOU!