DGRA Jahrestagung, Bonn
08.05.2014

Experiences with early G-BA advice and involvement of BfArM/PEI

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Set the scene…

- Support for HTA (G-BA) activities is a relatively new activity at a German affiliate level
- While Regulatory decisions are mostly done at a European level, HTA/Market access remains a “local” activity
- There is a strong connection between Regulatory and Market access activities as the Regulatory dossier and the outcome of the approval process form the basis of the value dossier
- Scientific Advice discussions with BfArM/PEI is a typical Regulatory activity
- G-BA advice discussions are lead by Market Access with input from DRA

Some similarities, some discrepancies between the two advice processes…

Note : Early G-BA advice may be an at-risk activity

Agenda

G-BA advice

- Why? Legal basis
- How does it work in practice?
- How can DRA contribute?
- Involvement of BfArM/PEI
- Experiences at Roche Germany
- Outlook/Discussion

Different legal basis for G-BA additional benefit assessment and Regulatory risk-benefit assessment (simplified…)

- **PEI/BfArM:**

  AMG (Drug law)

  - Quality
  - Safety
  - Efficacy

- **G-BA:**

  SGB V (Social code book)

  - Additional benefit over existing therapies

Legal basis G-BA advice („Request for consultation“) SGB V §35a (7)

„Eine Beratung vor Beginn von Zulassungsstudien der Phase drei oder zur Planung klinischer Prüfungen soll unter Beteiligung des Bundesinstituts für Arzneimittel und Medizinprodukte oder des Paul-Ehrlich-Instituts stattfinden.“

G-BA homepage:

Eine solche Beratung kann bereits vor Beginn von Zulassungsstudien der Phase drei und unter Beteiligung des Bundesinstituts für Arzneimittel und Medizinprodukte oder des Paul-Ehrlich-Instituts stattfinden.

This consultation can take place before the start of phase 3 authorization studies and can involve the Federal Institute for Drugs and Medical Devices or the Paul Ehrlich Institute.”

How does it work in practice?

- **G-BA meeting:**
  - F2F G-BA meeting will be scheduled approx 2 months upon receipt of request
  - Meeting duration 20min to 2h
  - Outcome of G-BA discussion will be presented to you
    - Provision of responses on slides (mostly)
    - BfArM/PEI position handed over in writing
    - Possibility to ask clarifying questions
- **Preparation phase:**
  - Request template provided on G-BA homepage
    - *Don´t forget to tick the box for involevement of BfArM/PEI*
- **Post-meeting:**
  - Receipt of protocol (written by G-BA) ca. 1 month later
  - 1 week time for comments

How can DRA contribute?

- **G-BA meeting:**
  - Provide Regulatory viewpoint at G-BA meeting
  - Interpretation of indication wording, approval status

- **Preparation phase:**
  - Provide/explain Regulatory context:
    - Global development timelines (incl. scenario planning)
      - Regulatory pathway
        - Help decide on best timing of G-BA advice
    - Provision/Interpretation of Scientific Advice from EU and FDA
      - And/or Regulatory guidelines
  - Input/review into G-BA „advice package“
    - Special emphasis on indication wording

- **Post-meeting:**
  - Discussion with BfArM/PEI

Involvement of BfArM/PEI

Paul-Ehrlich-Institut

BfArM

Before G-BA advice

- Discussion of study design
- Understanding of comparator therapy from Regulatory standpoint
- Indication wording

After G-BA advice

- Interpretation of indication wording
  - (mostly of comparator therapy but also on „own“ indications)
- „Formal“ Scientific Advice re G-BA proposed study design/comparator
- Discussion/Feasability of G-BA commitments

Experiences at Roche Germany

≈ Fifteen (15) G-BA advices

- Few true „**early“** advices
  - i.e. prior to start/protocol lock of phase III/registration study
- Mostly „**mid-stage“** advices
  - „heritage“ prior AMNOG
- Some „**dossier“** advices
  - i.e. structure of value dossier
  - Usually close to final regulatory approval
  - „stable“ indication

……3 development programs stopped ……..

Typical questions for G-BA advice…

- ZVT – comparator therapy
- Endpoints qualifying for G-BAs additional benefit assessment domains
  - Mortality
  - Morbidity
  - QoL
  - Safety
- Study design
- Homogeneity of population as per indication
- SOC

Discussion Points at G-BA meetings

- ZVT (comparator therapy):
  - ZVT needs to be approved in Germany
  - But „actual“ evidence base of approval status often not considered…
  - When does a new therapy becomes SOC and therefore ZVT?
- Endpoints (i.e. PFS in oncology…)
- Validity of PRO tools
- Problems that arise through global nature of drug develoment i.e.
  - concomittant therapies allowed in study protocol are not approved (or „differently“ approved) in Germany/EU

Outlook - Procedural questions

- When is a new G-BA advice needed?
  - When is the evidence for the G-BA advice “outdated”?
  - Will G-BA monitor this as well?

- “True” parallell/joint SA of G-BA and BfArM/PEI i.e.:
  - BfArM and/or PEI take part in the G-BA discussion
  - G-BA/IQWIQ join national scientific advice at BfArM/PEI
    - Start with Observer status?

True Joint Advice ...can we get there?

What is possible on an EU-level, should be possible on a national level?

Can we try a pilot?

THANK YOU