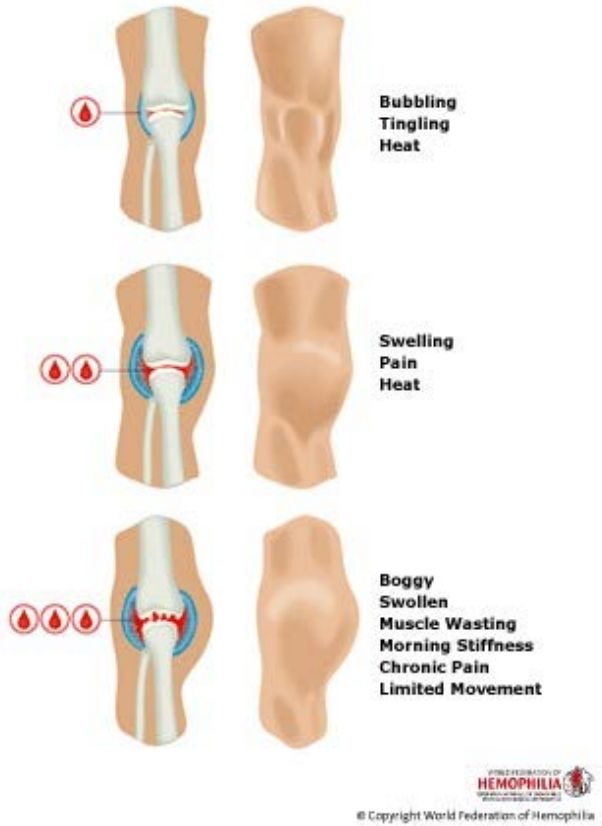
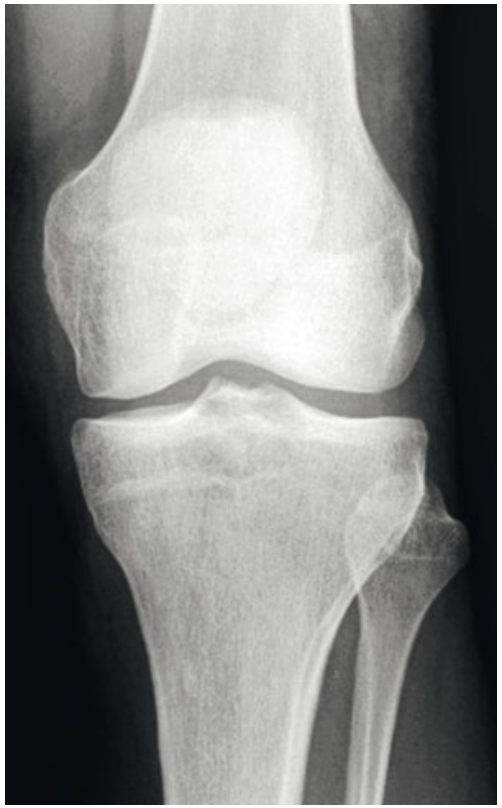
The German Experience in Policy Evolution for Haemophilia Therapies – From IQWIG to AMNOG to ACCESS

Dr. med. Uwe Schlenkrich

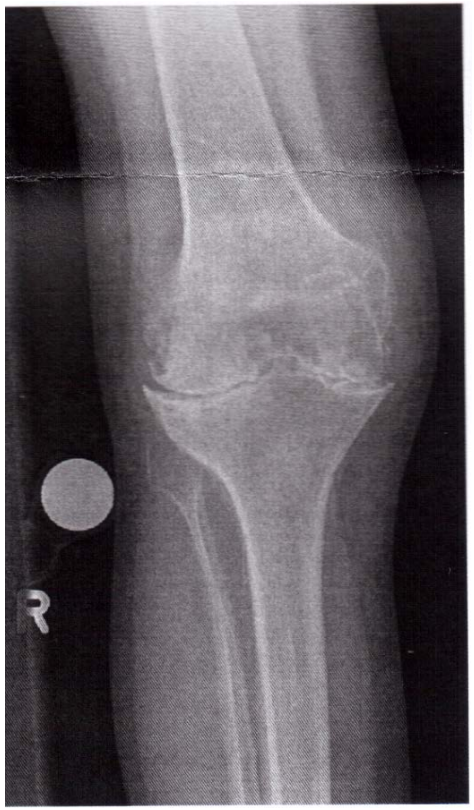
Joint Bleeding



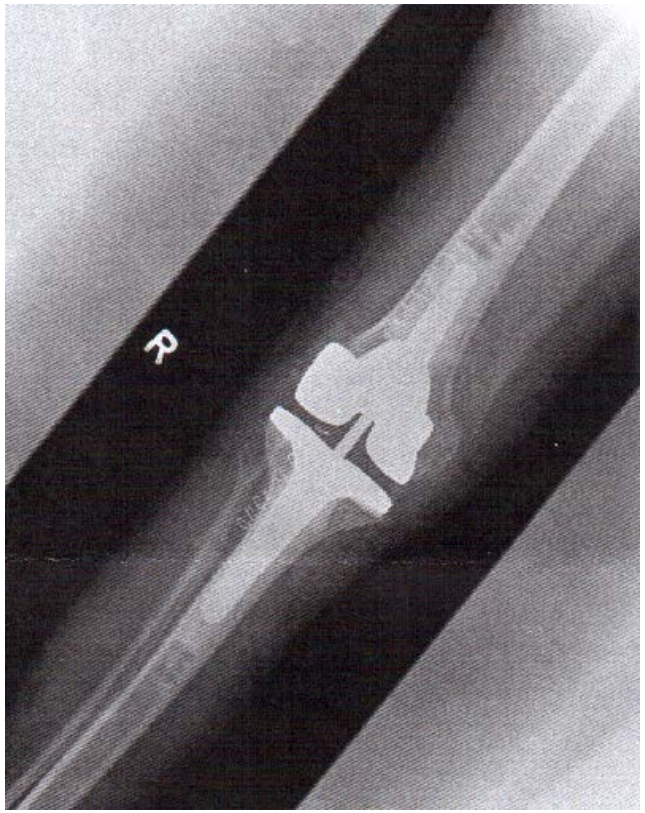
Normal Knee Joint



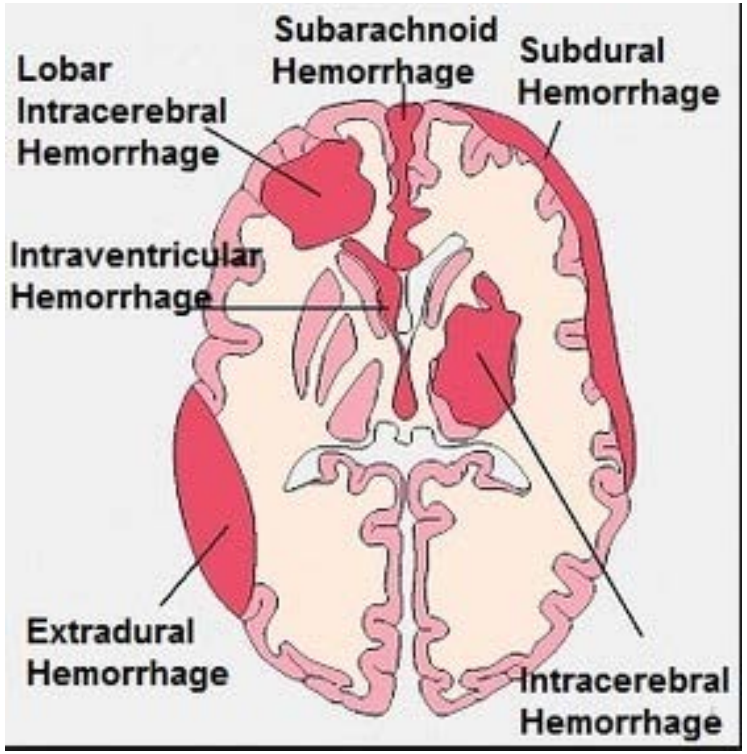
Knee Joint of a PWH



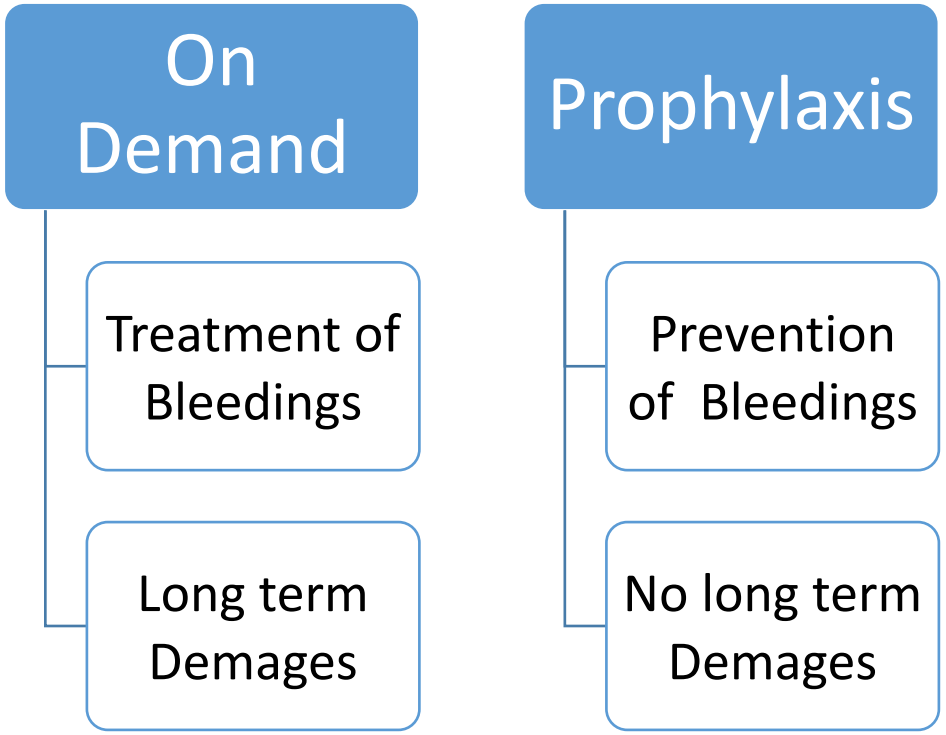
Joint Replacement



Intracranial Hemorrhage

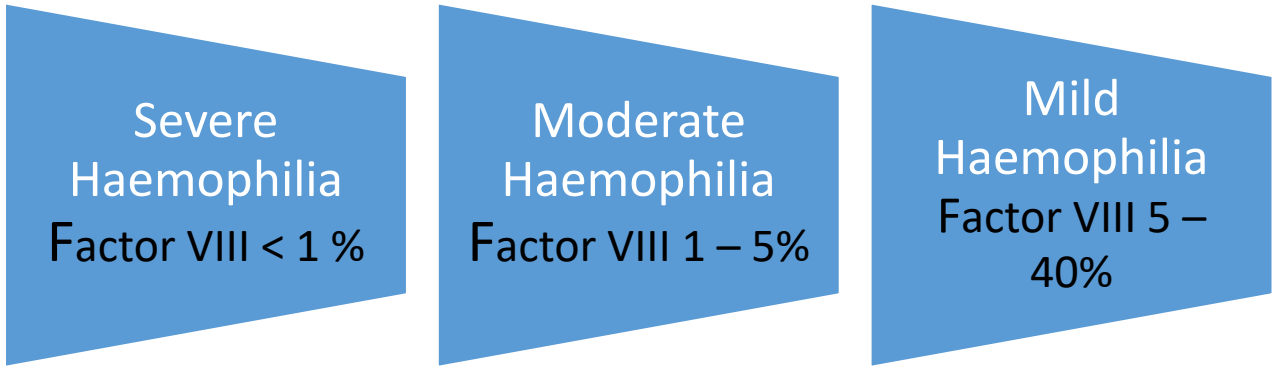


Types of Treatement



Prophylaxis

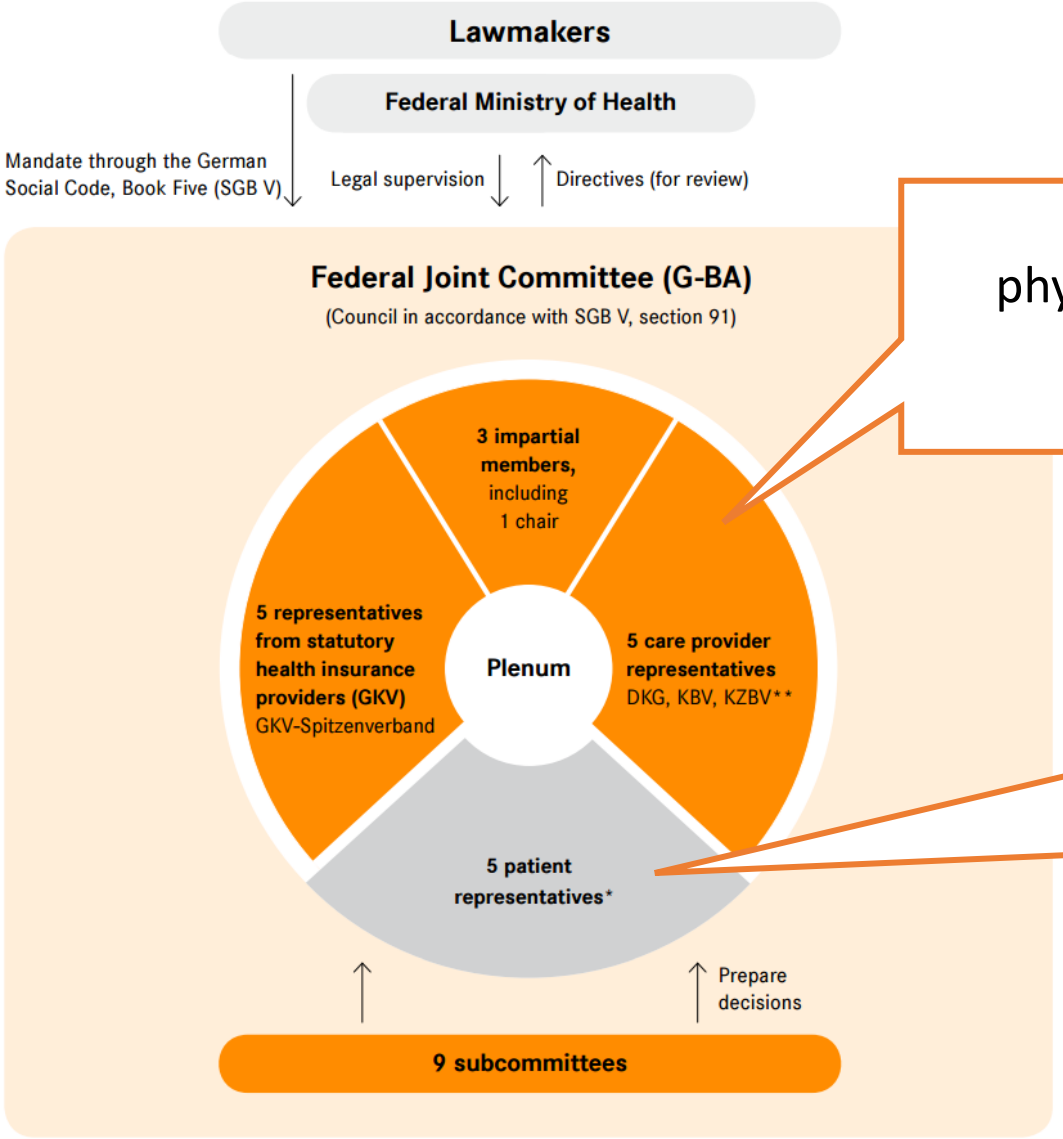
Change of the Phenotype



German health care system

- Health insurance is mandatory in Germany. About 90% of the people are insured at Statutory Health Insurance (SHI). 10 % are in a private insurance.
- Financed: 7.5 % of salary and about the same amount from employer go to a common fund
- Self-government of health care system
- G-BA (Federal joint committee) is the highest decision-making body of the joint self-government
  - specifies which services in medical care are reimbursed by the Statutory Health Insurance fund
  - Passes HTAs to IQWiG

Federal Joint Committee (G-BA)



physicians, dentists, hospitals

comprehensive discussion and petition rights on all agenda items
BUT: no voting right!

Responsibilities and Objectives of IQWiG -Institute for Quality and Efficiency in Health Care-

Receives tasks only from the Ministry of Health and the G-BA

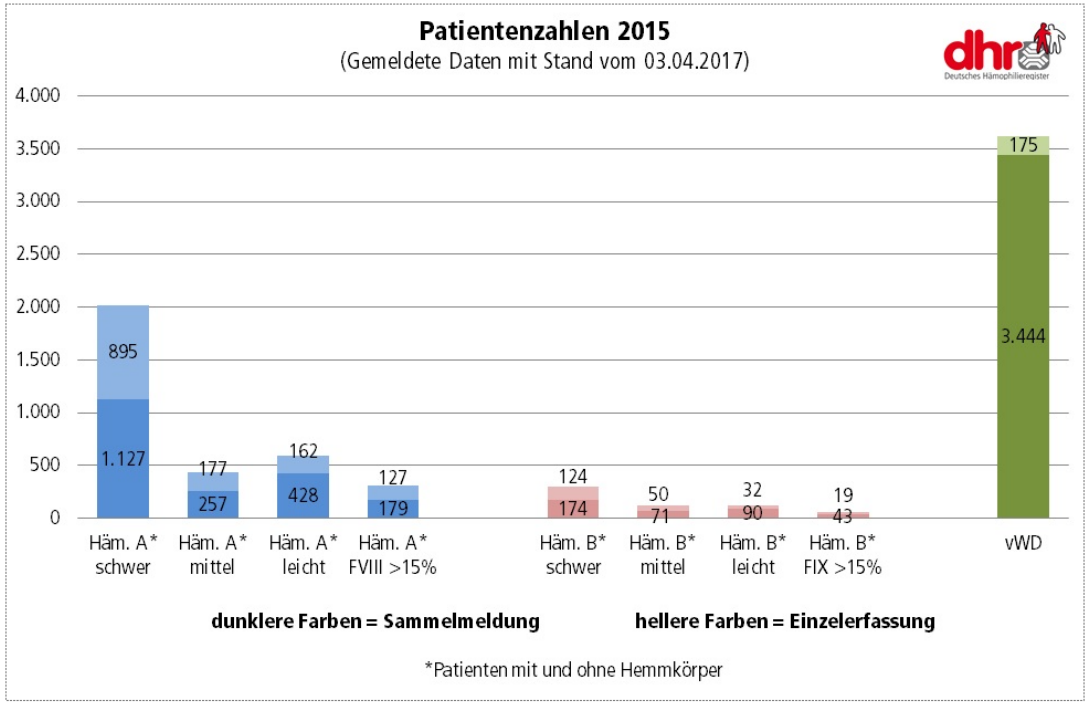
The Institute generates independent, evidence-based reports (HTAs), e.g. on:

- drugs
- non-drug interventions (e.g. surgical procedures)
- diagnostic tests and screening tests
- clinical practice guidelines (CPGs) and disease management programmes (DMPs)

Haemophilia treatment in Germany

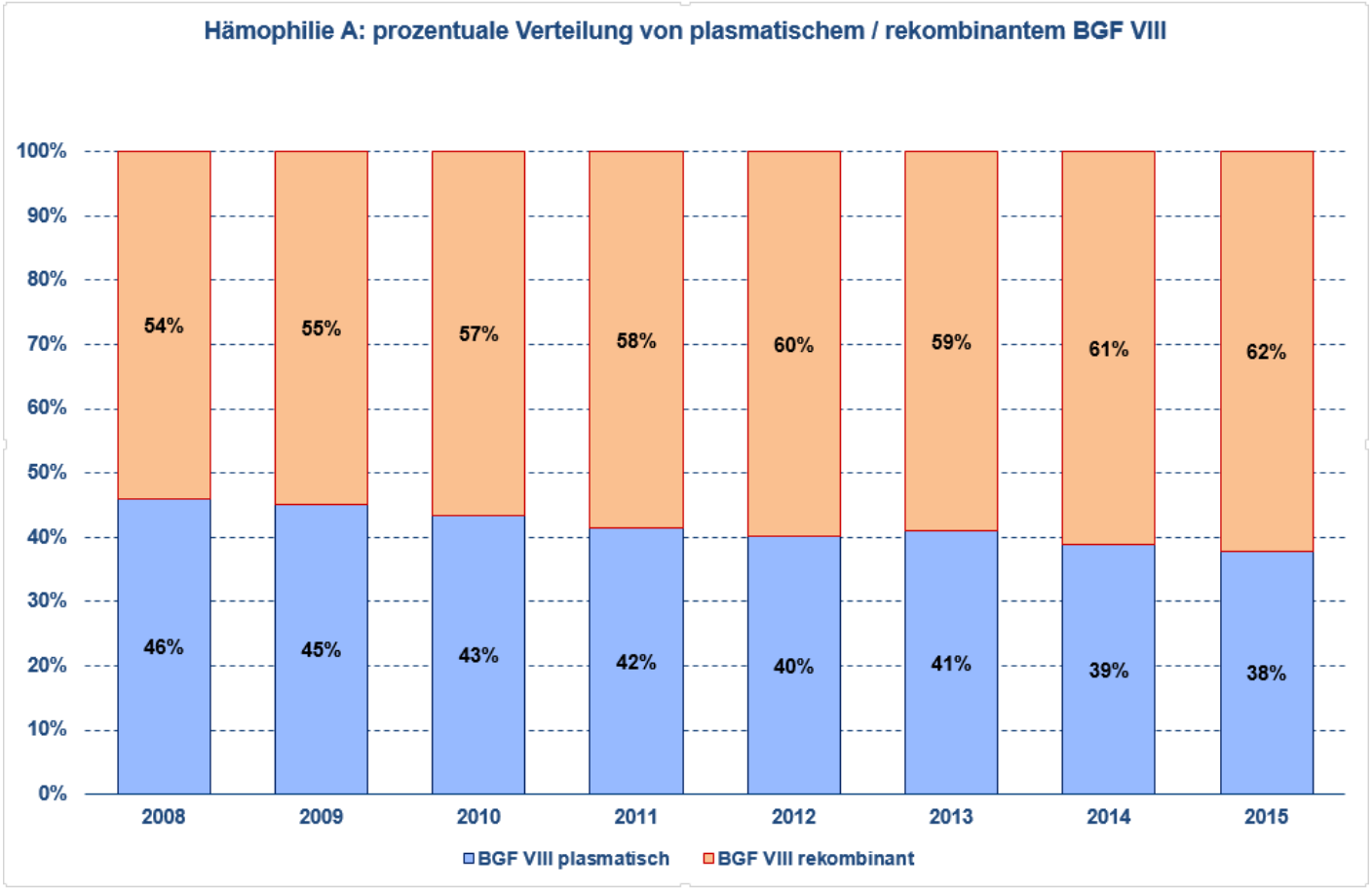
- Covered by health insurances:
  - ✓Prophylaxis for children and adults
  - ✓Immune tolerance therapy (ITT)
  - ✓Surgeries (replacement therapies)
  - ✓HCV therapies
  - ✓HIV therapies
- Choice of product done by physician and patient / parents
- Consumption is 760 millions IU factor VIII, about 8 IU/Capita
- Plasma derived clotting factors / recombinant factors 45%/55%

Patients with Haemophilia in Germany

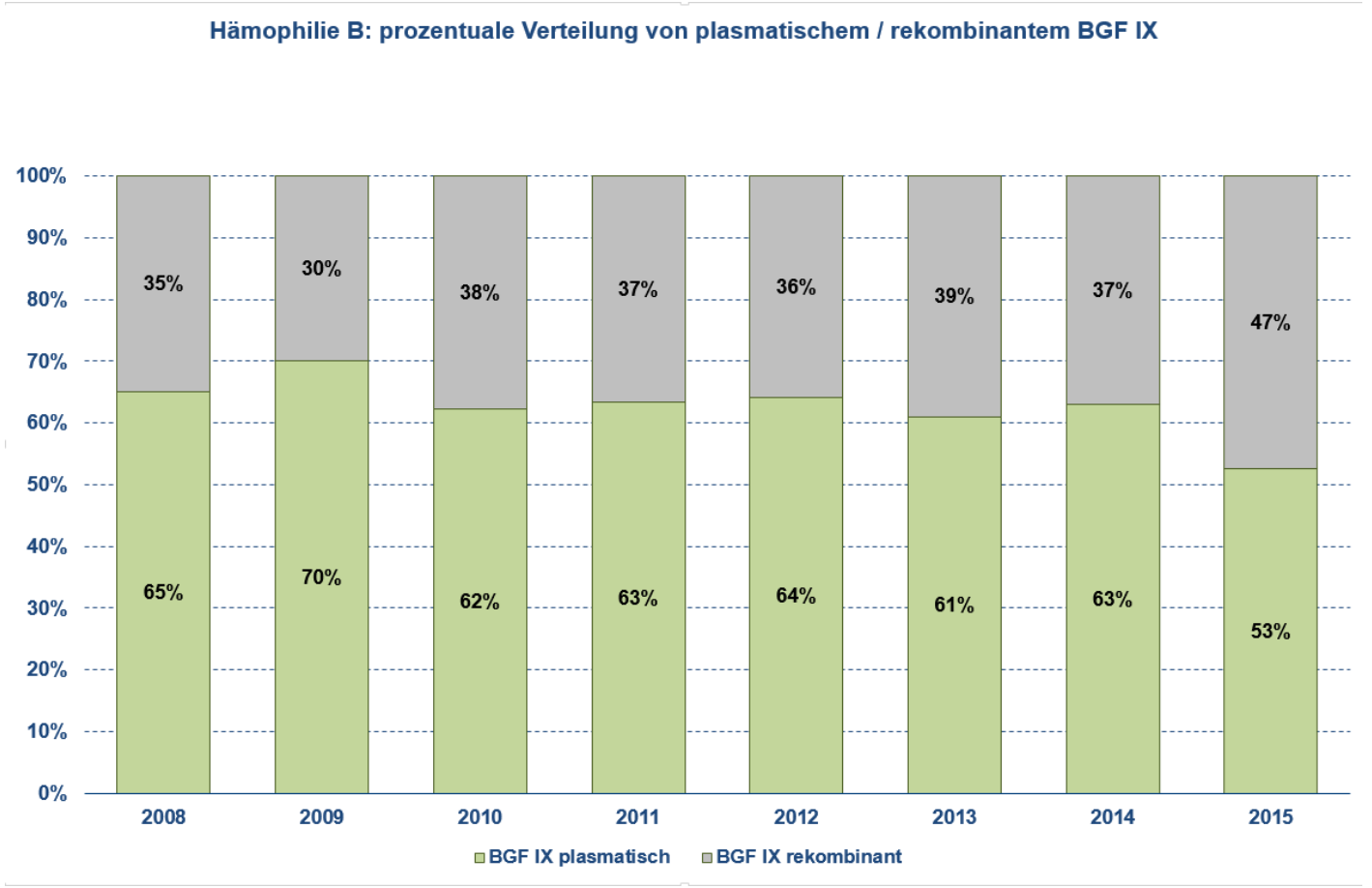


- Haemophilia A: 3352
- Haemophilia B: 603

Haemophilia A



Haemophilia B

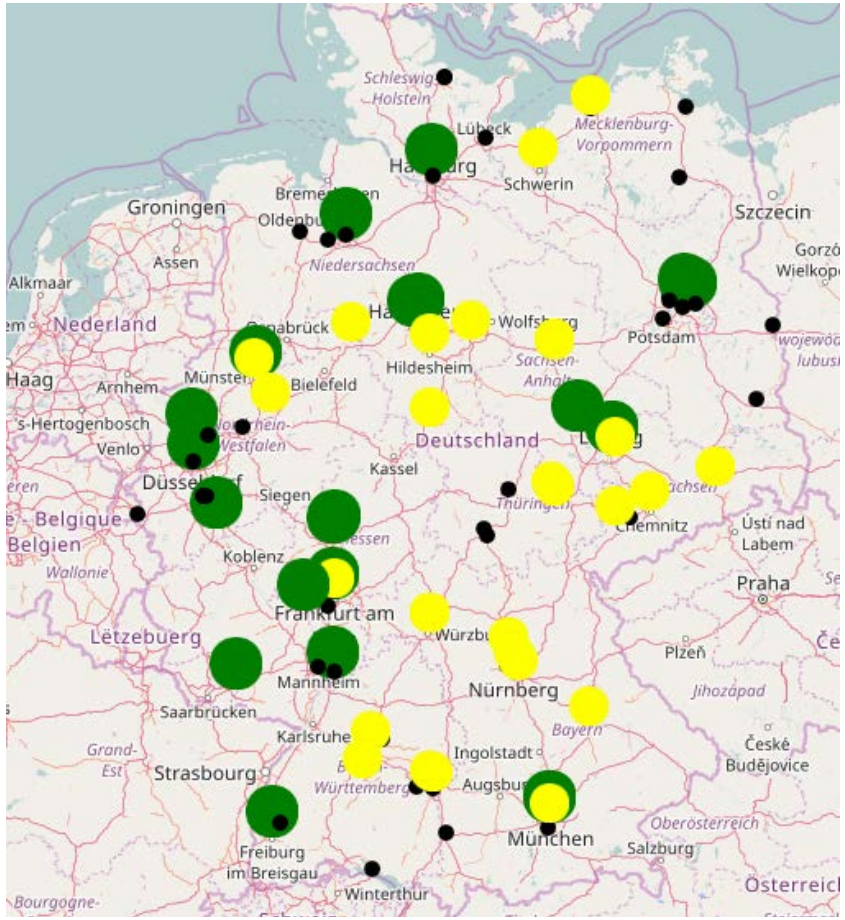


Prophylaxis

- Children: 76-100%
- Adults: 51-75%

B. O'MAHONY, D. NOONE, P. L. F. GIANGRANDE and L. PRIHODOVA. Haemophilia care in Europe – a survey of 35 countries. Haemophilia (2013), 19, e239–e247

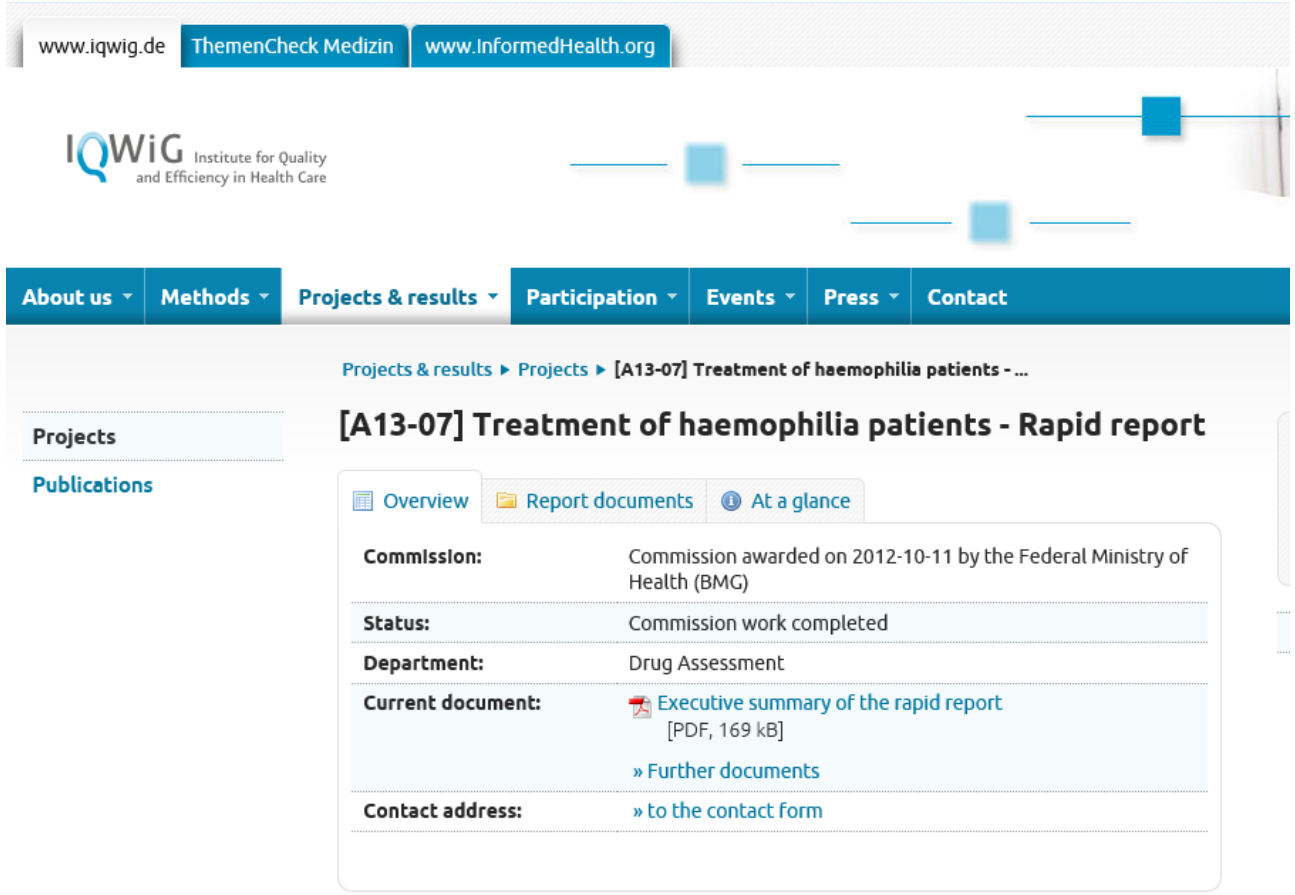
Treatment Centres in Germany



Guidelines for Treatment of PWH in Germany

- Society for Thrombosis and Haemostasis (GTH)
- The consensus recommendation of the medical board of the German Haemophilia Society (1994)
- Rapid report of the IQWiG (2015)

Rapid Report 2015



The conclusions on prophylaxis versus on-demand treatment with factor VIII are as follows:

Studies in adolescents and adults

- An **indication of an added benefit** with regard to **severe bleeding**
- A hint of an added benefit with regard to state of health
- **No hint of an added benefit** with regard to **joint function** (due to a lack of data)

Studies in children

- A **hint of an added benefit** with regard to severe bleeding
- **No hint of an added benefit** with regard to **joint function** and health-related quality of life (due to unevaluable data)

Experience with the Rapid report

- Criticised the conclusion of the IQWiG that there is no hint of an added benefit with regard to joint function for children (due to a lack of data)
- Statements from the PPTA and Medical board of the EHC
- Statement that there is an indication of an added benefit with regard to severe bleeding for children and adults is a good argument for discussions with health insurances to cover prophylaxis

Assessment of new Drugs in Germany

- The Act on the Reform of the Market for Medicinal Products – **AMNOG** is in force since 2011
- Completely revised pricing regulations for newly authorized pharmaceuticals with new active ingredients and their reimbursement
- Key responsibility: Federal Joint Committee (G-BA) and Institute for Quality and Efficiency in Health Care (IQWiG)
- Assessment **after** market authorization
- Benefit assessment - **no cost assessment**
- Companies must prove an **added benefit** of a newly authorized medicinal product compared to an already available drug or treatment

Assessment of new Drugs in Germany

Goal: negotiate prices based on outcome of assessment

Interests concerning Benefit Assessment

Patients

- Added benefit, better treatment or better way of diagnosis
- Accessibility / Market access
- Affordable price

Industry

- Added benefit, way to negotiate a higher price with health insurance companies

Challenges for the industry

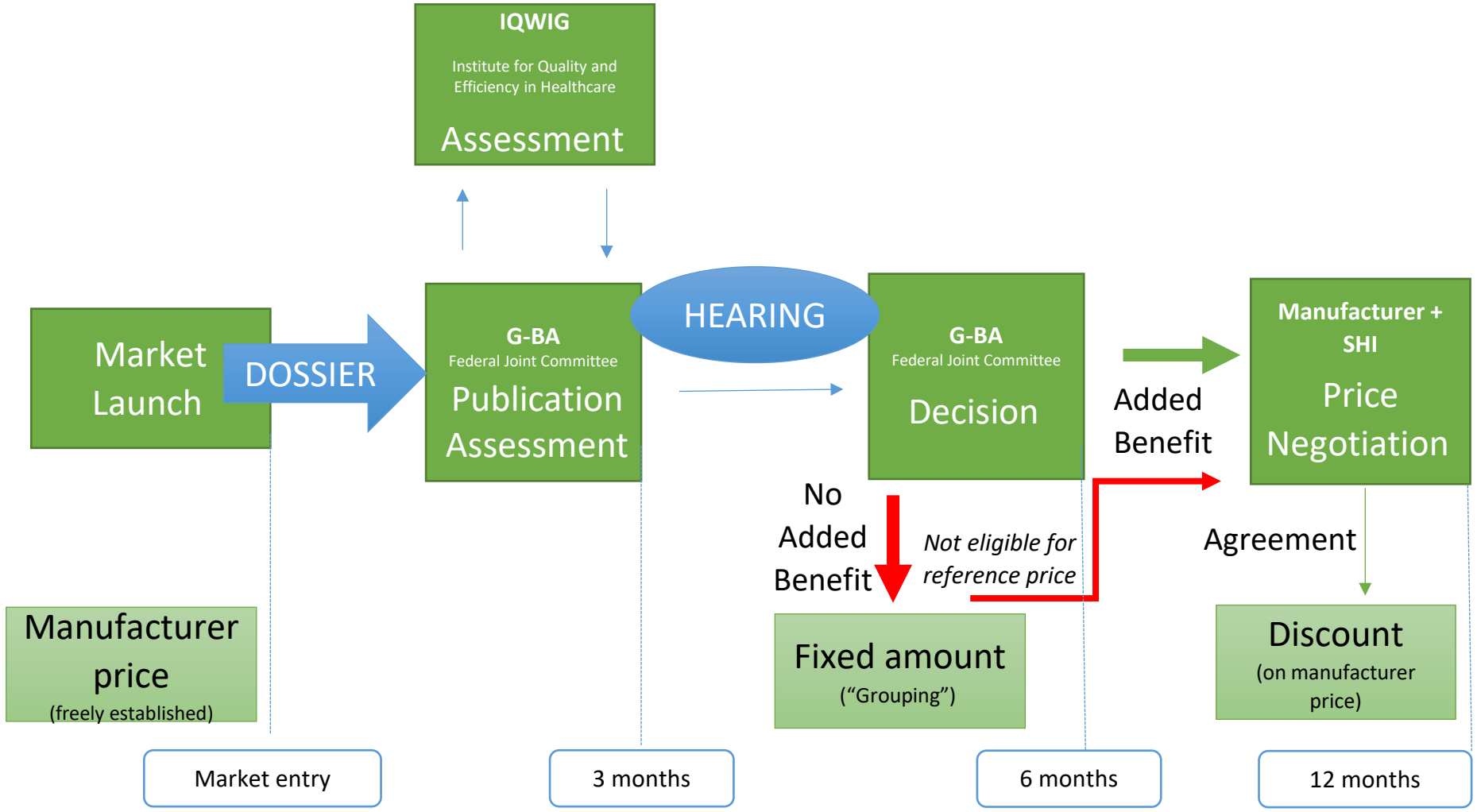
Requirements from regulators (EMA, FDA)

- Clinical trials:
  - Number of patients
  - Duration of treatment
  - Age of patients
- **Goal**: safety and efficacy

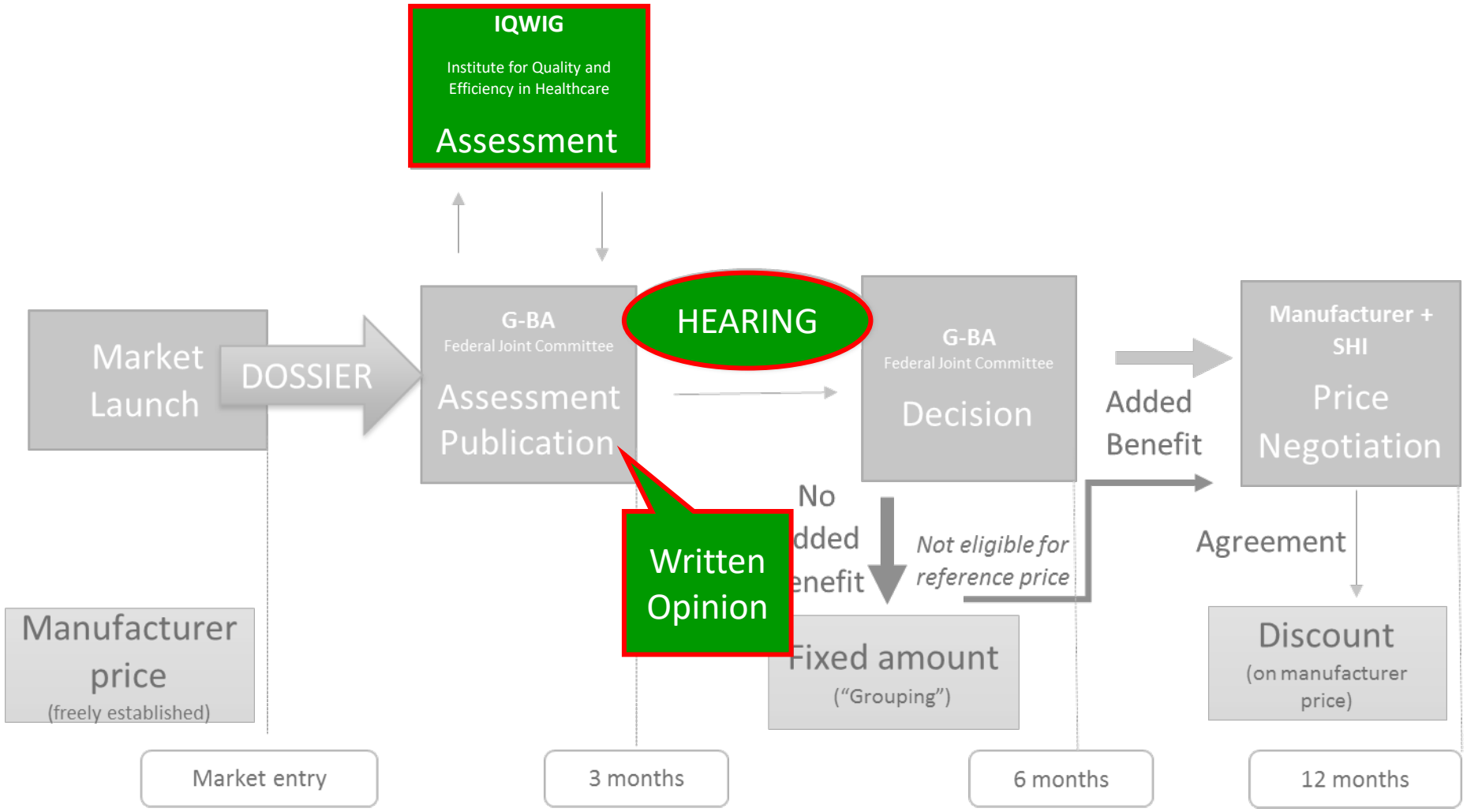
Requirements from national authorities (e.g. G-BA)

- RCTs
- Comparison to a certain already available therapy/drug
- **Goal**: added benefit

Early Benefit Assessment



Possible Patient Involvement



NovoEight (FVIII)

Nutzenbewertungsverfahren zum Wirkstoff Turoctocog alfa

Steckbrief

- **Wirkstoff:** Turoctocog alfa
- **Handelsname:** NovoEight®
- **Therapeutisches Gebiet:** Hämophilie A (Krankheiten des Blutes und der blutbildenden Organe)
- **Pharmazeutischer Unternehmer:** Novo Nordisk Pharma GmbH

Fristen

- **Beginn des Verfahrens:** 15.01.2014
- **Veröffentlichung der Nutzenbewertung und Beginn des schriftlichen Stellungnahmeverfahrens:** 15.04.2014
- **Fristende zur Abgabe einer schriftlichen Stellungnahme:** 06.05.2014
- **Beschlussfassung:** 03.07.2014
- **Verfahrensstatus:** Verfahren abgeschlossen

Claim:

- Additional recombinant factor on the marked, better supply
- Better storage condition (30°C)

Nuwiq (FVIII)

Nutzenbewertungsverfahren zum Wirkstoff Simoctocog alfa

Steckbrief

- **Wirkstoff:** Simoctocog alfa
- **Handelsname:** Nuwiq®
- **Therapeutisches Gebiet:** Hämophilie A (Krankheiten des Blutes und der blutbildenden Organe)
- **Pharmazeutischer Unternehmer:** Octapharma GmbH

Fristen

- **Beginn des Verfahrens:** 15.11.2014
- **Veröffentlichung der Nutzenbewertung und Beginn des schriftlichen Stellungnahmeverfahrens:** 16.02.2015
- **Fristende zur Abgabe einer schriftlichen Stellungnahme:** 09.03.2015
- **Beschlussfassung:** 07.05.2015
- **Verfahrensstatus:** Verfahren abgeschlossen

Claim:

- Less inhibitors in PUPs, because of use of a human cell line

Elocta (FVIII)

Nutzenbewertungsverfahren zum Wirkstoff Efmoroctocog alfa

Steckbrief

- **Wirkstoff:** Efmoroctocog alfa
- **Handelsname:** Elocta®
- **Therapeutisches Gebiet:** Hämophilie A (Krankheiten des Blutes und der blutbildenden Organe)
- **Pharmazeutischer Unternehmer:** Swedish Orphan Biovitrum GmbH

Fristen

- **Beginn des Verfahrens:** 01.01.2016
- **Veröffentlichung der Nutzenbewertung und Beginn des schriftlichen Stellungnahmeverfahrens:** 01.04.2016
- **Fristende zur Abgabe einer schriftlichen Stellungnahme:** 22.04.2016
- **Beschlussfassung:** 16.06.2016
- **Verfahrensstatus:** Verfahren abgeschlossen

Claim:

- Longer half live
- Better adherence
- Lower annual bleeding rate

Decision of the Federal Joint Committee

- All claims are denied
- No proof, as no company has done RCTs
- No added benefit for the new clotting factors
- But plasma derived CFCs and recombinant CFCs are seen as equal

Assessment and evaluation of clinical trials of Rare diseases (Rapid report 2014)

IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

IQWiG-Berichte – Nr. 241

Bewertung und Auswertung von Studien bei seltenen Erkrankungen

- EU (EMA): 2/3 of all new approved Orphan drugs used RCT
- USA (FDA): 54% of all new approved Orphan drugs used RCT
- **Conclusion: RCT are possible for rare diseases**

Orphan Drugs in the AMNOG process

- Special status in the early benefit assessments
- The additional medical benefit of these medications is **already proven** by market authorization (EMA)
- Additional benefit **is assumed**
- Only the extent of additional benefit must be proved
- It does not require a relevant scientific assessment by IQWiG
- Revenues must not exceed 50 million euros in the past twelve months

Alprolix (FIX)

Nutzenbewertungsverfahren zum Wirkstoff Eftrenonacog alfa

Steckbrief

- **Wirkstoff:** Eftrenonacog alfa
- **Handelsname:** Alprolix®
- **Therapeutisches Gebiet:** Hämophilie B (Krankheiten des Blutes und der blutbildenden Organe)
- **Pharmazeutischer Unternehmer:** Swedish Orphan Biovitrum GmbH
- **Orphan Drug:** ja

Fristen

- **Beginn des Verfahrens:** 15.06.2016
- **Veröffentlichung der Nutzenbewertung und Beginn des schriftlichen Stellungnahmeverfahrens:** 15.09.2016
- **Fristende zur Abgabe einer schriftlichen Stellungnahme:** 06.10.2016
- **Beschlussfassung:** Mitte Dezember 2016
- **Verfahrensstatus:** Beschlussfassung wird vorbereitet

Bemerkungen

Arzneimittel zur Behandlung eines seltenen Leidens (Orphan Drug)

Claim:

- Longer half live
- better adherence
- lower annual bleeding rate

Idelvion (FIX)

Nutzenbewertungsverfahren zum Wirkstoff Albutrepenonacog alfa

Steckbrief

- **Wirkstoff:** Albutrepenonacog alfa
- **Handelsname:** Idelvion®
- **Therapeutisches Gebiet:** Hämophilie B (Krankheiten des Blutes und der blutbildenden Organe)
- **Pharmazeutischer Unternehmer:** CSL Behring GmbH
- **Orphan Drug:** ja

Fristen

- **Beginn des Verfahrens:** 01.06.2016
- **Veröffentlichung der Nutzenbewertung und Beginn des schriftlichen Stellungnahmeverfahrens:** 01.09.2016
- **Fristende zur Abgabe einer schriftlichen Stellungnahme:** 22.09.2016
- **Beschlussfassung:** Anfang Dezember 2016
- **Verfahrensstatus:** Beschlussfassung wird vorbereitet

Bemerkungen

Arzneimittel zur Behandlung eines seltenen Leidens (Orphan Drug)

Claim:

- Longer half live
- better adherence
- less annual bleeding rate

Decision of the Federal Joint Committee

- Orphan Drugs (benefit is automatically assumed)
- “No quantifiable added benefit”

Conclusion

- Haemophilia therapy is on a high level in Germany
- Prophylaxis is available and reimbursed for everyone
- New drugs have to prove added benefit (AMNOG)
- The demand for RCTs (even for rare diseases) has been shown as an obstacle in the assessment. Other kind of evidence (apart from RCTs) as ways of indirect comparisons should be taken into consideration.
- Market access is always given
- Prices are depending on the outcome of the assessment

ABSTRACT

Haemophilia therapy is on a high level in Germany: prophylaxis is available and reimbursed for everyone. However, the Act on the Reform of the Market for Medicinal Products, which entered into force on the 1st of January 2011, brought a fundamental change in the pharmaceutical market. New drugs are assessed and have to prove an added benefit now.

The first new haemophilia drugs have gone through the process. The demand for RCTs (even for rare diseases) has been shown as an obstacle in the assessment. Other kind of evidence (e.g. indirect comparisons) should be taken into consideration in order to regard the special situation of the haemophila therapy.

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