IMPACT OF THE EARLY BENEFIT ASSESSMENT ON A PHARMACEUTICAL'S REAL CONSUMPTION IN GERMANY

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Objectives

The Act on the Reform of the Market for Medicinal Products ("AMNOG") introduced an early benefit assessment (EBA) of pharmaceuticals in Germany in 2011.
According to this law, all pharmaceuticals with a new active agent made available on the market for the first time have to go through a benefit assessment process. A benefit assessment dossier has to be submitted at the time of the market entry of the new pharmaceutical. In this benefit assessment dossier, the pharmaceutical company has to prove the additional benefit of the pharmaceutical compared to a given appropriate comparator.
Since the impact of the EBA results on a pharmaceutical's consumption is unclear, those effects were quantitatively analyzed.

Methods

All pharmaceuticals which were assessed by an EBA in 2011 or 2012 and were still available in 2012 and 2013 and gliptins launched before 2011 with an EBA in 2013 were considered. A pharmaceutical's real consumption (measured by the amount of defined daily doses dispensed by pharmacies for ambulatory care within the statutory health insurance) in 2012 and 2013 was compared to the expected consumption (EC) based on the highest possible number of patients defined by the Federal Joint Committee according to a pharmaceutical's label. For the EC only subpopulations with an acknowledged additional benefit (AB) were taken into account. Results are presented in terms of „shares" (= real consumption / EC).

Results

Pharmaceuticals with a low share (<10%) in 2013

Table 1: Shares* for pharmaceuticals with an acknowledged additional benefit in at least one subpopulation (%) - low shares

Pharmaceutical	2012	2013
Cabazitaxel	0.2	0.3
Saxagliptin/metformin	n/a	1.4
Belatacept	0.6	1.5
Boceprevir	3.4	1.9
Belimumab	1.6	2.6
Eribulin	3.3	3.3
Telaprevir	8.1	3.5
Vandetanib	n/a	5.5
Nabiximols	4.6	5.5
Saxagliptin	6.0	5.9
Rilpivirine	n/a	7.9

* Share = real consumption / expected consumption

Pharmaceuticals with a low share (<10%) in 2013 were cabazitaxel (0.3%), saxagliptin/metformin (1.4%), belatacept (1.5%), boceprevir (1.9%), belimumab (2.6%), eribulin (3.3%), telaprevir (3.5%), vandetanib (5.5%), nabiximols (5.5%), saxagliptin (5.9%) and rilpivirine (7.9%) (Table 1).
The share of abiraterone was higher by a factor of 300 (Table 3) compared to the share of cabazitaxel, although both pharmaceuticals have the same therapeutic indication (prostate cancer). This may be due to the restricted use of cabazitaxel in specialized treatment facilities and the lower acknowledged additional benefit.
The reduction of shares for protease inhibitors boceprevir and telaprevir from 2012 to 2013 needs to be interpreted in the light of guidelines recommending treatment with these pharmaceuticals to urgent chronic hepatitis c patients and the imminent interferon-free treatment alternatives.
The low shares of eribulin and vandetanib may arise from the inpatient setting and the use in palliative situations in conjunction with a high rate of adverse events, respectively.
Rilpivirine has to be prescribed concomitantly with other retroviral pharmaceuticals. This has probably led to a higher share of rilpivirine as part of the respective fixcombination (Table 3) than for the single pharmaceutical.

Pharmaceuticals with a midsize share (10-50%) in 2013

Table 2: Shares* for pharmaceuticals with an acknowledged additional benefit in at least one subpopulation (%) - midsize shares

Pharmaceutical	2012	2013
Pirfenidone	7.3	11.0
Ipilimumab	8.4	11.2
Pasireotide	n/a	13.7
Ticagrelor	9.4	17.6
Vemurafenib	n/a	21.0
Sitagliptin	12.4	21.0
Decitabine	n/a	25.7
Brentuximab vedotin	n/a	28.6
Crizotinib	n/a	31.4
Tafamidis	33.2	49.7

* Share = real consumption / expected consumption

Pharmaceuticals with a midsize share (10-50%) in 2013 were pirfenidone (11.0%), ipilimumab (11.2%), pasireotide (13.7%), ticagrelor (17.6%), vemurafenib (21.0%), sitagliptin (21.0%), decitabine (25.7%), brentuximab vedotin (28.6%), crizotinib (31.4%) and tafamidis (49.7%) (Table 2).
Out of the gliptins, only saxagliptin, sitagliptin and their fixed combinations with metformin were awarded an additional benefit. However, it can be asssumed that all gliptins are perceived equally in practice, regardless of an additional benefit.
Ticagrelor almost doubled its share but it can be assumed that it has not yet completed its market penetration. Furthermore, there are still more economic therapeutic alternatives in this indication which lead to a relatively low share.
When interpreting the shares of the melanoma treatments (ipilimumab and vemurafenib), it has to be considered that the target population of vemurafenib is a subset of the target population of ipilimumab. When exluding patients which exlusively pertain to the indication of vemurafenib, the share of ipilimumab would have increased to 20% in 2013.

Pharmaceuticals with a large share (>50%) in 2013

Table 3: Shares* for pharmaceuticals with an acknowledged additional benefit in at least one subpopulation (%) - large shares

Pharmaceutical	2012	2013
Ivacaftor	n/a	53.4
Abiraterone	38.3	77.9
Emtricitabine/rilpivirine/ tenofovir	n/a	195.2
Apixaban	1.5	261.4
Fingolimod	246.5	397.8
Axitinib	n/a	not meaningful**

* Share = real consumption / expected consumption
** The subpopulation with an additional benefit encompasses <1% (n=6) of the total target population. Considering axitinib's real consumption in 2013 it can be concluded that a treatment with axitinib was not limited to the patient population with an additional benefit.

Pharmaceuticals with a large share (>50%) in 2013 were ivacaftor (53.4%), abiraterone (77.9%), emtricitabine/rilpivirine/tenofovir (195.2%), apixaban (261.4%) and fingolimod (397.8%) (Table 3).
Ivacaftor has reached a share of 53.4% in its first year of availability. This may be due to the relatively small target population of about 170 patients in which ivacaftor targets a specific genetic mutation in cystic fibrosis.
Abiraterone, used in prostate cancer, has doubled its share from 2012 to 2013 to 77.9%. The extended market authorization during 2013, considering patients not yet eligible for chemotherapy, has not been taken into account. This would have led to an EC more than three times larger than for the initial patient population and a decrease in abiraterone's share to 15% in 2013.
The large shares of emtricitabine/rilpivirine/tenofovir and fingolimod might have been caused by an underestimated target population or by additionally treated patients as compared to the label (or subgroups without an acknowledged AB).
The vast increase of apixaban's share from 2012 to 2013 can be ascribed to the label extension in early 2013, leading to an additional one million possible patients.

Conclusions

The shares of pharmaceuticals considered in this analysis vary between 0.2% and 398%. No correlation between share and extent of AB could be identified. It is assumed that label restrictions regarding the use of a pharmaceutical, competing alternatives in the same therapeutic indication, a pharmaceutical's life-cycle or an overestimation of the EC influence a pharmaceutical's share. Shares >100% indicate that also subpopulations without an acknowledged AB receive treatment with the respective pharmaceutical. Further research is needed to confirm these assumptions.

References

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