Price Erosion for Haemato-oncology Drugs in European Markets

HPR33

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OBJECTIVE

To examine price evolution over time for three haemato-oncology drugs (ibrutinib [Imbruvica], obinutuzumab [Gazyvaro], venetoclax [Venclyxto]) in four key European markets.

METHODS

Historical prices for ibrutinib, obinutuzumab, and venetoclax were obtained from nationally available list price databases, covering the period 2015 to 2022.

Changes in price since 2015 (or first available) were plotted over time as additional indications were obtained from the European Medicines Agency (EMA) and reimbursement decisions were made in France (French National Authority for Health; HAS), Germany (Federal Joint Committee; GBA), Italy (Italian Medicines Agency; AIFA), and England (National Institute for Health and Care Excellence; NICE).

Background

The EMA issued the following marketing authorisation for ibrutinib, obinutuzumab and ventoclax

- In 2014, the EMA recommended marketing authorisation for ibrutinib for the treatment of relapsed of refractory mantle cell lymphoma (MCL) and for the treatment of adult patients with chronic lymphocytic leukaemia (CLL) who have received at least one prior therapy, or in first line in the presence of 17p deletion or TP53 mutation in patients unsuitable for chemo-immunotherapy (EMA/CHMP/645137/2014).
- In 2014, the EMA authorized obinutuzumab in combination with chlorambucil for the treatment of adult patients with previously untreated CLL and with comorbidities making them unsuitable for full-dose fludarabine based therapy (EMA/CHMP/231450/2014).
- In 2016, the EMA authorised venetoclax monotherapy for the treatment of CLL in the presence of 17p deletion or TP53 mutation in adult patients who are unsuitable for or have failed a B-cell receptor pathway inhibitor, or in the absence of 17p deletion or TP53 mutation in adult patients who have failed both chemoimmunotherapy and a B-cell receptor pathway inhibitor (EMA/725631/2016).

Results

Price reductions were seen in France, Germany and Italy as additional indications or sub-populations were reimbursed or recommended by respective national Health Technology Assessment (HTA) agencies.

In France, the list prices for ibrutinib, obinutuzumab, and venetoclax decreased (Figure 1). Each of the products had additional indications and/or populations approved by the HAS during the period analysed. Ibrutinib price decreased by 33% and had expanded indications in CLL (2017, 2020, 2021). The price of obinutuzumab decreased by 10% as indications in FL (2017, 2018) were added. Venetoclax price decreased by 8% while indications in CLL were expanded (2019).

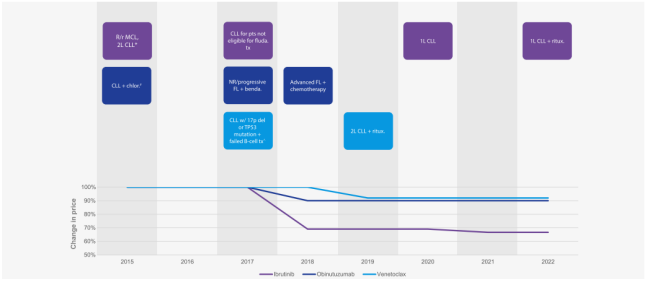
In Italy, the price for ibrutinib decreased by 10% while gaining an additional indication in Waldenstrom macroglobulinemia (WM) (2016) and expanding the population in CLL (2018). The price for obinutuzumab decreased by 21% while gaining reimbursement for a subpopulation of FL patients in 2019. Venetoclax price stayed the same and had expanded indications in CLL (2019, 2022) (Figure 2).

In Germany, the price for ibrutinib slightly increased from 2020 to 2022 (prices before 2020 were unavailable). The price for obintuzumab decreased by 46%. During this period, reimbursement for obintuzumab expanded to additional patient populations in CLL and FL. The price for venetoclax decreased by 9%. Reimbursement expanded to additional populations in CLL, and AML was added in 2021 (Figure 3).

In England, public list prices for each of the three drugs stayed the same across the time period. Nevertheless, references to updated Patient Access Schemes (PAS) can be used to infer that confidential discounts have been applied and increased at various stages in the lifecycle of each product.

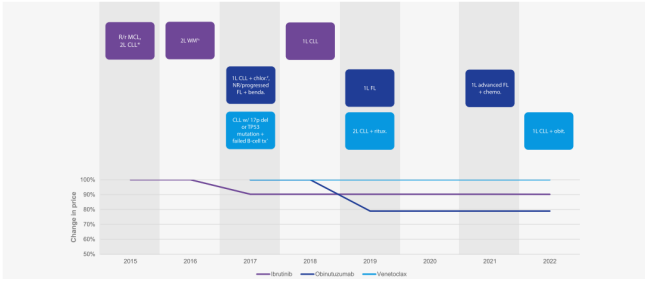
- NICE submission for ibrutinib for previously treated CLL and untreated CLL with 17p deletion or TP53 mutation (TA429, 2017) included a PAS. Subsequently, the final appraisal document (FAD) for TA502 (for treating relapsed or refractory MCL 2018) refers to "a patient access scheme agreed with the Department of Health that applied to all indications for ibrutinib", implying a change to the original PAS.
- Original guidance for obinutuzumab for untreated CLL (TA343, 2015) included a PAS. When assessed for untreated advanced FL (TA513, 2018), the ERG's critique of the ACD response notes a: "revised patient access scheme (PAS) for obinutuzumab consisting of an increased discount."
- Publicly available papers for Venetoclax do not make reference to revised or updated PAS, or increased discounts (TA487, TA561, TA663, TA765, TA787, TA796). Papers do refer to "a simple discount PAS", apparently unchanged from the original assessment in 2017 (TA487, for treating CLL). A subsequent "managed access agreement with NHS England" or "commercial arrangement", is first referred to in TA561 (2019, with rituximab for previously treated CLL) and potentially updated in 2022 (TA796, updated appraisal for treating CLL).

Figure 1: Price evolution of ibrutinib, obinutuzumab, and venetoclax in France from 2015 to 2022



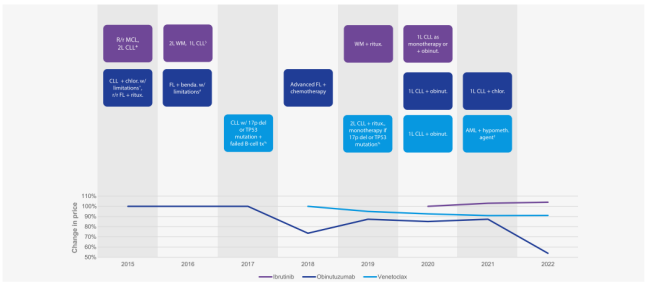
*or IL if 17p deletion or TP53 mutation in patients unsuitable for immunochemotherapy
#: for patients with comorbidities ineligible for full-dose fludarabine therapy
† or in the absence of 17p del or TP53 mutation if failed both chemoimmunotherapy and a B-cell receptor pathway inhibitor
CLL: chronic lymphocytic leukaemia, FL: follicular lymphoma, MCL: mantle cell lymphoma, NR: not responsive, r/r: relapsed or refractory

Figure 2: Price evolution of ibrutinib, obinutuzumab, and venetoclax in Italy from 2015 to 2022



*or IL if 17p deletion or TP53 mutation + unsuitable for chemoimmunotherapy
† or in the absence of 17p del or TP53 mutation if failed both chemoimmunotherapy and a B-cell receptor pathway inhibitor
% or IL in pts unsuitable for chemoimmunotherapy
#: in patients with comorbidities unsuitable for full-dose fludarabine based therapy
CLL: chronic lymphocytic leukaemia, FL: follicular lymphoma, MCL: mantle cell lymphoma, NR: not responsive, r/r: relapsed or refractory, WM: Waldenström's macroglobulinaemia

Figure 3: Price evolution of ibrutinib, obinutuzumab, and venetoclax in Germany from 2015 to 2022



*or IL if 17p deletion or TP53 mutation + unsuitable for chemoimmunotherapy
†indicated in combination with chlorambucil of adult patients with previously untreated CLL and with comorbidities making them unsuitable for full - dose fludarabine based therapy
‡ for patients who did not respond or who progressed during or up to 6 months after treatment with rituximab or a rituximab-containing regimen.
% or in the absence of 17p del or TP53 mutation if failed both chemoimmunotherapy and a B-cell receptor pathway inhibitor
$ for patients eligible for FCR therapy
ǂ in newly-diagnosed pts ineligible for intensive chemotherapy
AML: acute myeloid leukaemia, CLL: chronic lymphocytic leukaemia, FCR: fludarabine, cyclophosphamide and rituximab, FL: follicular lymphoma, MCL: mantle cell lymphoma, r/r: relapsed or refractory, WM: Waldenström's macroglobulinaemia

CONCLUSIONS

- **In this analysis, the initial list price achieved for a product was the highest price in its lifecycle.**
- **By adding indications or populations and increasing volume, prices go down even if the additive population is smaller and has a greater positive effect and might therefore on its own have attracted a higher price.**
- **When considering additional indications for a product reimbursed in Europe, modeling price erosion and additional volumes to understand revenue implications is essential.**
- **Policymakers might also consider whether the fact that prices only ever go down is creating a barrier to innovation or to access for European patients in need of new treatments.**

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