Characterizing the continued relevance of IRP in Italy: A simulation analysis of top prescribed molecules in oncology

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Objective

While international reference pricing (IRP) is recognized as a prevalent tool, there is some debate surrounding its continued relevance amid the rise of confidential discounting. In a country such as Italy, where IRP is used informally, and managed-entry agreements (MEAs) as well as other confidential agreements are relatively common, its continued influence is uncertain. The present analysis sought to identify whether there is evidence that IRP continues to hold relevance in the Italian context.

Results

73% of the molecules exhibited simulated prices falling within a delta of ±5% of actual launch prices in Italy. In general, the smallest deltas were observed with reference to the EU-wide average simulated price, as opposed to simulated prices in individual reference countries. Actual Italian prices tended to remain largely stable, despite increasing deltas relative to simulated prices over time.

Figure 1 – Analysis results for each of the 23 active ingredients (AIs) under analysis.

Active Ingredient	Date of first price in Italy	Date of first price in Reference countries (EU)	Date of first price in the main 5 Reference countries	EU Average		Average among the main 5		% CAGR in Italy (from time of first price to June 2019)
				L	TD	L	TD	
Abatacept *125 MG/ml, SOLUTION FOR INJECTION,4 iu*	Jun 2013	Dec 2012	Mar 2013	+13.2%	+3.6%	-3.4%	-10.3%	-5.42%
Abiraterone *250 MG, ORAL, 120 iu*	May 2013	Nov 2011	Nov 2012	+2.4%	+16.9%	-4.3%	+11.8%	0.00%
Adalimumab *100 MG/ML, 20 ML, SOLUTION FOR INJECTION, 2 iu*	Jan 2019	Mar 2018	Apr 2018	+0.7%	+9.89%	-4.4%	-4.16%	0.00%
Bevacizumab *400 MG, CONCENTRATE SOLUTION FOR INFUSION, 1 iu*	Mar 2007	Oct 2005	Oct 2005	-4.6%	+25.38%	-4.6%	+25.38%	-0.41%
Bortezomib *3.5 MG, POWDER, 1 iu*	Oct 2006	Oct 2004	Oct 2009	+2.2%	+14.2%	NR	NR	0.00%
Dasatinib *50 MG, ORAL, 60 iu*	Dec 2010	Apr 2007	Nov 2007	-5.6%	+16.79%	-0.4%	+14.90%	-0.60%
Eculizumab *300 MG, CONCENTRATE SOLUTION FOR INFUSION, 1 iu*	Sept 2008	Jan 2008	Feb 2008	-2.2%	-1.7%	-1.5%	-0.68%	0.00%
Etanercept *10 MG, POWDER, 4 iu*	Jan 2014	Mar 2009	Mar 2012	-0.4%	+10.5%	-5.1%	-2.8%	-0.93%
Fingolimod *0.5 MG, ORAL, 28 iu*	Jan 2012	May 2011	May 2011	+3.1%	+7.5%	+2.1%	+5.3%	-1.36%
Golimumab *50 MG, SOLUTION FOR INJECTION, 1 iu*	Sep 2010	Mar 2010	Marl 2010	-27.2%	-0.01%	-46.0%	-2.98%	0.00%
Ibrutinib *140 MG, ORAL, 90 iu*	Feb 2016	Dec 2014	Dec 2014	+0.12%	+2.1%	-9.72%	-1.8%	-2.96%
Infliximab *100 MG, POWDER, 1 iu*	Mar 2007	Jul 2008	Jul 2008	NR	NR	NR	NR	-0.01%
Lenalidomide *25 MG, ORAL, 21 iu*	Jul 2008	Nov 2007	Nov 2007	+3.2%	+16.7%	+3.9%	+11.3%	0.00%
Leuprorelin *3.75 MG, 3.75 MG/ML, POWDER, 1 iu*	Oct 2013	Feb 2007	Feb 2007	-9.2%	-15.2%	+4.0%	-5.12%	0.00%
Natalizumab *300 MG, 20 MG/ML, CONCENTRATE SOLUTION FOR INFUSION, 1 iu*	Jan 2007	Dec 2006	Mar 2007	NR	NR	NR	NR	0.00%
Nilotinib *300 MG, ORAL, 112 iu*	Nov 2009	Apr 2008	May 2008	+0.8%	+14.3%	+1.5%	+7.6%	0.00%
Nivolumab *100 MG, CONCENTRATE SOLUTION FOR INFUSION, 1 iu*	Dec 2015	Aug 2015	Aug 2015	+28.0%	+6.5%	+24.4%	+7.3%	-10.31%
Pembrolizumab *100 MG, CONCENTRATE SOLUTION FOR INFUSION, 1 iu*	Sep 2017	Nov 2016	Feb 2017	+3.9%	+10.1%	+3.8%	+13.6%	0.00%
Pertuzumab *420 MG, CONCENTRATE SOLUTION FOR INFUSION, 1 iu*	Oct 2013	Apr 2013	Jun 2013	+28.7%	+11.3%	+27.3%	+5.3%	-5.7%
Rituximab *1400 MG, SOLUTION FOR INJECTION, 1 iu*	Apr 2015	Oct 2012	Sep 2013	-2.7%	+0.77%	-20.0%	-11.3%	-1.20%
Ruxolitinib *15 MG, ORAL, 56 iu*	Nov 2014	Apr 2013	Oct 2013	+5.9%	+17.5%	+12.9%	+18.2%	0.00%
Trastuzumab *600 MG, SOLUTION FOR INJECTION, 1 iu*	Oct 2014	Apr 2013	Oct 2013	-0.0%	+11.1%	-2.6%	+4.90%	-1.07%
Ustekinumab *130 MG, CONCENTRATE SOLUTION FOR INFUSION, 1 iu*	Dec 2018	Jan 2017	Jan 2017	-2.0%	-0.9%	-2.8%	-4.3%	0.00%

Source: IHS Markit

Notes to Figure 1:

- L: % delta between the actual list price in Italy and the simulated average price at time of launch.
- TD: % delta between the actual list price in Italy and the simulated average price to date (as of June 2019).
- CAGR: Compound Annual Growth Rate
- NR: Not relevant (in case the product was launched in Italy prior to any other country in the EU).
- The main 5 reference countries are the ones reported in primary research to be the most frequently used during informal IRP, namely France, Germany, the Netherlands, Spain and the United Kingdom. This is the rationale for performing the analysis on the average of these 5 countries, as well as on the EU-wide average.
- In green are highlighted cases where simulated prices fall within a delta of ±5% of actual launch prices in Italy; in blue are highlighted cases where price fall within the same range in June 2019, just for comparison purposes.
- Please note we selected just one preparation per AI as an example, ensuring a wide variety in the date of first price in Italy.

Conclusions

The present analysis suggests that IRP continues to exert influence on Italian list prices, particularly at time of launch. Moreover, the EU average price may be an important benchmark in price negotiations. Although pricing contracts may be re-negotiated every couple of years, the present results suggest that IRP may not be an extensive driver of price erosion downstream of launch. Additional analysis on larger sample sizes is needed to clarify the generalizability of these findings.

Methodology

An Excel model was developed to simulate IRP application, drawing on ex-manufacturer prices in potential reference countries from three months prior, and calculating the delta relative to historic Italian prices. A basket of 23 drugs selected among the top prescribed molecules in oncology (as reported by OsMed, the National Observatory on the Use of Medicines) was used. Controlling for active ingredient, pack size, strength, form and market authorization holder, Italian prices were compared to simulated prices in individual EU countries and the EU-wide arithmetic average, on a monthly basis over a period of 15 years (from January 2004 until June 2019).

Figure 2 – Actual price evolution comparison (in EUR) for ustekinumab (130 MG, Concentrate solution for infusion, 1 unit) between Italy and all EU countries with the product available on the market, from 2017 to present

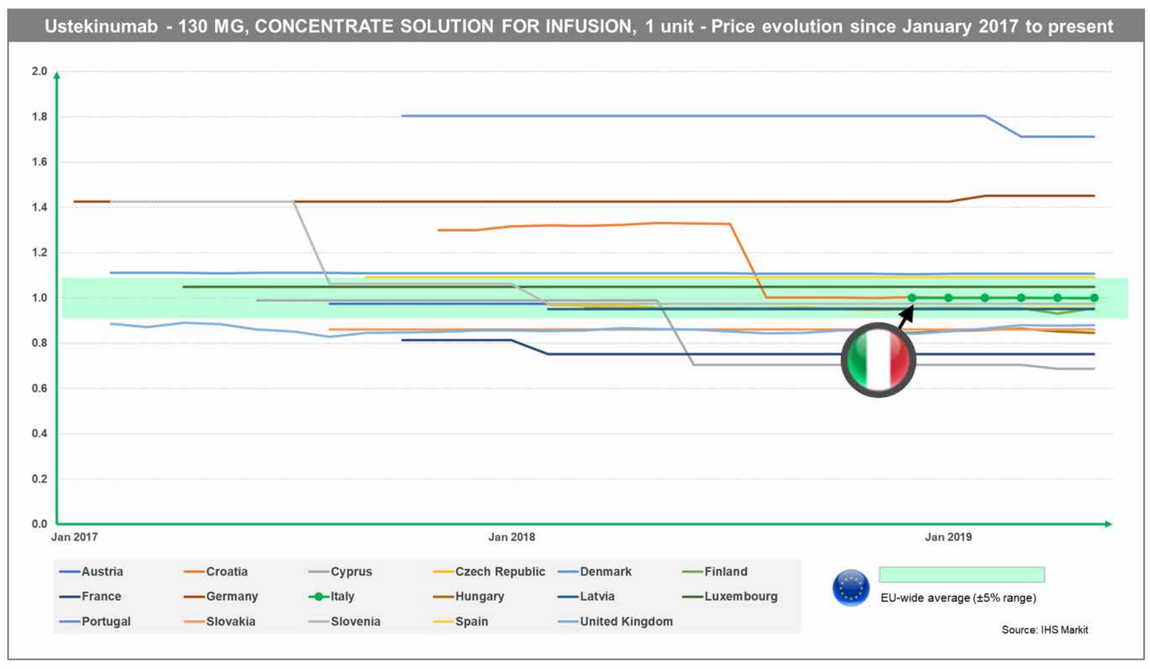

Figure 3 – Actual price evolution comparison (in EUR) for bortezomib (3.5 MG, Powder, 1 unit) between Italy and all EU countries with the product available on the market, from 2004 to present

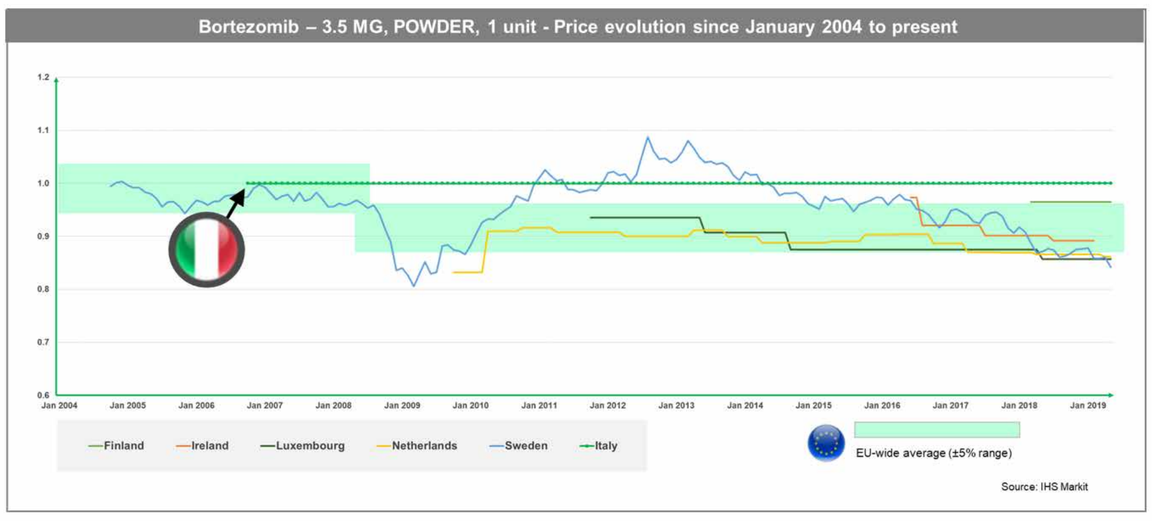

Figure 4 – Actual price evolution comparison (in EUR) for trastuzumab (600 MG, Solution for injection, 1 unit) between Italy and all EU countries with the product available in the market, from 2013 to present