Impact of restricted EU market access decisions on patient access to medicines in Multiple Myeloma

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Objective

Approaches to health technology assessment (HTA) vary around Europe and include evaluation of clinical effectiveness and cost-effectiveness (CE). Previous research indicated that countries relying primarily on CE place more access restrictions on oncology and rare disease medicines than non-CE markets[1].

This case study assessed the impact of HTA decisions and restrictions on the proportion of eligible patients that can access drugs/ indications for multiple myeloma (MM) in markets that primarily take a CE vs. a non-CE approach to HTA.

Methods

Identifying drug/indications & market access decisions

- HTA decisions from CE markets (England (NICE), Scotland (SMC), Sweden (TLV)) and clinical-effectiveness markets (France (HAS), Germany (G-BA), Italy (AIFA), Spain (AEMPS)) were reviewed for MM treatments with EMA approval (2016-2021): yielding three drugs Darzalex®, Empliciti®, Ninlaro®) with nine indications (Table 1).
- Differences between the reimbursed population and the EMA indication were considered HTA restrictions.

Table 1. Drug/ Indications included in the analysis

Brand name (generic name)	MOA	Indication	EMA approval
Darzalex® (daratumumab)	Monoclonal antibody; anti-CD38	(1) Monotherapy for the treatment of adult patients with relapsed and refractory MM, whose prior therapy included a PI and an immunomodulatory agent and who have demonstrated disease progression on the last therapy.	20 May 2016
		(2) In combo with Len and Dex, or Bor and Dex, for the treatment of adult patients with MM who have received at least one prior therapy.	28 Apr 2017
		(3) In combo with Bor, melphalan, and prednisone for the treatment of adult patients with newly diagnosed MM who are ineligible for autologous stem cell transplant.	31 Aug 2018
		(4) In combo with Len and Dex or with Bor, melphalan, and prednisone for the treatment of newly diagnosed adult patients with MM who are not eligible for autologous stem cell transplantation.	19 Nov 2019
		(5) In combo with Bor, thalidomide, and Dex for the treatment of adult patients with newly diagnosed MM who are eligible for autologous stem cell transplant.	20 Jan 2020
		(6) In combo with Pom and Dex for the treatment of adult patients with MM who have received one prior therapy containing a PI and Len and who were Len refractory, or who have received at least two prior therapies that included Len and a PI and who have demonstrated disease progression on or after the last therapy.	21 Jun 2021
Empliciti® (elotuzumab)	Monoclonal antibody; anti-SLAMF7	(1) In combo with Len and Dex for the treatment of MM in adult patients who have received at least one prior therapy.	21 May 2016
		(2) In combo with Pom and Dex for the treatment of adult patients with RRMM who have received at least two prior therapies including Len and PI and who have demonstrated disease progression on the last therapy.	23 Aug 2019
Ninlaro® (ixazomib)	PI	(1) In combo with Len and Dex for the treatment of adult patients with MM who have received at least one prior therapy.	21 Nov 2016

MM, Multiple Myeloma; RRMM, relapsed and refractory MM; Len, lenalidomide; Dex, dexamethasone; Pom, pomalidomide; PI, proteasome inhibitor; Bor, bortezomib

References

1. Katsikostas-Michopoulos G, et al. Impact of the use of cost-effectiveness analysis (CEA) on patient access to medicines: A comparison of CEA vs non-CEA markets. Value in Health, Abstract, Vol 25, Issue 12, Suppl S299. Dec 2022.
2. Raab MS, Cavo M, Delforge M, Multiple myeloma: practice patterns across Europe. British Journal of Haematology, 2016, 175, 66–76

- Note: in some countries, mechanisms at national, regional, or local levels may grant access subsequent to the HTA decision; this was not considered in this analysis.

Impact of restrictions on patient access & cumulative impact over time

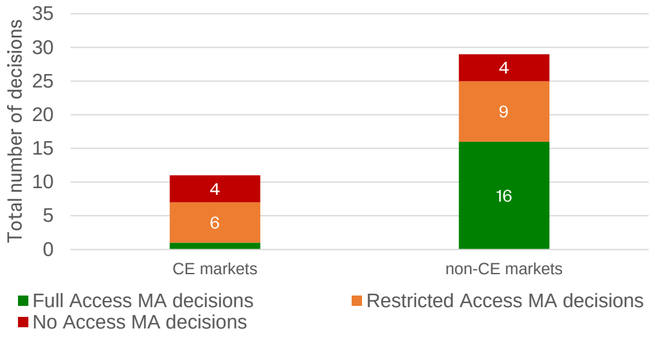
- Drugs for the treatment of MM are typically initially launched as treatments for relapsed/refractory disease. Subsequent approved indications are likely for use in earlier lines of therapy, sometimes in newly diagnosed patients, sometimes in different drug combinations. Therefore, the overall eligible patient population may be smaller for the initial approved indication and then broadens over time as subsequent indications are approved.
- To determine the percentage patients with access in each market, the percentage of patients with access from each HTA assessment was multiplied by the relevant proportion of the MM population; this was also calculated cumulatively over time and all indications.
- The proportion of the total MM population covered for each indication was estimated using published treatment pattern data from a European observational chart review2: indication 1: 26%; indication 2: 28%; indications 3 & 4: 13%; indication 5: 20%.

Results

Access decisions in CE vs. non-CE markets

- There was a higher number of MA decisions in non-CE vs. CE markets (29 vs. 11), with a greater proportion of restricted decisions in CE markets (Figure 1).
- There was a greater number of full market access decisions (i.e., no restrictions beyond the EMA label) in non-CE markets (Figure 1).

Figure 1. Market access decision across CE and non-CE markets (based on HTA decision).



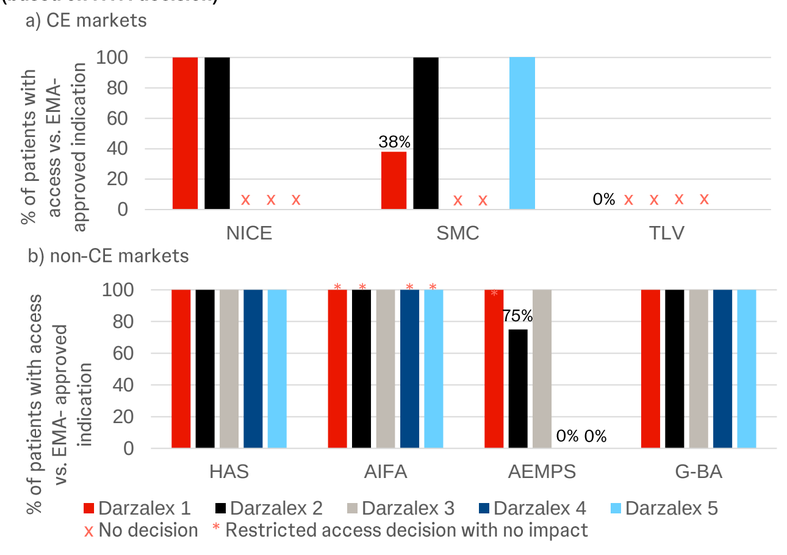
Access decisions & impact of restrictions

- Empliciti® had two EMA approvals, with country-level patient access to 0-2 indications; the two restricted reimbursement decisions did not limit the number of patients with access.
- Ninlaro's® one EMA approval had two full access plus three restricted HTA decisions, limiting patient access to an estimated 89% (NICE), 85% (AIFA), and 69% (TLV) of the EMA label population.
- Of six Darzalex® EMA-approved indications, patients had access to 0-5 indications by country after HTA review; there were no decisions available for the 6th indication during the period of analysis:
  - Four markets (England, Italy, Scotland, Spain), applied further access restrictions beyond the regulatory label.
  - Four out of five EMA approved indications received restricted market access decisions in at least one market.
  - Two of these restriction decisions limited the number of patients with access (SMC, estimated 38% eligible patients; AEMPS, estimated 75%) (Figure 2).
  - AIFA restrictions related to being included in the patient registry and were not considered to lead to restricted patient access for all indications.
  - A decision report from the TLV was available only for the first indication.
- Beyond decisions aligning patient access with trial criteria, HTA restrictions impacting the highest proportion of patients were related to treatment line, combination therapy, or disease characteristics.

Cumulative impact of market access restrictions

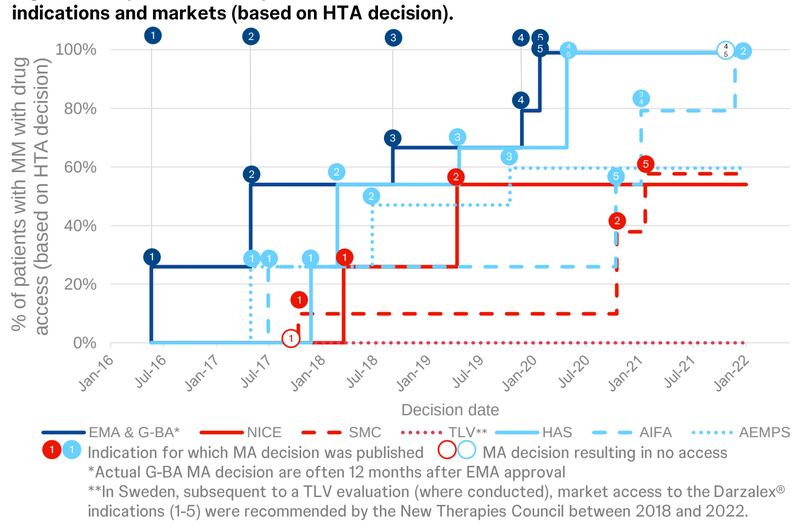
- Cumulatively across indications, a lower proportion of patients had access to MM treatments in CE markets, given published HTA decisions and restrictions.

Figure 2. Market access restrictions for Darzalex® with EMA approval (2016-2019) (based on HTA decision)



- Case study Darzalex® (Figure 3):
  - Since its launch, a larger percentage of patients had access to Darzalex® in non-CE vs. CE-markets when compared with the eligible EMA approved population.
  - Additionally, non-CE markets generally took less time to reach a MA decision
  - No clear difference was observed between time to first or subsequent MA decisions after EMA regulatory approval

Figure 3. Proportion of MM patients with access to Darzalex® over time and across indications and markets (based on HTA decision).



Conclusion

HTA agencies reach distinct conclusions and apply different restrictions beyond the regulatory label, impacting the number of patients who can access a new medicine. Overall, a lower proportion of patients had access to MM medicines in markets that take a CE vs. non-CE approach to HTA, in part due to access restrictions beyond the regulatory label. This impact on access can accumulate over time with each new indication. Further research could facilitate additional understanding the impact of HTA restrictions on patient access.