ISPOR EU 2021. Virtual Conference. December 01 - 03, 2021.

PAYER PERCEPTIONS OF VALUE DRIVERS BEYOND CLINICAL OUTCOMES

Ismailoglu I, PhD[1], Mock G[1], Amata H[1], Hunt M[1]
[1]CBPartners, New York, USA

HAVE A QUESTION? maximilian.hunt@cbpartners.com

OBJECTIVE

Our research aims to understand payer acceptance of value attributes of therapies beyond clinical outcomes and determine their impact on pricing and access outcomes in the EU5.

METHODOLOGY

Three recently launched products (ixazomib, ravulizumab, and onasemnogene abeparvovec) were selected as case studies. HTA reports were analyzed to understand how key attributes, including oral route of administration vs. infusion, decreased frequency of administration vs. competitors, and a decrease in need for continued care, was evaluated by payers and contributed to the overall HTA outcomes.

RESULTS

Attributes of a medicine beyond clinical efficacy and safety can provide value by addressing unmet needs for patients and the healthcare system, such as improved convenience or decreased healthcare resource utilization.

However, challenges remain in demonstrating the value of these improvement to HTA bodies across countries.
In GBR and FRA, potential quality of life gains and cost savings from a less frequent dosing schedule vs. other alternative treatments and patient preference for the fewer infusions were noted as value drivers in assessments.

On the other hand, assessments in DEU, ITA, and ESP largely focused on clinical criteria and the direct budget impact of each drug to inform decision-making. Payers in these countries did not see the value in potential cost-savings from reduced resource use or the benefit to patients who preferred the less frequent dosing or less intensive administration of the selected therapies.

CONCLUSIONS

Challenges in quantifying and formally demonstrating value drivers beyond clinical outcomes limited the perception of these attributes and decrease their contribution to the overall opportunity. While outcomes impacting, economic factors can be incorporated within modelling and leveraged in some markets, more qualitative outcomes (e.g., patient preferences) are likely to be challenged by payers. Development of standardized and validated metrics to better outline and capture these attributes can increase their acceptance across the EU markets.

Clinical Value Drivers

- **Efficacy**
- **Safety**
- **Quality of Life (QoL)**

Traditionally, clinical value drivers, such as efficacy / safety and to a lesser extent quality of life have constituted the basis of value assessment for pharmaceuticals

Non-Clinical Value Drivers

- **Route of Administration**
- **Frequency of Administration**
- **Treatment Setting**

With differences in clinical benefit across pharmaceutical products narrowing, payers may increasingly focus on other attributes that can provide additional value for patients and healthcare systems

www.cbpartners.com /company/cbpartners /cbpartners

CASE STUDIES

Case Study: Ixazomib in Relapsed / Refractory Multiple Myeloma

	GBR	DEU	FRA	ESP	ITA
Value Drivers	Ixazomib was **approved by the EMA[1] in November 2016** as part of an **all-oral triplet** regimen to treat Relapsed / Refractory Multiple Myeloma (RRMM)				
	As the **first oral proteasome inhibitor**, ixazomib was considered to be an agent that can **potentially improve patient convenience** during long-term treatment[2]				
HTA Summary	**Managed access through CDF[3]**	**ODD / unquantifiable benefit[4]**	**SMR: Important ASMR V[5]**	**Not listed**	**Class C[6]**
	No mention of non-clinical value drivers in HTA report	No mention of non-clinical value drivers in HTA report	No mention of non-clinical value drivers in HTA report	N / A	No mention of non-clinical value drivers in HTA report
Takeaways	Assessment of ixazomib largely focused on the clinical outcomes and **oral route of administration was not considered to be a value driver**				

Case Study: Ravulizumab in Paroxysmal Nocturnal Hemoglobinuria

	GBR	DEU	FRA	ESP	ITA
Value Drivers	Ravulizumab, an engineered version of the molecule eculizumab, was approved by the EMA[7] in July 2019, based on **two non-inferiority trials vs. the original molecule**				
	Ravulizumab is administered through infusion **every 8 weeks** vs. eculizumab which requires infusions **every 2 weeks[8]**				
HTA Summary	**Recommended with simple discount[9]**	**No additional benefit vs. eculizumab[10]**	**SMR: Important ASMR: IV[11]**	**Not listed**	**Class C[12]**
	Mention of less frequent dosing schedule vs. eculizumab, which may result in cost-savings	No mention of non-clinical value drivers in HTA; costs for eculizumab shown to be €1,100-1,700 higher	Mention of expected improvement in care conditions due to the infusion frequency reduction vs. eculizumab	N / A	No mention of non-clinical value drivers in HTA
Takeaways	**Less frequent administration** for ravulizumab vs. eculizaumab was cited as a **minor advantage** from the **treatment cost and patient convenience** perspectives in some markets				

Case Study: Onasemnogene Abeparvovec In Spinal Muscular Atrophy

	GBR	DEU	FRA	ESP	ITA
Value Drivers	Onasemnogene abeparvovec was approved by the EMA[13] in 2020 as the **first one-time gene therapy in SMA**, following nusinersen into the space				
	While a direct comparison between the two therapies has not been performed, the gene therapy may provide value for patients by **eliminating the need for ongoing infusions**				
HTA Summary	**Recommended with simple discount[14]**	**No additional benefit vs. nusinersen (IQWiG)[15]**	**SMR: Important ASMR: III (shared with nusinersen)[16]**	**Not listed**	**Class H[17]**
	Potential benefits associated with normal life of patients and caregivers noted	No mention of non-clinical value drivers in HTA	No mention of non-clinical value drivers in HTA	N / A	No mention of non-clinical value drivers in HTA
Takeaways	Assessments of onasemnogene focused on the **clinical outcomes**, with no mention of potential **value of a one-time infusion**				

CONCLUSIONS & DISCUSSION

- With **increasing competition in the pharmaceutical space**, it has become more common for new medicines to come into space **without significant clinical differentiation vs. existing therapies**, but offering **advantages from a non-clinical perspective** (e.g., patient convenience, treatment frequency, decrease in administration burden)
- Furthermore, **new technologies**, such as cell and gene therapies **offer long-term benefit for patients** and **potential relief in costs** for healthcare systems by eliminating the need for ongoing use of expensive and intrusive therapies
- Our analysis of **three recent case studies** indicates HTA evaluations in the EU-5 countries continue to **focus on clinical drivers**, with **non-clinical attributes not considered** or seen only as **minor drivers**
- As the **frequency of such launch and assessment scenarios increase**, payer authorities might pay **further attention to non-clinical value drivers** to determine the value of each new agent in comparison to existing alternatives; efforts towards decreasing frequency of hospital visits (e.g., due to the COVID-19 pandemic) may also emphasize certain value attributes, such as self administration or longer duration between doses
- **Increased prominence of the patient voice** and health of the overall system may compel a more **holistic evaluation of value**, necessitating additional evidence tools and manufacturer / payer engagement

REFERENCES

1. European Medicines Agency (EMA). Ninlaro (ixazomib) EPAR. https://www.ema.europa.eu/en/medicines/human/EPAR/ninlaro, 3 August 2021.
2. S.V. Rajkumar. Ixazomib: A Relevant Addition to Myeloma Therapy. https://ascopost.com/issues/june-25-2016/ixazomib-a-relevant-addition-to-myeloma-therapy/, 25 June 2016.
3. National Institute for Health and Care Excellence (NICE). Ixazomib with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma. https://www.nice.org.uk/guidance/ta505, 7 February 2018.
4. Gemeinsamer Bundesausschuss (G-BA). Benefit assessment procedure for the active ingredient ixazomib (multiple myeloma at least 1 previous therapy, combination with lenalid omide and dexamethasone). https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/275/#beschluesse, 18 April 2017.
5. Haute Autorite de Sante (HAS). NINLARO (ixazomib). https://www.has-sante.fr/upload/docs/application/pdf/2021-03/ninlaro_09092020_summary_ct18381.pdf, 9 September 2020.
6. Gazzetta Ufficiale della Republica Italiana. Ninlaro (ixazomib). https://www.gazzettaufficiale.it/atto/serie_generale/caricaDettaglioAtto/originario?atto.dataPubblicazioneGazzet ta=2019-03-08&atto.codiceRedazionale=19A01444, 19 February 2019.
7. European Medicines Agency (EMA). Ultomiris (ravulizumab) EPAR. https://www.ema.europa.eu/en/medicines/human/EPAR/ultomiris, 18 August 2021.
8. European Medicines Agency (EMA). Soliris (eculizumab) EPAR. https://www.ema.europa.eu/en/medicines/human/EPAR/soliris, 9 September 2021.
9. National Institute for Health and Care Excellence (NICE). Ravulizumab for treating paroxysmal nocturnal haemoglobinuria. https://www.nice.org.uk/guidance/ta698, 19 May 2021.
10. Gemeinsamer Bundesausschuss (G-BA). Benefit assessment procedure for the active ingredient ravulizumab. https://www.g-ba.de/downloads/39-1464-4155/ceb2181be 9055025daa6b2b363fb64d3/2020-02-06_AM-RL-XII_Ravulizumab_D-463_EN.pdf, 6 February 2020.
11. Haute Autorite de Sante (HAS). ULTOMIRIS (ravulizumab). https://www.has-sante.fr/jcms/p_3202251/en/ultomiris-ravulizumab#smr, 16 September 2020.
12. Gazzetta Ufficiale della Republica Italiana. Ultomiris (ravulizumab). https://www.gazzettaufficiale.it/atto/serie_generale/caricaDettaglioAtto/originario?atto.dataPubblicazioneGazzet ta=2021-03-18&atto.codiceRedazionale=21A01525, 8 March 2021.
13. European Medicines Agency (EMA). Zolgensma (onasemnogene abeparvovec) EPAR. https://www.ema.europa.eu/en/medicines/human/EPAR/zolgensma, 17 August 2021.
14. National Institute for Health and Care Excellence (NICE). Onasemnogene abeparvovec for treating spinal muscular atrophy. https://www.nice.org.uk/guidance/hst15, 7 July 2021.
15. Gemeinsamer Bundesausschuss (G-BA). Benefit assessment procedure for the active ingredient Onasemnogen-Abeparvovec (spinal muscular atrophy). https://www.g-ba.de/bew ertungsverfahren/nutzenbewertung/561/#beschluesse, 3 December 2020.
16. Haute Authorité de Santé (HAS). SPINRAZA (nusinersen), antisense oligonucleotide. https://www.has-sante.fr/jcms/c_2826600/en/spinraza-nusinersen-antisense-oligonucleotide, 6 July 2018.
17. Gazzetta Ufficiale della Republica Italiana. Zolgensma (onasemnogene abeparvovec). https://www.gazzettaufficiale.it/atto/serie_generale/caricaDettaglioAtto/originario?atto.dat aPubblicazioneGazzetta=2020-11-17&atto.codiceRedazionale=20A06264, 12 November 2020.