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Impact of Long-Acting Modality on Health Technology Assessments and Formulary Decision Making in the EU4 and USA

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Background

- Relapse is a substantial risk factor for chronic diseases and is strongly associated with treatment discontinuation, where a major challenge in the management is maintaining treatment adherence
- Existing evidence indicates non-compliance increases clinical and economic burden. Therefore, pharmaceutical companies are entering the market with long-acting modalities to address these compliance issues
- The traditional Health Technology Assessment (HTA) therapeutic benefit assessment, however, is independent of the mode of treatment

Objectives

To outline the impact of long-acting modality on inherent HTA and formulary access in the EU4 (Germany, France, Italy, and Spain) and USA

Methodology

- Identified products with long-acting modality across various therapeutic areas and outlined their respective dosing schedule, HTA ratings, and price
- Developed detailed discussion aids, such as a discussion guide and interview handout, assuring capture of all key parameters needed by payers to understand the long-acting space
- Payer insight investigation was conducted through in-depth, 1.5-hour interviews with twenty Payers across the EU4 and USA, which outlined payer perceptions on the impact of long-acting mechanism of therapies on HTA ratings/ formulary decisions and price

Findings

- Long-acting therapies perceived to provide greater advantages for patients & physicians
  - Convenient for patients who tend to be non-adherent with/do not prefer daily regimens, and easier to manage given the lower number of doses per year
  - Payers were not concerned with increased compliance due to long-acting modality, and would not be considered relevant for formulary decisions / HTA, unless associated with improved clinical outcomes
  - However, payers cite difficulty in linking improvements in clinical outcomes to compliance, as it is difficult to measure in the real world given the lack of validated and standardized measurement tools
- Among the identified long-acting therapies, payers perceived formulary decisions / HTA ratings to be based on attributes such as clinical outcomes, innovativeness, safety, cost-effectiveness, ability to address the unmet needs, and number of therapeutic alternatives
  - Payer perceive long-acting modality to have little-to-no impact, unless being assessed in a disease area wherein adherence is considered extremely important (such as HIV, epilepsy, and schizophrenia)
  - RWE data linking long-acting modality to improved clinical outcomes would be considered acceptable, given that the data is subject to a low risk of bias, and the results are clinically relevant & meaningful

"Anytime we're talking about long-acting, it's really patient convenience issues to potentially improve compliance and adherence. Now, payers really have a difficult time paying for "convenience," and I'm quoting that word. Payers pay for outcomes. Payers pay for higher percent of patients who achieve clinical benefit. Payers are more willing to pay and consider drugs that improve clinical outcomes, markers, surrogate markers, et cetera. So, just because something is long-acting, it doesn't mean it's going to work better. There could be some therapeutic areas where this might be a more salient point to fit an unmet need versus others. Think of things like HIV" - ***Vice President Contracting, Large Plan, US***

Table 1.0: Examples of LA Therapies with a Summary of their HTA Evaluations in EU5

Product / EMA approval date	Therapeutic area	Dosing schedule	FR	DE	IT	ES	UK
Prolia May 2010	Postmenopausal osteoporosis	Once every 6 months	ASMR V, SMR Important ⊘	No data	Class A, Non-Innovative ⊘	Additional monitoring ⊘	Reimbursed with restrictions ⊘
Evenity Sep 2019	Postmenopausal osteoporosis*	Once monthly for 12 months	ASMR IV, SMR Important ⊘	Minor additional benefit ✓	Class "Cnn" ?	Not reimbursed ⊗	(Not yet published) ?
Leqvio Sep 2020	Primary hypercholesterolemia and mixed dyslipidemia	Single SC initially, again at 3 months, followed by every 6 months	No data	Additional benefit is not proven ⊘	Class "Cnn" Additional monitoring ⊗	Not marketed ?	Reimbursed with restrictions ⊘
Praluent Sep 2015	Primary hypercholesterolemia and mixed dyslipidemia	Once monthly or once every 2 week	ASMR V, SMR Important ⊘	Additional benefit not proven ⊘	Class A, Non-Innovative ⊘	Reimbursed with restrictions ⊘	Reimbursed with restrictions ⊘
Ajovy Mar 2019	Migraine prophylaxis	Once monthly/ once quarterly	ASMR V, SMR Moderate ⊗	Considerable added benefit for sub-population C ⊘	Class A, Non-Innovative ⊘	Follow-up conditions ⊘	Reimbursed with restrictions ⊘
Vyepti Jan 2022	Migraine prophylaxis	Once every 3 months	No data	No data	Class "Cnn"	No data	Ongoing assessment

✓ Reimbursed ⊘ Reimbursed with restrictions ⊗ Not reimbursed ? P&R / HTA on-going Conditional / restricted recommendation Not recommended / no HTA

*with a history of at least one severe fracture

Table 2.0: Payer Perceptions on Lon-acting Therapies

Drug	US		EU	
	Annual WAC price ($)	Perceptions	Annual DE price (€)	Perceptions
Prolia	$2,868	• Most payers agreed that long-acting modality had no effect – formulary and coverage decisions were based solely on demonstration of clinical improvements • All analogs assessed require prior authorizations (PAs), with failure to at least 1 therapy in their respective indications • Uptake of products / preferred status of branded long-acting drugs is highly dependent on competitive contracting	€598	• LA modality played no role in HTA assessments of analogs across Europe except for Prolia in France ○ Initial ASMR IV rating was attributed to better adherence & efficacy, however, re-evaluation led to ASMR V due to safety issues, unclear added value, and lower real-world compliance • Positive ratings for Evenity in FR and DE were attributed to the superiority shown against bisphosphonates in a H2H trial • Ajovy received a positive benefit rating in Germany only in last-line patients where a clinically meaningful impact was shown
Evenity	$10,496		€10,508	
Leqvio	$9,750		€5,464	
Praluent	$5,556		€8,931	
Ajovy	$5,320		€7,652	
Vyepti	$6,283		N/A	

Conclusion

While the long-acting modality is an important benefit at the patient and prescriber level to achieve a relatively higher uptake / adherence, Payers and HTA bodies look beyond the long-acting mechanism to assess the therapeutic benefit, HTA rating, and pricing / reimbursement status of a novel therapy. Furthermore, there is a lack of relevant data to show that increased adherence / compliance leads to better clinical outcomes. Payers perceive the long-acting modality to have a greater value potential in chronic diseases having significant consequences due to non-adherence, such as HIV, epilepsy, and chronic obstructive pulmonary disorder (COPD).

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