Optimizing Drug Market Exclusivity in the US and EU Markets

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INTRODUCTION

Market exclusivity (ME) allows a drug to have a monopoly on the market and to be protected from generic drug competition for a given period of time. ME incentivizes manufacturers to develop innovative drugs including in niche populations where there's an unmet need. MEs can run concurrently with or extend beyond the patent protection term (PT), which is 20 years both in the US and EU. The ME types granted by the FDA and EMA and the associated strategic evidence requirements to support these are contrasted across the US and EU.

METHODS

We reviewed regulatory guidance from the EMA and FDA around ME to identify the different exclusivity types and associated exclusivity time gained (Tables 1 and 2). We also extracted the application for each type as well as evidence required to support each (Table 3). We evaluated mechanisms for patent extension, which comprise Patent Term Extension (PTE) in the US, which allows for up to 14 years of marketing, and Supplemental Protection Certificate (SPC) in the EU which allows for up to 15 years of marketing. The various ME types in each market are visualized in timelines against patent lengths and applicable extensions (Figures 1 and 2). We summarized the drivers of ME along with additional considerations for special populations (Figure 3).

Table 1. Market Exclusivity Types - US

ODE	Orphan Drug Exclusivity	7 years
NCE	New Chemical Entity	5 years
GAIN	Generating Antibiotic Incentives Now Exclusivity	5 years
CIE	Clinical Investigation Exclusivity	3 years
PE	Pediatric Exclusivity	0.5 years

Table 2. Market Exclusivity Types - EU

MEO	Market Exclusivity for Orphan Drugs	10 years
PIP	Pediatric Investigation Plan Completion if applied to MEO; +0.5 years extension of Supplemental Protection Certificate (SPC); for a maximum of 5.5 years) for all other applications that complete PIP	2 years
DE	Data Exclusivity	8 years
DE +	Data Exclusivity for 1) new therapeutic indication with significant clinical benefit of new or known substance OR 2) change in classification on basis of significant pre-clinical tests or clinical trials	9 years*
MP	Market Protection (beyond DE)	2 years

*Additional year granted if submitted during the initial 8 years of DE

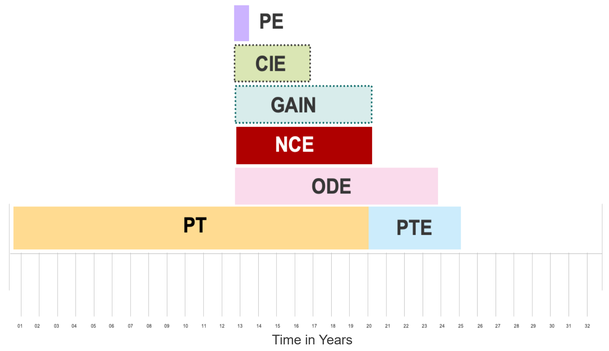

Figure 1. Market Exclusivity Types for US Market Mapped Against Patent Length

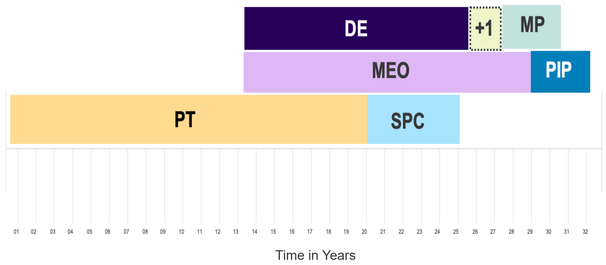

Figure 2. Market Exclusivity Types for EU Market Mapped Against Patent Length

RESULTS

There are 5 non-mutually exclusive pathways to ME in the US granting 6 months to 7 years of exclusivity. In the EU, there are 2 distinct approaches: 1) market exclusivity for orphan drugs (MEO) of 8 years +/- Pediatric investigation plan (PIP) for an additional 2 years and 2) "8+2+1" approach of data exclusivity and market protection +/- new therapeutic indication or change in classification. Marketing for the approved drug can begin during the patent term, but the marketing cannot exceed 14 years if PTE is applied, or 15 years if SPC is applied.

Table 3. Market Exclusivity Types, Applications and Pros/Cons

US-FDA	NCE	Brand-name drug with a new active moiety not previously approved by the FDA **PROS:** No requirement to apply
	PE	Sponsor has conducted and submitted pediatric studies on the active moiety in response to a written request from FDA **PROS:** Added to the end of listed patents and/or exclusivities **CONS:** Clinical trial recruitment challenges
	CIE	Drug with a previously approved moiety when application/supplement contains reports of new clinical investigations (not bioavailability studies) conducted or sponsored by applicant • Include: change in active ingredient(s), strength, dosage, administration route, use condition **PROS:** Can supplement an NCE
	ODE	To treat diseases or conditions affecting fewer than 200,000 in the US **PROS:** Can apply for designation prior to receiving NDA approval; Can be granted for new indications of existing drugs **CONS:** Clinical superiority must be demonstrated if targeting an indication with a previously approved ODE drug; High cost of approved medications
	GAIN	To treat serious or life-threatening infections, including those caused by: (1) an antibacterial/antifungal resistant pathogen, including novel/emerging infectious; or (2) qualifying pathogens listed by the Secretary under subsection (f) [of section 505E of the Food, Drug, and Cosmetic Act (FD&C Act)] **PROS:** Added to the end of listed patents and/or exclusivity **CONS:** Limited scope of products that qualify for this exclusivity
EU-EMA	MEO	Specific to orphan drugs for rare diseases • No mix of orphan and non-orphan indications in the same MA allowed **PROS:** Protocol assistance throughout development; access to centralized procedure; fee reductions; therapeutic indication for a separate orphan designation benefits from 10 years market exclusivity **CONS:** Limited in application to orphan indications only if choosing this pathway. Runs parallel with normal rules on data exclusivity and market protection
	DE	Bars others from using the approved drug's data for the purposes of submitting an application, obtaining marketing authorization or placing the product on the market - hindering generic/biosimilar/hybrid production of a new active substance (Annex I) **PROS:** Possible to extend exclusivity of an existing drug for a new indication **CONS:** Need to prove significant clinical benefit over existing therapies through improved **efficacy, safety** or **contribution to patient care**. Assessed at discretion of CHMP
	MP	Generic, hybrid or biosimilar cannot be placed on the market, even if the medicinal product has received a marketing authorization • **2 years** beyond data exclusivity, even if new drug attempting to enter the market is using their own data from preclinical stage or clinical trials • Can extend for **1 additional year** with approval for a new, significantly beneficial therapeutic indication

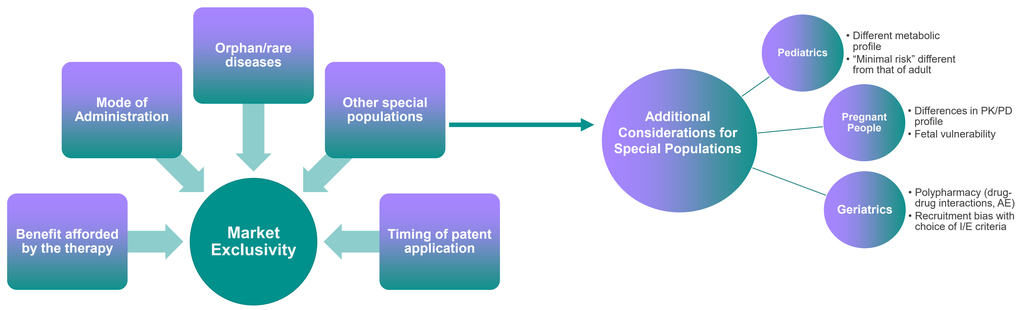

Figure 3. Drivers of ME and additional considerations for special populations

CONCLUSION

There are many pathways to gaining market exclusivity in the US and EU, however the exclusivities granted may not in the end exceed the remaining patent length afforded by the regulator, depending on the timing of the new marketing application. In both markets, orphan drug exclusivity presents the greatest opportunity for market exclusivity extension. A market-specific approach is recommended to maximize ME globally, taking into consideration relevant drivers such as special populations, drug benefits or mode of administration. The ability to enter an expedited approval program will also impact entry to market and should be considered alongside ME approaches.

References: 21 CFR 314 Subparts C, D, H, I; FDA Draft Guidance for Industry. Pregnant Women: Scientific and Ethical Considerations for Inclusion in Clinical Trials Draft Guidance for Industry; FDA Draft Guidance for Industry. Pediatric Drug Development: Regulatory Considerations – Complying with the Pediatric Research Equity Act and Qualifying for Pediatric Exclusivity Under the Best Pharmaceuticals for Children Act. Rinku Patel. Exclusivity – Which one is for me?. FDA Office of Generic Drugs; Sonia Riberio. Data Exclusivity, market protection, orphan and pediatric rewards. EMA. 26 October 2018.; Regulation (EC) No. 726/2004; Directive 2001/83/EC.