White Paper

Not All Fixed Dose Combinations (FDCs) are Equal

Key strategic considerations for pricing and market access

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Overview

Fixed-dose combinations (FDCs) are coformulations of two or more active ingredients within a single dosage form. These active ingredients can be both marketed as monotherapies prior to FDC launch (referred to within this paper as 'mono:mono') or be a combination of marketed and novel (described here as 'mono:new'). FDC components can also be on- or off-patent, or represent the standard of care (SoC) within the target indication.

FDC pricing and market access (P&MA) outcomes depend on the launch context, the benefits they offer compared to existing therapies, and how payers perceive their value. Payers can perceive FDCs as lifecycle extension strategies, by manufacturers of key brands approaching LoE (loss of exclusivity), to defend against generic or biosimilar competition. But what about FDCs that bring novel active ingredients, enable improved drug delivery, enhance outcomes through greater treatment compliance, or provide safety benefits? Are these considered innovative and assessed in the same way as other novel therapeutics, i.e., priced according to value, with the potential for achieving favorable price and access outcomes relative to SoC and/or component ingredients?

In this report, we describe how different types of FDCs are perceived by payers, outlining their P&MA drivers, challenges, and outcomes. To conclude, we summarise the "rules of thumb" for FDC P&MA outcomes and discuss how these can inform the development of appropriate pricing, reimbursement, and evidence generation strategies depending on the type of FDC in question.

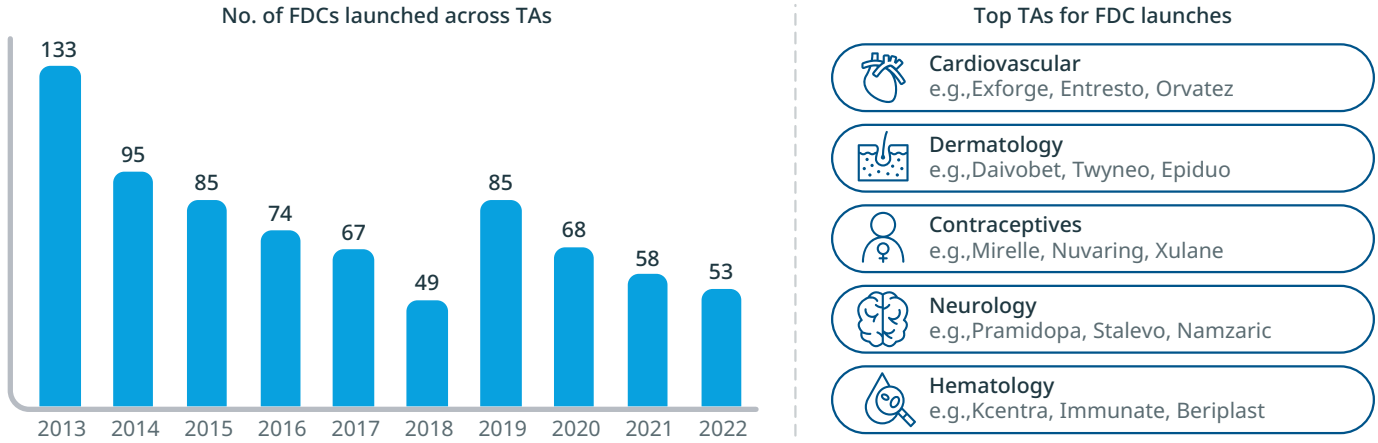
Since 2013, approximately 750 branded FDCs have launched across therapy areas (TAs), with the greatest concentration seen in cardiovascular and dermatology indications.

Introduction

Since 2013, approximately 750 branded FDCs have launched across therapy areas (TAs), with the greatest concentration seen in cardiovascular and dermatology indications (see Figure 1).

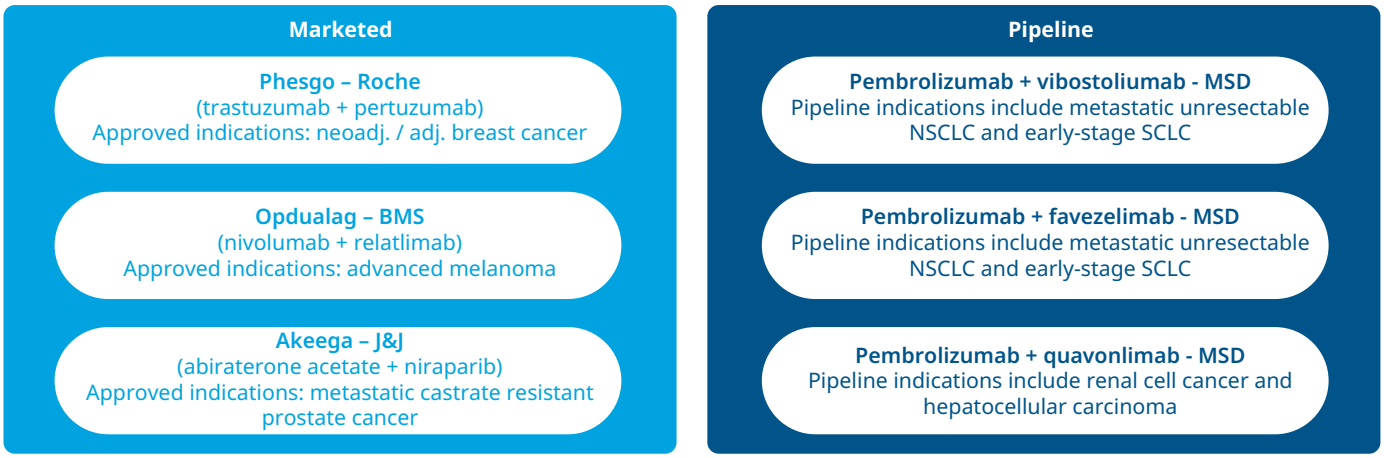
Although overall there is a downward trend in the number of FDC launches year on year, we have recently seen the launch of FDCs in oncology, with Phesgo (trastuzumab + pertuzumab) and Opdualag (nivolumab + relatlimab) in Q4 2020 and Q3 2022, respectively (see Figure 2). Further oncology FDC launches are anticipated. These represent a significant change in clinical approach, switching from treatment with two separate therapies in the form of a 'traditional, loose' combination, as seen with most oncology combinations, to providing two separate therapies for use in a single dosage form. In our next whitepaper we discuss combination strategies in oncology in more detail, covering both loose combination regimens and fixed/single doses, and explore how to navigate the complexities of combination price setting and negotiate favourable P&MA outcomes with payers. Additionally, some of the FDCs discussed in this paper with off-patent components have been characterized as "Value Added Medicines" in reports developed following a collaboration between Medicines for Europe and IQVIA (see *'A digital future for value added medicines'* whitepaper for the latest in this series).

Figure 1: Overview of number of branded FDCs and most common TAs in which they launch



Source: IQVIA MIDAS® data analysis.
Note: Analysis considers Rx products launched post-2013 (generic products, multivitamins/supplements and imaging agents & diagnostics are excluded); country scope: FR, DE, IT, ES, UK, US. Top 10 TAs for FDC launches are cardiovascular, dermatology, contraceptives, neurology (inc. pain), hematology, respiratory, gastrointestinal, ophthalmology, diabetes and HIV.

Figure 2: FDCs emerging in oncology space (non-exhaustive)



Source: clinicaltrials.gov

Pricing and market access outcomes for FDCs

We observe different patterns of P&MA outcomes for mono:mono vs. mono:new FDCs when assessed relative to the available monotherapy(ies) (i.e., the mono-component(s)) and/or the established standard of care (SoC).

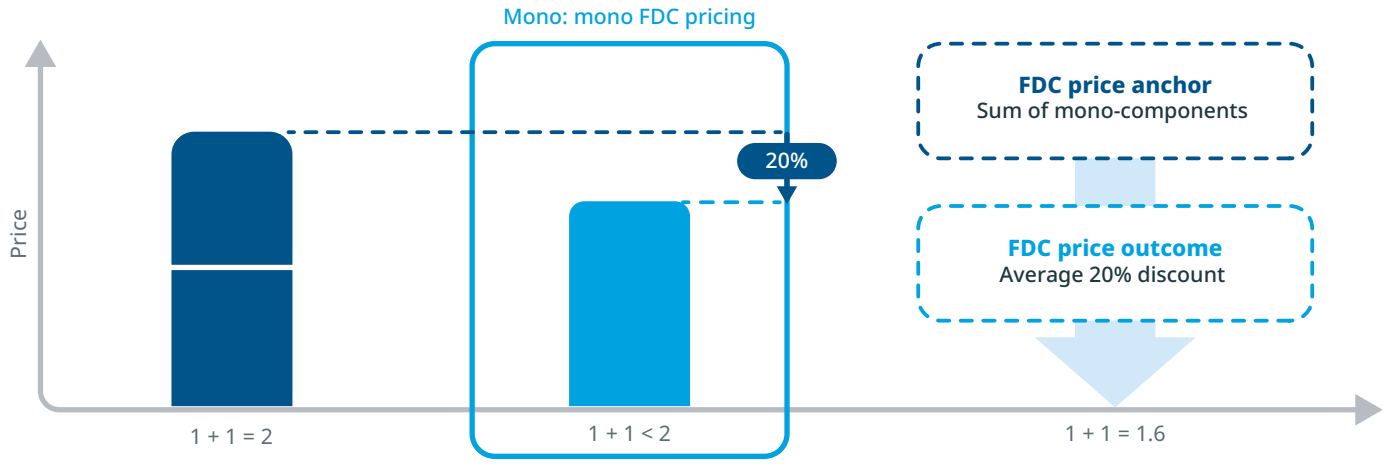
P&MA OUTCOMES FOR MONO: MONO FDCS

For 'mono:mono' FDCs, price and market access are typically determined relative to the available mono-components, meaning the sum of the mono-component costs serves as a price benchmark. Our analysis shows that for all mono:mono FDCs, while "1+1 =2" pricing is possible, it is not the norm. Instead "1+1 = 1.6" is the average price achieved by the FDC, which equates to a ~20% discount vs. the sum of monotherapies (see Figure 3). Despite typically offering price discounts, all FDCs received access that was equivalent to or more restricted than the mono-components (e.g., requiring patients to be initiated on individual components and well controlled prior to switching to the FDC, as seen with Glyxambi — combination of empagliflozin and linagliptin for Type 2 diabetes in Spain).

Only in exceptional circumstances are 'mono:mono' FDCs reimbursed at a cost equivalent to or greater than the sum of the mono-components (1+1 ≥ 2). Such cases are rare and contingent on FDCs demonstrating a meaningful clinical, or cost benefit vs. the established, parent combination (see Spotlight 1).

Our analysis shows that for all mono:mono FDCs … "1+1 = 1.6" is the average price achieved by the FDC.

Figure 3: Overview of average ex-manufacturer price at launch vs. individual monotherapy components for FDCs combining existing therapies – mono:mono



Source: IQVIA MIDAS® analysis.
Note: Country scope: US, DE, FR, UK, IT, CN, JP. Figures represent the average FDC price achieved observed across countries (calculated based on 10 FDCs, with prices ranging from 30% discount relative to the sum of mono components to approx. parity prices; Vyxeos excluded from analysis due to atypical launch context – see below for description). Analogues assessed include key launches in the top FDC therapy areas shown in Fig 1.

Spotlight 1: 'mono:mono' FDCs that achieved price premiums relative to mono-components

PHESGO (subcutaneous fixed dose combination of pertuzumab + trastuzumab, two existing agents) **achieved a slight price premium (1-7%) vs. the loose combination with intravenously administered trastuzumab**. Phesgo was reimbursed at a cost similar to the parent combination, despite only demonstrating non-inferiority, **because its subcutaneous formulation supported treatment outside the hospital, reduced administration time to 5-15minutes and was expected to reduce healthcare resource utilisation**. This was particularly valuable given it launched during the COVID pandemic, when hospital resources were stretched. Limited value* demonstrated in original pertuzumab trials meant Phesgo received the same limited access as the loose combination following HTA review.

*In the NeoShere trial: the loose combo plus chemo demonstrated a 1% improvement in 3-year IDFS rate and lack of significant OS effect (vs. trastuzumab plus chemo), leading to ASMR insufficient for both the parent combination and Phesgo.

VYXEOS (daunorubicin + cytarabine) which combined two chemotherapy agents in a new liposomal formulation that **improved absorption and enhanced clinical outcomes** (median OS was 9.6 months with Vyxeos vs. 5.9 months with the loose regimen). Vyxeos **was priced at a substantial premium of 319% to 2900% vs. the loose combination** in European countries and, despite the large price differential, saw uptake across markets. It is important to highlight that the high premium achieved by Vyxeos is in part due to the genericization and low cost of both the component chemotherapy agents. In Europe, Vyxeos received access in-line with the parent monotherapies, achieving positive clinical benefit ratings and demonstrating acceptable cost-effectiveness for a life-extending treatment. In the US, Vyxeos is considered medically necessary for t-AML and AML-MRC and is covered as a Tier 2 treatment by major government and commercial plans. Vyxeos is an example of a Value-Added Medicine.

It is also important to examine the scenario in which FDCs are introduced after generic versions of one of the mono-components have launched at a significantly lower cost in comparison to the original patented component. While our analysis showed these FDCs technically achieve a price of '1+1 = 2'; in reality, '1+0.01 = 1.01' is a more accurate description, as payers will consider the generic benchmark and the FDC price will be close to the non-genericised branded mono-component price (i.e., the genericised component will have a negligible impact). For example, Nexlizet combined ezetimibe — a highly genericized molecule, with bempedoic acid — a newly launched innovative molecule. In this case, the generic component had no impact on achievable price with the Nexlizet combination achieving the same price as bempedoic acid monotherapy.

Finally, in addition to price, we conclude that FDCs are unlikely to overcome access challenges associated with parent mono-components and the level achieved is typically similar or worse. With the recent assessment of Phesgo in France, HAS accepted bioequivalence as demonstrated in the FeDeriCa trial, however had previously rejected the loose combination (insufficient SMR) in the neoadjuvant (in 2016) and the adjuvant (in 2019) setting, meaning that the FDC could not achieve a positive recommendation. Furthermore, in France and Spain, a general pattern of restricted or no access is observed, suggesting an anti-FDC payer management philosophy, resulting in limited company appetite to launch mono:mono FDCs. For example, Suliqua (insulin glargine + lixisenatide) failed to achieve access in both markets and Nexlizet (bempedoic acid + ezetimibe) was never marketed, while both were reimbursed in the UK and/or Italy.

P&MA OUTCOMES FOR MONO:NEW FDCS

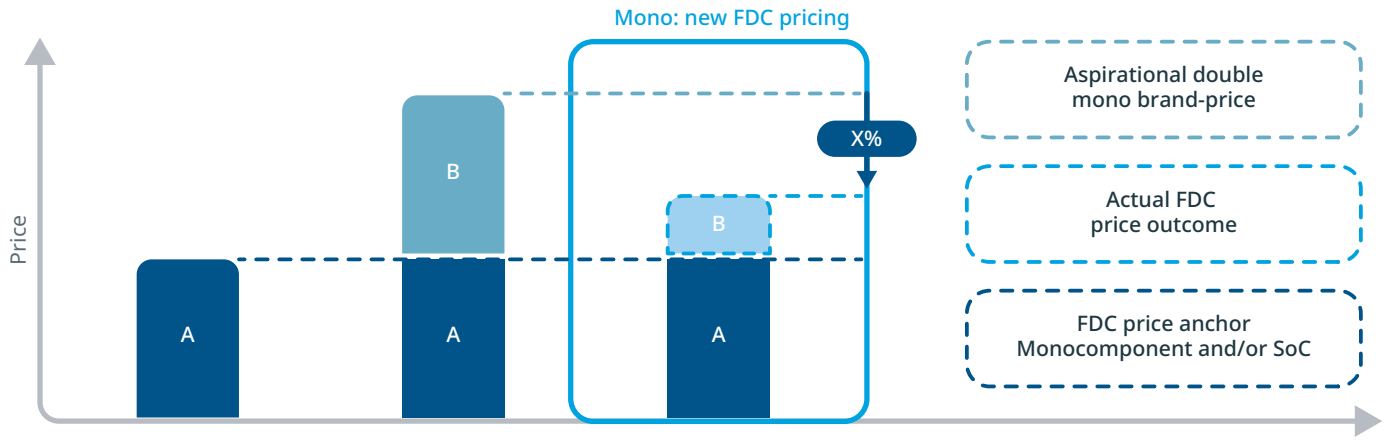
With 'mono:new' FDCs, if the marketed mono-component is the standard of care (SoC) then payers will consider it as a benchmark when assessing the FDC price; with the level of added benefit vs. the SoC determining the extent of the price premium. In practice, the premium awarded vs. the mono-component is modest and the new component does not get a full "monotherapy brand-like" price. For example, the price of Harvoni (ledipasvir+ sofosbuvir) was anchored to that of Sovaldi (sofosbuvir), the SoC at time of FDC launch, and received a 10% premium in Europe and the US (30% in Japan), based on a 10% improvement in hepatitis C cure rate.

Another such example is Anoro Ellipta, a once-daily combination treatment comprising two bronchodilators, umeclidinium, a long-acting muscarinic antagonist (LAMA), and vilanterol, a long-acting beta (2) agonist (LABA), in a single inhaler. At the time of launch, vilanterol was not available as a monotherapy. Anoro Ellipta was able to demonstrate robust clinical benefit (20% risk of a moderate/severe COPD exacerbation compared with umeclidinium) relative to umeclidinium monotherapy, while also enhancing response rates, reducing rescue medicine usage, and sustaining a higher quality of life. Anoro achieved a significant premium vs. the established monotherapy (~45%) and the SoC (~50%). This is at the higher end of the range observed for mono:new FDCs, however it still does not reach the "monotherapy brand-like" price of 100% of the established mono-component. Despite the cost differential, Anoro achieved access equivalent to the mono-components in EU countries and is covered without accompanying step edits or prior authorizations for the majority of US patients (~77% of Medicare Part D patients; ~94% of commercial patients nationally).

Price can be de-linked from the FDC mono-components if they do not represent current SoC (i.e., if the FDC targets a different population vs the established monotherapy), and the combination price is therefore assessed vs. other treatments. This situation is far less common among the FDCs in our analysis, but Entresto is one such example. With Entresto (sacubitril + valsartan), sacubitril was a novel component, while valsartan was not used in Entresto's target indication (chronic heart failure), meaning that payers benchmarked the FDC price vs. enalapril, the SoC at time of launch and trial comparator, instead of vs valsartan. Entresto was reimbursed at a significant premium to generic enalapril (9000% in Europe and 5100% in the US) which equated to a substantial premium to the branded valsartan (555% in Europe and 125% in the US) mono-component.

In summary, our analysis highlights the opportunity for 'mono:new' FDCs to achieve a price premium vs. available mono-component prices and/or SoC comparators, if incremental efficacy is demonstrated (see Figure 4). However, it also reveals that the price levels typically achieved are constrained by the existing mono-component (i.e., the novel ingredient does not receive a 'monotherapy brand-like' price). We therefore conclude that launching novel therapies as part of an FDC may in fact limit the price potential versus that which could be achieved if launched as a monotherapy (assuming the monotherapy profile is sufficient to achieve favorable pricing outcomes vs. SoC). Furthermore, having a high-priced mono-benchmark may further constrain the pricing headroom and premium achievable for the FDC, due to payer budgetary sensitivities.

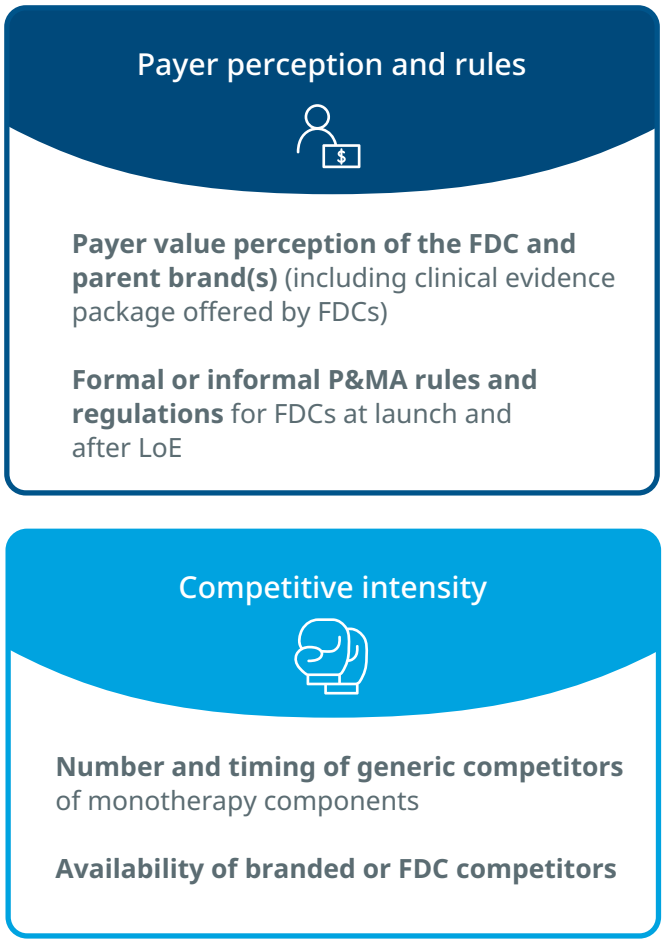
Figure 4: Illustrative ex-manufacturer prices at launch vs. established monotherapy component for FDCs combining new and existing therapies – mono:new)



Drivers of FDC P&MA outcomes

P&MA is driven by both external drivers and manufacturer strategy. First, we will focus on the two key overarching external drivers of P&MA outcomes of FDCs at launch (see Figure 5).

Figure 5: – Key overarching external drivers of P&MA outcomes of FDCs



In our analysis, no 'payer perceived lifecycle extension' FDC was able to secure parity or premium relative to the combined cost of its mono-components (1+1 does not equal 2).

Payer perception and rules

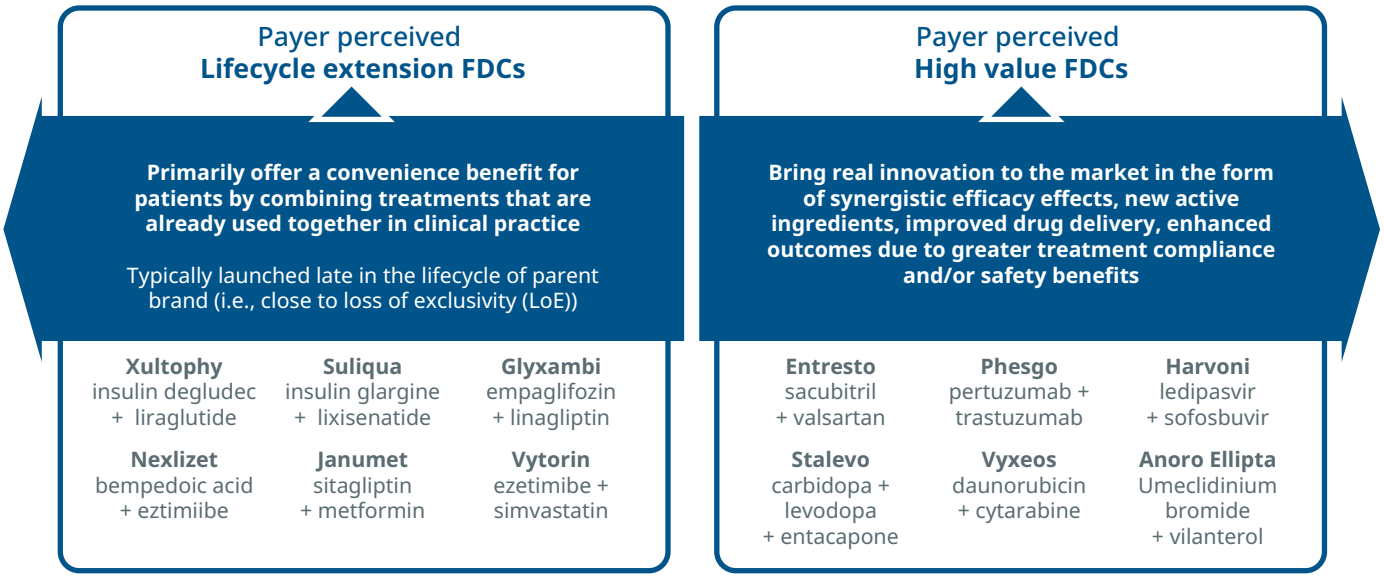
PAYER VALUE PERCEPTION

"Not all FDCs are equal" in the eyes of a payer. This IQVIA analysis identifies two broad groups of FDCs based on the level of payer-perceived value – 'payer perceived lifecycle extension' FDCs and 'payer perceived high value' FDCs (see Figure 6). While payers express general concerns around the limited dosing flexibility, risks of therapeutic duplication, or unclear positioning in treatment paradigms/ protocols associated with FDCs, they are typically much more skeptical of perceived 'lifecycle extension' FDCs, which represent the majority of coformulations available today. These FDCs are usually launched late in the lifecycle of the parent brand and are perceived by payers as strategies to extend patent life and market exclusivity with limited tangible impact on patient outcomes

The second category, 'payer perceived high value' FDCs, are those which payers perceive as bringing real clinical or cost benefits - for example, where one of the components is novel (i.e., not previously marketed as monotherapy) or a reformulation of established monotherapies offers synergistic efficacy improvements. These FDCs are less common and will often be launched earlier in the lifecycle of the parent brand, with similar P&MA expectations to those of a new product.

In our analysis, no 'payer perceived lifecycle extension' FDC was able to secure parity or premium relative to the combined cost of its mono-components (1+1 does not equal 2). For these FDCs, a significant price discount (e.g., 1+1=1.6) should be expected. Therapy area, product characteristics, and commercial strategy will ultimately determine the extent of that discount. For example, in TAs where monotherapy dosing is particularly complex (e.g., asthma, oncology) or treatment adherence is a known issue and vital to achieving near-cure status (e.g., HIV), payers have allowed for the FDC price to be closer to the sum of the mono-components. For example, in HIV, Dovato and Truvada were not considered to offer clinical innovation by payers (seen as lifecycle extension FDCs) but achieved prices within 10% of their respective individual mono-components due to the value of reducing pill burden for these patients.

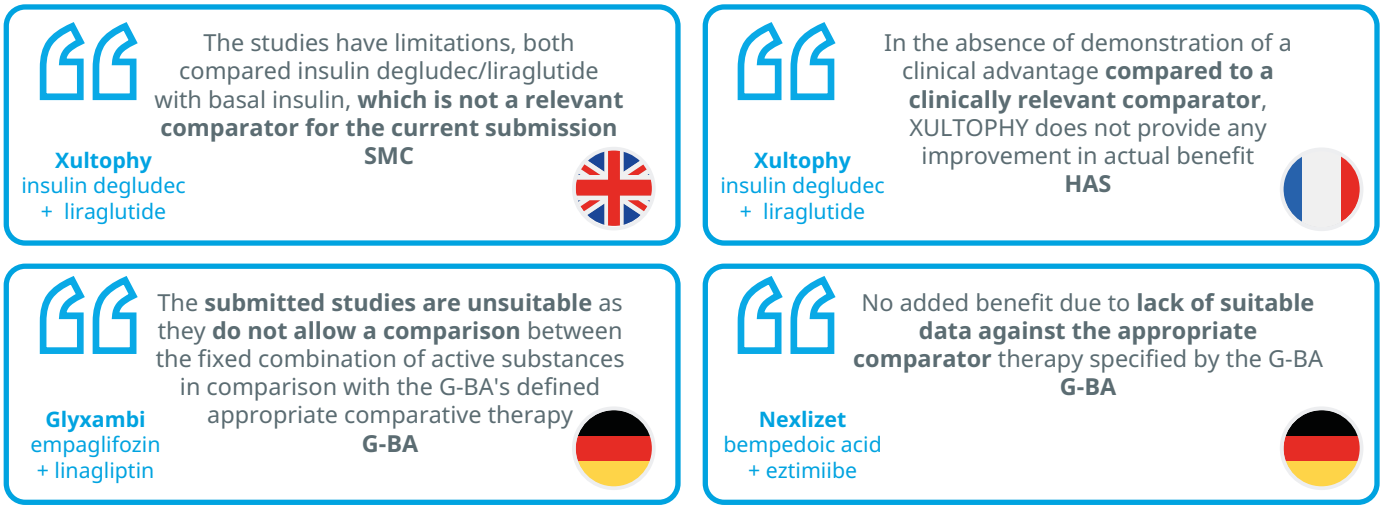
Figure 6: FDC payer value perception spectrum



Notes: Figure indicates expected categorization based on payer value perception. Most marketed FDCs are perceived by payers as lifecycle extension FDCs – payer perceived high-value FDCs are far less common. For the current analysis, FDCs falling under both categories were deliberately assessed.

The challenge with 'payer perceived lifecycle extension' FDCs is that while, from a regulatory perspective, FDCs only need to demonstrate an absolute efficacy benefit, and bioequivalence vs. monotherapy components, this approach does not satisfy payer requirements in terms of appropriate comparators or comparative clinical benefit, and typically leads to poor HTA outcomes (see Figure 7). Furthermore, the clinical rationale for most 'payer perceived lifecycle extension' FDCs (i.e., patient convenience and enhanced compliance vs. the loose combination) is challenging to capture in a clinical trial setting and companies do not typically invest in subsequent RWE generation due to the associated costs, risk of not demonstrating sufficient benefit, or misalignment with brand priorities. Ultimately payers do not pay for convenience unless it has been proven with robust evidence to improve patient outcomes.

Figure 7: EU payer critique for selected payer perceived lifecycle extension FDCs



After COVID, the access environment across countries is becoming ever more challenging for poorly differentiated products that do not offer unambiguously improved clinical benefit vs. SoC. This trend is particularly impacting FDCs perceived by payers 'lifecycle extension' strategies (see France example in Spotlight 2).

Spotlight 2: Steglujan was not reimbursed in France

STEGLUJAN is Merck's ertugliflozin / sitagliptin (SGLT2 / DPP-4) FDC indicated for T2D patients. The clinical evidence package was composed of a bioequivalence study (FDC vs. loose combination) and a placebo-based efficacy trial (HbA1c).

In 2019, France's CT attributed SMR insufficient (i.e., no reimbursement / access) given the inappropriate comparator choice and lack of CVOT data.

However, payers are open to rewarding innovation demonstrated by 'payer perceived high value' FDCs providing the value is illustrated with a robust evidence package demonstrating incremental clinical benefit vs. SoC (in terms of efficacy and/or safety) through accepted, hard outcomes (see Spotlight 3). In our analysis, only when FDCs offered meaningful clinical or cost benefits, and are perceived by payers as 'high value', were they reimbursed at or above the price of the sum of the mono-components, or SoC.

Payers are open to rewarding innovation demonstrated by 'payer perceived high value' FDCs providing the value is illustrated with a robust evidence package.

Spotlight 3: Entresto & Harvoni Price Premiums vs. SoC

ENTRESTO is Novartis' sacubitril / valsartan FDC for heart failure. At launch, sacubitril was a novel component (not available as a monotherapy), while valsartan (Diovan) was a well-established angiotensin receptor blocker; a genericised class. Entresto launched as the first-in-class angiotensin receptor neprilysin inhibitor (ARNI).

In the pivotal trial, Entresto was compared to the then standard of care (i.e., enalapril) and showed clinical superiority based on a composite of CV endpoints (20% relative risk reduction). Payers did not use the genericised mono component as a price benchmark and rewarded innovation with an **ex-manufacturer price of ~€5/day in the EU** ($12/day in the US) despite a generic SoC.

> **"Novartis launched Entresto as an LCM strategy following the LoE of their blockbuster Diovan, but they tried to distance themselves from it being perceived as a 'Diovan plus' to avoid it being bucketed with valsartan generics. I don't recall they ever referred to Entresto as an FDC"**
> IQVIA Expert

HARVONI is Gilead's ledipasvir / sofosbuvir FDC for Hepatitis C. Ledipasvir was a new component (not available as monotherapy), but sofosbuvir (Sovaldi) had been launched as monotherapy. Harvoni's cure rate vs. placebo was ~10% higher than Sovaldi's (from ~90% to nearly 100%). Payers rewarded innovation with a **~10-15% price premium vs. Sovaldi** in EU5 and US (30% in JP) with no change in access conditions.

A positive payer perception of the established mono-component(s) can also be a driver of improved P&MA outcomes of the FDC. It is challenging to single out the specific impact of this driver, but IQVIA believes that it can support improved P&MA outcomes compared to the abovementioned 'norm', if the FDC clinical evidence package allows for it. For example, Sovaldi's perception as a first-in-class curative treatment of HCV is likely to have acted as a catalyst for payers' appreciation of Harvoni's placebo-based trial that indirectly showed superiority vs. its parent brand. Similarly, the reputation of Herceptin (trastuzumab) and Perjeta (pertuzumab) as effective, well-established treatment options for HER2+ breast cancer patients is likely to have played a supportive role in Phesgo being able to achieve a price of 1+1=~2.

PAYER RULES AND REGULATIONS

At FDC launch, there are no formal price setting regulations for FDCs vs. mono-components established in any market except for Japan*. However, in several markets informal precedents exist for significant discounts on FDC pricing relative to branded mono-components. These will likely intensify as more FDCs are introduced, given the macroeconomic climate and payer budgetary constraints.

At loss of exclusivity (LoE) of a mono component, there are also no formal price revision rules for FDCs in any market. However, payers can introduce access restrictions to favour the use of the less-expensive individual mono-components vs. the more expensive FDC. Hence, a more important driver for FDC outcomes is the level of generic competition, and the impact on price and access dynamics (see next section).

Competitive intensity

LEVEL OF GENERIC COMPETITION

As previously noted, at FDC launch, when generic versions of one of the mono-components are available (and at a significant discount to the off-patent brand), payers will consider generic benchmarks when assessing achievable FDC price. Effectively, this means the FDC price will be close to the non-genericised mono-component. Similarly, when genericised competitors are part of the SoC, FDCs perceived by payers as lifecycle extension strategies will be priced at the lower end of the price range. Both Suliqua (Soliqua in US) and Xultophy (GLP-1/insulin FDCs) had lower cost basal / bolus insulin biosimilars as part of the SoC, which was reflected in their pricing outcomes (1+1=1.4).

Once generic alternatives of mono-components are available then, depending on the relative price differential, payers could implement generic favoring policies vs the FDC. Payer perceived 'Lifecycle extension FDCs' are at most risk of access restrictions. With Vytorin, given the genericization of ezetimibe and simvastatin, some providers in the US applied prior authorization criteria requiring patients to step-through generic ezetimibe and only covered the FDC for patients with swallowing difficulties. Similarly, payers may shift cost sharing onto patients due to budgetary pressures and a perception that FDCs are more "convenient' options that assist patients in terms of reduced pill burden that offer little "payer value". In some countries manufacturers have a degree of freedom to negotiate price/access trade-offs with payers and reduce the likelihood of implementation of generic-favouring policies (see Spotlight 4 below).

A positive payer perception of the established mono-component(s) can also be a driver of improved P&MA outcomes of the FDC.

* In Japan: with FDCs containing of two components that are marketed as monotherapies (i.e., mono:mono), the price is set at 80% of the sum of the NHI reimbursement price for each patented component; if the FDC contains generics, the cheapest marketed generic is the price considered for the calculation + 80% of the patented products.

Spotlight 4: US price-access trade-offs with FDCs and mono-components

US payers primarily make access decisions based on the economics of covering FDCs vs. individual components. In other words, they scrutinize their own net spend between outflow (i.e., payments to manufacturers) and inflow (i.e., co-pays from patients).

Manufacturers can negotiate net price and tiering status of both FDCs and the mono component(s) they own to 'make payers whole' (i.e., ensuring payers are not financially disadvantaged by providing access to the FDC vs. individual components) while pursuing their own FDC strategy in terms of price and volume ambitions. Contracts can be dynamic and change over time, for example upon LoE of one of the components.

Future outlook

Over time, the US market has become much more fragmented in terms of coverage economics and benefit design (e.g., deductibles, co-insurance for expensive drugs, co-pay cards and accumulator adjusters). In addition, drug costs on average have increased at a proportionally higher rate than co-pays, thereby reducing the impact of the latter on payer cost.

However, price-access trade-offs based on product tiering and corresponding co-pay level in the US are still an important option for companies to explore and implement in order to realize their FDC and portfolio strategies.

Illustrative examples of price-access trade-offs upon LoE of a FDC component

Assumption: Tier 1 (generics); ~10 USD; Tier 2 (originators); co-pay ~35 USD; Tier 3 (originators); co-pay ~65 USD

Pre-LoE scenario A

Based on price and tiering status, **there may be no advantage/ disadvantage for payers to favour FDCs** or single components

Illustrative Example	Drug A Tier 2	Drug B Tier 2	FDC (A+B) Tier 2
Net price	$95	$60	$120
Co-pay	$35	$35	$35
Payer cost	$60	$25	$85
Total payer net spend	$85 =		$85

Post-LoE scenario B

Based on price and tiering status, **there may be no advantage/ disadvantage for payers to favour FDCs** or single components

Illustrative Example	Drug A Tier 2	Drug B Tier 2 (Gx now available)	FDC (A+B) Tier 2
Net price	$95	$15	$120
Co-pay	$35	$10	$35
Payer cost	$60	$5	$85
Total payer net spend	$65 <		$85

Post-LoE scenario C

Alternatively, tiering status and correspondent co-pay level may actually make **FDCs more convenient for payers to cover**

Illustrative Example	Drug A Tier 2	Drug B Tier 2 (Gx now available)	FDC (A+B) Tier 2
Net price	$95	$15	$120
Co-pay	$35	$10	$65
Payer cost	$60	$5	$55
Total payer net spend	$65 >		$55

LEVEL OF BRANDED COMPETITION

The influence of branded competition on FDC P&MA outcomes plays out largely like other, non-combination therapies. FDCs must demonstrate a clinical or cost/ healthcare system benefit versus the current SoC therapies, or else face a penalty in the form of relative price discounts, or less favorable access. Branded competition also has the potential to influence payer perceptions of FDC value and their assignment as either 'high value', or 'lifecycle extension'. For example, an FDC that demonstrates a meaningful benefit and includes a novel ingredient but does not represent a 1st in-class or best in class launch for that mechanism of action within the therapy area is unlikely to be perceived as 'high value' (vs. a first in class FDC – e.g., Entresto) and will be limited to the price benchmark for the class as a ceiling.

Manufacturer portfolio strategy

Manufacturer strategy is a key internal driver of FDC P&MA outcomes. There are a range of portfolio considerations that drive the decision to launch an FDC (see Figure 8) and this also determines the manufacturer's strategy; for example, Merck launched Vytorin around the same time as Zetia (ezetimibe monotherapy) with the aim of stepping patients quicker through early line monotherapy (i.e., Lipitor and Zocor) onto Zetia-based regimens. They did this by positioning Vytorin FDC as the first product with a combined mode of action offering enhanced efficacy for lowering cholesterol levels compared to statins alone. Alternatively, Nexlizet, which offered a convenience benefit vs. SoC, was launched as an upgrade option prior to Nexletol (bempedoic acid) LoE and appeared to serve as a means of maximizing bempedoic acid volume and offering an intensification option, with the FDC priced at parity to bempedoic acid monotherapy. The portfolio rationale for launching FDCs in turn guides the strategic objectives at launch: price maximization vs volume maximization, thus contributing to observed FDC P&MA outcomes.

Figure 8: Potential portfolio rationale for FDC launch

UPGRADE
Switch patients from an established brand to FDC (e.g., prior to LoE) to retain and drive overall market share

ENHANCE
Launch FDC to improve patient outcomes and generate a new revenue source (e.g., by addressing a clear clinical need with an innovative product)

SUSTAIN
Leverage the FDC to sustain a brand, or device, loyal customer base (e.g., prior to launch of a follow-on product with a similar device)

REINFORCE
Help reinforce manufacturer or brand leadership and/or reputation in a particular therapy area

Conclusions and strategic considerations for FDC launches

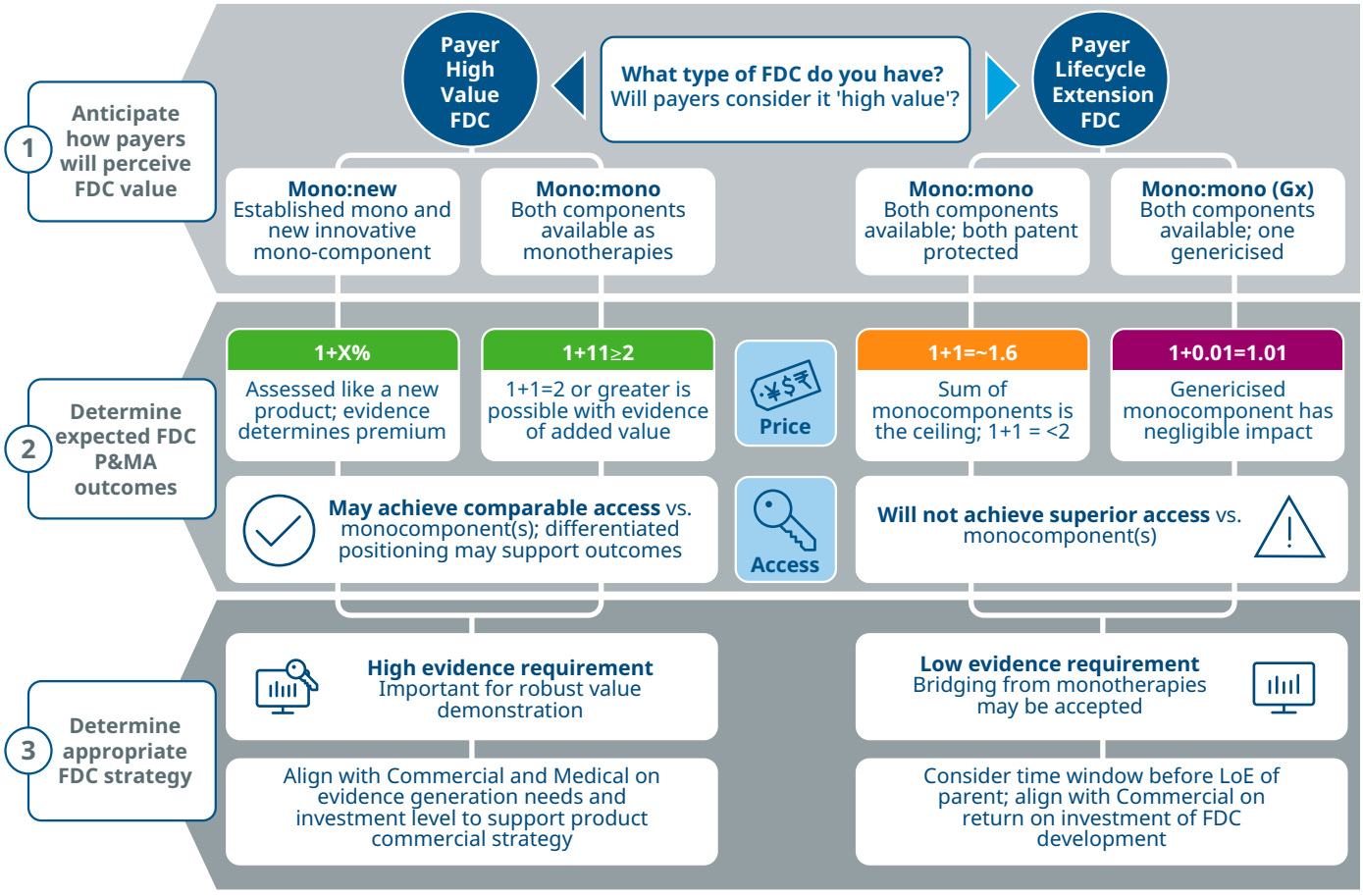
Payer perceptions of FDCs have been critical to P&MA outcomes. Late-launched FDCs without a compelling patient or economic benefit will be perceived by payers as clear life-cycle extension strategies and achieve sub-optimal P&MA. This is the likely reason for the decreasing number of FDC launches year on year (Figure 1). To make smart decisions about developing and positioning FDCs, it is essential that market access teams take a structured approach that reflects how payers will perceive the value of the asset, i.e., lifecycle extension vs high value (see strategic planning framework; Figure 9).

Each pipeline FDC should have a clear objective that maximizes strategic value while remaining anchored to achievable P&MA outcomes, based on the payer value perception categorization.

STEP 1: ANTICIPATE HOW PAYERS WILL PERCEIVE FDC VALUE

The starting point is to anticipate how payers will categorise the FDC — as high value or lifecycle extension. Within this approach market access should collaborate with cross-functional teams to identify the likely payer perception and categorization by asking important questions: Does it have any payer-relevant 'high-value' characteristics (e.g., can the FDC address high unmet need in a differentiated patient population vs the established mono-component?), and can the value be robustly proven? If not, what evidence would be needed to enable 'high value' perceptions, and is this feasible to collect with the right level of investment? By determining this early on, market access teams can better anticipate P&MA challenges and outcomes, facilitating greater organizational alignment on FDC strategic planning

Figure 9: Strategic planning framework for an FDC asset



Notes: Bridging studies are conducted to compare pharmacokinetic data between the FDC and authorized active substances taken simultaneously in order to demonstrate bioequivalence and are typically sufficient for achieving regulatory approval in the same target population (without the need for comparative phase III trials).

STEP 2: DETERMINE EXPECTED FDC P&MA OUTCOMES

Second, based on the payer categorization, understand expected P&MA outcomes using IQVIA "rules of thumb" (see Fig. 9). It is important to note that significant variation in outcomes is observed even within categories, depending on the unique launch conditions and presence of drivers discussed in the earlier section.

STEP 3. DETERMINE APPROPRIATE FDC STRATEGY

The payer perception and resulting P&MA flexibility determines the strategic options available with FDCs and critical success factors for each strategy, such as, evidence investment needs and launch timing vs. competitors, or relative to the LoE of established mono-components.

For example, to achieve P&MA success with a FDC identified as potentially being 'payer perceived high value', the team need to consider two key factors: launch timing vs competition and the level of clinical differentiation – in other words, is the asset first in class or best in class? If yes, then a high level of investment in a payer-relevant integrated evidence package that substantiates the product value differentiation is required to support FDC success. The level of investment in the pivotal RCT and supporting RWE required is like that for development of a new drug (payers will not accept bridging of the evidence package from the established monotherapy).

On the other hand, if the asset is identified as a 'payer perceived lifecycle extension' FDC, and the value perceived by the payer is limited, investing in additional evidence is unlikely to make a tangible difference. In such situations, the key to success is to offer a price advantage over competitors. The level of competition will ultimately determine the viability of such a strategy – e.g., is there sufficient time before the parent mono-component loses exclusivity (and payers favour lower cost generic alternatives) to establish the FDC. If no, does it make financial sense to develop the FDC, taking into account potential revenue loss following patent expiry? Therefore, market access teams need to provide realistic, discounted price and access assumptions to inform the FDC business cases. In turn, ensuring the organisation makes well-informed decisions about FDC development.

In conclusion, payers do not view all FDCs equally. Therefore, there isn't a "one-size fits all" FDC strategy. It is fundamental to consider the payer value perception in strategic planning. IQVIA can offer expert advice to assist market access teams in navigating these challenges. Please contact us for more information.

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List of abbreviations

AIFA: Agenzia Italiana del Farmaco

ARNI: Angiotensin receptor neprilysin inhibitor

CCG: Clinical Commissioning Group

COPD: Chronic obstructive pulmonary disease

CV: Cardiovascular

CVOT: Cardiovascular outcome trial

DTC: Direct To Consumer

FDC: Fixed dose combination

FEV: Forced expiratory volume

Gx: Generic

G-BA: Gemeinsamer Bundesausschuss (Federal Joint Committee)

GLP-1: Glucagon-like peptide 1 agonist

HAS: Haute Autorité de Santé (French National Authority for Health)

HIV: Human immunodeficiency virus

HTA: Health Technology Assessment

IDFS: Invasive disease-free survival

LABA: Long-acting beta-agonist

LAMA: Long-acting muscarinic antagonist

LCM: Lifecycle Management

LoE: Loss of exclusivity

MoA: Mechanism of action

NHS: National Health Service

NICE: National Institute for Health and Care Excellence

P&MA: Pricing and market access

RWE: Real world evidence

Rx: Prescription

SoC: Standard of Care

SMC: Scottish Medicines Consortium

SMR: Service Medical Rendu (medical benefit)

TA: Therapy area

References

1. Anoro Ellipta: EPAR - Product Information (EMA). Available at: https://www.ema.europa.eu/en/documents/product-information/anoro-ellipta-epar-product-information_en.pdf
2. Nustendi: EPAR - Product Information (EMA). Available at: https://www.ema.europa.eu/en/documents/product-information/nustendi-epar-product-information_en.pdf
3. Phesgo: EPAR - Product Information (EMA). Available at: https://www.ema.europa.eu/en/medicines/human/EPAR/phesgo
4. Vyxeos: EPAR - Product Information (EMA). Available at: https://www.ema.europa.eu/en/medicines/human/EPAR/vyxeos-liposomal
5. Guideline on clinical development of fixed combination medicinal products (EMA). Available at: https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-clinical-development-fixed-combination-medicinal-products-revision-2_en.pdf
6. American Medical Association. 2016 AMA Prior Authorization Physician Survey. 2016, 1–2
7. IQVIA HTA Accelerator
8. IQVIA MIDAS data
9. IQVIA's Pharma Pricing & Reimbursement Country Guide

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