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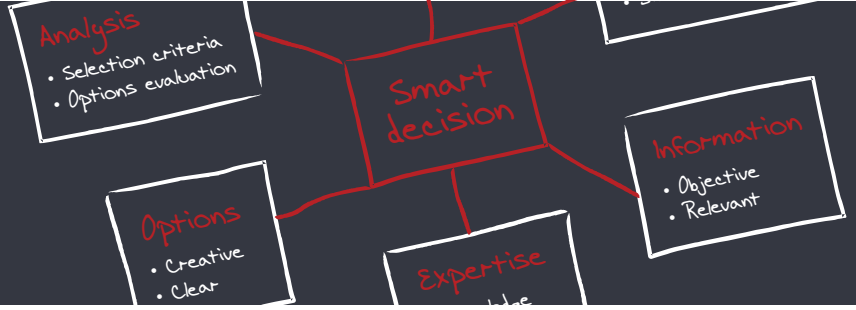


Decision making and value creation along the pharmaceutical product journey

In today's world everybody is in search of value – arguably you no longer sell useful products or services, you sell added value. It is with this concept in mind that this ePaper explores the relationship between decision making and value creation at four key points along the pharmaceutical product journey. At each of these touch points we examine a recent case study looking at specific decisions that have either added or subtracted value from a drug product. Finally, we address the question of whether pharmaceutical businesses can enhance their decision making, thereby benefiting product value.

1. The concept of value in pharmaceuticals

If we examine the very essence of value, which is defined by the Oxford English Dictionary as *"... the importance, worth, or usefulness of something"*,[1] it is apparent that if a drug is to be of value it must be of use to someone. It follows, therefore, that to create added value a new product must be of more use than the alternative products available at launch.

It is also apparent that whilst drug developers attempt to create value, the judgement of that value rests with the customers (typically physicians, payers, patients); hence, we need to understand what constitutes value to them. This remains true throughout the pharmaceutical product journey, from its beginnings in early R&D to its post-genericization end.

2. The opportunity for value creation along the pharmaceutical product journey

Common practice under the traditional business model was that once you had a drug ready to market you distilled its differentiating benefits into compelling marketing messages and started selling. And herein lies the problem that pharma is adjusting to, in an ever more saturated market – 'usefulness', or value, is not something that comes at the end, like an advanced packaging that can be wrapped around a product before hitting the 'go' button. Wait until launch day and you are too late. Value is not created at a single point in time, but evolves layer by layer over the course of the product journey.

It follows, therefore, that the decisions taken throughout that journey, which are unique to that product, are responsible for creating (or failing to create) its value offering.

Over the product journey there are, of course, many decisions to be made, and hence many opportunities to impact value. In the remainder of Section 2 we focus on four specific areas that are particularly significant in this regard. In each area we look at a recent case study, highlighting specific decisions that led to value being gained or lost.

When considering the case studies it must be remembered that decision making is not easy; the intention of this ePaper is not to praise or criticize the decision makers, rather to illustrate the very real impact that decision making can have on product value.

The four areas reviewed are:

1. Selecting unmet needs
2. Clinical trial design
3. Product positioning
4. Beyond the pill

2.1. Selecting unmet needs

In order to create added value we must identify a suitable patient need around which we can build our product, thereby making it more useful than its competitors.

This is where decision making on the product journey typically begins. Indeed, the unmet need(s) will form a central pillar of the product's story and will stay with it throughout its journey.

Identifying, prioritizing and selecting suitable unmet needs is challenging, not least as it requires assumptions to be made about the shape of the market in the future, at the expected time of launch. Whilst being challenging, this is one of the most significant opportunities to impact value through decision making.

Case study 1 – Exubera

The situation. In October 2007, approximately 1 year after launch, Pfizer withdrew the inhaled insulin product Exubera from the market. Despite being the first inhaled insulin, and despite being launched among much hype and expectation, uptake was low; the market was not sufficiently interested.[2]

What went wrong? There was, and arguably still is, an unmet need for less invasive methods of insulin delivery; however, the Exubera inhaler was large and bulky (likened to the size of a tin of tennis balls). When given the choice between thin modern needles, which can be quickly and discretely injected, and a bulky inhaler that was also time-consuming to use, the market saw limited value in Exubera. High costs and various other factors have also been cited, but ultimately the developers failed to predict end-user behaviour – they failed to sufficiently understand the nuances of the unmet need.[2,3]

The decision. The decision to progress through development with the cumbersome device, which was presumably based on the expectation that it would meet the unmet need and be valued by sufficient numbers of patients, was flawed. Obviously there were many other decisions along the journey that eventually brought Exubera to the market; however, this key decision, made many years earlier, was responsible for subtracting significant value.

Good decisions at this stage (including a clear vision of a minimally acceptable product profile to aid go/no go decisions) essentially purchase the opportunity to develop a product with the *potential* to be highly valuable. If the decision making falls short, however, and there is a failure to understand the needs of the market, the product's potential value is capped from the start.

Case study 1 looks at a decision to bring a novel drug formulation to market, under the assumption that it would meet a patient need and hence be valued.

2.2. Clinical trial design

Having identified a suitable unmet need, the next step on the product journey is to develop a product that addresses it.

Good decision making on clinical trial design is vital. Your product may target a significant unmet need, but if the trial programme falls short of demonstrating it, how will anybody know? At worst, your value story will end, at best, your product's value has diminished.

The design of any clinical trial is essentially a series of decisions. Make these decisions well and you gain the opportunity to maximize the potential end value of your product. Make poor decisions, however, and the opposite is true. With visionary insight, 15 years ago Daniel Von Hoff published his treatise that *"There are no bad anticancer agents, only bad clinical trial designs"*.[4] Arguably, the industry still has a lot to learn, especially in the field of oncology.[5-6]

Case study 2 looks at how decisions made on a specific element of trial design thwarted approval of a new indication, despite the primary endpoint of the supporting study being met.

Case study 2 – Xarelto

The situation. First in 2012 and again in 2013, the FDA blocked approval of the factor Xa inhibitor Xarelto (from Bayer/Janssen) for a new indication, *"reducing the risk of thrombotic cardiovascular events in patients with acute coronary syndrome or unstable angina in combination with aspirin, aspirin plus clopidogrel, or ticlopidine"*. The trial met its primary endpoint; however, the major issue was the high number of patients of unknown vital status (12% of patients at the 2012 rejection and 3.2% of patients in 2013, following efforts to track down missing patients). The extent of the missing data was greater than the 1–1.5% differences in endpoint rates between Xarelto and placebo.[7-9]

What went wrong? The trial design utilized a 'modified intention-to-treat analysis', whereby every patient who begins the treatment statistically remained part of the trial, whether they finished or not. In this study, around 1300 patients who had withdrawn from the study were lost to follow-up and their status remained unknown (although efforts by the manufacturers subsequently reduced this number to around 500). This missing data made statistical interpretation of the trial problematic and introduced sufficient doubt for the FDA to reject the indication.[7-9]

The decision. The decision to use this intention-to-treat analysis was reputedly against the FDA's suggestion to observe all patients until the end of the trial.[7] While there are many confounding factors, not least the challenges and costs associated with designing and running large-scale cardiovascular studies, with hindsight this decision appears to have hindered approval for the new indication, despite the primary endpoint of the study being met.

2.3. Product positioning

Product positioning can be considered a classic 'chicken or egg' scenario: *does clinical trial data dictate positioning, or does desired positioning dictate clinical trial design (and hence data)?* Compelling arguments could be made either way, but it is clear that positioning and trial data are inextricably linked.

Best-practice drug development would involve design of a trial programme that allows for an adequate demonstration that an unmet need can be met, thereby proving value within the desired target population.

However, this premise relies heavily on the trial data being positive. The reality is that you can decide on a *target* positioning only for the trial data to take the product in a different direction. Hence, it is only upon completion of the clinical programme that you can transition from a target product profile (TPP), with *target positioning*, to an acceptable actual profile (AAP) that reflects *realistic positioning*. It is not uncommon for marketing strategies to fail because the APP is never defined or the TPP never modified in the face of real data, resulting in mirage marketing of an unrealistic positioning.

To return to the product journey, upon completion of the trial programme and development of the APP there is now a clear picture (and evidence) of how well the product fulfils the unmet need(s) behind its conception. It is also now clearer how significant the unmet need is, what the competitive landscape looks like, and if there have been any notable market environment developments (eg epidemiology, guideline, or pricing trends). This information should, therefore, yield a clear vision of:

i) What the product positioning might realistically look like

ii) The viewpoint of all stakeholders (internal and external) on this positioning

iii) The value judgement of customers on that positioning

iv) The commercial implications of those value judgements

Case study 3 examines a product where good decision making brought about much-needed clarity on its positioning.

Case study 3 – Brintellix

The situation. In May 2012, Lundbeck announced positive data from a Phase III programme on their new multimodal antidepressant, Brintellix. In six of eight studies, the drug demonstrated statistically significant efficacy versus placebo.[10] Based on these data Lundbeck (and partner Takeda) filed for approval. However, while regulators considered the application the market also passed judgement. With only placebo-controlled data there was confusion over its positioning. The benefits versus existing treatments were being questioned and given the generic (low cost) status of certain competitors it was not clear in which patients it should be used: "*Without showing superiority, there is no way a mechanistically new agent can compete with generic drugs for the same disease.*"[11]

What went right? In April 2013, Lundbeck published results of the REVIVE study, which amongst other findings demonstrated success of Brintellix in patients who had failed standard therapy.[12] In doing so, Lundbeck clearly identified their initial target patient segment and target positioning, "*by showing that Brintellix is effective in first-line treatment failures, if it is approved, Lundbeck can have entry into this patient population who need a treatment alternative.*"[11]

The decision. Matching proven benefit with a need is the key to good positioning. Rather than go head-to-head against the existing generic first-line therapies, by targeting the first-line failures Lundbeck is aiming at a segment in which Brintellix has been shown to directly benefit patients. The decision to perform the REVIVE study to support this very clear positioning may, therefore, prove to be one that adds significant value.

2.4. Beyond the pill

The central tenet of the most effective beyond the pill strategies is to improve fulfilment of the market's unmet need(s). That is to go beyond simply providing a medicine that addresses a pharmaceutical need and address wider unmet needs that are significant in the provision of care.

Beyond the pill strategies and activities can be helpful either directly to patients – a good example being Bayer's integrated disease portal for multiple sclerosis sufferers; **www.ms-gateway.com** – or indirectly through the provision of support for physicians, payers, or other stakeholders who are significant in the care pathway for a given disease.

The concept of beyond the pill can be thought of as simply making the product offering more useful, or more valuable, to its customers.

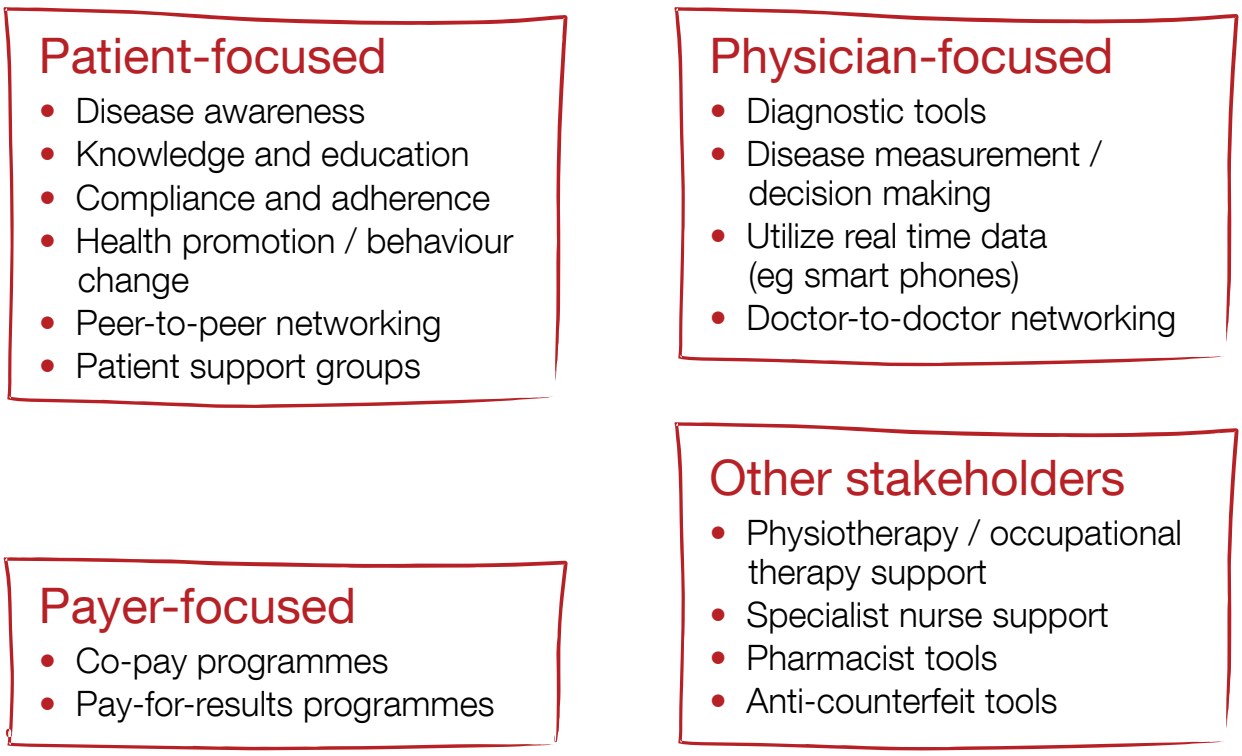
Several common areas of beyond the pill support are given in **Figure 1**; it should be remembered that by definition of being 'useful', all beyond the pill strategies and tactics should be tailored to the disease in question.

From the pharma perspective there are two main questions that underpin the examples given in **Figure 1**:

- What else can pharma do to help customers?
- What skills/facilities does pharma have that customers need but do not have?

Embracing these questions is a significant and challenging step, as it requires a fundamental shift in the pharmaceutical business model, quite literally beyond the pill. Nonetheless, progress is being made, for example in January 2013 Novartis CEO Joseph Jimenez stated: *"I also started to shift our business away from a transactional model that was focused on physically selling the drugs to delivering an outcome-based approach to add value beyond just the pill. I really believe that, in the future, companies like Novartis are going to be paid on patient outcomes as opposed to selling the pill."*[13]

Figure 1. Example areas of beyond the pill support that can potentially add product value



The decision making in this rapidly evolving area is certainly challenging, not least because this is a move off the familiar ground of drug development. However, sound decision-making principles and techniques will help with the tough decisions that need to be made (for example the identification, prioritization and selection of programmes to pursue, the assessment of return on investment, and the development of execution and key performance indicator strategies).

Case study 4 illustrates a series of decisions taken by a manufacturer to deploy a substantial beyond the pill strategy and in doing so create added value.

Case study 4 – Pain

The situation. Pfizer has long been a leader in the area of pain.[14] However, pain management remains an area of huge unmet need. The basic mechanisms of pain (in particular chronic pain) remain poorly understood, while patient experiences of living with pain remain under-appreciated by the healthcare community. In other words, there are significant unmet needs extending beyond the basic provision of pain relief medicines.

What went right? Over the last couple of years Pfizer has implemented a significant beyond the pill strategy in pain. This includes launch of the 'Pain Exchange', a Twitter-esque forum for sharing experiences of living with pain, with the aim of building a user-generated database of pain experiences to improve understanding between patients and healthcare providers.[15] Another development was the establishment of the 'Pfizer Integrated Health' business unit whose vision is *'to be the leader in delivering services and solutions to improve global health through integrated care'.* One of the early offerings from this dedicated 'beyond the pill' unit has been the development of an integrated approach to chronic pain management that includes digital decision support tools to help healthcare providers and patient engagement tools to support therapy and behaviour modification.[16]

The decision. Given Pfizer's heritage in the field of pain, it is well placed to extend the provision of care beyond the pill. Whilst the impact of these initiatives on patients, physicians, healthcare budgets, or drug sales is not yet publically known, data from other initiatives from the unit have reputedly produced positive patient outcomes.[17] We suggest, therefore, that the decision to set up these initiatives can only be positive for patients and Pfizer.

3. Improving decision making

As noted previously, decision making is not easy; doubtless there are many decisions we are proud of and many we would reverse if we could.

"Hindsight explains the injury that foresight would have prevented"

Charles Caleb Colton (1780–1832)

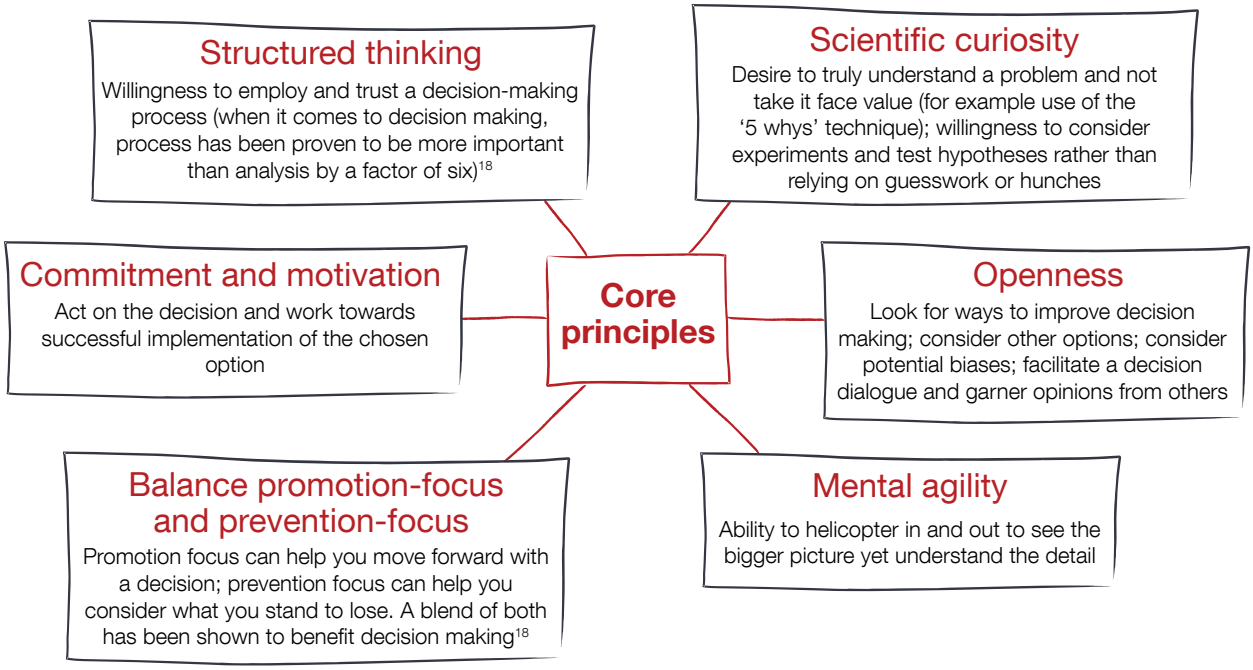
Yet we strive to improve, and with that in mind the final section of this ePaper addresses the question of whether pharmaceutical businesses can improve their decision making and hence product value.

The literature in the field of decision making is vast, with numerous theories put forward by leading minds from academia and industry. However, here, we look from a more practical perspective at how the application of a small number of principles and decision-making techniques can help.

3.1. A philosophy of decision making

Good decision making starts with the right frame of mind. In **Figure 2** we list the important attitudinal principles that we recommend are embraced; failure to do so is likely to hinder the decision-making process from the start.

Figure 2. Core principles for good decision making



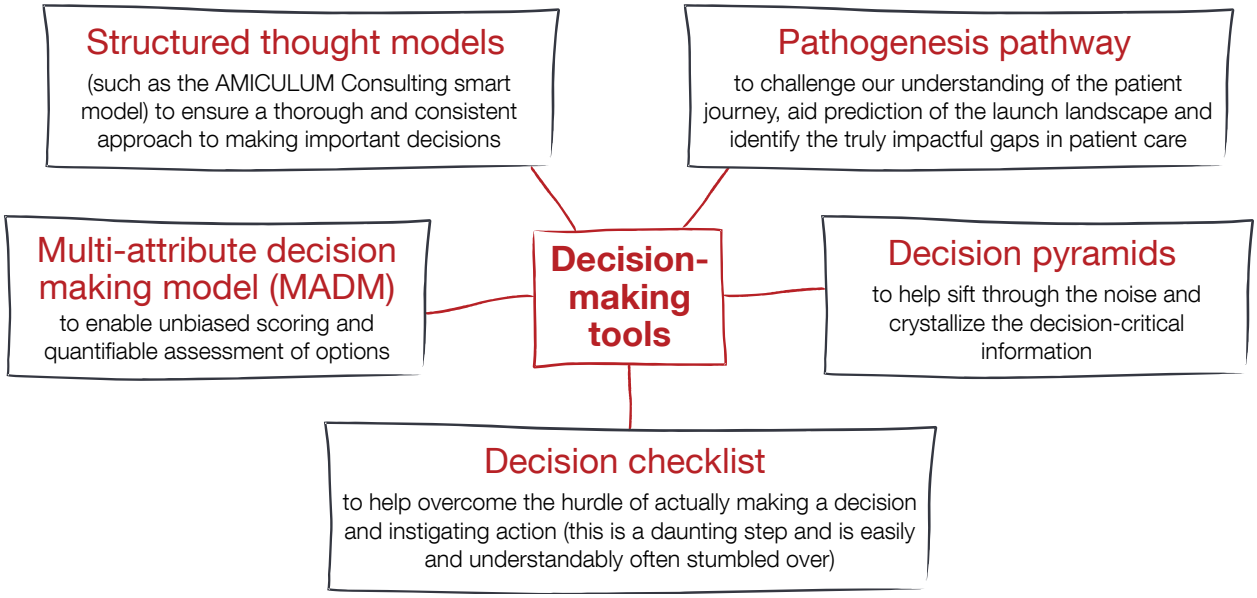
3.2. Decision support tools

In addition to the right philosophy, accepted best practice in pharma today is to use a combination of market information (typically audit data and primary/secondary research) and structured decision-making techniques to identify and quantify the potential benefits and risks of the options available; and in doing so make an informed choice.

These tools need not be overly complicated, their real value lies in forcing you to step back and think through all aspects of a decision. In doing so you can identify what is really important, regardless of bias, preconception and political constraint. A selection of established decision support tools is shown in **Figure 3**.

By employing a combination of the right mindset and right tools at the right time along the pharmaceutical product journey, it is possible to add structure, direction and the clarity required to tackle the complex decisions encountered in a pragmatic and time-effective manner. Done well, this can positively impact product value.

Figure 3. Decision-making tools



4. Conclusion

In posing and addressing the question of whether pharmaceutical businesses can enhance their decision making for the benefit of product value, we are essentially issuing a challenge to reflect on our decision making across the industry and to look for ways to improve.

As the case studies illustrate, good decision making can potentially drive significant gains in product value throughout the product journey. Embracing this philosophy will not only benefit our businesses, but will also benefit physicians, payers and patients who, let us not forget, are the true endpoint of the product journey and the ultimate recipients and judge of any value that we can create.

For more information or to discuss any of the points raised in the ePaper please contact the author (see details below).

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