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Reducing Uncertainty in Value-Based Pricing Using Evidence Development Agreements

The Case of Continuous Intraduodenal Infusion of Levodopa/Carbidopa (Duodopa®) in Sweden

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Abstract

Background: Value-based pricing (VBP), whereby prices are set according to the perceived benefits offered to the consumer at a time when costs and benefits are characterized by considerable uncertainty and are then reviewed *ex post*, is a much discussed topic in pharmaceutical reimbursement. It is usually combined with coverage with evidence development (CED), a tool in which manufacturers are granted temporary reimbursement but are required to collect and submit additional health economic data at review. Many countries, including the UK, are signalling shifts in this direction. Several countries, including Sweden, have already adopted this approach and offer good insight into the benefits and pitfalls in actual practice.

Objective: To describe VBP reimbursement decision making using CED in actual practice in Sweden.

Methods: Decision making by The Dental and Pharmaceutical Benefits Agency (TLV) in Sweden was reviewed using a case study of continuous intraduodenal infusion of levodopa/carbidopa (Duodopa®) in the treatment of advanced Parkinson's disease (PD) with severe motor fluctuations.

Results: The manufacturer of Duodopa® applied for reimbursement in late 2003. While the proper economic data were not included in the submission, TLV granted reimbursement until early 2005 to provide time for the manufacturer to submit a formal economic evaluation. The re-submission with economic data was considered inadequate to judge cost effectiveness, so TLV granted an additional extension of reimbursement until August 2007, at which time conclusive data were expected. The manufacturer initiated a 3-year, prospective health economic study and a formal economic model. Data from a pre-planned interim analysis of the data were loaded into the model and the cost-effectiveness ratio was the basis of the next re-submission. TLV concluded that the data were suitable for making a definite decision and that the drug was not cost effective, deciding to discontinue reimbursement for any new patients (current patients were unaffected). The manufacturer continued to collect data and to improve the economic model and re-submitted in 2008. New data and the improved model resulted in reduced uncertainty and a lower cost-effectiveness ratio in the range of Swedish kronor (SEK)430 000 per QALY gained in the base-case analysis, ranging up to SEK900 000 in the most conservative sensitivity analysis, resulting in reimbursement being granted.
Discussion: The case of Duodopa® provides excellent insight into VBP reimbursement decision making in combination with CED and *ex post* review in actual practice. Publicly available decisions document the rigorous, time-consuming process (four iterations were required before a final decision could be reached). The data generated as part of the risk-sharing agreement proved correct the initial decision to grant limited coverage despite lack of economic data. Access was provided to 100 patients while evidence was generated.
Conclusions: Economic appraisal differs from clinical assessment, and decision makers benefit from analysis of naturalistic, actual practice data. Despite reviewing the initial trial-based, 'piggy-back' economic analysis, TLV was uncertain of the cost effectiveness in actual practice and deferred a final decision until observational data from the DAPHNE study became available. Second, acceptance of economic modelling and use of temporary reimbursement conditional on additional evidence development provide a mechanism for risk sharing between TLV and manufacturers, which enabled patient access to a drug with proven clinical benefit while necessary evidence to support claims of cost effectiveness could be generated.

1. Background

Value-based pricing (VBP), whereby prices are set according to the perceived benefits offered by a product rather than such metrics as the cost of production, competitor's prices or historical prices, is allocatively and dynamically efficient when information is symmetric, agency is perfect and intellectual property rights are guaranteed (e.g. because of patent protection). It is consequently the norm in market-based economies, where most industries approximate these conditions.

VBP is difficult to implement in the healthcare sector because individuals (patients) and their agents (physicians) are not usually qualified to identify and synthesize all the relevant evidence and to

conduct the economic evaluation necessary to assess the value of competing healthcare interventions.[1] Moreover, even if such assessments were possible, it is unlikely in traditional insurance-based (collective) healthcare systems that this would lead to decisions that were consistent with collectively agreed objectives and that conformed to resource constraints, because neither doctors nor patients face the same resource constraints as the payer, and incentive compatible contracts (agency) cannot be specified perfectly.[1]

Decision making in the healthcare setting is, thus, often conducted using inefficient models such as free pricing with profit controls and internal reference pricing.[2]

Greater use of VBP in the healthcare setting could yield improved allocative efficiency, since technologies are adopted only if their prices ensure that the expected health benefits exceed the health that will be displaced elsewhere in the healthcare sector as other technologies go unfunded. Greater use of VBP would also yield improved dynamic efficiency, since prices based on value provide clear long-run economic incentives to invest in the development of technologies that are likely to be cost effective.[1] Moreover, if VBP is used prior to product launch (i.e. *ex ante*), earlier patient access to innovative cost-effective therapies can be promoted.

One remedy to the above-mentioned problems of information asymmetry and imperfect agency in the healthcare sector is to create independent health technology assessment (HTA) authorities and to give them responsibility for ascertaining the value to society of pharmaceutical interventions and signalling to producers the market demand curve. This has been used successfully in recent years in a small number of countries (notably, Australia, Canada and Sweden). There are signs that other countries such as the UK are also moving in this direction.[3]

VBP-based HTA decision-making bodies must address several important issues that are resolved reflexively in normally functioning markets. Chief among them, they must identify and apply an appropriate willingness-to-pay threshold for health benefits (often the cost-effectiveness threshold), a difficult empirical question based on both the productivity of existing health sector activities and the overall healthcare budget.[1] An overly generous threshold yields decisions in which drugs will be reimbursed at overly high prices, for instance, which displaces more health elsewhere in the healthcare system than will be created. Overly stringent criteria, on the other hand, yield decisions in which drugs would not be reimbursed at prices that would improve net health.

Centralized decision makers must also account for differences in cost effectiveness across patient groups, indications and disease severities. Using the benefits derived from patient subgroups that are particularly cost effective to treat to 'subsidize' the treatment of other subgroups that would not otherwise be cost effective to treat is inefficient, so decision makers will ideally employ marginal rather than average pricing despite increased complexity and data burdens (see Claxton[1] for a comprehensive exposition).

VBP can take numerous forms in the healthcare setting, although it can generally be divided into *ex post* (after launch) and *ex ante* (prior to launch). *Ex post* decision making generally consists of free pricing at product launch followed by subsequent review post-launch, in which cost-effectiveness analysis is used to revise the price or, more frequently, reimbursement coverage (which can be used to influence price indirectly). *Ex ante* decision making generally consists of using cost-effectiveness analysis to make initial (i.e. at or prior to launch) pricing or, more frequently, reimbursement coverage decisions. The data available for *ex ante* evaluations are typically limited, preliminary and uncertain, often making data synthesis with economic models indispensable. Moreover, periodic *ex post* reassessment is routinely used to lessen the potential negative consequences of making *ex ante* choices under uncertainty. Frequently, 'coverage with evidence development' (CED), a tool in which pharmaceutical companies are granted temporary reimbursement but are required to generate additional evidence that substantiates their claims to retain coverage following the expiry date, is employed to ensure that new data are available to inform these *ex post* reassessments (see Hutton et al.[4]).

The VBP approach using CED has now been used in several countries for a number of years.

Unfortunately, relatively little is known about how pricing and reimbursement occurs. As the authorities responsible for pharmaceutical benefits in Sweden are relatively transparent, use CED to inform *ex post* review extensively and were an early adopter of VBP (in 2002), they provide an excellent case study to illustrate the VBP approach in actual decision making. A careful review of Swedish decision making may offer insights for those seeking to submit price and reimbursement applications to VBP institutions as well as insights for decision makers in countries considering transition to a VBP system.

2. Objective

The objective of this article is to describe actual VBP reimbursement decision making and the application of CED in Sweden, using a case study of continuous intraduodenal infusion of levodopa/carbidopa (Duodopa®) in the treatment of advanced Parkinson's disease (PD) with severe motor fluctuations.

3. The Setting

3.1 The Dental and Pharmaceutical Benefits Agency in Sweden

The Swedish central Government established the Pharmaceutical Benefits Board (LFN) in 2002 to determine which pharmaceutical products would be subsidized by the national health system. In 2008, LFN was expanded to also include dental procedures and was renamed the Dental and Pharmaceutical Benefits Agency (TLV). Any company that markets medicine in Sweden may apply to TLV for a price and for reimbursement coverage.[1] The application must include a health economic analysis. A cost-minimization analysis is sufficient for medicines with the same effect as treatment alternatives. More uncertainty is accepted when expected sales volumes are low, in which case rough estimates of costs and effects will be considered. Retail prices should be used for pharmaceuticals, including the anticipated price of the drug under application. Price and reimbursement coverage are not granted when the application is not considered to fulfil TLV's criteria.

TLV applies three, sometimes conflicting, criteria in their decision making: (i) human dignity; (ii) need and solidarity; and (iii) cost effectiveness. Human dignity and need and solidarity are difficult to operationalize in actual decision making, but it is widely understood that TLV prioritizes more severe diseases and diseases with few or no treatment alternatives (e.g. orphan diseases) by employing different thresholds for cost effectiveness. The same criteria are used for orphan drugs, although orphans may also be included in the pharmaceutical benefits scheme for special conditions and humanitarian reasons.

Cost-effectiveness evaluation is the central element of decisions on which products will be granted reimbursement. TLV does not systematically require *ex post* review of decisions, but because of uncertainty in decision making at the time of launch, TLV routinely employs temporary reimbursement combined with demands for additional evidence generation (CED) and *ex post* review. Decisions have been reversed during *ex post* reassessment, either because the additional evidence generated did not support initial conclusions or because market conditions changed. A good example is the recent *ex post* review of antihypertensive treatments that resulted in the de-listing of three drug therapies.[5]

In recognition of diminishing marginal utility, separate cost-effectiveness calculations are required for subgroups (e.g. by age, sex or disease severity) in which the cost effectiveness of treatment is expected to vary. TLV has the authority to grant reimbursement to only particular indications and subgroups, and frequently does.

TLV welcomes economic modelling, particularly as part of the initial submission, to synthesize the often limited data available at the time. TLV frequently requests electronic copies of manufacturer-submitted models, both to test model reliability and to conduct independent (often subgroup) analyses. By international standards, TLV is generally seen as transparent and effective, willing to work

1 TLV neither directly sets nor negotiates price.

with companies to determine the evidence to be collected and submitted and the subgroups to be affected. TLV cooperates with patient organizations in a 'user council'. Concerned patient organizations may also submit comments.

3.2 Duodopa® in the Treatment of Advanced Parkinson's Disease with Severe Motor Fluctuations

PD is a degenerative movement disorder of the CNS. There is currently no cure and the goal of treatment is to alleviate symptoms, primarily consisting of resting tremor, bradykinesia (slowness of movement), rigidity and postural instability, and thereby enable patients to maintain as normal a lifestyle as possible, with good opportunities for social interaction and good quality of life (QOL).[6]

Treatment has, for decades, consisted initially of oral administration of levodopa (usually in combination with carbidopa or benserazide), which is metabolized into dopamine in the body. In patients with PD, the body's ability to produce dopamine diminishes over time, rendering them more sensitive to fluctuations in delivery of the supplemental levodopa (e.g. due to erratic gastric emptying and interference from dietary amino acids). As a result, symptom relief becomes less consistent and disabling side effects arise. At this stage, a number of alternative oral medications (e.g. dopamine agonists and catechol-O-methyl transferase inhibitors) can provide good symptom relief in combination with oral levodopa, but even these lose effect over time.[7,8]

A small number of patients exhaust the conventional treatment alternatives and are left with severely disabling symptoms and the accompanying need for help in the performance of nearly all activities of daily living.[6] Neurosurgery has shown promise in relieving symptoms in these patients, but it is highly invasive and often unsuitable because of patient age, contraindicated co-morbidities (e.g. depression, cognitive impairment) and poor general health.[9] Another therapeutic approach is continuous intraduodenal infusion of levodopa/carbidopa (Duodopa®) using a portable, patient-operated pump to deliver the drug through a surgically implanted tube directly into the upper small intestine, where it is rapidly absorbed (ensuring a constant supply) and independent of gastric emptying (ensuring regular uptake). Clinical trial data have confirmed the benefits of avoiding fluctuations in dopamine levels, although (consistent with a treatment with a narrow patient population such as advanced PD) the clinical trials have been relatively small and estimation of the exact magnitude of the treatment effects has been uncertain.[10]

The scarcity of patients, severity of the condition and lack of suitable alternatives qualifies Duodopa® as an orphan drug in several jurisdictions, including the EU (since 2001), the US (since 2000), Australia (since 2006) and Japan (since 2009). Duodopa® was developed and first used in Sweden and was originally used restrictively outside of the pharmaceutical benefits scheme (until it was first covered in early 2004).

4. Submission for Reimbursement for Duodopa®

The application process for Duodopa® is illustrated in table I. Neopharma first submitted an application for reimbursement for Duodopa® in Sweden at the end of 2003. While not strictly *ex ante*, the available data describing the few patients who had previously been treated with Duodopa® were extremely limited and the case had the uncertainty characteristic of *ex ante* decision making. This initial submission included data from the clinical studies available at the time, primarily small studies with short follow-up times, including studies comparing pharmacokinetic fluctuations of intraduodenal versus oral delivery of levodopa/carbidopa but also including a randomized crossover comparison of motor function for patients treated with individualized conventional treatment versus with Duodopa®.[12] No health economic data were submitted.

TLV issued a decision early in 2004. While they did not accept Neopharma's application for reimbursement because there were no cost-effectiveness data, they did grant temporary reimbursement for the period 23 January 2004 to 31 January 2005 to provide the time for Neopharma

Table I. Duodopa® submission timeline

Date	Event
2003 Nov	Neopharma applies to TLV for reimbursement at a price of SEK6910 (ex factory)
2004 Jan	TLV grants temporary reimbursement until 31 January 2005 with continued reimbursement contingent upon submission of health economic data
2004 Nov	Neopharma re-submits for reimbursement at a price of SEK6910 (ex factory), including an economic analysis[11]
2005 Jan	TLV extends reimbursement until 31 August 2007 with continued reimbursement contingent upon submission of new evidence of the health economic benefits and costs Neopharma acquired by Solvay Pharmaceuticals Solvay Pharmaceuticals begins DAPHNE study
2006 Jan	First patient recruited to DAPHNE study
2007 May	First interim analysis of DAPHNE
2007 Jun	Solvay Pharmaceuticals re-submits for reimbursement at a price of SEK6910 (ex factory), including a new economic model partly populated with data from the first interim analysis of DAPHNE
2007 Sep	TLV halts reimbursement for all new patients
2007 Dec	Second interim analysis of DAPHNE
2008 Feb	Solvay Pharmaceuticals re-submits for reimbursement at a price of SEK6688 (ex factory), including a revised model populated more heavily with DAPHNE data (and additional patients and follow-up)
2008 Jun	TLV grants reimbursement

SEK = Swedish kronor; **TLV** = Dental and Pharmaceutical Benefits Agency.

to conduct a formal economic evaluation.[13] Their reasoning was described as follows. First, TLV had, under their own initiative, identified data showing that the costs of PD in Sweden increase with symptom severity, which, when combined with the clinical trial data, suggested that treatment could provide benefits at reasonable incremental cost. Second, TLV viewed the indication as serious and concluded that the need for effective new treatments was high, and their review of the clinical data convinced them that the drug improved patient movement, self-management of activities of daily living and QOL. Indeed, they cited special circumstances, humanitarian need and the EU decree on orphan drugs.[13] A total of 100 patients were granted access to treatment under the temporary reimbursement.

Neopharma resubmitted at the end of 2004. The new submission included a cost-effectiveness evaluation, which made use of a 'piggy-back'-style model constructed from the limited data available at the time, namely a 24-patient, 6-week crossover design study (DIREQT [Duodopa Infusion: Randomized Efficacy and Quality of Life Trial]).[12] This model is described in detail in a previous issue of *Applied Health Economics and Health Policy*.[14] The estimated incremental cost-effectiveness ratio (ICER) of Duodopa® treatment versus conventional oral treatment was approximately Swedish kronor (SEK)6.1 million per QALY gained (roughly $US915 000 at the time), which TLV judged to be high.[11] However, there were a number of shortcomings in the analysis, including uncertainty about the magnitude of improvements in QOL, and costs of home-based and institutional care, and foregone productivity, which led TLV to conclude that the data were inadequate to judge actual cost effectiveness.[11] Indeed, TLV interpreted the data submitted as suggesting that Duodopa® may actually be cost effective for treating patients with severe motor complications, for whom there are very few alternative treatments, and decided to grant continued temporary reimbursement to allow for additional data to be gathered (this time until 31 August 2007).

Neopharma was acquired by Solvay Pharmaceuticals in early 2005. Solvay Pharmaceuticals responded to the demands for new economic data by initiating an open and uncontrolled 3-year prospective study called DAPHNE (Duodopa in Advanced Parkinson's: Health Outcomes and Net Economic Impact), which assesses the resource use and QOL in two cohorts of patients, namely treatment-naïve patients and patients already treated with Duodopa in Sweden;[2] 1-year data for the treatment-naïve group has been presented elsewhere.[15] In total, DAPHNE enrolled 75 patients and presents an unusually large study including health economic parameters for an orphan drug. In accordance with TLV wishes, and in contrast to data in the earlier submission, the study was naturalistic and thus not driven by intervention protocol. A scheduled preliminary

2 A small number of patients were recruited in neighbouring Norway.

analysis of the data would permit DAPHNE to support the re-submission.[3] The interim analysis of both patient cohorts was performed in the third quarter of 2009, which included 1-year observations of some patients. Final results will be available 2 years thereafter.

In parallel, Solvay Pharmaceuticals commissioned a more comprehensive economic model, not based on a 'piggy-back' analysis of a single clinical trial, which included an extension of the time horizon from 2 years to up to 10 years (5 years was used in most of the submitted analyses) to allow better capture of the longer-run effects; inclusion of direct medical costs, direct non-medical costs (e.g. home help, nursing home care and transportation) and indirect costs; and explicit accounting for first- and second-order uncertainty. The basis for modelling the treatment effect for time spent in the 'off' state was DIREQT;[12] the effect of treatment on the Hoehn & Yahr (HY) rating scale was derived from an expert panel.

The model was loaded with direct medical costs, direct non-medical costs and QOL data from a preliminary analysis of DAPHNE. There were too few data as yet available to model indirect costs reliably, so they were derived from a previous Swedish study.[16] The ICER was approximately SEK1 million per QALY in the base case, with the difference largely explained by the longer timeframe and the inclusion of a broader array of costs. In sensitivity analyses, the ICER ranged up to SEK4 million in the most conservative treatment efficacy scenarios.

TLV decided that the economic analysis was well conducted and, even if it included several uncertain assumptions, was sufficient for making a decision, and it concluded that Duodopa® was not cost effective at the requested price.[17] Furthermore, while DAPHNE was as yet still incomplete, TLV saw no indications that further data from DAPHNE would change the cost-effectiveness calculations. Duodopa® was thus withdrawn for new patients from the reimbursement benefits list on 1 September 2007. Because discontinuation would require surgery to remove the tubes, lead to patient suffering and impose considerable transition costs, reimbursement was continued for the 100 patients who had by then already been initiated on Duodopa®.

Solvay Pharmaceuticals, like all manufacturers, had an additional chance to submit data. The model, which was submitted to TLV as part of the submission, was revised to separate direct non-medical costs into home help and assistance, nursing home care and informal care (i.e. friends and family); to incorporate QOL reductions for informal caregivers; and to include the ability to specify apomorphine explicitly as a comparator (in response to a request from TLV). A second preliminary analysis of DAPHNE was undertaken, including more patients and more follow-up visits (and this time there were enough data to analyse the costs of foregone productivity). In this version, direct non-medical costs were analysed separately by subcategories, making the importance of home help more apparent. In addition, better treatment efficacy data were available. A study of the change in motor fluctuations in nine patients was chosen because it had a relatively long follow-up time of 12 months,[18] and the DIREQT data were used in sensitivity analysis. Moreover, in response to concerns about the HY treatment effect data from the expert panel, Solvay conducted a meta-analysis of clinical trial data that was used as the new baseline.

The ICER for Duodopa® against conventional care (primarily with oral drugs but even with continuous apomorphine infusion for some patients) was found to be SEK430 000 per QALY in the base-case analysis, ranging up to SEK900 000 in the most conservative sensitivity analysis.[19] The most important difference in results was the increase in direct non-medical unit costs. The increase can be explained both by heavy resource use in the new patients and follow-ups that became available in the second preliminary analysis (this was especially true for home help, where a number of patients received around-the-clock home assistance) and by the decision to unbundle the

3 Some modelling was required to overcome gaps in data coverage for many of the cells (health states) required by the model.

costs into separate components, which led to more follow-up visits with zero costs and hence increased uncertainty in the regression coefficients. The use of more robust treatment effect data for time spent 'off' also had a sizable impact on the results. However, sensitivity analyses showed that reductions in caregiver QOL had only a small impact on the ICER.

Even though there were still several assumptions that were considered uncertain, TLV judged, in June 2008, the economic analysis to be well conducted and a sound basis for reasonable estimation of the cost effectiveness.[19] Having already accepted that advanced PD with severe motor fluctuations satisfied conditions for human dignity and need and solidarity, TLV concluded that Duodopa® was cost effective versus the existing alternatives and granted reimbursement coverage.

5. Discussion

The case of Duodopa®, which is summarized in figure 1, provides excellent insight into TLV's decision-making process, partly because the process was long and resulted in three re-submissions requiring an extensive exchange of data.

TLV (as an agent for the Swedish taxpayer), in the face of considerable initial uncertainty about the realistic cost effectiveness of Duodopa® in actual practice, took a chance in granting reimbursement coverage to allow time for convincing data to be compiled. A total of 100 patients benefited. However, the risk to Swedish taxpayers was limited by *ex post* review (CED), in which the initial uncertainty (not uncommon, especially for orphan drugs) could be reduced by replacing the 'piggy-back' data presented early on with naturalistic, actual practice data analysed using a cost-effectiveness model, thus increasing the certainty of making a correct decision.

The process may also have downsides from the societal perspective. In particular, it was administratively costly to conduct so many reviews (four in total), both to TLV and to the manufacturer. However, such complicated processes may be particularly likely in decision making for orphan drugs where uncertainty is considerable because underlying data for economic evaluation are by nature scarce and sample sizes necessarily small. TLV learned a key lesson from such cases, and they instituted a pilot project in September 2009 to provide scientific advice jointly with the Swedish Medical Product Agencies (the national authority responsible for regulation and surveillance of the development, manufacturing and marketing of drugs and other medicinal products) to companies planning to submit products for reimbursement.[20] Clear communication of both clinical and economic requirements will likely reduce the rate of resource-intensive *ex post* reviews.

From the manufacturer's perspective, the VBP decision-making process enabled market access from initial product launch, uninterrupted until the present (with the exception that new patients

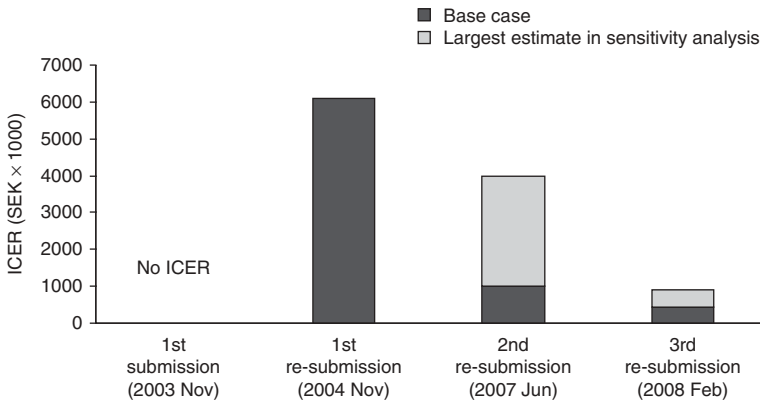

Fig. 1. The estimated cost effectiveness of Duodopa® versus standard care at each step in the submission process. **ICER** = incremental cost-effectiveness ratio; **SEK** = Swedish kronor.

could not be initiated between September 2007 and June 2008). However, the initial submission and three re-submissions were costly, and temporary coverage came with substantial CED requirements. The 75-patient, 3-year health economic study that resulted is extremely large (and costly) for orphan drugs. While uncertainty about recovering the expenses of the clinical study will certainly enter decision making about investing in the development of new orphan drugs, the manufacturer has also found the study useful in seeking reimbursement in other countries.

The patients were the beneficiaries of access to a drug with proven benefits but initially uncertain cost effectiveness (with the exception that new patients could not be initiated for nearly a year). While the *ex ante* decision-making process does entail uncertainty for the patients in that their treatments can be de-listed as the result of *ex post* review, this must be weighed against the benefits of early adoption. Moreover, review as circumstances change is a common feature of even *ex post* decision making, so uncertainty about treatment de-listing is not unique to *ex ante* decision making.

In summary, the key insight from this case study is that manufacturers need a better understanding of which health economic information best informs decision makers and that HTA bodies need the capacity to guide manufacturers in their data collection.

6. Conclusions

This article describes actual VBP reimbursement decision making combined with CED in Sweden, using continuous intraduodenal infusion of levodopa/carbidopa (Duodopa®) in the treatment of advanced PD with severe motor fluctuations. The process was long, consisting of an initial submission and three re-submissions, perhaps not surprising given the timing (just after the inauguration of LFN [now TLV]) and the complexity of the case. Status as an orphan drug, moreover, compounded the usual shortage of data observed with initial *ex ante* submissions.

The case of Duodopa® highlights a couple of important points. First, economic appraisal differs from clinical assessment, and decision makers benefit from analysis of naturalistic, actual practice data. Despite reviewing the initial trial-based, 'piggy-back' economic analysis, for example, TLV was uncertain of the cost effectiveness in actual practice and deferred a final decision until observational data from the DAPHNE study became available. Second, the acceptance of economic modelling and the use of temporary reimbursement conditional on CED provide a mechanism for risk sharing between TLV and manufacturers, which in this case enabled patient access to a drug with proven clinical benefit while the necessary evidence to support claims of cost effectiveness could be generated. The commitment of taxpayer money was limited.

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