Should lifecycle pricing be considered in HTA? Practical considerations for incorporation into HTA policy

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Introduction

- Many health technology assessments (HTAs) require cost-utility modelling as part of the HTA submission. The incremental cost-effectiveness ratio (ICER) of a new patented drug is normally compared with a comparator drug, which may be a generic or a patented drug at the time of HTA submission.
- Drug costs within cost-effectiveness analysis (CEA) are usually limited to the price of both drugs at the time of model conception. However, the price of the new drug is expected to decrease once generic versions of the molecule are introduced following expiration of the drug patent.[1] Therefore, standard CEA may not accurately capture the true value of a drug over its lifecycle.
- In order to more accurately reflect actual practice, Canadian and international guidelines recommend that the future introduction of lower-cost generic versions of patented molecules, if they are expected to appear within the examined time horizon, be considered within economic models.[2]
- A lifecycle pricing approach was recently proposed by the manufacturer in a NICE appraisal of a cystic fibrosis treatment, whereby a price reduction for the intervention was modelled after patent expiration.[3]

Objectives

- The objective of this study was to assess practical considerations for incorporating lifecycle pricing into HTA policy.

Methods

- A targeted literature review was conducted to identify studies describing elements of lifecycle pricing. These studies were used to assess the evidence supporting a lifecycle pricing approach.
- Databases searched included PubMed, Ovid Embase, EconLit, and Google Scholar.

Results

- The following studies **(Table 1)** were identified and examined to demonstrate key elements for consideration of lifecycle pricing in HTA policy.

Table 1: Included studies

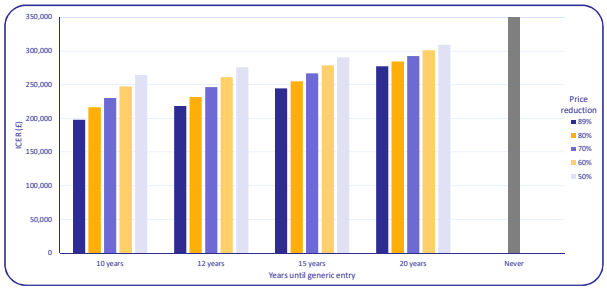
Author	Drug	Disease	Model	Country
Guertin (2015)	Dabigatran etexilate	Stroke and embolism in atrial fibrillation	Simplified Markov model	Canada
Garrison (2009)	Trastuzumab	HER2+ Breast cancer	Dynamic life cycle cost utility: 1998-2016	US
Lu (2012)	Paclitaxel and docetaxel	Oncology (multi-indication)	Dynamic life cycle cost utility building on model framework developed by Garrison (2009)	US
NICE TA398 (2016)	Lumacaftor and Ivacaftor (LUM-IVA)	Cystic fibrosis	Lifetime Individual patient microsimulation	UK
Malatestinic (2015)	IL-17 inhibitor	Psoriasis	N/A	Global

HER2+, human epidermal growth factor receptor 2-positive; IL-17, interleukin-17.

Magnitude and timing of the reduction in drug price on patent expiry

- **Canada (dabigatran etexilate)[1]:** Data protection laws in Canada guarantee 8 years of market exclusivity when a drug receives its Notice of Compliance from Health Canada. Assuming a 75% decrease in price on generic entry, the incremental cost of dabigatran etexilate compared to warfarin, when ignoring the future introduction of generics, would be overestimated by 70.1%.
- **UK (lumacaftor and ivacaftor)[3]:** In CEA of LUM-IVA, it was assumed that generics would be available 12 years after commercialisation with an 89% price reduction. Sensitivity analysis highlighted that uncertainty in the timeframe for availability of generics and the expected price reduction has a substantial impact on the ICER **(Figure 1)**.

Figure 1: Impact of price reductions and timeframe for generic entry on ICERs[3]



Effect of multiple indications on long-term cost-effectiveness

- **US (paclitaxel and docetaxel)[4]**: Lifecycle ICERs can decrease substantially when new indications and price decreases after patent expiry are incorporated into CEA. The ICER for paclitaxel decreased by 39% and 72%, 10 and 20 years, respectively, after product launch while the ICER for docetaxel decreased by 38% and 59%, respectively, over the same time periods.
- **US (trastuzumab)[5]**: Average ICERs for multi-indication drugs can increase or decrease over the drug lifecycle **(Table 2)**. This may be particularly relevant in oncology where the initial indication is often in patients with more advanced disease with subsequent indications in patients who experience greater benefit.

Table 2: Indication-specific and cumulative lifecycle cost-effectiveness

Treatment	ICER (metastatic setting)	ICER (adjuvant setting)	Cumulative lifecycle ICER
Trastuzumab (vs. SOC)[5]	$85,700	$26,400	$35,600

ICER, incremental cost-effectiveness ratio; SOC, standard of care.

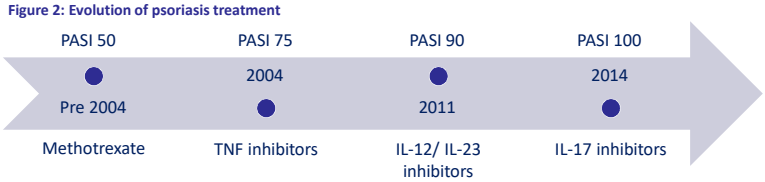
Not all medicines will face significant generic challenge

- **Oral formulations:** Small molecules are expected to be easy to replicate. Whilst there are exceptions (e.g. osmotic release oral system), oral administration may be easier for generic development and for a healthcare system to implement versus other methods of administration.
- **Biologics:** Randomised controlled trial requirements and manufacturing process and patent litigation challenges in biosimilar development are often cited as reasons why market entry and subsequent price reductions are more difficult to predict for biologics than traditional generics.
- **Cell and gene therapy:** It is unlikely that cell and gene therapies will face generic challenge.
- **Market attractiveness:** Biosimilar/ generic manufacturer interest has focused on market attractiveness raising the question if lifecycle pricing would be appropriate for rare illnesses.

Is the drug likely to be superseded in the modelled time horizon?

- For example, the evolution of science should be considered whereby new technologies may be quickly replaced by superior products ahead of patent expiry. In psoriasis, a 50% reduction in PASI score was originally determined to be an indicator of clinical effectiveness. However a PASI score of 75% is now required to show clinical effectiveness **(Figure 2)**. Such leaps in clinical outcomes will mean older drugs are no longer used and cost savings will not be realised.[6]

Figure 2: Evolution of psoriasis treatment



IL, interleukin; PASI, psoriasis area and severity index; TNF, tumour necrosis factor.

- While there will always be a degree of uncertainty on whether a major clinical advancement will occur in any disease area, manufacturers will be aware of all potential comparators in development. Should there be a drug showing potential to revolutionise the disease area (such as HER2 positive breast cancer treatment, trastuzumab[4]) it could be argued this should be considered in pricing negotiations.

Conclusion

- Pricing strategy after patent expiration is influenced by several factors including regulatory aspects, market incentives, medication class, and the market power of the patented drug. As a result, the magnitude and timing of price reductions after patent expiry is uncertain.
- Key considerations for the inclusion of lifecycle pricing in HTA policy are:
  - Is the ICER above the threshold and will lifecycle pricing bring this down?
  - Does the modelled time horizon include the period after patent expiry of the intervention and/ or comparators?
  - Is there a reasonable prospect of lower priced generics/ biosimilars entering the market (market attractiveness and formulation/ legal barriers)?
  - Can the timing and extent of the price reduction be estimated using sensitivity analysis as required?
  - Will the intervention/ comparator be superseded in long term use so that modelled future cost reductions will not be realised?
- There appears to be a strong methodological rationale for a lifecycle pricing approach. However, there are caveats that need to be considered when incorporating this approach into policy.

References
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