Health Technology Assessment in Singapore: Shining a Light in the Darkness

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Objective

- This research explored possible factors influencing health technology assessment subsidy decisions in Singapore.

Background

- The Agency for Care Effectiveness (ACE) was established in 2015 to expand health technology assessment (HTA) capabilities for subsidy decisions in Singapore.[1]
- The Singapore Ministry of Health (MOH) provides subsidies for drugs under the Standard Drug Lists (SDL 1 and 2) and the Medication Assistance Fund (MAF). Most SDL drugs are capped at S$1.40 per week for subsidised patients, while higher cost SDL and MAF drugs are subsidised at 50% or 75% of the retail price.[2]

Methods

- The 14 appraisals published by ACE in 2017 (May and October) were reviewed.[3]
- For each appraisal, the type of evaluation (full or expedited), subsidy recommendation, and factors that were considered by the MOH Drug Advisory Committee (DAC) to inform subsidy recommendation were recorded.
- Further information on ACE's drug evaluation methods and processes were obtained at the ACE Industry Briefing held in May 2017.[4]

Results

- Out of the 14 appraisals of 19 drugs, 5 led to subsidy listing on the SDL 1 or 2, 7 led to inclusion in the MAF, and 2 led to no subsidy.
- 13 evaluations were expedited evaluations as they were generics or had a low budget impact, with trastuzumab being the only therapy that was considered in a full evaluation due to its high cost.
  - In full evaluations, manufacturers must submit their proposed price and may be invited to submit clinical and economic data. ACE will also conduct a review of available clinical and economic data, and will develop local cost-utility and budget impact models.[4]
  - In expedited evaluations, manufacturers must submit their proposed price and ACE will review published clinical and economic evidence, and will develop a local budget impact model.[4]
- The factors that influenced subsidy decisions are summarised in **Table 1**.
- Three of the subsidised drugs (somatropin, trastuzumab and Botox®) were in areas of substantial clinical need. In the absence of clinical need, the price relative to existing alternatives appeared to be a key consideration: compared to other subsidised anti-TNFs, golimumab was cost-effective at the manufacturer's proposed price but ustekinumab was not, as its price was higher than existing subsidised treatments.
- In the 3 appraisals where more than 1 technology in the same class were compared, only the cheapest drug was subsidised in each case (rivaroxaban, dapagliflozin and Botox®), further indicating the importance of drug cost in subsidy decisions.
- In 3 appraisals (gliclazide, golimumab and trastuzumab), restrictions were imposed on the type of formulation covered by the subsidy.
  - The modified-release version of gliclazide was not subsidised due to its higher cost and equivalent outcomes to the immediate-release formulations.
  - Basaglar® Kwikpen version was not subsidised as its price was higher than that of Lantus® pen, which is currently listed on the SDL for the same indication.
  - The subcutaneous (SC) version of trastuzumab was not subsidised as use of this may reduce potential savings from the entry of biosimilar intravenous trastuzumab in the next 1–2 years.
  - The intravenous (IV) formulation of golimumab was not subsidised, likely to avoid additional healthcare costs associated with IV administration, although this was not specifically stated.
- Only 6 evaluations reported incremental cost-effectiveness ratios (ICERs), half were derived from UK cost-effectiveness studies while the other half were from Singaporean studies. Among Singaporean cost-effectiveness studies, an ICER of up to S$75,000 per quality-adjusted life-year gained was considered cost-effective. However, given the small number of appraisals reporting ICERs, no conclusions around a formal willingness-to-pay threshold can be drawn.
- Budget impact was a key consideration across all appraisals. However, both drugs that were not recommended for subsidy had a lower budget impact (below S$1 million per year) than rivaroxaban, which was subsidised despite having the highest budget impact of S$3–S$5 million per year.

Table 1 | Summary of guidance published by ACE in May and October 2017

	Drug evaluation	Indication	ICER	Budget impact	Factors considered by the DAC to inform subsidy decision
SDL	**Gliclazide**	Type 2 diabetes	–	–	• Better safety profile vs other sulfonylureas • Low annual cost of subsidy
SDL	**Insulin glargine biosimilar, Basaglar® (cartridge)**	Type 1 and 2 diabetes	–	–	• Comparable efficacy and safety vs originator insulin glargine (Lantus®) • Price of Basaglar® cartridge was lower than the price of Lantus® pen
SDL	**Sumatriptan** (in combination with naproxen)	Acute migraine	–	–	• Superior efficacy in combination with naproxen vs monotherapy • Low annual cost of subsidy
SDL	**Gemcitabine** (monotherapy or combination therapy)	Advanced bladder cancer and non-small cell lung cancer	–	–	• Comparable efficacy and safety vs other standard chemotherapy regimens • Low annual cost of subsidy
SDL	**Temozolomide**	Malignant glioma	–	Less than S$500,000 in the first year	• Acceptable clinical effectiveness and safety vs other treatment options • Likely to be cost-effective due to the availability of generic temozolomide in Singapore
MAF	**Denosumab**	Post-menopausal women with osteoporosis at high risk of fracture	Dominant to <£18,000 per QALY gained vs no treatment or strontium ranelate	Less than S$1 million in the first year	• Superior efficacy vs placebo • Cost-effective at proposed price vs zoledronic acid
MAF	**Somatropin**	Growth failure in children	Less than £30,000 per QALY gained	Less than S$1 million in the first year	• High clinical need (only treatment in this indication) • Cost-effective when evidence from published overseas economic analyses were generalised to the local context
MAF	**Golimumab** (subcutaneous formulation)	RA, AS, PsA and UC	–	Less than S$1 million in the first year	• No therapeutic gap but cost-effective at proposed price vs other subcutaneous biological TNF inhibitors, adalimumab and etanercept, which are listed on the MAF
MAF	**Trastuzumab** (in combination with a taxane or an aromatase inhibitor)	Metastatic breast cancer	Within the range of S$45,000 to S$75,000 per QALY gained	S$1 to S$3 million per year	• High clinical need • Superior efficacy vs taxane monotherapy • Cost-effective when an 8-cycle stopping rule was implemented
MAF	**Rivaroxaban**, dabigatran and apixaban	Prevention of stroke in non-valvular AF	Less than S$15,000 per QALY gained compared with warfarin	S$3 to S$5 million per year	• Superior efficacy and cost-effective at the proposed price vs warfarin • Rivaroxaban had the lowest price among the NOACs and was thus the only NOAC selected for subsidy
MAF	**Dapagliflozin**, canagliflozin and empagliflozin (in combination with metformin and/ or sulfonylurea)	Type 2 diabetes	Less than S$15,000 per QALY gained compared with sulfonylureas	S$1 to S$3 million per year	• Superior efficacy vs other therapies in combination with metformin, and in triple therapy with metformin and sulfonylurea • Dapagliflozin had the lowest price among the SGLT2 inhibitors and was cost-effective vs other therapies. It was thus the only SGLT2 inhibitor selected for subsidy
MAF	**Botox®**, Dysport® and Xeomin®	Focal spasticity of the upper limbs associated with stroke in adults	£10,000 to £27,000 per QALY gained	Less than S$1 million in the first year	• Unmet clinical need • Superior efficacy and safety vs placebo • Botox® (50U vial) had the lowest cost and was considered the most cost-effective among the 3 brands. It was thus the only botulinum toxin A selected for subsidy
	Denosumab	Prevention of skeletal-related events in adults with bone metastases from solid tumours	–	Less than S$1 million in the first year	• Superior efficacy vs zoledronic acid • Inconsistent cost-effectiveness results from the UK vs branded zoledronic acid • Unlikely to be cost-effective in Singapore at the proposed price (more than five times higher than generic zoledronic acid)
	Ustekinumab	Chronic plaque psoriasis and PsA	–	Less than S$1 million per year	• No clinical need as anti-TNFs are already listed on the MAF for the same indication • Superior efficacy vs etanercept and comparable efficacy vs adalimumab in plaque psoriasis, but inferior to anti-TNFs in PsA • Unlikely to be cost-effective in Singapore as price was higher than the anti-TNFs already listed in the MAF

AF: atrial fibrillation; AS: ankylosing spondylitis; DAC: Drug Advisory Committee; ICER: incremental cost-effectiveness ratio; NOAC: novel oral anticoagulant; PsA: psoriatric arthritis; QALY: quality-adjusted life-year; RA: rheumatoid arthritis; SGLT2: sodium-glucose co-transporter 2; TNF: tumour necrosis factor; UC: ulcerative colitis.

Conclusions

- This analysis highlights the importance of technology cost in HTA decisions in Singapore. In the absence of a clinical need, the price relative to treatments already subsidised appears to be a key factor in decision-making. The cost of different formulations was also considered for formulation-specific recommendations.
- This research was limited by the small number of appraisals and will be updated in future as further evaluation decisions are published.

References

1. Agency for Care Effectiveness (2017). About Us. Available at: https://www.moh.gov.sg/content/dam/moh_web/ACE-HTA/about-us.html [Last accessed 02.10.17]; **2.** Ministry of Health, Singapore (2012). Health Scope. Available at: https://www.moh.gov.sg/content/dam/moh_web/healthscope/archive/2012/MOH%20Healthscope_July-August%202012%20Issue.pdf [Last accessed 06.10.17]; **3.** Agency for Care Effectiveness (2017). Our Guidance. Available at: https://www.moh.gov.sg/content/dam/moh_web/ACE-HTA/our-guidance.html [Last accessed 02.10.17]; **4.** Agency for Care Effectiveness (2017). Industry Briefing-ACE Drug Evaluation Methods and Processes.

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