Towards a Transparent, Credible, Evidence-based Decision-making Process of New Drugs Listing on the Hong Kong Hospital Authority Drug Formulary: Challenges and Suggestions

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Abstract

The aim of this article is to describe the process, evaluation criteria and possible outcomes of decision-making for new drugs listed in the Hong Kong Hospital Authority Drug Formulary in comparison to the health technology assessment (HTA) policy overseas. Details of decision-making processes including the new drug listing submission, Drug Advisory Committee (DAC) meeting, and procedures prior to and following the meeting, were extracted from the official Hong Kong Hospital Authority drug formulary management website and manual. Publicly-available information related to the new drug decision-making process for five HTA agencies (the National Institute of Health and Care Excellence (NICE), the Scottish Medicines Consortium (SMC), the Australia Pharmaceutical Benefits Advisory Committee (PBAC), the Canadian Agency for Drugs and Technologies in Health (CADTH), and the New Zealand Pharmaceutical Management Agency (PHARMAC)) were reviewed and retrieved from official documents from public domains. The DAC is in charge of systemically and critically appraising new drugs before they are listed on the formulary, reviewing submitted applications, and making the decision to list the drug based on scientific evidence to which safety, efficacy and cost-effectiveness are the primary considerations. When compared with other HTA agencies, transparency of the decision-making process of the DAC, the relevance of clinical and health economic evidence, and the lack of health economic and methodological input of submissions are the major challenges to the new-drug listing policy in Hong Kong. Despite these challenges, this review provides suggestions for the establishment of a more transparent, credible, and evidence-based decision-making process in the Hong Kong Hospital Authority Drug Formulary. Proposals for improvement in the listing of new drugs in the formulary should be a priority of healthcare reforms.

Key Points for Decision-Makers

- Improvement of the transparency of decision-making processes, including disclosure of the rules governing decision in terms of cost-effectiveness, conflict-of-interest declaration from those initiating submissions, and the engagement of key external stakeholders, would support the credibility and accountability of decisions made by the Drug Advisory Committee.
- Detailed information on costs of new and alternative drugs, healthcare services due to the uptake of new drugs and other condition-related health care services, as well as other important aspects within the budget-impact analysis framework would allow the Drug Advisory Committee to better understand the value of new and alternative drugs.

Manuscript Text

Introduction

Due to the necessity of efficiently allocating resources under fixed budgetary control, there has been increase in demand for a systematic process of health technology assessment (HTA), placing emphasis on the value of emerging and conventional drugs. Drug appraisal and the review process involves an initial assessment of clinical evidence and health economic evidence for certain developed countries, which leads to recommendations or the decision to reimburse new drugs based on appraisal of the best-available evidence[1]. This approach to review has been adopted in the Hong Kong drug listing formulary system and new drug reimbursement systems in many developed commonwealth countries[2-5] and some Asian countries such as South Korea[6-8], Japan[9], Thailand[8], and Malaysia[10]. Recommendations for new drugs may vary from country to country because of the differences in jurisdictions and decision-making processes[11].

In Hong Kong, the Drug Advisory Committee (DAC) evaluates and advises on new drugs to be included in listing on Hospital Authority Drug Formulary[12], the largest public healthcare service provider. New and existing drugs approved by the DAC are included in the Hospital Authority Drug Formulary which was established in July 2005. Missions of the Drug Formulary include the standardization of drug and drug-use policies in affiliated hospitals and clinics across regional clusters, and ensuring equal access of patients to cost-effective drugs, the safety and efficacy of which are proven. In the past decade, prevailing drugs listed on the drug formulary has rapidly expanded with the increased budget allocated to new drugs that patients can access. In response to intense public scrutiny over the decisions of new drugs listed on the Drug Formulary, the Hospital Authority drug formulary management system was

reformed in 2015. However, the drug review process challenged due to its lack of transparency to members of the public and scientific documentation as the base for the decisions made[13].

The purpose of this paper is to describe the process, evaluation criteria and possible outcomes of the decision for new drugs to be listed in the Hong Kong Hospital Authority Drug Formulary. This review summarizes the decision-making trajectory from submission to final outcomes within the context of Hong Kong in comparison to existing policies of countries overseas that adopt the HTA for submission of new-drug reimbursement. Hence, this review outlines the challenges and suggestions for the establishment of a more transparent, credible, and evidence-based decision-making process in Hong Kong.

Method

Details of decision-making processes including submissions for new drug listings, DAC meetings, and procedures prior to and following the meeting, were extracted from the official Hong Kong Hospital Authority drug formulary management website[12] and manual[14]. To compare HTA policy in Hong Kong to overseas commonwealth countries, information related to the new drug decision-making process for HTA agencies with a centralized drug review process[1] were reviewed and retrieved from official English guidelines published on the website of advisory bodies. Decision-making processes of neighboring Asian countries such as China[8, 15, 16], South Korea[6-8], Japan[9], Thailand[8] and Malaysia[10] were only reported in published literature but not on the official advisory body websites. Therefore, these countries are not included in the comparisons. All publicly-available information related to the new drug decision-making process of the England National Institute of Health and Care Excellence (NICE)[2], the Scotland Scottish Medicines Consortium (SMC)[3], the Australia

Pharmaceutical Benefits Advisory Committee (PBAC)[4], the Canadian Agency for Drugs and Technologies in Health (CADTH) Canadian Drug Expert Committee(CDEC)[5], and the New Zealand Pharmaceutical Management Agency (PHARMAC) Pharmacology and Therapeutics Advisory Committee (PTAC) were assessed, reviewed and synthesized by the author (CW). Information was extracted in May 2017.

Results

Current New Drug Listing Policy in Hong Kong

Prior to 2013 the Drug Utilization Review Committee (DURC) was the advisory body responsible for appraising new and existing drugs for inclusion into the formulary. Due to fundamental changes in governance structure in 2013, the Drug Management Committee (DMC) was established to supersede the former Drug Utilization Review Committee (DURC), and is supported by five functional sub-committees: the Drug Advisory Committee (DAC), the Drug Formulary Committee, the Drug Selection Committee, the Medication Safety Committee, and the Cluster Drug and Therapeutics Committees. In 2015, the Hospital Authority published the Drug Formulary Management Manual to explicitly describe overall formulary management in terms of: 1) the governance structure of drug management and the composition of the five functional sub-committees, 2) mechanism, principles, the decision-making process of new drugs listed on the Formulary, and 3) consultation, engagement and participation of internal and external stakeholders. According to the latest version of the management manual[14], the sub-committee of the DAC is in charge of systematically and critically appraising new drugs for listing on the formulary, reviewing submitted applications, and making the decision to list drugs based on scientific evidence to which safety, efficacy and cost-effectiveness are the primary considerations. Notably, new drug applications are

only accepted through the Hospital Authority clinicians, not through pharmaceutical companies or clinicians outside the Hospital Authority. Other practical considerations include referring to international recommendations and practices for drugs already assessed, innovation and advanced technology to which a new drug is expected to bring significant advantages over similar, existing drugs on the formulary, disease state, patients' needs, patient compliance, quality of life, clinical effectiveness of a new drug in terms of the use of the drug in the local population, and suggestions and feedback from relevant patient group and expert panels.

DAC meetings are held four times per year in January, April, July and October. New drug submissions received three months prior to a DAC meeting are scheduled to be reviewed and thus listed on the agenda of the meeting to come. In brief, prerequisite information for submissions includes general information on the new drug, the target population (proposed location of treatment, administration criteria, exit criteria and indication for this new drug), choice of main comparators (existing alternatives already available in the Hospital Authority), clinical evidence and its level (benefits in term of efficacy, safety issues, and other benefits), international guidelines and overseas reimbursement assessment status, and cost comparisons of the new drug and similar ones already available and budget impact mainly about hospital expenditure, specifically medicine expenditure rather than the total costs including ambulatory care. Detailed information required for the submission form for a new drug is shown in the Electronic Supplementary Material - *Appendix A*. The decision on new drugs is made during the following DAC meeting, and is made publicly available within 3 weeks.

Following the DAC meeting, the decision on the submissions of each new drug falls into one of the following categories: 1) Approval for use as a 'General Drug' which is made available for general use by patients with relevant clinical conditions under the Hospital Authority; 2)

Approval for use as a ‘Special Drug’ with restriction on specific specialty, subject to the prescriber or clinical condition; 3) Approval for use as ‘Self-financed Items’ with a safety net provided through the Samaritan Fund or the Community Care Fund Medical Assistance Programme; 4) Pending; or 5) Rejection. The third category is not covered by standard fees and charges in public hospitals and clinics but by patients who require these drugs and can afford the costs to purchase them at their own expense. A safety net is provided through relevant funds to subsidize the costs of drugs for patients who have financial difficulties. In cases when the DAC solicits further information and advice from expert opinions on clinical guidelines or protocols related to drugs before making a decision, the recommendation is noted as ‘pending’. Meanwhile, relevant specialties from an expert panel are invited to submit recommendations. Decisions are made publicly available on the designated website of the formulary within 3 weeks following the DAC meetings, accompanied by a list of references that were considered during decision-making process. Although the primary reason for rejection is made public, reasons for acceptance and approval of new drugs are not available. Reasons for rejection are primarily categorized as ‘insufficient justification of the treatment’s cost in relation to its benefits’, ‘alternative(s) available in Hospital Authority Drug Formulary with comparable benefits’, ‘insufficient evidence to demonstrate clinical outcome benefits’, ‘lack of high quality level of evidence to demonstrate its efficacy’, ‘insufficient evidence to address safety concern’, and ‘insufficient evidence to demonstrate improvement in quality of life’, etc.

Based on the established mechanism, a total of 164 new drugs were listed on the drug formulary between July 2005 and March 2014[17]. However, the transparency, relevance and consistency of the current drug listing policy are subject major challenges such as the comparison to the new drug reimbursement decision-making process of the five HTA agencies and the international good practice guidelines for conducting budget-impact

analysis[18-20]. Table 1 summarizes the decision-making process of new drug submissions in Hong Kong, England and Scotland (in the UK), Australia, Canada, and New Zealand.

Transparency of the decision-making process

A closed committee meeting format is adopted by the DAC. In the SMC, PBAC, CADTH and PHARMAC meetings, only committee members are eligible to attend but non-committee members may be invited to attend as observers. In contrast, NICE technology appraisal meetings are semi-open for members of the public to attend and observe the introduction and presentation sessions. Moreover, all DAC members, except for the Chairperson who must disclose his/her name and position, remain anonymous on the formulary management website. Unlike the practice in Hong Kong, the identity of each committee member overseas is made publicly available.

All available evidence considered relevant to the decision-making process is unknown to external stakeholders including patient groups, pharmaceutical companies, and members of the public, however it is made known to groups or hospital Drug and Therapeutics Committees which comprise of internal stakeholders. For overseas HTA agencies, commercially-sensitive information such as confidential discounts due to risk sharing arrangements[21] and managed entry agreements[22] as well as drug tender price[23] are coloured out in publicly-available documents.

Although patient groups are invited to provide suggestions and feedback prior to the meeting, neither members of the public nor pharmaceutical companies are represented during the meeting or are involved in the decision-making process. A similar stakeholder arrangement is found in Canada where representatives of the patient group and manufacturer are not

permitted to attend the CADTH meetings. The Patient and Clinical Engagement (PACE) Group has been established to give patient groups and clinicians a stronger voice in the SMC's decisions of new medicines for end-of-life and very rare conditions[24].

Following the DAC meeting, there is no final decision report on the drug appraisal published or relevant DAC meeting minutes detailing evidence regarding the effectiveness of the treatment, safety concerns and cost-effectiveness, or comments from patient groups or expert panels. Compared to past submissions to the NICE[25] and the SMC[26], there is no quantitative or composite weighting assigned to each factor when making the decision reimbursing a new drug. However, health economic evidence concerning the outcomes of the cost-effectiveness analysis is one of the evaluation criteria for making the decision (Table 1). The factors that heavily influence past decisions of the DAC and individual members, i.e. the approval and rejection of new drugs, cannot be ascertained. In DAC meetings between October 2015 and July 2016, 25 submissions of new drugs were rejected[12]. The most frequent reason for rejections given was 'Alternative(s) available in the HADF with comparable benefits' (10; 40%) followed by 'Insufficient justification of the treatment's cost in relation to its benefits' (6; 24%). Around one-fourth of rejections were due to the latter reason, reflecting a barrier of submission initiators to justify the value and economic evidence of the submission of a new drug. The central rule of decision-making as to how the drug is considered cost-effective is not transparent to external stakeholders such as patient groups, academics or pharmaceutical companies. The experience of European countries involved submitting physicians to establish a 'Wise List' of new medicines jointly recommended for primary and hospital care, which consequently increased the approval rates of prescribed medicines that are recommended in the 'Wise List'[27, 28].

Clinical evidence

Clinical evidence such as efficacy and safety of a new drug compared to similar ones that are already available is a key consideration. It is mandatory to list the efficacy and safety issues of a new drug compared to existing ones when submitting for approval (*Appendix A*). Claimed benefits must be clearly referred to supporting documents that detail information and data from clinical trials published as full articles. Clinical evidence of the highest level is considered. Mounting evidence from meta-analysis or network meta-analysis of randomized controlled trials is desirable. Head-to-head direct comparative randomized trials are preferred over indirect comparisons and placebo-controlled trials. Despite taking leading clinical evidence into account, this approach largely relies on the information submitted by the initiators, through which conflicts of interest may occur. Although the evidence submitted may be incomplete or biased, a detailed report must also be prepared by the Chief Pharmacist's Office.

Health economic evidence

'Cost-effectiveness' is one of three principal considerations for evaluating new drug listing applications. In the new drug submission form, only information related to occurrence of the disease (such as in relation to the population size) and the impact of the drug listing on the formulary on the Hospital Authority budget with possible savings are mandatory for submission (*Appendix A*). In principle, 'cost-effectiveness' and 'budget impact' are conceptually different. When assessing health economic evidence of submissions, the current policy is to adopt the 'budget impact' and 'cost consequence' approach in term of whether the new drug will impose a direct monetary consequence or significantly higher direct medical costs from the perspective of the Hospital Authority as a justification of the affordability or 'willingness-to-pay' of the Hospital Authority healthcare services for the clinical benefit of

the drug. Based on the experience abroad, the budget impact analysis together with the cost-effectiveness analysis have a significant impact on decision-making.

Although a budget impact analysis is essential for making the decision to list a new drug[29], current input and data sources required in the submission form are insufficient to estimate the budget impact from the perspective of the Hospital Authority. Reports of the Society for Pharmacoeconomics and Outcomes Research (ISPOR)[18, 19] on good research practices have made general recommendations on the input and data sources for the budget impact analysis which is informed not only by costs of new and alternative drugs but also costs of other condition-related healthcare services provided by the Hospital Authority. The cost comparison is limited to the purchasing costs of new and alternative drugs but direct costs of monitoring and surveillance associated with new drug are seldom considered. Thus, the introduction of new drugs may alter the use of other condition-related healthcare services in terms of physician visits, emergency visits, hospitalization, laboratory testing, diagnostic and surgical procedures, the result changes of symptoms, duration and progression of the disease, or complications associated with the condition. Several aspects such as the time horizon, time dependency and discounts, and an uncertainty and scenario analysis, within budget impact analysis framework are not taken into consideration. Furthermore, a Canadian budget impact analyses guideline[20] provided recommendations regarding the analytic framework, inputs and data sources, and reporting format of the budget-impact analysis evidence submitted to the CADTH. However, the data input and sources of the budget impact analysis required in the submission form are not required to adhere to the key characteristics for good practices in the international budget-impact analysis guidelines.

Classical health economics literature[30, 31] defined three major forms of health economic evaluation: a cost-benefit analysis, cost-effectiveness analysis, or cost-utility analysis. A cost-

minimization analysis is considered a subcategory of a cost-effectiveness analysis. While the concept of 'cost-minimization' is easy to comprehend and thus disseminate to both professional and public audiences, it can only be used under the assumption of equal treatment and the effectiveness of the new and existing drugs. There have been major debates and criticism [32, 33] on the use of the cost-minimization analysis because of its biased estimation of uncertainty, leading to a higher chance of making the wrong decision. Furthermore, new drugs are, in general, more expensive than existing ones. Clearly, one possible consequence is the inclusion of a cost-saving drug which is less effective than ones that already exist. Unless non-inferiority or equal-effectiveness withstands, the cost-minimization analysis is a less appropriate approach than the other three methods of analysis (i.e. cost-effectiveness analysis, cost-utility analysis, and cost-benefit analysis) that account for both costs and effectiveness associated with new and existing drugs. A calculation of the incremental cost-effectiveness ratio (ICER) that explicitly demonstrates the clinical benefits at the expense of additional costs is not required by the DAC for the evaluation of a new drug. However, an ICER value of the new drug versus the main competitor drugs is an important attribute and a preferred cost-effectiveness measure for decision making in the UK, Australia, and Canada. For instance, in England, the decision-making process in the NICE relies on the ICER value of less than the formal ICER threshold of £20,000-30,000 (US$21,880-32,823) per quality-adjusted life-year (QALY) for being normally accepted for reimbursement[2], and less than £50,000 (US$54,700) per QALY for new cancer drugs extending life expectancy towards the end of the patient's life. An empirical estimate of the ICER threshold based on the effects of changes in NHS expenditure on patients' health was likely to be £12,936 (US$14,152) per QALY[34]. From 1991 to 1996, based on submissions to the PBAC, the ICER threshold for recommending a new drug for listing by PBS ranged from AUS$42,000-76,000 (US$31,168-56,400) per life-year[35]. In Hong Kong, the potential ICER threshold is US$61,600 per effectiveness unit for what was considered to be a cost-

effective cancer screening program for recommendation[36]. Whilst the DAC does not have a preferred cost-effectiveness threshold or a formal ICER threshold, the input of cost-comparison and budget-impact values contributes to the conclusion of whether the new drug is cost-saving or simply costs the Hospital Authority, as opposed to a conclusion of whether the new drug is cost-effective compared to existing drugs.

Health economic and methodological data on submissions

In overseas countries, health economists and methodologists in review committees and independent parties serve the role of reviewing health economic and other technical aspects of submissions in terms of long-term model simulation, budget impact and cost-effectiveness of a new drug versus existing ones. Representatives with expertise in health economics, mainly academics, are members of the NICE Technology Appraisals Committee and SMC in the UK, the PBAC in Australia, and the CADTH in Canada. In the UK, submissions are independently reviewed by the Evidence Review Group and New Drugs Committee, specifically providing health economic and methodological input prior to the review by the Technology Appraisals Committees and SMC, respectively. Methodologists and health economists are not part of the PTAC in New Zealand but PHARMAC contracts health economists to prepare health economic analyses.

The DAC comprises of 12 members[37] including administrators, pharmacists, academics, and clinical experts from different specialties (medicine, surgery, orthopaedics and traumatology, paediatrics, psychiatry, oncology, anaesthesiology and pain medicine, dermatology, infectious disease, family medicine, obstetrics and gynaecology, ophthalmology, ear, nose and throat), providing balanced views on the clinical effectiveness and safety of drugs assessed. However, the composition of the DAC and the expert panel

lacks input from health economists.

Discussions and Conclusions

This paper reviews the decision-making process of new drugs listed on the formulary in Hong Kong, and compares it to the HTA process of new drug reimbursement overseas. Discrepancies in the decision-making process from several countries are presented in this review. There is no perfect new drug reimbursement system anywhere in the world, and it is unrealistic to transfer a whole new system to Hong Kong. Nevertheless, lessons from overseas countries provide valuable insights into the Hospital Authority, which aims to establish transparent, credible, objective, and robust decision-making in the formulary management system. Firstly, improvement in the transparency of the decision-making process, including the disclosure of the rules of making decisions in terms of cost-effectiveness, declarations of conflicts of interest from submitters, and engagement of key external stakeholders would support the credibility and accountability of the decisions made by the DAC. Secondly, the adoption of a budget-impact analysis framework from international guidelines would enhance the standardization and improve the quality of budget-impact analysis[38], and thus present a better picture of the budget impact to health-policy makers. Detailed information on costs of new and alternative drugs and healthcare services due to the uptake of new drugs, and other condition-related healthcare services and important aspects within the framework of budget-impact analysis would allow the DAC to better understand the value of new and alternative drugs. Thirdly, a cost-effectiveness measure, expressed in either ICER or a net monetary benefit, should be presented in the submission to determine whether a new drug is considered cost-effective. Finally, health economists and methodologists are required to review the calculations regardless of whether the cost-effectiveness analysis is based on local or overseas data. The DAC should consider

including members with expertise in health economics on the expert panels.

In summary, there are a number of challenges facing the Hong Kong Hospital Authority regarding the Drug Formulary. Proposals for the improvement of the listing of new drugs in the formulary should be a priority when implementing healthcare reforms.

Author contributions

CW conceived these ideas, drafted the plan and wrote the first version of this paper. OW contributed to the development of the idea. All authors reviewed drafts and approved the final version of the manuscript prior to its submission.

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Table Legend

Table 1. Comparisons of New Drug Submission and Decision-making Process in Hong Kong and Overseas Countries

Appendix Legend

Appendix A Hospital Authority Drug Formulary Submission Form

Table 1. Comparisons of New Drug Submission and Decision-making Process in Hong Kong and Overseas Countries

		Overseas Countries				
	Hong Kong	**UK England**	**UK Scotland**	**Australia**	**Canada**	**New Zealand**
Drug listing	Hospital Authority	NHS England	NHS Scotland	Pharmaceutical Benefits Scheme (PBS)	Canada's public drug plans, except for Quebec	New Zealand pharmaceutical schedule
Advisory body and review committee	Drug Advisory Committee (DAC)	NICE Technology Appraisals committees (TAC)	Scottish Medicines Consortium (SMC)	Pharmaceutical Benefits Advisory Committee (PBAC)	CADTH Canadian Drug Expert Committee (CDEC)	PHARMAC Pharmacology and Therapeutics Advisory Committee (PTAC)
Composition of review committee members	12 members including Hospital Authority pharmaceutical service management corporate director, chief pharmacist, clinicians from different specialties, and academics in healthcare-related disciplines from local universities	96 members with representatives of the NHS, patient and carer organisations, academia, and pharmaceutical and medical devices industries, evenly across 4 individual committees	Representatives of Area Drugs and Therapeutics Committee leads from each heath board in Scotland	Representatives of medical practitioners, pharmacists, patient support group, health economists, and company	14 members with representatives of technical experts with qualifications as physician, pharmacist, economist, or other health professionals, and lay public	Senior health practitioners nominated by professional medical bodies
Initiator	Hospital Authority clinicians	Manufacturers	Manufacturers	Manufacturers	Manufacturers	Pharmaceutical suppliers, health professionals, patients and consumers
Evaluation criteria	Three principal criteria (safety, efficacy and cost-effectiveness), International recommendations and practices, advance in technology, disease state, patient compliance, quality of life, actual experience in use of drugs, and views of professionals and patient groups	Clinical and cost effectiveness of treatments for use within the NHS	Clinical and cost effectiveness of treatments	Comparative health gain, comparative cost-effectiveness, patient affordability in the absence of PBS subsidy, and predicted use in practice and financial implications	Patient group input, safety, efficacy, effectiveness, therapeutic advantages and disadvantages, cost and cost-effectiveness of new drug relative to current accepted therapy	Health needs, availability and suitability of existing medicines, clinical benefits and risks of pharmaceuticals, cost-effectiveness, budgetary impact, direct cost to health service users, Government's priorities for health funding, and other criteria
Independent assessors	Expert panel	Evidence Review Group	New Drugs Committee	Economics Sub-Committee and Drug Utilisation Sub-Committee	Common Drug Review team	PTAC Subcommittees in specialist areas
Patient and carer group engagement	Notification of meeting agenda to patient group. Report suggestions and feedback received from patient group during the meeting. No engagement in carer group	Invitation of patient group or their carer to submit narrative summaries about disease and treatment experience, acceptability of, preferences for and expectations about treatment	Invitation of patient groups to submit experiences of patients, their families and carers, advantages and disadvantages of new drugs. A Patient and Clinical Engagement (PACE) Group to give patient groups a stronger voice in decisions of new medicines for end-of-life and very rare conditions	Invitation of patient groups to comment benefits and harms of new drug. No engagement in carer group	Invitation of patient input to provide experiences of condition, currently available treatments and new drug, and expectations of for new drug	No engagement in patient and carer group but patient and carer group may be a initiator
Meeting						

		Overseas Countries				
	Hong Kong	**UK England**	**UK Scotland**	**Australia**	**Canada**	**New Zealand**
Format and attendance	Closed; DAC Members	Public & Private; TAC Members, patient experts, clinical specialists, commissioning experts (Evidence Review Group), and public observers	Public; SMC Members, invited experts, industry, patient group, public observers	Closed; PBAC Members and other attendees by invitation only (sponsors, clinical experts, patient groups)	Closed; CDEC Members and other attendees by invitation only (health ministry officials, specialist experts, contracted external reviewers, and invited observers). Manufacturers and patients are not entitled to attend.	Closed; PTAC members, secretary, observers
Quorum	50% of committee membership	50% of committee membership	1/3 of committee membership	Not available	66% of committee membership	Six members
Voting	Consensus of committee members present normally. Voting in exceptional cases	Consensus of committee members present normally. Voting in exceptional cases	Decision based on a majority vote	Not available	Decision based on a majority vote	Consensus of committee members present normally. Voting if consensus cannot be achieved
Preferred cost-effectiveness measure	Not available	ICER in term of cost per QALY gain	ICER in term of cost per QALY gain	ICER; Unspecified effectiveness unit	ICER; Unspecified effectiveness unit	Cost-utility analysis as recommended economy analysis. ICER in term of cost per QALY gain
Decision making approach	Not available	<£20,000 per QALY; £20,000-30,000 per QALY plus four criteria satisfied (degree of uncertainty around the ICER, adequacy of health-related quality of life captured, innovation, and relation to non-health objectives of NHS); <£50,000 per QALY for end-of-life drugs	<£20,000 per QALY; £20,000-30,000 per QALY plus significant benefits over existing treatments	Not available	Not available	Not available
Decision categories	Approval for use as 'General Drug'; Approval for use as 'Special Drug'; Self-financed Items; Pending; Rejection	Recommended; Optimised; Only in research; Not recommended	Accepted for use; Accepted for restricted use; Not recommended for use	Recommended; Deferrals of a recommendation; Not recommended	List; List with clinical criteria and/or conditions; Do not list at the submitted price; Do not list	Recommended; Defer a final recommendation; Not recommended
Post-meeting						
Decision publicly available	Within 3 weeks after the meeting	About 3 months after the meeting	About four weeks after the meeting	6 weeks after the meeting	After an embargo period of 10-30 business days	Not available
Report on decision publicly available	Not available	Draft minutes are submitted to the next meeting for approval. Within 20 working days of approval	Not available	16-18 weeks after the meeting	Same day as final decision	Not available
Implementation of approved drugs listed	Around 3 months after the meeting	Within 3 months of decision published	Not available	After the price agreement and budget-impact evaluation	Not available	Not available
Appeal mechanism	No	Within 15 working days of final draft guidance published	Yes (but deadline of appeal unknown)	Within 90 days of decision made	A procedural review Request submitted within 10 working days of final recommendation published	No

NHS = National Health Services; NICE = National Institute of Health and Care Excellence; PBS = Pharmaceutical Benefits Scheme; PBAC = Pharmaceutical Benefits Advisory Committee; CADTH = Canadian Agency for Drugs and Technologies in Health; CDEC = Canadian Drug Expert Committee; DAC = Drug Advisory Committee; PHARMAC = Pharmaceutical Management Agency; PTAC = Pharmacology and Therapeutics Advisory Committee; ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life-year; TAC = Technology Appraisals committees; PACE = Patient and Clinical Engagement

HA Drug Advisory Committee

New Drug Submission Form

An application can be submitted, via Cluster / Hospital DTC, for consideration of listing on the HA Drug Formulary if the concerned drug entity or indication fulfills the following criteria:

a) It is indicated for prevention or treatment of conditions which are not covered by drugs in the existing HA Drug Formulary;
b) It has an advantage in terms of efficacy and adverse effects over agents in the existing HA Drug Formulary for the same indication; or
c) It is equivalent in terms of safety and efficacy as compared to existing agents in the HA Drug Formulary for the same indication and of lower treatment costs.

Please complete ALL sections and attach relevant supporting documents in order to facilitate the evaluation. Incomplete information may lead to delay in the submission process.

FOR INTERNAL USE ONLY	
DAC Ref. No.:	Date received:

1. GENERAL INFORMATION

1.1 Submitting hospital:
1.2 Name of drug: Generic (Trade)
1.3 Name of manufacturer / supplier:
1.4 Strength & form:
1.5 Cost (per unit):
1.6 Current formulary status of this drug:
☐ Non-Formulary use – SFI ☐ Non-Formulary use – Hospital-funded ☐ Sample use
1.7 Proposed financing method:
☐ Hospital-funded ☐ SFI
1.8 Status of application:
1.8.1 Approved by hospital DTC: ☐ Yes ☐ pending 1.8.2 Date of DTC meeting:
1.9 Applying doctor (name, rank, specialty)
Name: Rank: Specialty:

2. PROPOSED PLACE IN THERAPY IF INTRODUCED INTO HADF

2.1 Licensed indication(s) of this new drug in HK (specific for this submission)

e.g. Erosive Esophagitis

2.2 Worldwide registration status for this indication (if known)
(e.g. registration status and month/year in Australia, Canada, EU, US)

e.g.

Country	Dosage	Indication	Approval Date
Hong Kong	30mg capsules 60mg capsules	Erosive Esophagitis	Nov 2010
USA	30mg capsules 60mg capsules	Erosive Esophagitis ~~Maintenance of healed EE~~ ~~Symptomatic non-erosive GERD~~ (no need to list these indications which are unlicensed in HK/not for this application	Jan 2009 ~~May 2005~~ ~~May 2005~~
Australia	30mg capsules 60mg capsules	Erosive Esophagitis ~~Maintenance of healed EE~~ ~~Symptomatic non-erosive GERD~~	Jul 2010 ~~Apr 2006~~ ~~Apr 2006~~

2.3 Natural History of the disease
(e.g. survival time, time to progression of the disease)

e.g. The median survival for patients with the disease ranges from approximately 2–11 years depending on risk stratification; the median survival time for patients with intermediate–2–risk is 4 years and 2 years for patients with high-risk disease.

2.4 Existing treatment protocol for this disease in HA

(Please list out all existing treatment alternatives, dose regimens and sequence of use)

2.4.1 Existing treatment alternatives with dose regimens

(Note:- alternatives must be available in HA):

e.g.
Insulin Lispro – individualised dose
Insulin Aspart – individualised dose

e.g.
sitagliptin 5mg once daily
vildagliptin 50mg-100mg once daily

2.4.2 Sequence of use:

e.g.
In patients with T2DM
Step 1: Initiate with metformin
Step 2: After failed the optimal doses of metformin, add a sulphylurea
Step 3: After failed the optimal doses of metformin and a sulphonylurea, add DPP-4
Step 4: After failed all oral anti-diabetic agents, give insulin

2.5 Proposed place in therapy of this new drug in relation to 2.4.2

(Proposed treatment protocol or algorithm for this disease after introduction of this new drug)

e.g.(1) IF NEW DRUG IS IN ADDITION TO EXISTING TREATMENT
Use the new drug as an alternative to insulin:-
In patients with T2DM
Step 1: Initiate with metformin
Step 2: After failed the optimal doses of metformin, add a sulphylurea
Step 3: After failed the optimal doses of metformin and a sulphonylurea, add DPP-4
Step 4: *After failed all the above treatments, give Drug A (new drug)*
Step 5: After failed all the above treatments, give insulin

e.g.(2) IF NEW DRUG IS AN ALTERNATIVE TO EXISTING TREATMENT
e.g. The new drug Insulin A is another option for existing short-acting insulin available in HA

e.g. (3) IF THERE IS NO EXISTING ALTERNATIVE
e.g. Bosentan for pulmonary aterial hypertension NYHA/WHO Functional Class IV symptoms

2.6 Treatment initiation and exit criteria for the new drug

2.6.1 Initiation criteria:

e.g. (1) in patients refractory to the alternatives stated in Section 2.4.1

e.g. (2) patients who had received at least 1 prior course of chemotherapy and had disease progression or relapse since chemotherapy

2.6.2 Exit criteria:

e.g. (1) patient not responding after 3 months of treatment

e.g. (2) Treatment will be terminated if the patient develops progressive disease or unmanageable toxicities

e.g. (3) discontinue if fail to achieve HbA_{1c}<8% within 6-8 months

2.7 Proposed HA Drug Formulary Indication(s) for this new drug
(Please list out proposed indication wordings as would appear in MOE, each indication should be within 200 characters including punctuation marks and spacing)

e.g. Short-term treatment of moderate to severe atopic dermatitis in non-immunocompromised patients unresponsive to other topical treatments or when those treatments are not advisable (total 177 characters)

2.8 Authorisation for prescribing this new drug for this indication (which specialty)

e.g. Specialists: Derm / Paed

2.9 Proposed HA Drug Formulary status
(General / Special / SFI)

e.g. Special

3. SUMMARY OF BENEFITS OF THIS NEW DRUG OVER EXISTING OPTIONS LISTED IN SECTION 2.4

(DETAILS TO BE PROVIDED IN SECTION 4)

3.1 Benefit in Efficacy

e.g. (1) Median time to progression was significantly longer in patients receiving the new drug compared to drug A [drug A must be currently available in HA] (14.3 months vs. 6 months, HR=0.34, p=0.001)

e.g. (2) The percentage of 24-h heartburn-free days and night was significantly greater in patients receiving the new drug than placebo (69% vs. 15%, p=0.001)

e.g. (3) Improvement in symptom severity and overall quality of life were maintained over 6 month

3.2 Benefit / Concerns in Safety Issues

e.g. (1) The new drug has lower incidence of EPS than both haloperidol (13% vs. 25%, p<0.001) and risperidone (17% vs. 22%, p=0.1), but a significantly higher increase in QT interval (7% vs. 0.5%, p<0.001) and a weight gain of 4.6kg over 1 year

e.g. (2) The new drug is well tolerated with an adverse event profile similar to that of placebo; however, the incidence of hypoglycemia was higher than existing alternatives listed in Section 2.4.1 (8% vs. 3%, p<0.001)

3.3 Other Benefit(s)

e.g. (1) Less drug-drug interaction than existing alternatives listed in Section 2.4.1

e.g. (2) First drug in the class available in oral form, more convenient than the existing alternatives; more acceptable by patients

e.g. (3) The controlled released formulation improves compliance than the multiple dosing of the immediate-release formulation.

4. DETAILS ON CLAIMED BENEFIT(S) OF THIS NEW DRUG AS SUMMARISED IN SECTION 3

- All supporting documents MUST be clearly referred to
- Do not include any data on unlicensed indication(s)
- Only provide the highest level of evidence for each individual claimed benefit listed in Section 3
  (e.g. if efficacy has already been proven in phase III randomised-controlled trials, there is no need to provide evidence from placebo-controlled trials etc.)
- Only accept fully published clinical trials (no abstracts or posters)

4.1 Benefit in Efficacy
4.2 Benefit in Safety Issues
4.3 Other Benefit(s)

5. AVAILABLE INTERNATIONAL GUIDELINES AND OVERSEAS REIMBURSEMENT ASSESSMENT DOCUMENTS

(All supporting documents MUST be clearly referred to)

5.1 Please list out relevant international guidelines and their summaries

e.g. The new drug has been recommended in the US guidelines (American College of Cardiology Foundation / American heart Association Take Force on Practice Guidelines) as an alternative to warfarin for the prevention of stroke and systemic thromboembolsim in patients with paroxysmal to permanent AF and risk factors for stroke or systemic embolisation who do not have a prosthetic heart valve or haemodynamically significant valve disease, severe renal failures (CrCL<15 ml/min), or advanced liver disease (impaired baseline clotting function).

5.2 Please indicate if this new drug has been evaluated by Australia Pharmaceutical Benefits Scheme (PBS), UK National Institute of Clinical Excellence (NICE), Scottish Medicines Consortium (SMC), and their recommendation(s)

5.2.1 PBS: e.g. not listed in PBS

5.2.2 NICE: e.g. under review

5.2.3 SMC: e.g. accepted for use as first-line treatment in patients with locally advanced or metastatic non-small cell lung cancer with epidermal growth factor receptor activating mutations.

6. COST COMPARISON AND BUDGET IMPACT

6.1 Cost comparison of this new drug with existing alternatives in HADF as listed in 2.4.1

HADF status	Drug	Strength	Unit cost $	Dose regimen (also provide maximum maintenance dose)	Daily cost/cost per cycle	Annual/ Treatment cost $
	New Drug	e.g. (1) 150mg	$520	50mg once daily continuous till remission/ progression/ lifetime Max 50mg once daily	$520/day	Annual cost $189,800

HADF status	Drug	Strength	Unit cost $	Dose regimen (also provide maximum maintenance dose)	Daily cost/cost per cycle	Annual/ Treatment cost $
		e.g. (2) 50mg	$8400/ vial	e.g. 50mg/m^2 i.v. on day 1 every 3 week, rest 1 week, then repeat; max 75mg/m^2 for 8 cycles	$16,800/ cycle Max $25,200 (@1.6$m^2$)	Total treatment cost for 8 cycles $134,400 Max $201,600
		e.g. (3) 50mg	$8400/ vial	e.g. 70mg/m^2 s.c. every 2 weeks; max 100mg, for 6 months	$25,200/ 2 weeks Max $33,600/ 2 weeks (@1.6$m^2$)	Total treatment cost for 6 months $302,400 Max $403,200
G/S/SFI/ SN	Alternative					
G/S/SFI/ SN	Alternative					
G/S/SFI/ SN	Alternative					
G/S/SFI/ SN	Alternative					

6.2 Budget impact	
(1) Prevalence data	(1) Total no. of patients with this disease in HK = e.g. 200,000 (2) Total no. of patients with this disease in HA = e.g. 100,000 (3) Total no. of patients in HA who fulfil the proposed HADF indication as stated in Section 2.7 = e.g. 6,000 (4) Total no. of NEW patients in HA who fulfil the proposed HADF indication as stated in Section 2.7 = e.g. 800 (5) Data source *(Please state how this is estimated e.g. patient registry, CDARS, recommendation from HADF Expert Panel) :* e.g. Cancer registry 2012
(2) Total budget impact per annum in HA	(Please indicate if there is any increase in patient no. in the next few years) e.g. Year 1 = 6,000 (backlog) + 800 (NEW) = 6,800 Year 2 = 6,800 + 800 – 200 (withdrawal/progression) = 7,400
(3) Possible cost saving	(1) Replacement of existing option(s) as stated in Section 2.4 *(please list out)* = (2) Other resource(s) = *(e.g. lab, shorten hospitalisation, delay of surgery etc.)*

7. SUPPORTING DOCUMENTS FOR THIS SUBMISSION

Please submit the following documents for evaluation (in hard and soft copies)

(1) Prescribing information sheet (package insert)

(2) Supporting references for sections 1 – 6 where applicable

* List out the references under this section
* Please ensure that all supporting documents are clearly numbered and referred to
* Provide soft copy of the references in PDF format and the full reference list in Microsoft word

References:

8. CHAIRPERSON OF THE DRUG AND THERAPEUTICS COMMITTEE

Name:

Designation:

Signature:

Date: