A PROPOSAL FOR CLASSIFICATION OF PUBLIC FUNDING RESTRICTIONS

Norbert M. Wilk

Director for Research and Quality Development, Arcana Institute, Cracow, Poland

BACKGROUND

Increasingly difficult situation of health care systems forces decision makers to limit access to publicly funded drugs compared to registration conditions. To keep the transparency, the decisions to deny health intervention to some group of patients have to be publicly justified – simple intuition is not enough.

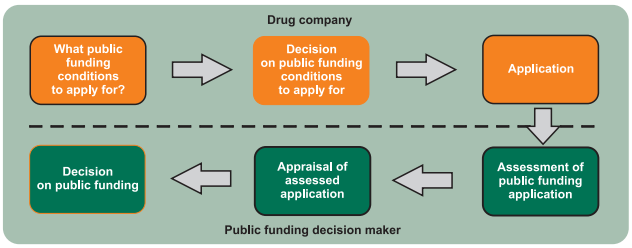
The common model for public funding decision making is based on an application for funding submitted to administration by the producer.

The drug company sets the funding condition that they apply for – e.g. the price and populational restrictions, if any are deemed necessary within the application.

The administration, usually represented by the Minister of Health, is a decision maker. In some countries the part of the process performed by the public funding decision maker is divided into substeps: assessment and appraisal of the assessed application, leading to the decision on public funding.

Any drug to be applied in humans has to be registered first and within a registration decision there are indications and contraindications listed. When the drug is decided on being publicly funded, some restrictions may be applied for numerous reasons – and this is analysed further.

Figure 1. The process of public funding applying and decision making



OBJECTIVES

The objective is to present initial classification of public funding restrictions. The details of methods to generate such restrictions are also explored.

METHODS

A pool of public funding decisions has been identified through search of internet websites of the institutions that recommend or actually make public funding decisions. To ensure highest probability of identifying both a restriction and its mechanism (on the basis of detailed justification) and because of exploratory nature of the work, the results were filtered to those that originate from the institution known for probably most detailed justifications of its decisions: National Institute for Health and Clinical Excellence (NICE, England and Wales, UK).

The specific conditions restricting access to publicly funded drugs were identified, analyzed and draft classification proposed.

RESULTS

There are three general types of public funding restrictions:

- Financial – e.g. price, limited allocated budget;
- Populational – e.g. regarding the features related to indications;
- Mixed – risk- and cost-sharing solutions.

In this presentation only populational restrictions are explored and initially classified for the two drugs:

- Hycamtin for small cell lung cancer;
- Erbitux in combination with chemotherapy for colorectal cancer.

In the following tables the registration and public funding conditions for these drugs are contained.

Table 1. Erbitux in combination with chemotherapy for colorectal cancer appraised by NICE

Registration conditions	Reimbursement restrictions	Justification	Mechanism/type of restriction
Cetuximab is indicated for the treatment of patients with EGFR-expressing, KRAS wild-type metastatic colorectal cancer in combination with chemotherapy.	Cetuximab with FOLFOX or FOLFIRI combination, within its licensed indication, is recommended for the first-line treatment of metastatic colorectal cancer only when all of the following criteria are met:	*The Committee noted that the manufacturer had not provided an economic analysis that included the entire population for which cetuximab is licensed.* *The economic model focused on a subgroup of patients with a good performance status and metastatic disease confined to the liver.*	indirect voluntary manufacturer's restrictions
	– the primary colorectal tumour has been resected or is potentially operable;	*The Committee noted that in people who have undergone primary colorectal surgery with curative intent and whose liver metastases are rendered resectable following a successful response to chemotherapy, the 5- and 10-year survival rate is approximately 30% and 20% respectively.*	**because of improved efficacy**
	– the metastatic disease is confined to the liver and is unresectable;	*The Committee thought that the QALYs gain ed for the whole population [not restricted to liver metastases only] would be substantially lower than that of the subgroup, while the incremental costs would not be any lower.*	**to improve cost-effectiveness**
	– the patient is fit enough to undergo surgery to resect the primary colorectal tumour and to undergo liver surgery if the metastases become resectable after treatment with cetuximab;	*The majority of KRAS wild-type patients in the CRYSTAL and OPUS trials (96% and 90%, respectively] had an ECOG performance status of 0 or 1, so this was reflected in the modelled cohort.* *The Committee noted that for patients who are not well enough to have surgery to remove liver metastases, adding cetuximab to their chemothe-rapy would not help in enabling a curative operation.*	**because of too limited evidence to improve effectiveness**
	– the manufacturer rebates 16% of the amount of cetuximab used on a per patient basis (FOLFOX only);	proposed by the manufacturer	**to improve cost-effectiveness**
	– the patient is unable to tolerate or has contraindications to oxaliplatin (FOLFIRI only).	*adding cetuximab to [FOLFOX] withthe intention of reducing the size of liver metastases would be the combination of choice for [patients with liver-only metastases]. However the Committee was aware that there may be some patients who are unable to tolerate, or have a contraindication to oxaliplatin, and it agreed that for these patients the most appropriate comparator would be FOLFIRI.*	**to improve efficacy-safety relation because it is the only effective treatment**
	Patients [...] should receive treatment with cetuximab for no more than 16 weeks. At 16 weeks treatment with cetuximab should stop and the patient should be assessed for resection of liver metastases	*The Committee heard from the clinical specialists that in current UK clinical practice, all patients would normally stop receiving treatment with cetuximab at the time of the assessment for possible liver resection (that is, after approximately12-16 weeks).* *The Committee noted that the 16-week analysis provided by the manufacturer only explored stopping the costs of cetuximab treatment at 16 weeks. [...] The Committee considered this to be the most optimistic scenario.*	**to reflect current clinical practice to limit budget impact**
	Refers to all restrictions	*The Committee agreed that the most likely ICER for cetuximab in combination with FOLFOX compared with FOLFOX alone was between GBP26,700 (estimated by the manufacturer) and GBP33,300 per QALY gained (estimated by the DSU), and that this was within a range that could be considered a cost-effective use of NHS resources.* For combination therapy of cetuximab with FOLFIRI *the ICER would likely be within a range considered to be a cost-effective use of NHS resources.*	**to improve cost-effectiveness**

Sources:
1. European Medicines Agency (EMEA). Erbitux SMPC
2. National Institute for Health and Clinical Excellence (NICE): Cetuximab for the first-line treatment of metastatic colorectal cancer. August 2009

Table 2. Hycamtin for SCLC appraised by NICE

Registration conditions	Reimbursement restrictions	Justification	Mechanism/type of restriction
Oral and intravenous topotecan is recommended to treat relapsed small cell lung cancer (SCLC) in patients for whom re-treatment with the first line regimen is not considered appropriate.	Oral – as registered. Intravenous topotecan is not recommended for people with relapsed small-cell lung cancer	*Severe or life-threatening adverse events were similar between intravenous topotecan and oral topotecan in the studies, with the exception of neutropenia, which appeared to occur more frequently with intravenous topotecan*	**To improve efficacy-safety relation**
		[...] the ICER for intravenous topotecan versus oral topotecan was either very high or that intravenous topotecan was dominated. [...] the ICER for intravenous topotecan compared with best supportive care was very high	**To improve cost-effectiveness**
		[...] alternative to intravenous therapy only required patients to attend hospital once per cycle compared with five times for intravenous topotecan	**To improve patient compliance**

Sources:
1. European Medicines Agency (EMEA). Topotecan SMPC
2. National Institute for Health and Clinical Excellence (NICE): Topotecan for the treatment of relapsed small-cell lung cancer. November 2009

The main types of restrictions identified either because of the target public funding parameter affected or because of the reasoning are presented in Table 3.

Table 3. Main types of public funding restrictions (draft)

Basis/simplified justification	Mechanism
„because of lack of evidence" "because of too limited evidence"	Exclude from public financing those patients for whom there is no evidence (though they might fall within the registered population)
„because it is the only effective treatment" (rule of rescue)	Exclude from public financing those patients who are NOT in such a tragic situation when the treatment is the only effective option
„because there is so few patients with a condition"	Accept public financing for indications with very few patients in order to avoid accusations of discrimination on grounds of sparseness (and perceived lack of political power) – applicable rather when referred to whole registered population
„because of improved efficacy"	Exclude from public financing those patients for whom health benefits gained with treatment in trials are particularly relatively small
„to improve efficacy-safety relation"	Exclude from public financing those patients for whom there are safety issues which decrease net health benefit
„to improve effectiveness"	Exclude from public financing those patients who have relatively low health benefit
„to improve cost-effectiveness"	Exclude from public financing those patients who generate higher costs (e.g. high dosing) or who have relatively low health benefit
„to limit budget impact"	Exclude from public funding some group of patients (particularly beneficial when leads to better defined remaining funded population) or limit length of use of a given health technology
„to improve patient compliance"	Exclude from public financing those treatment modalities that are more tiresome for patients without adequate additional benefit
„to reflect current clinical practice"	Incorporate limitations that are in line with current clinical practice in a given country

The proposed categories are based on the above public funding decisions, but also supplemented with author's experience:

- as a deputy director of Agency for HTA in Poland (AOTM), where he was responsible for organizing the two step (assessment/appraisal) decision making process and took part in meetings of Polish appraisal body – Consultative Council;
- as a director for Research and Quality Development at Arcana Institute (Krakow, Poland), where he is responsible for Market Access consulting services.

CONCLUSIONS

Why investigate reasons for public funding restrictions? Because to know the outcome is just about nothing, but to know the mechanism is just about everything. A mechanism is a linkage between the evidence that the decision was based on, the environmental circumstances for the decision (usually difficult to formally identify) and the public funding decision or its recommendation. To know how a restriction is generated and applied is a must to foresee public funding decisions in similar circumstances.

The restrictions should be perceived as tools to enable a positive public funding decision when the registration scope of financing is just behind the hypothetical threshold.

Exploring and further analyzing methods and aspects concerning generating public funding restrictions is important for:

- **Public funding decision makers – a reason for the public to believe, so they be**
  - more aware of the consequences and impact of their decisions on the people/patients they serve, and
  - could make more transparent decisions.
- **HTA analysts**
  - to focus their interest on the subsequent use of HTAs to help decision makers identify all potential options to rationally limit funding.
- **Market Access managers – to be a better partner for discussion with decision makers, so they used the identified mechanisms and methods to ensure best compromise between probability for positive public funding decisions and company's earnings, to**
  - better foresee the public funding decisions concerning their drugs;
  - anticipate restrictions and use them in public funding applications.

Arcana Institute, 8 St. Dąbka street, 30-732 Cracow, Poland, tel./fax +48 12 263 60 38, e-mail: kontakt@inar.pl www.arcanainstitute.com