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Access to medicines for breast, colorectal, and lung cancer in Thailand

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ABSTRACT

Aim: Cancer drugs have become prohibitive, and consequently their accessibility has increasingly been of great concern in many countries. Particularly, the information about cancer drug access in Thailand has been sporadic. Therefore, the goal of the study was to examine the antineoplastic drug accessibility in Thailand in terms of both market access and patient access. In addition, this study evaluated antineoplastic drugs based on cancer incidence in Thailand, and especially those for the top 3 common cancer types: Breast cancer, colorectal cancer, and lung cancer. **Method:** The study method was descriptive in nature to evaluate the number of antineoplastic drugs in both Thai market and reimbursement list or National List of Essential Medicines to reflect the market access and patient access, respectively. In determining Thailand's market access, the number of active ingredients (APIs) of antineoplastic drugs was obtained from the WHO website as a reference to the number of Thailand's marketing authorization approvals (MAAs) of antineoplastic drugs as per the Thai FDA website. For the determination of patient access, the number of antineoplastic drugs available to Thai patients was extracted from 2016 NLEM so that it can be compared to Thailand's MAAs. For further delineation with respect to treatments for each cancer type (ranked by cancer incidence in Thailand), the total number of APIs for each cancer type was used to determine market access and patient access. **Results:** The accessibility of antineoplastic drugs was 49% (88 of 180 APIs of WHO) for Thailand's market access and 43% (38 of 88 APIs in Thailand) for the patient access. For the top 3 cancer types, the market access was of a high percentage while the patient access from NLEM list was of low percentage. **Conclusions**: The market accessibility of antineoplastic drugs did not pose a problem for Thailand. Registrations of anti-cancer drugs undoubtedly played a key role for the market accessibility. However, new innovative antineoplastic drugs have presented a rather considerable concern for Thai patients, which are further complicated by the NLEM selection process and the limitation of use according to the categories outlined in the NLEM requirements. Therefore, improvement is clearly needed for patient access to new innovative antineoplastic drugs.

Keywords: Antineoplastic drug, drug access, market access, patient access

INTRODUCTION

Fourteen million new cancer cases and 8.2 million cancer deaths were reported in 2012. The three most common cancers were lung (1.82 million), breast (1.67 million), and colorectal (1.36 million); while the most common causes of cancer death were lung (1.6 million deaths), liver (745,000 deaths), and stomach (723,000 deaths).[1]

Through the search in Thailand's 5 cancer registries, which were representative of the country's 4 major geographic regions, during the span of at least 15 years (from 1989 to 2004), Sriplung *et al*. analyzed the trends in incidence of certain cancer types and reported a statistical significance of increasing trend for colorectal and breast cancers.[2] Coinciding with a more recent cancer registry data collected during 2009–2014, breast cancer was, thereafter, reported

Table 1: Registry of annual new cancer patients in Thailand during 2009–2014

Cancer types	Number of new cancer patient registry*(2009-2014)						
	2009	2010	2011	2012	2013	2014	Total
Breast	768	821	761	943	926	1006	5225
Colon and rectum	342	369	417	454	389	483	2454
Trachea bronchus, lung	371	332	336	407	450	425	2321
Cervix uteri	298	276	289	340	356	288	1847
Liver and bile duct	236	215	336	285	323	348	1743
Lip and oral cavity	165	135	175	188	139	124	926
Non-Hodgkin lymphoma	100	98	96	109	51	100	554
Esophagus	70	87	80	105	101	94	537
Ovary	77	69	90	87	73	82	478
Prostate gland	70	19	45	79	75	70	358
Other types	817	715	716	920	1042	948	5158
Total without other types	2,497	2,421	2,625	2,997	2,883	3,020	16,443
Total all types	3,314	3,136	3,341	3,917	3,925	3,968	21,601

*Number of new cancer patient registry during year 2009–2014, data from the website of National Cancer Institute (NCI), Thailand. http://www.nci.go.th/th/cancer_record/cancer_rec1.html, accessed date on Mar 23, 2017

as the most common among the 10 common cancer types [Table 1].[3]

Treating cancers have long been a challenging undertaking. Many cancers become refractory or resistant to cancer treatments, particularly to the conventional therapies, which subsequently lead to recurrent and/or metastatic stages. Therefore, new innovative therapies are desperately needed.[4] The landscape of current cancer therapies has transformed tremendously from the treatments with cytotoxic drugs to various newer classes of pharmacological drug agents (e.g., kinase inhibitors and monoclonal antibodies) as well as to innovative, targeted therapies such as trastuzumab, bevacizumab, and regorafenib.[5-8] The upsides to the targeted cancer therapies are their premises of better safety, tolerability and efficacy profiles as well as better quality of life as compared to the conventional cancer treatments with traditionally common cytotoxic drugs. However, the downsides to the innovative drug therapies are their inherently prohibitive development costs. In addition, as cancer is rarely cured and likely to be recurrent to progress to an advanced stage and/or metastasize to other organ(s), the cost of cancer treatments has thus far wreaked havoc on the health-care systems globally. Contingent on a country's economic power and the availability of cost-effective cancer drugs in each country, accesses to cancer drugs among countries, set forth by their health-care policies, are accordingly diverged.[9,10] Prevalence of cancer in Thailand has been increasingly reported, on the contrary, the knowledge of the access of cancer drugs is rather sparse, or lack thereof, whose awareness is hoped to ultimately be raised.

Access to medicine is crucial. Drug access has been quantified in various studies into market access and patient access.[11-14] Drug accessibility, as defined by the United Nations, is to have medicine continuously available and affordable at public or private health facilities or medicine outlets that are within 1 h walk from his/her residence.[15] The pathway to access new medicines includes various steps, starting from the completed R & D of the drug, market authorization approval (MAA), the drug product launching, and medicine outlet to the product listed for reimbursement. Some studies, however, referred "accessibility" as time lag to access of medicines such as from completed R & D of the drug to MAA or from MAA to reimbursement decision.[16-18] In addition, one study in Malaysia considered the total numbers of cancer drug available in Malaysia National Essential Medicines to determine the current status of accessibility to essential cancer drugs.[19]

All Thais are covered under the public health insurance system. They are insured through one of the three health insurance schemes - the Civil Servants Medical Benefit Scheme, the social security scheme (SSS) or the universal coverage. Cancer treatments in Thailand are mainly based on the clinical practice guideline set forth by the national health security office, adopted from the well-established institutes such as the US National Cancer Institute (US NCI), American Cancer Society (ACS), the UK Cancer Research, as well as Thai Royal College.

Drug expenditure has outpaced the growth of another health-care cost, and payers have taken the brunt of shouldering the increasing cost for the reimbursement providing that the prescribed medicines are listed in the National List of Essential Medicines (NLEM). The Thai Food and Drug Administration (FDA) is mandated in arriving the NLEM, whereby the consideration of evidence-based approach, such as the ISafE scoring system, is taken into account in the selection of appropriate medicines.[20]

As previously alluded, antineoplastic drug is costly. Therefore, the NLEM is a saving grace for those patients to drug access. Patients will be reimbursed for their drug treatments as long as the medicines are prescribed according to the criteria/requirements stipulated in the NLEM. In general, NLEM classifies drugs into 5 categories (A, B, C, D, and E) depending on how they are prescribed: Categories A, B, and C refer to

those for standard treatments. Drugs in Categories D and E are expensive and prone to misuse, and thus, hospitals are required to conduct drug use evaluation. Category E imposes stricter requirements and special mechanism on drug use monitoring, and pre-authorization. In addition, Category E is further categorized into E1 (medicines for special projects of government) and E2 (for special situation customized for a particular patient given that the access to this medicine is reasonable and sustainable).[21]

The aim of this study was to examine the antineoplastic drug accessibility in Thailand with respect to market access and patient access. In addition, the antineoplastic drug accessibility was further delineated among various cancer types, particularly in the three most common cancer types in Thailand, i.e., breast, colorectal, and lung.

MATERIALS AND METHODS

In this study, market access for antineoplastic drug accessibility was defined as the existence of medicines in the market while patient access referred to drug availability of antineoplastic drugs under NLEM. Market access was then operationalized as the number of available active pharmaceutical ingredients (APIs) approved in Thailand for the treatments of each cancer type, and patient access was measured by the number of available antineoplastic drugs listed in NLEM for the treatments of each cancer type. The study was aimed to report the findings of the cancer drug accessibility, the results were reported as the percentage of available antineoplastic drugs approved in Thailand relative to the number of antineoplastic drugs listed in 2015 World Health Organization (2015 WHO); and antineoplastic drugs in list of 2016 NLEM relative to the number of antineoplastic drugs approved in Thailand.

This study defined market access (%) as the number of antineoplastic APIs approved in Thailand as the percentage of the number of APIs available in 2015 WHO and patient access (%) as the number of antineoplastic API listed in 2016 NLEM as the percentage of the number of APIs approved in Thailand.

Data Sources

According to the WHO's Anatomical Therapeutic Chemical (ATC) classification system, APIs are divided into different groups pertinent to the organ or system on which they act and their therapeutic, pharmacological, and chemical properties. As such, antineoplastic drugs are classified into groups at five different levels. Designated by lettering for the 1st level, drugs are divided into 14 main groups. In addition, subsequent divisions are further delineated for the 2nd level (pharmacological/therapeutic subgroups), 3rd and 4th levels (chemical/pharmacological/therapeutic subgroups), and 5th level (chemical substance).

Accordingly, all cancer APIs from the main therapeutic class "L01: Antineoplastic drug" were extracted from the WHO website,[22] which reflected the number of APIs available worldwide as previously described to derive the market access and patient access.

In general, an marketing authorization approval (MAA) is granted in Thailand once the application was accepted for registration in Thailand. Through the database as per the Thai FDA website,[23] a list of available antineoplastic APIs (considered as L01 per the WHO's ATC classification system) were compiled from the MAAs granted by the Thai FDA between 1982 and April 2016. In addition, the information on their approved indications per cancer types was collected so that the accessibility for the treatments of each cancer type was determined.

NLEM version 2016 was used to compile the list of available antineoplastic APIs for the analysis of patient access based on the NLEM's prescribing criteria/requirements for the treatments of each cancer type.

In addition, the original approvals of the antineoplastic APIs were traced back to their reference countries (e.g. the US FDA, the UK medicines and health-care products regulatory agency, Australia therapeutic goods administration, Health Canada, European medicines agency, and Pharmaceuticals and medical devices agency) to verify their approved indications. Treatment guidelines for each cancer type from the US NCI, ACS, and the UK Cancer Research were also reviewed for their recommendations based on the best available evidence with the aims to inform clinicians of when there is no evidence and to help clinicians deliver the best possible health care.

RESULTS

There were 180 antineoplastic APIs listed in the 2015 WHO. Of those, 88 were found in Thailand's MAAs and 38 in Thailand's 2016 NLEM. As such, the accessibility of antineoplastic drug was 49% (88/180) for market access in Thailand and 43% (38/88) for patient access.

According to Thailand's prevalence [Table 2], of 180 APIs listed in 2015 WHO for treating these 10 cancer types, 170 APIs were approved worldwide. However, only 72 unique APIs were identified of the 170 APIs, resulting in 40% (72/180) for treating these 10 cancer types. Compared to the worldwide pool of 72 unique APIs, 54 unique APIs approved in Thailand (75%) were accessible for treating these 10 cancer types. Only 27 unique, APIs listed in NLEM (50%) were accessible for treating Thais patient (when compared to the unique API number in Thailand).

Per cancer type, market access (as shown in column Approvals in Thailand) was quite high (>71%), where 100% market access was observed in cervix uteri, liver and bile duct, and prostate gland and 71% to 95% market access for the remaining cancer types. Meanwhile, patient access (as shown in column 2016 NLEM) was relatively lower when compared to the market access - ranging from 33% to 63% except for Non-Hodgkin Lymphoma (70%). Of note, the patient access below 50% was observed in colorectal (33%), esophagus (37%), and cervix uteri (38%).

Specific to top 3 cancer types (breast, colorectal, and lung cancer), although their market access was high, their patient access was around 50% or lower. The precise details are presented in Tables 3-5.

Breast Cancer

Of the 25 APIs listed under 2015 WHO for breast cancer [Tables 2 and 3], Thailand's market access was 88% (22/25);

Table 2: Drug access for each cancer type by the number of active pharmaceutical ingredient

Cancer types	The total of patients [A](2009-2014)	Number of API: *n* (%)		
		Approval worldwide - December 2015 (N: 180)[B] (%)	Approval in Thailand - April 2016 (N:88)[C] (%)	2016 NLEM (N:38)[D] (%)
Breast	5225	25 (100)	22 (88)	11 (50)
Colon and rectum	2454	12 (100)	9 (75)	3 (33.33)
Trachea bronchus, lung	2321	28 (100)	22 (78.57)	12 (54.55)
Cervix uteri	1847	13 (100)	13 (100)	5 (38.46)
Liver and bile duct	1743	8 (100)	8 (100)	5 (62.5)
Lip and oral cavity	926	15 (100)	13 (86.67)	7 (53.85)
Non-Hodgkin lymphoma	554	28 (100)	20 (71.43)	14 (70)
Esophagus	537	17 (100)	16 (94.11)	6 (37.5)
Ovary	478	20 (100)	19 (95)	12 (63.16)
Prostate gland	358	4 (100)	4 (100)	2 (50)
Total (N)	16443	170 (100)	146 (85.88)	77 (52.73)
Total (N) of API uniqueness		72 (100)	54 (75)	27 (50)

[A]: Number of new cancer patient registry during year 2009–2014, data from the website of National Cancer Institute (NCI), Thailand. http://www.nci.go.th/th/cancer_record/cancer_rec1.html, accessed date on Mar 23, 2017. API: Number of Active pharmaceutical ingredient, [B]: Total number of Antineoplastic API listed by the WHO in December 2015, [C]: Total number of Antineoplastic API found in Thailand in April 2016, [D]: Total number of Antineoplastic API found in 2016 NLEM in Thailand for reimbursement under three health insurance schemes

while the patient access of only 50% was observed. Nevertheless, drug access (in terms of market and patient access) in Thailand represented in all 5 pharmacological groups according to the WHO's ATC classification system but varied in percentages [Table 3].

Thiotepa is no longer used as an Alkylating Agent. If thiotepa was to be excluded, 100% market access would be reported in the 4 pharmacological groups except for 80% in other antineoplastic agents. Other antineoplastic agents mostly included innovative drugs (targeted cancer therapies), except carboplatin and cisplatin. During the study period, 2 APIs, trastuzumab emtansine and palbociclib were not included, as they were under the regulatory review and expected to be approved soon in Thailand. Once these 2 APIs were to be approved, that would have resulted in 100% market access for the pharmacological group of Other Antineoplastic Agents.

Under NLEM categories, the antineoplastic drugs for breast cancer were listed as Categories C, D, and E2 only. Reportedly, patient access per pharmacological groups were 100% in alkylating agents, 75% for antimetabolites, 75% for plant alkaloids and other natural products, 20% for cytotoxic antibiotics and related substances, and 38% for other antineoplastic agents. All of these 5 groups are of primary treatments for patients according to their fulfillment to the NLEM criteria. Interestingly within the pharmacological group of other antineoplastic agents, patient access to the innovative drug (trastuzumab), was only 12.5% (1/8).

Lung Cancer

Of the 28 APIs for treating lung cancer [Table 4], the market access in Thailand was 79% (22/28); while the patient access was only 55% (12/22). Similar to breast cancer, the patient could access all five pharmacological groups but varied in percentages.

Excluding chlormethine (not commonly used as an alkylating agent), 100% market access was observed in 4 pharmacological groups except other antineoplastic agents (67% market access). If newer innovative drugs (necitumumab, nivolumab, pembrolizumab ramucirumab, and ceritinib) were not in other antineoplastic agents, 100% market access would otherwise be claimed for treating lung cancer.

As per patient access, similar pattern as breast cancer was observed; high percentage of accessibility for older drugs in pharmacological groups such as alkylating agents (100%), cytotoxic antibiotics and related substances (100%), plant alkaloids and other natural products (83%), and antimetabolites (67%). Only 20% of patient access was other antineoplastic agents. However, if excluding older APIs such as carboplatin and cisplatin, the patient access to new innovative APIs would have been 0%.

Colorectal Cancer

For colorectal cancer [Table 5], only 2 pharmacological groups (antimetabolites and other antineoplastic agents) were found. Of the 12 APIs for treating colorectal cancer, market access was 75% (9/12) in Thailand and 33% (3/9) for patient access.

Market access was 75% in antimetabolites and other antineoplastic agents. As panitumumab and ramucirumab were soon to be granted approvals (MAAs) in Thailand, till then the market access would be 100% for other antineoplastic agents. However, patient access is low for both pharmacological groups especially other antineoplastic agents (about 17%). Although new innovative drugs were accessible in Thailand, only oxaliplatin was listed in the NLEM.

Table 3: Drug access to treating breast cancer in Thailand by the number of active pharmaceutical ingredient

Pharmacological groups and API name	Number of API for breast cancer			Number of pharmaceutical company in Thailand
	Approval worldwide (%)	Approval in Thailand (%)	Approval category in 2016 NLEM (%)	
Alkylating Agents: *n* (%)	2 (100)	1 (50)	1 (100)	-
L01AA				
Cyclophosphamide	✓	✓	C	4
Thiotepa	✓	-	-	-
Antimetabolites: *n* (%)	4 (100)	4 (100)	3 (75)	-
L01BA				
Methotrexate	✓	✓	C	21
L01BC				
Capecitabine	✓	✓	D	3
Fluorouracil	✓	✓	C	6
Gemcitabine	✓	✓	-*	18
Plant alkaloids and other natural products: *n* (%)	4 (100)	4 (100)	3 (75)	-
L01CA				
Vinblastine	✓	✓	C	1
Vinorelbine	✓	✓	-	3
L01CD				
Docetaxel	✓	✓	E2	10
Paclitaxel	✓	✓	D	18
Cytotoxic antibiotics and related substances: *n* (%)	5 (100)	5 (100)	1 (20)	-
L01DB				
Doxorubicin	✓	✓	C	11
Epirubicin	✓	✓	-	2
Mitoxantrone	✓	✓	-*	2
L01DC				
Ixabepilone	✓	✓	-	1
Mitomycin	✓	✓	-*	3
Other antineoplastic agents: *n* (%)	10 (100)	8 (80)	3 (37.5)	-
L01XA				
Carboplatin	✓	✓	C	12
Cisplatin	✓	✓	C	11
L01XC				
Bevacizumab	✓	✓	-	1
Pertuzumab	✓	✓	-	1
Trastuzumab	✓	✓	E2	1
Trastuzumab emtansine	✓	-	-	-
L01XE				
Everolimus	✓	✓	-	1
Lapatinib	✓	✓	-	1
Palbociclib	✓	-	-	-

(Contd...)

Table 3: *(Continued)*

Pharmacological groups and API name	Number of API for breast cancer			Number of pharmaceutical company in Thailand
	Approval worldwide (%)	Approval in Thailand (%)	Approval category in 2016 NLEM (%)	
L01XX				
Eribulin	✓	✓	-	1
Total APIs: N (%)	25 (100)	22 (88)	11 (50)	-

*Active pharmaceutical ingredient (API) is available in 2016 NLEM (National list of Essential Medicines – Thailand), but not recommended to use for this cancer type, C: Category C, D: Category D, and E2: Category E2, ✓: Available, - : Not applicable

DISCUSSIONS AND CONCLUSIONS

Apparently, market access of antineoplastic drugs to Thai market was considered high, and the trend is likely to increase in the future due to the drive of market growth and global trend. One other factor that potentially affects market access is the lapse between the MAA of a particular drug in the reference/original country and the MAA in Thailand, the impact of such elapsed time will be a subject of future study.

Many pharmaceutical companies have keen interest to register their drug products in Thailand because of: (1) Low cost for drug registration compared to other countries and (2) A life-long MAA (no expiry date). Therefore, after innovative drugs receive their first MAAs in one country, the products are very likely planned to be registered in Thailand especially those from USA, EU, Australia, Canada, etc. Cost of drug registration in Thailand is soon to be increased. Such increase in cost, although considered low, could not have been foreseen to adversely affect Thailand's market access for antineoplastic drugs.

Patient access was trending toward lower than market access, especially for the innovative drugs such as targeted cell therapy, which possesses low side effects and provides a better quality of life to the patient. Antineoplastic drugs were found in NLEM under Categories C, D, and E2 only; the majority of which were in Category C (standard drug for treating cancers). Few antineoplastic APIs were in Category D (which is for treating an advanced stage of cancer), and even fewer were in Category E2 (which intended to control the use of an innovative drug or high-cost medicine). In the case of these high-cost medicines, it is unlikely that a pharmacoeconomic analysis of the high cost, innovative drugs could demonstrate cost-effective or cost saving, which could have resulted in lower patient access.

Based on the government policy, the E2 Access Program, which aims to improve clinical outcomes and drug affordability,[14] may facilitate increasing innovative cancer drug in Category E2. However, drugs listed in Category E2 are of limited use based on the criteria/requirements stipulated in the NLEM. As long as the drug is monopolized by a single company, drug price would not easily be reduced given that no competitor exists. Therefore, the patient access to cancer drugs is unlikely to be altered without proactive approach on pricing (e.g., negotiation by the main payer).

Mostly, the MAAs for each API were held by more than one single company. Therefore, as listed in the NLEM, the chance to monopolize the selling of the API by a single company would be very rare, except trastuzumab and vinblastine. Trastuzumab (Targeted cell therapies) was recommended by NCI (US), American Cancer Society and Cancer Research UK for treating breast cancer. Therefore, trastuzumab was deemed necessary and effective to be listed in the NLEM under Category E2 with price negotiated by government. Vinblastine, on the other hand, was classified as an orphan drug in Thailand.

MAAs for docetaxel were granted for 10 pharmaceutical companies; thus, price competition has been enjoyed accordingly. Therefore, Category D (rather than the currently assigned Category E2) should be warranted to docetaxel to improve the patient accessibility to this drug.

Although some antineoplastic drugs were listed in the NLEM, the limitation of use as per the NLEM conditions has hindered patient access. For an example, gemcitabine (for metastatic breast cancer) was granted MAAs to 18 companies, and also existed on the NLEM list, but gemcitabine was not recommended for treating breast cancer according to the condition stipulated by the NLEM. If prescribed by a physician, reimbursement for gemcitabine would not be fulfilled. More APIs for antineoplastic drugs should be added to the NLEM such that patient access can be enhanced. One avenue to increase the number of drugs in NLEM and to also share the burden of drug cost (when not fully meeting the prescribing conditions according to NLEM requirements) was to impose copayment as an option for Thai patients to access antineoplastic drugs in the future.

To our knowledge, this was the first study to systemically examine the findings of the cancer drug accessibility in Thailand in terms of both market access and patient access, where the following were discovered: the information about cancer drug access in Thailand was rather sparse, and the study aspired to raise such awareness; drug access among the top 3 cancer types (breast, colorectal and lung cancer) was presented by pharmacological classes with patient access around 50% or lower despite relatively high market access 75% or higher; and, the numbers of the pharmaceutical companies in Thailand granted MAA for each API were revealed, which in turn reflected competition and consequently drug price. Although this study was mainly focused on examining the numbers of APIs, access to cancer drug is matter-of-factly complex. It is well recognized that the cancer drug access could potentially be influenced by other factors, for instance, price (particularly in the situation of little or no competition among

Table 4: Drug access to treating lung cancer (NSCLC and SMLL) in Thailand by number of active pharmaceutical ingredient

Pharmacological groups and API name	Number of API for lung cancer (NSCLC & SMLL)			Number of pharmaceutical company in Thailand
	Approval worldwide	Approval in Thailand	Approval category in 2016 NLEM	
Alkylating agents: n (%)	2 (100)	1 (50)	1 (100)	-
L01AA				
Chlormethine	✓	-	-	-
Cyclophosphamide	✓	✓	C	4
Antimetabolites: n (%)	3 (100)	3 (100)	2 (66.67)	-
L01BA				
Methotrexate	✓	✓	C	21
Pemetrexed	✓	✓	-	3
L01BC				
Gemcitabine	✓	✓	D	18
Plant alkaloids and other natural Products: n (%)	6 (100)	6 (100)	5 (83.33)	-
L01CA				
Vinorelbine	✓	✓	-	3
Vinblastine	✓	✓	C	1
Vincristine	✓	✓	C	6
L01CB				
Etoposide	✓	✓	C	9
L01CD				
Docetaxel	✓	✓	E2	10
Paclitaxel	✓	✓	D	18
Cytotoxic antibiotics and related substances: n (%)	2 (100)	2 (100)	2 (100)	-
L01DB doxorubician	✓	✓	C	11
L01DC mitomycin	✓	✓	D	3
Other antineoplastic agents: n (%)	15 (100)	10 (66.67)	2 (20)	-
L01XA				6
Carboplatin	✓	✓	C	12
Cisplatin	✓	✓	C	11
L01XC				
Bevacizumab	✓	✓	-	1
Necitumumab	✓	-	-	-
Nivolumab	✓	-	-	-
Pembrolizumab	✓	-	-	-
Ramucirumab	✓	-	-	-
L01XE				
Afatinib	✓	✓	-	1
Ceritinib	✓	-	-	
Crizotinib	✓	✓	-	1
Erlotinib	✓	✓	-	1
Everolimus	✓	✓	-	1
Gefitinib	✓	✓	-	1
L01XX				
Irinotecan	✓	✓	-	13
Topotecan	✓	✓	-	2
Total APIs: N (%)	28 (100%)	22 (78.57)	12 (54.55)	-

API: Active pharmaceutical ingredient, C: Category C of NLEM, D: Category D of NLEM, and E2: Category E2 of NLEM, ✓: Available, - : Not applicable

Table 5: Drug access to treating colorectal cancer in Thailand by number of active pharmaceutical ingredient

Pharmacological groups and API name	Number of API for colorectal cancer			Number of pharmaceutical company in Thailand
	Approval worldwide (%)	Approval in Thailand (%)	Approval category in 2016 NLEM (%)	
Antimetabolites: n (%)	4 (100)	3 (75)	2 (66.66)	-
L01BC				
Capecitabine	✓	✓	-*	3
Fluorouracil	✓	✓	C	6
Tegafur+Uracil	✓	✓	D	2
Trifluridine+Tiparacil	✓	-	-	-
Other antineoplastic agents: n (%)	8 (100)	6 (75)	1 (16.66)	-
L01XA				
Oxaliplatin	✓	✓	D	17
L01XC				
Bevacizumab	✓	✓	-	1
Cetuximab	✓	✓	-	1
Panitumumab	✓	-	-	-
Ramucirumab	✓	-	-	-
L01XE				
Regorafenib	✓	✓	-	1
L01XX				
Aflibercept (ZIV)	✓	✓	-	1
Irinotecan	✓	✓	-	13
Total APIs: N (%)	12 (100)	9 (75)	3 (33.33)	-

*: Active pharmaceutical ingredient (API) is available in 2016 NLEM (National list of Essential Medicine - Thailand), but not recommended to use for this cancer type, C: Category C, D: Category D, and E2: Category E2, ✓: Available, - : Not applicable

the pharmaceutical companies), drug registration regulations (entries of generic drugs to increase competition) and time lag to access of cancer medicines (from completed R&D of drug to MAA or from MAA to reimbursement decision). Thorough understanding of such factors is in dire need, and ultimately patient access could be enhanced.

Consequently, the healthcare policy should incentivize competition in drug access such that, for instance, increase in entries of generic drugs; enlist more APIs in the same pharmacological class, if generic unavailable; and revise NLEM and reimbursement processes to be more up-to-date given that information on cancer treatment is rapidly evolving.

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