Cetuximab is provided for mCRC patients with positive KRAS wild type, and also head and neck cancer patients as indicated in the Indonesian National Drug Formulary. However, currently, it is also used for indications not specified in the National Drug Formulary.

Adding cetuximab to chemotherapy for mCRC is unlikely to offer “good value for money” in Indonesia. Furthermore, there are meager benefit, in terms of life years gained.

With regards to affordability, government requires a lot of money to provide cetuximab as an adjuvant therapy for mCRC patients. There should be a careful consideration whether cetuximab remains on benefit package in national health insurance scheme.

More than half of cetuximab prescriptions do not follow National Drug Formulary:

- Appropriate use of cetuximab: 45%
- Inappropriate use of cetuximab: 55%
There are currently 8,000 patients with colorectal cancer in Indonesia, of which 12% are at metastatic stage. If left untreated, only 25% of patients with advanced disease survive in 2-year time.

The main treatment of mCRC remains the use of standard chemotherapy, i.e. 5-fluorouracil, leucovorin, combined with irinotecan (FOLFIRI) or oxaliplatin (FOLFOX). The National Drug Formulary indicates that cetuximab should be used in combination with standard chemotherapy for mCRC patients with positive KRAS wild type and for patients with head and neck cancer. However, in practice, cetuximab is used for the indications other than those stated in the National Drug Formulary. Total claims data from Badan Penyelenggara Jaminan Sosial Kesehatan (BPJS, the healthcare payer) shows an enormous economic burden up to 140 billion IDR or over 1 million USD from 2014 until mid of 2017.

The Indonesian HTA Committee commissioned University of Indonesia to assess the clinical effectiveness and economic evaluation of adding cetuximab to the standard chemotherapy for mCRC patients with KRAS wild type. Our study aims to assess whether the cost of cetuximab outweighs the benefit for mCRC treatment and to understand the utilization pattern of this drug among the study sites.

The following interventions were compared: 1) FOLFIRI; 2) FOLFOX; 3) cetuximab plus FOLFIRI; and 4) cetuximab plus FOLFOX. A Markov model was constructed to estimate the cost-utility of the interventions from societal perspective and budget impact from payer perspective. The life-time cost for adding cetuximab to standard chemotherapy requires 300 million IDR more than chemotherapy alone while it improves the patient’s quality adjusted life years (QALY) for 2.3 months. Compared to FOLFIRI alone, the incremental cost-effectiveness ratio (ICER) of FOLFOX alone is around 700 million IDR per QALY gained while cetuximab plus FOLFOX yields 1.8 billion IDR per QALY and cetuximab plus FOLFIRI generates 3 billion IDR per QALY.
Effect of cetuximab price reduction towards ICER

At the threshold of 3 gross domestic products (GDP), i.e. IDR 140 million, it was shown that the current price of cetuximab, i.e. 3.7 million IDR per vial is not cost-effective. Even when the price is reduced to 80% of the original price or less, the ICER remains far above the threshold value.

Budget impact of adding cetuximab for mCRC treatment

The budget impact analysis compares between two scenarios, i.e. with cetuximab (50% of patients use it with FOLFOX and 50% with FOLFIRI), and without cetuximab (50% of patients use FOLFOX and 50% use FOLFIRI). If cetuximab is removed from the benefits package, about 0.7 trillion IDR would potentially be saved.

Utilization pattern

Based on the data from BPJS and hospital information system, it was found cetuximab was mainly used for mCRC patients, head and neck cancer, and nasopharyngeal cancer. Among our study sites, around 45% of cetuximab use is for indications not specified in the National Drug Formulary. We try to extrapolate this number using data claims for cetuximab use. The National Health Insurance (JKN) would be able to save approximately 25 billion IDR per year if cetuximab was used according to the indications stated in National Drug Formulary.
Policy Recommendations

- Since the current practice on the use of cetuximab is not fully compliant with the national regulation, BPJS together with the Ministry of Health should regularly monitor the use and prescription of cetuximab. A rigid verification system should be developed to regulate the use of cetuximab.

- The addition of cetuximab on the chemotherapy for mCRC patients with KRAS wild type in the benefit package should be re-considered.

- The potential savings from excluding cetuximab from the benefit package could be re-allocated to other health measures, e.g. colorectal cancer screening program, which would promote early diagnosis of colorectal cancer, so less patients would transition into an advanced stage.

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Authors, investigators and co-investigators

1. Amila Megraini¹
2. Septiara Putri¹
3. Ery Setiawan²
4. Levina Chandra Khoe³
5. Siti Rizny F. Saldi⁴
6. Vety Yulianty⁵
7. Ryan R. Nugraha²

¹ Faculty of Public Health, University of Indonesia
² Center for Health Economics and Policy Studies, University of Indonesia
³ Faculty of Medicine, University of Indonesia
⁴ Clinical Epidemiology and Evidence-Based Medicine, Cipto Mangunkusumo Hospital/University of Indonesia
⁵ Center for Health Economics and Policy Studies, University of Indonesia

Contact

1. Ery Setiawan: setiawan.ery@cheps.or.id
2. Levina Chandra Khoe: levina.chandra01@ui.ac.id
3. Manushi Sharma: manushi.s@hitap.net

For more information on this study, please go to www.globalhitap.net/projects/idsi-indonesia