OHTAC Recommendation

Emerging Pharmacogenomic Tests

Presented to the Ontario Health Technology Advisory Committee in August, 2010

June 2011

OHTAC Ontario Health Technology Advisory Committee

Issue Background

As part of the Provincial Pharmacogenomics Expert Panel (PEPP), two subgroup committees were established to determine a preliminary list of emerging pharmacogenetic tests and scan the pharmacogenetic /horizon to recommend priorities for health technology assessment (HTA) from specialties outside of oncology.

Objective

The objectives of the subgroup committees were to provide recommendations to PEPP on the following:

1. scan the horizon regarding pharmacogenetic tests to be considered in the province of Ontario
2. identification of potential oncology biomarkers in the imminent phase
3. creation of a potential priority list of pharmacogenomic tests outside of oncology which are ready for HTA evaluation

Methods

The two subcommittees were formed by the chair of PEPP. Each committee was chaired by a core member of the PEPP. Additional members were added to the committees by the chairs to represent a range of therapeutic areas and expertise. The subcommittees met twice over the course of a month and then met jointly for a third meeting.

Priorities for HTA Evaluation (other specialities)

The first three evidence-based reviews undertaken by the Medical Advisory Secretariat (MAS) focused on oncology pharmacogenomic tests (insert weblinks). The subgroup committee formed through PEPP was tasked with identifying pharmacogenomic tests in other specialties which are ready for HTA evaluation. In order to come up with a prioritization list, the committee agreed to examine five prioritization criteria which were derived from a systematic review by Noorani HZ et al. in 2007 of various practical and current approaches of HTA priority setting. The prioritization criteria used were Disease Burden, Clinical impact, budget impact, evidence, and ethical, legal or psychosocial implications.

A list of drugs and their associated pharmacogenomic tests were identified by the subgroup committee (table 1). A template was then created for each member to use when presenting for discussion the drugs and the associated pharmacogenomic tests by the Expert Panel (Appendix 1).

Table 1: Drugs Identified for Consideration of Prioritization for HTA Evaluation

Drug	Therapeutic Area
Codeine	Pain Management
Abacavir	HIV
Carbamazepine	Epilepsy
Isoniazid (INH)	Tuberculosis
Warfarin	Cardiovascular Disease
Azathioprine	Thiopurine drugs
Clopidogrel	Cardiovascular Disease

Paediatric Drugs	
TPMT	IBD
PPI	GERD
Codeine	Adenotonsillectomy
Carbamazepine	Epilepsy

IBD: Inflammatory bowel disease; GERD: Gastroesophageal reflux disease; TPMT: Thiopurine methyltransferase; PPI: Proton-pump inhibitors

Based on the criteria developed for each of the tests, the committee concluded that Carbamazepine, Warfarin, Abacavir and Azathioprine were considered ready for HTA evaluation. Isoniazid (INH), Codeine and Allopurinol were not deemed to warrant examination at this time. Pharmacogenetic tests associates with clopidogrel and statins were identified as potential tests that could be examined when more evidence becomes available.

Emerging Pharmacogenetic Tests

The subgroup committee formed through PEPP was tasked with identifying oncology biomarkers which are considered emerging markers for pharmacogenetic testing. They were also asked to recommend steps needed for future identification of emerging markers and their associated pharmacogenetic tests by the province of Ontario. A quick scan of the literature was completed to identify the state of horizon scanning for pharmacogenomics. Five horizon scanning systems were identified (Table 2).

Table 2: Horizon Scanning Systems for Pharmacogenomic Tests

Horizon Scanning System	Method	Includes PGx Tests
UK National horizon Scanning Centre (NHSC)	• New & emerging technology briefings • Specific program for "Gene-based diagnosis and therapy"	YES
EuroScan	• Technology search	YES
The Canadian Health Technology Agency (CADTH)	• Environmental scanning service	YES
Australia and New Zealand Horizon Scanning Network (ANZHSN)	• Horizon Scanning Program	?
Evaluation of Genomic Applications in Practice and Prevention (EGAPP)	• Topic Identification • Specific to genetic tests	YES

PGx: Pharmacogenomic

As indicated above, a number of organizations carry out horizon scanning efforts, typically HTA agencies. Few horizon scanning systems however are designed specifically for pharmacogenomic tests.

The committee then developed a list of oncology biomarkers which are considered in the horizon scanning phase (table 3 & 4).

Table 3: A Selection of Oncology Biomarkers Identified in the Horizon Scanning Phase

Drug	Therapeutic Area
HER2 amplicfication/trastuzumab	Gastric cancer
B-Raf mutations/B-Raf inhibitors	Melanoma
BRCA 1 and 2	Ovarian Cancer
ALK mutation/ ALK inhibitors	Lung cancer, Neuroblastoma

Table 4: A Selection of Oncology Biomarkers Identified in the Horizon Scanning Phase

Drug	Therapeutic Area
HPV or p16	Head and Neck Cancer
IDH-1 and IDH-2 mutations	Glioma
Flt-3 mutation	AML
TMPRSS2: ERG gene fusion	Prostate Cancer
Numerous leukemia (ALL/AML)	Ongoing – in phase III
T(2;13) or t(1:13) [Pax3/Pax7-FKHR]	Alveolar rhabdomyosarcoma
T(11;22) [EWS-Fli1] and variant translocations	Ewing sarcoma
PTEN	Prostate cancer
N-myc amplification	Neuroblastoma

Table 3 presents a selection of biomarkers that are likely to put a pressure on the health care system more immediately than those biomarkers listed in Table 4.

Recommendations to PEPP

The following recommendations were made by the two subgroup committees.

1. Identify who will be doing horizon scanning for pharmacogenomic tests in the province
2. Identify of sources for proactive horizon scanning and validate by experts on a 6 month basis (include Cancer Care Ontario Disease Site Groups)
3. Define scope of horizon scanning timeframe
4. Assess what technologies/ tests/ instruments are currently being used by centres and what they think they will be doing in the future
5. Decide on the threshold of minimum evidence needed to move biomarkers from horizon scanning phase to prioritization for a full HTA

OHTAC Recommendation

- Based on expert opinion the following tests will present a real pressure to the health care system in the next 12 months. Therefore, OHTAC urges that provincial capacity to conduct evidence-based analyses be identified and secured as soon as possible.

1. Pharmacogenomic testing for Warfarin
2. Pharmacogenomic testing for Carbamazepine
3. Pharmacogenomic testing for Abacavir
4. Pharmacogenomic testing for Azathioprine
5. Pharmacogenomic testing for HER-2 /neu in Gastric Cancer
6. Pharmacogenomic testing for B-Raf mutations/B-Raf inhibitors in Melanoma
7. Pharmacogenomic testing for BRCA 1 and 2 in Ovarian Cancer
8. Pharmacogenomic testing for ALK mutation/ ALK inhibitors in Lung Cancer and Neuroblastoma

Note: Tests 1-4 include paediatrics and Azathioprine includes paediatrics for Inflammatory Bowel Disease (IBD)

- OHTAC supports the PEPP Recommendation that there is a need in Ontario for a mechanism to be established to identify and determine which pharmacogenetic tests are emerging and to ensure that these are assessed and prioritized for health technology assessment appropriately.

References:

Noorani HZ, Husereau DR, Boudreau R. Priority setting for health technology assessments: A systematic review of current practical approaches. International Journal of Technology Assessment in Health Care, 23:3 (2007), 310–315.

APPENDIX 1

Template for Prioritization of Drugs and their Associated Pharmacogenomic Tests

Criteria	ON Population	Comments	References
Disease Burden			
Prevalence/Incidence			
# of people taking drug			
% of people who are expected to have a clinically significant reduction in drug response (i.e.% UMs, IMs, PMs*)	= x # Ontarians		
% of people expected to have an ADR	= x # Ontarians		
Clinical Impact			
Effect of variant on clinical response (partial or complete loss of effectiveness)			
ADR life-threatening or causes life-long disability	Yes/No/n/a		
Estimated impact and burden for the ADR in terms of severity of the reaction	High/moderate/low n/a		
Budget Impact			
Cost of test x # of people eligible for test			
Evidence			
Availability of recent HTA* reports, systematic reviews or economic analyses by HTA or similar agencies on this topic?	Yes/No		
Availability of studies evaluating the clinical utility or validity of test?	Yes/No		
Ethical, legal, or psychosocial implications			
Ethical, legal, or psychosocial implications associated with the use of this technology for the given clinical condition			