June 19, 2011

Diane McArthur
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Ontario Ministry of Health and Long-Term Care
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Dear Diane McArthur

I am pleased to submit another report from your Citizens' Council, this one representing the outcome of Council deliberations that took place in Toronto during the weekend of April 15th through17th, 2011.

The Council was particularly pleased that the Ministry accepted the recommendations regarding the Management of the Drug Formulary in its report following the 2010 meeting.

Specifically, those recommendations were

"The Ministry should raise awareness of its policies and procedures for approving and adding new drugs to the Formulary and removing those no longer found to be effective; these explanations should be aimed not only at those suffering from rare diseases, but also directed to the public at large."
(Recommendation 10)

"The Ministry should develop a transparent and periodic and systematic review for removing from the Formulary drugs that are no longer found to be effective."
(Recommendation 16)

You responded to those Recommendations by asking the Council to meet again and to consider the following question - ***"... under what conditions or situations should the Executive Officer consider delisting or limiting the use of drug products on the Ontario Formulary?"***

The Council approached the subject in general terms by first studying three cases in specific terms -

1. The Harm/Benefit Ratio: The Example of Avandia.
2. The Cost/Benefit Ratio: The Example of Diabetes Test Strips.
3. When is Enough Enough? The Example of Me Too Drugs.

A REPORT OF THE ONTARIO CITIZENS' COUNCIL

MANAGING THE DRUG FORMULARY

Submitted to:

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June 19, 2011

Submitted by:

Gerri Gershon, Chair
ONTARIO CITIZENS' COUNCIL

TABLE OF CONTENTS

APPENDICES

RELEVANT WEBSITES

For information about the Citizens' Council, including its Terms of Reference and its members, click here or see www.health.gov.on.ca/en/public/programs/drugs/councils/citizens_council.aspx

For information about how drugs are approved in Ontario, click here or see www.health.gov.on.ca/english/providers/program/drugs/how_drugs_approv/how_drugs_approv.html

For a glossary of terms related to Ontario Public Drug Programs, click here or see www.health.gov.on.ca/english/providers/program/drugs/dr_glossary/opdp_glossary.pdf

For information about the Ontario Drug Benefit Program, click here or see www.health.gov.on.ca/en/public/programs/drugs/funded drug/

For information about the Committee to Evaluate Drugs, click here or see www.health.gov.on.ca/english/providers/program/drugs/how_drugs_approv/funding_ced.html

EXECUTIVE SUMMARY

The Ontario Citizens' Council is mandated to provide advice to the Executive Officer of the Ontario Public Drug Programs on the values that reflect the needs, culture and attitudes of Ontario's citizens about government drug policy.

At its April 2011 meeting, the Council was asked to provide advice on the values that should influence the management of the Ontario Drug Benefit Formulary (ODBF).

Through presentations by experts and through facilitated discussions, Council members reiterated the values they had identified in previous meetings, added additional values and, based on those values, set out ten recommendations intended to assist the Ministry in more effectively managing the Formulary.

Overall, recommendations relate to:

- The need for a systematic review of all drugs on the Formulary and the need for drug manufacturers to share in the cost of such a review
- The need to respond quickly to concern over unexpected adverse effects or accumulated evidence of harm
- Concern for the impacts changes to the Formulary may have on patients
- Responsibility for drug manufacturers to provide complete and comprehensive information in their application to list drugs, as well as on an ongoing basis after listing
- Accountability and cost-effectiveness of the OPDP

RECOMMENDATION 1

The Executive Officer should develop and implement a systematic process for periodic review of all drugs on the Formulary with clear timelines and milestones.

RECOMMENDATION 2

To assist with the ongoing costs of a systematic review process, an arms-length fund or levy should be created, paid for by drug manufacturers.

RECOMMENDATION 3

Drugs found to be harmful should be delisted (removed from the Formulary) immediately.

RECOMMENDATION 4

The implementation of a delisting decision must be preceded by an appropriate notice period and adequate education of health professionals, patients and the general public.

RECOMMENDATION 5

The contractual agreement required for listing a drug in the Formulary should include a commitment from the manufacturer to give adequate notice before ceasing production or distribution of the drug in Ontario.

RECOMMENDATION 6

If for clinical reasons a patient cannot benefit from an alternative drug after delisting of a harmful drug, he/she could remain eligible for funding of the delisted drug under the Exceptional Access Program (EAP).

RECOMMENDATION 7

Any new listing agreements should require full disclosure by the manufacturer of all trial results (positive and negative) related to the use of that drug.

RECOMMENDATION 8

In cases where the effectiveness of a drug or self-monitoring device varies with the severity of symptoms, strategic adaptation of the limited-use/exceptional access categories should be considered.

RECOMMENDATION 9

The Ministry of Health and Long-Term Care should open discussions with Health Canada specifically about the manner in which it discharges its approval authority and its responsibility for prompt advisories on problematic drugs.

RECOMMENDATION 10

Council should, in future sessions, consider other issues related to updating and modernizing the Ontario Drug Benefit Formulary.

The discussion of the Council was rich and substantive. The Council offers its recommendations to the Executive Officer as ways to update the Ontario Drug Benefit Formulary. It also suggests that the Ontario Public Drug Programs itself present any forthcoming changes to the Formulary as important ways to modernize and streamline the Formulary to better serve the people of Ontario and in so doing, make it more efficient and effective.

1.0 THE QUESTION

The Report issued by the Citizens' Council following its session on Drugs for Rare Diseases[1] contained a strong recommendation to examine the underlying policies and procedures followed by the Ministry in the listing and delisting of drugs on the Ontario Drug Benefit Formulary (the Formulary). The Ministry accepted that recommendation. Accordingly, for the April 2011 meeting, the Ministry asked the Citizens' Council to consider one aspect of 'Managing the Drug Formulary'.

The Assistant Deputy Minister and Executive Officer for the Ontario Public Drug Programs is the Provincial official who ultimately makes the decision to list or delist (remove) a drug or drug product on the Formulary for the Ontario Public Drug Programs. She posed the following question for the Council's consideration:

Under what conditions or situations should the Executive Officer of the Ontario Public Drug Programs consider delisting or limiting the use of drug products on the Ontario Formulary?

In its deliberations on this question, the Council was asked to identify the values that should be taken into account as decisions are being made to remove drugs from the Formulary.

Many of the problems in managing the Formulary are created by factors beyond the Ministry's control. An aging population, including a large number of baby boomers, has resulted in a major demographic shift. People are also living longer. The majority of people now using drugs funded by the Ontario government are seniors. A pervasive flow of pharmaceutical information – not always accurate or credible – has raised the public's expectations to such a degree that Ontario's Health Care system and its drug programs, although among the best in the world, are straining the province's financial resources to an unprecedented and barely sustainable level.

The Ontario Public Drug Programs currently has a budget of $4.3 billion, or over 10% of total health care spending in Ontario. Health care in Ontario accounts for approximately 50% of the overall provincial budget. The compelling image of a suitcase with limited capacity is a metaphor for the provincial drug budget (and for the health care budget in general). There are few options available to address the pressure to increase the size of the suitcase: raise taxes, decrease spending on other initiatives such as education or social services, or work to free up space in the suitcase by taking things out and/or packing better.

There is clearly some urgency concerning the problem of managing a Formulary that includes more than three thousand drugs, with new additions being proposed on a regular basis. Currently, there is no systematic process for removing drugs from the Formulary. This happens only rarely and primarily on the grounds of safety. However, having clear reasons for removing drugs from the Formulary could be an important management strategy.

[1] http://www.health.gov.on.ca/en/public/programs/drugs/councils/reports.aspx

2.0 PREPARING FOR DELIBERATIONS

In order for the Council to respond to the question posed by the Executive Officer, it was necessary for the members to understand the environment in which the Formulary management presently operates.

The Council was provided in advance with a range of background material, including scientific and media reports. At the session itself, there were presentations from physicians, economists and pharmacists on relevant topics such as

- Managing the Formulary
- The concept of harm and benefit related to the Formulary
- 'Me too' drugs
- Arguments in favour of removing drugs from the Formulary
- Arguments that a wide range of options should be available in the management of the Formulary.

See Appendix 2 for the session agenda, which includes the names of presenters. See Appendix 3 for biographies of presenters. For a glossary of relevant terms, click here or see www.health.gov.on.ca/english/providers/program/drugs/dr_glossary/opdp_glossary.pdf.

The Council also heard from presenters on three case studies that highlight key challenges to the Formulary. These examples were used to help explore considerations potentially relevant to delisting.

1. The Harm/Benefit Ratio: The Example of Avandia

- The purpose of this case study was to examine a situation in which a drug was found, following its listing and use, to have increased health concerns. Avandia, widely used to treat diabetes, was found to increase the risk of congestive heart failure or make it worse in certain high risk patients.

2. The Cost/Benefit Ratio: The Example of Diabetes Test Strips

- The purpose of this case study was to examine a situation in which a drug product, diabetes test strips, is potentially being over-used at considerable cost to the Ontario Public Drug Programs.

3. When Is Enough Enough? 'Me Too' Drugs, the Example of COX2 Inhibitors.

- The purpose of this case study was to consider a situation in which many drugs that are similarly effective – in this case COX2 inhibitors for treatment of hypertension - are all listed on the Formulary, at considerable cost to the overall drug provision and distribution system.

See Appendix 4 for background material on each case study.

3.0 CONSIDERATION OF HOW THE FORMULARY WORKS

3.1 What is the Formulary?

The Ontario Drug Benefit Formulary of the Ontario Public Drug Programs is a list of drugs that are eligible for funding for Ontarians aged 65 and older, residents of long-term care homes and homes for special care, recipients of professional home services and social assistance and beneficiaries of the Trillium Drug Program.

The Formulary provides the interface between the patient and the drug manufacturer. Neither the practicing physician nor the pharmacist can guarantee that a drug will live up to the manufacturer's claims. They all depend upon a Formulary listing to provide that assurance.

Few drugs have ever been removed from the Formulary. Even drugs that are found to be harmful after listing on the Formulary have proved difficult to remove from use.

3.2 What is the Role of Health Canada?

In order for a drug to be listed on the Ontario Drug Benefit Formulary, pharmaceutical companies must first receive approval from Health Canada: http://www.hc-sc.gc.ca/dhp-mps/homologation-licensing/system/map-carte/index-eng.php

A manufacturer must submit a Clinical Trial Application (CTA) for authorization to conduct a clinical trial in Canada and prepare a New Drug Submission (NDS) for Health Canada to establish that a drug is safe, efficacious, and of high quality.

Once the marketing of a drug is authorized, Health Canada also conducts surveillance, inspection and investigations. It has regulatory authority during the clinical trial application and the submission review, and it conducts post-market supervision. It also issues advisories: http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2011/index-eng.php

It maintains the Canada Vigilance Program - a post-market surveillance program that collects and assesses reports of suspected adverse reactions to health products, including drugs, marketed in Canada. Through the portal MedEffect, consumers, patients and health professionals can report adverse reactions and obtain updated safety information: http://www.hc-sc.gc.ca/dhp-mps/medeff/index-eng.php

When a drug has been approved by Health Canada for marketing, Ontario has the responsibility of authorizing its distribution in the province and of listing it as eligible for public funding under the Ontario Public Drug Programs.

3.3 What is the Role of the Ontario Ministry of Health and Long-Term Care?

Ontario has a process for reviewing requests for drug funding under the Ontario Drug Benefit (ODB) program. Drug products may be considered for reimbursement by the ODB program under the *Ontario Drug Benefit Act (ODBA)* or the *Drug Interchangeability and Dispensing Fee Act (DIDFA)*, if the manufacturer's submission to the Ministry is complete. All submissions

require a review by the CED (Committee to Evaluate Drugs) as well as a thorough assessment of the scientific and clinical evidence contained in a manufacturer's submission. The CED then makes a recommendation to the Executive Officer of Ontario Public Drug Programs on whether or not the drug should be funded under the ODB program, the New Drug Funding Program for Cancer Care or through the Exceptional Access Program (EAP). The Executive Officer makes the final decision, taking into consideration the CED recommendations and public interest.

The current Formulary of the Ontario Public Drug Programs lists approximately 3300 drugs. http://www.health.gov.on.ca/english/providers/program/drugs/odbf_mn.html

There are three types of listings in the Formulary, in addition to the Exceptional Use Program (EAP): General Benefit, Conditional Listing, and Limited Use.[2]

3.4 How Do Drugs come off the Formulary?

Disinvestment is the process of withdrawing, partially or completely, resources from any existing health practices, procedures, technologies and pharmaceuticals that are deemed to deliver no or low health gain and thus are not an efficient health resource for allocation. As disinvestment applies to the Formulary it is referred to as delisting.

In the past decade only nineteen drugs have been delisted as a result of Government decision. Listing new drugs is a priority; delisting receives scant attention from the Ministry for a variety of reasons, including:

- Whenever the Ministry considers delisting a drug, the affected pharmaceutical company rallies patient support and can sometimes create fear in the general population that a supposedly effective drug will be denied to them.
- Reviewing a drug for delisting is costly and time consuming.
- There is no systematic process for review
- There is no systematic process for collecting ongoing research or assessment of the real-life use of drugs.

On the other hand, drug companies on occasion stop manufacturing a drug because it is not generating sufficient profit - often without notice to patients - effectively delisting that product on their own determination.

4.0 HOW THE COUNCIL DID ITS WORK

With the information provided by the speakers, Council members developed their response to the Executive Officer's question:

[2] http://www.health.gov.on.ca/english/providers/program/drugs/how_drugs_approv/review_types.html

Under what conditions or situations should the Executive Officer consider delisting or limiting the use of drug products on the Ontario Formulary?

The process for discussion of the three case studies was a modified World Café, a process designed to build ideas and understandings, and carry those ideas through three rounds of discussion. See Appendix 4 for an overview of the World Café Process.

The council was divided into three groups and every member was able to choose whether to stay with a case for two or three sessions or rotate through all three sessions. At the end of the first World Café session, some members took fresh concepts and/or interesting ideas into their second group; and similarly into the third discussion group. This meant that everyone would hear from all other Council members over the three "rounds" and might reconsider or alter their view over the course of the process.

Throughout the discussions, several Council members drew on personal experiences to convey to others the importance of access to appropriate drugs/products as well as to full information about them. The personal stories of the members added insights to ideas of risks and benefits. This shed further light on the issues under consideration and provided Council members with additional perspectives.

5.0 THREE CASE STUDIES

5.1 *Case 1 - The Harm/Benefit Ratio: The Example of Avandia*

This case study focused on the situation that arises when harmful effects appear after a drug has been in use in the general population for some time. Avandia is such a drug.

Warnings about Avandia began in May 2007, by the Food and Drug Administration in the United States. Similar information was slower getting out to the Canadian population.

In November 2007, Health Canada announced that access to Avandia would be restricted. In December 2007, a new Canadian study showed that Avandia increased the risk of heart failure, heart attacks and death. A new funding agreement with the manufacturer, GlaxoSmith Kline, followed that study. In June 2009, Avandia's status was changed and it was funded only through the Exceptional Access Program. This agreement also meant that patients who had been approved for the drug up to 12 months prior to the change in listing status would continue to have coverage, with their physician's approval.

HIGHLIGHTS OF THE DISCUSSION

In the discussion of this case, Council members questioned the delay in the Health Canada announcement and wondered whether the lack of information put Ontarians at risk. There was general agreement that dangerous or ineffective drugs should not remain on the Formulary. Council members also felt that a better tracking system is necessary in order to streamline the process of alerting health professionals and the public.

Council members felt that members of the public should have full information from the outset about the possible effects of a drug and have the opportunity to decide if they want to pursue taking it. The Council also felt there would be an advantage in demanding wider testing and full disclosure of results before listing a drug on the Formulary.

Across the three discussion groups, the following points were made:

- MOHLTC has to protect people taking drugs as well as taxpayers who pay for the drugs;
- Full disclosure of all studies, positive and negative, is necessary and should be a statutory requirement when accepting drugs for listing;
- Where there are potential issues (such as adverse side effects), the patient must clearly understand the consequences of taking the drug. There should be informed consent, clearly documented by both physician and patient. It is also important to provide alternative medication for those individuals losing access to a drug that may be effective though potentially dangerous. This would minimize concern and fear in patients;
- Drug companies should help fund reviews of the Formulary (in an arms-length way, to avoid conflict of interest);
- A formal process is needed for listing and delisting, with conditions attached, such as notice for discontinuing distribution and full and transparent disclosure of all study results;
- It is important to find a way to monitor adverse reactions and gather this information in a systematic way, without overburdening the system. Responsibility for this should be shared among patients, doctors and pharmacists;
- It is important to look to best practices in other jurisdictions, to see how they set up their review process of drugs as well as criteria for listing and delisting;
- It is important to safeguard security of individual personal medical information, especially in the documentation of adverse reactions.

5.2 *Case 2 - The Cost/Benefit Ratio: The Example of Diabetes Test Strips*

The issue underlying this case study was a situation in which escalating costs are not necessarily matched by increasing benefits.

Self-monitoring test strips for diabetes are widely used in Ontario. Those who benefit most from their use are people who depend on insulin to control their blood glucose levels. Self-monitoring is very important for newly diagnosed individuals. As their condition becomes better understood and managed, it may be possible to lower their frequency of testing. In some cases, the use of test strips when not medically justified has actually been found to contribute to fear and depression.

Currently, the Formulary places no restrictions on diabetes test strips. The substantial increase

in the cost to OPDP of funding test strips is not due to more cases of diabetes in the population but rather to greater use of the test strips. Some doctors are suggesting that people who are "pre-diabetic" start using the strips, claiming that this helps patients understand and learn from the results and adjust their lifestyles accordingly.

Recent research indicates that people with Type 2 Diabetes could use them less frequently with no appreciable risk to their health, thus providing a considerable cost saving to the Government.

HIGHLIGHTS OF THE DISCUSSION

In their discussions, Council members explored the cost of test strips (approximately seventy cents for each; $2 per day; $730 per year) and felt that the soaring costs of funding test strips are a constant reminder that attention must be paid to limiting access to funding for this particular product.

On the other hand, some members felt that doctors may not be considering the stress and anxiety that testing may cause for some pre-diabetic patients, even though there is little evidence that the test strips are effectively controlling diabetes.

As part of their discussion of options, Council members were informed that there are other methods of testing but these are even more expensive and are not available in all rural areas of Ontario.

Council members also noted the following concerns or problems:

- Patients who use the test strips may not know what to do or may not act upon the test strip information; therefore benefit/improvement will not likely occur.
- The number of test strips needed varies from patient to patient; some patients choose to test once a day, while others may test three times a day.
- Different medical opinions exist as to how often a patient should be tested. There are so many variables that it would be difficult to identify a maximum number of test strips per patient.

Overall, Council members felt that diabetes is a silent illness whose consequences, if untreated, can be extremely serious. This would result in even higher costs to the Ontario health budget. They felt that self-monitoring with test strips can provide a sense of empowerment for the patient, and agreed that it is crucial to keep them on the Formulary while at the same time finding ways to appropriately limit their use.

5.3 *Case 3 - When is Enough Enough?: The Example of 'Me Too' Drugs*

There are a large number of drugs on the Formulary that perform the same function; these are sometimes known as 'me too' drugs. They are structurally (chemically) comparable to already known drugs and have clinical benefits and safety profiles similar to other drugs in the same class. They are a significant reason for the growing number of drugs on the Formulary – with

one expert indicating that up to 70% of new drugs on the Formulary are 'me too' drugs.

There are varying views on the financial impact of 'me too' drugs. Some suggest that they simply replace current drugs and have little net impact on the Formulary budget. Others suggest that the presence of such drugs increases competition and drives prices down. And still others suggest that the marketing of 'me too' drugs - (largely a result of manufacturers' high marketing budgets and the prevalence in the US of direct-to-consumer advertising) - actually increases market demand, resulting in an increase in overall costs.

Some of the debate about the benefits and costs of 'me too' drugs are summarized in the case study document (see Appendix 4).

In this case study, Council members were asked to consider whether the number of these drugs should be limited and, if so, on what basis.

HIGHLIGHTS OF THE DISCUSSION

Council members considered the importance of freedom of choice and of convenience in discussing the availability of many 'me too' drugs on the Formulary.

In most cases, bio-equivalents on the Formulary can easily be substituted. Members were concerned about situations where slight differences in formulae or in stabilizers may cause allergic reactions, or not be tolerated. They were also concerned about regimens which may be less convenient or less comfortable for the patient (e.g. frequency of administering, a requirement to refrain from lying down and to refrain from food and liquids other than water for a period of time). Overall, they felt that it was up to the doctor and patient to come to a decision about which drug was most appropriate.

Members were concerned that delisting a drug may mean it will no longer be produced by the pharmaceutical company; several members agreed that this was an acceptable trade-off in managing the number of 'me too' drugs on the Formulary.

With physicians as busy and pressured as they are to provide good patient care, Council members were concerned that it would be difficult – if some 'me too' drugs are removed from the Formulary - to convince doctors to change their prescription habits. There may be resistance from the medical profession to delisting the brands they are accustomed to prescribing.

Several factors that could be considered in a systematic approach to considering the delisting of 'me too' drugs were agreed to:

- Cost
- Comparable effectiveness
- Frequency of use (perhaps by looking at physicians' prescribing patterns)
- Harm (e.g. allergies to non-medicinal ingredients in the drug)
- Compassion (e.g. the regimen for administrating a different 'me too' drug causing undue

discomfort or inconvenience

- Length of time on Formulary (time since listing)

Members also discussed whether there should be a limit on the number of 'me too' drugs in any classification. There were mixed views on this. The Council agreed that this discussion needed more time for further consideration.

6.0 COUNCIL VIEWS ON RELEVANT SOCIETAL VALUES

Council members reviewed the values and principles that, in January 2010, they agreed should underlie decisions about public funding of drugs for rare diseases. In the current discussion on Formulary management, the Council reaffirmed these values and added several more.

The resulting values and principles that Council members felt needed to be considered in decision-making on Formulary management were:

COMPASSION AND THE IMPORTANCE OF QUALITY OF LIFE

Consideration needs to be given to any undue discomfort and inconvenience that a delisting decision may result in for individual patients.

EQUITY AND FAIRNESS

Equity and fairness do not imply equality.

BALANCE THE COMMON GOOD WITH THE NEEDS OF PARTICULAR INDIVIDUALS

The government has a mandate to serve all citizens, including those with special needs, but it must provide prudent management of available resources for the benefit of all.

FISCAL RESPONSIBILITY

Decisions must be made responsibly. The legislation mandates that dollars be spent wisely.

ACCOUNTABILITY TO TAXPAYERS

The public drug program uses public funds. Taxpayers are entitled to know how those funds are used.

ADVANCING MEDICAL KNOWLEDGE

All observations on the use of a drug become part of the bank of knowledge that can support continuous improvement of treatments and alert the medical community to potential harmful effects of a drug that might only emerge as the drug is used in the real world.

EVIDENCE-BASED DECISIONS

Decisions must be made on a full range of evidence, both positive and negative, including evidence based on ongoing reporting of adverse effects.

PUBLIC SAFETY

Decisions that err on the side of caution need to be taken effectively and in a timely manner when there is emerging evidence that a drug already on the Formulary produces harmful effects.

SHARED RESPONSIBILITY/COLLABORATION

All parties have a role to play in ensuring the ongoing viability and effectiveness of the Formulary system[3], particularly in building and providing up-to-date and balanced information related to the risks and benefits of Formulary drugs. Governments and manufacturers also have a responsibility for sharing the financial costs of reviewing drugs after the drugs have been listed, to ensure that information is kept relevant and up-to-date.

INFORMED PUBLIC

It is essential that members of the public, patients and medical professionals have the information they need to make informed decisions about taking a drug, staying on a drug or discontinuing its use.

TRANSPARENCY

The decision-making process for both listing and delisting drugs must be fully transparent. Full disclosure of all research findings is essential. There must be a transparent plan for removing drugs from the Formulary if they are found to be harmful or ineffective.

7.0 COUNCIL RESPONSES TO THE EXECUTIVE OFFICER'S QUESTION

7.1 *There Is A Need To "Right-Size" The Formulary*

Ontario legislation stipulates that drug funding decisions be based on the best clinical and economic evidence available and that the decisions ensure that taxpayers' dollars are spent wisely. Council members respect the freedom of choice of both patients and health professionals, as well as the values of fiscal responsibility, accountability to taxpayers and achieving balance between the common good and the needs of individuals.

Members agreed that efficacy, safety and cost-effectiveness are the most important criteria for listing drugs on the Formulary. New drugs are constantly being developed but the Formulary cannot continue to grow without due regard to the overall budget of Ontario.

The Citizens' Council unanimously agreed that there is a need to "right size" the Formulary and to manage the number of drugs more effectively. It sees the need for a formal process, with time lines and milestones, to systematically review drugs on the Formulary.

The Council recommends negotiation of contractual agreements with pharmaceutical companies prior to listing a drug, providing commitment to full disclosure of all clinical trials,

[3] The Council defined parties broadly to include the federal and provincial governments, drug companies, and medical professionals (including pharmacists).

submission to periodic reviews throughout the period of use of the drug (the possibility of delisting based on the results of such reviews), and adequate notice if the drug's production or distribution will be discontinued or interrupted. It further recommends that pharmaceutical companies share the cost of such reviews. The Council also discussed the possibility of a fee system for listing a drug, although this would have to contain a procedure that would remove any perceived conflict of interest.

The Council supports the immediate delisting of drugs for which harmful effects are clinically proven during use in the general population. It also suggests that consideration be given to retaining the use of such drugs where needed, provided there is an appropriate professional recommendation as well as informed consent on the part of the patient.

For purposes of fiscal responsibility and accountability to tax payers, the Council supports in principle the approach of limiting the number of 'me too' drugs on the Formulary, though it would prefer to discuss this issue further before finalizing a position. There should also be more discussion on strengthening the policies and procedures for adding drugs to the Formulary.

The Council also recognized that some of its discussions may relate to Health Canada's roles and responsibilities in light of overlapping jurisdictions, and suggests that the MOHLTC open relevant discussions with Health Canada where appropriate.

7.2 Recommendations

The following recommendations are grounded in the values set out above and reflect the Citizens' Council deliberations. These recommendations emerged from discussion of the case studies and related matters, with the Council working to craft advice that can also be applied to better managing the Formulary.

Overall, recommendations relate to:

- The need for a systematic review of all drugs on the Formulary and the need for drug manufacturers to share in the cost of such a review
- The need to respond quickly to concern over unexpected adverse effects or accumulated evidence of harm
- Concern for the impacts that changes to the Formulary may have on patients
- Responsibility for drug manufacturers to provide complete and comprehensive information in their application to list drugs
- Accountability and cost-effectiveness of the OPDP

There was considerable discussion, though no agreement, on whether there should be a cap on the number of 'me too' drugs or the total number of drugs on the Formulary. These discussions may warrant further consideration.

Further, Council members recognize that education, information and advance notice of new listing and delisting conditions will be essential for physicians as well as for pharmacists and other health professionals.

The recommendations are an effort to "formalize" these concerns and guide the Ministry as it looks for ways to better manage the Formulary, in particular in regard to delisting.

RECOMMENDATION 1

The Executive Officer should develop and implement a systematic process for periodic review of all drugs on the Formulary with clear timelines and milestones

There was strong consensus for a periodic review of all drugs on the Formulary to determine their ongoing eligibility for listing.

The Council explored a range of options for a periodic systematic review process. Suggestions included: meta-analysis on a 5-year basis by class of drugs (e.g. statins, PPIs, narcotics), by year of inclusion on the Formulary, by DIN category, or by frequency of use. The Council feels that the Executive Officer and her advisors should choose the most appropriate and feasible method.

Members agreed that criteria for the review be clear and transparent and include such aspects as cost of the drug, availability of bio-equivalents, effectiveness, efficacy, full disclosure of all study results, etc.

The Council recognized that a review process is likely to be resource-intensive. Information technology, the eventual advent of e-Health and ongoing data collection could simplify the management of this process, though it is likely to remain costly and time-consuming. To that end, the Council agreed on the establishment of an arms-length fund, supported by drug manufacturers, to enable these reviews. This is the subject of the next recommendation.

RECOMMENDATION 2

To assist with the ongoing costs of a systematic review process, an arms-length fund or levy should be created, paid for by drug manufacturers.

The Council believes that the costs of Formulary reviews should be borne, at least in part, by drug manufacturers who benefit enormously from having their products listed on the Formulary. Members felt that any new listing agreements should require the manufacturer's agreement to participate in such a fund or levy, and agreed that a fund at "arms-length" was important in order to avoid any conflict of interest.

A number of possible approaches were mentioned:

- A contractual arrangement as a condition of listing that includes a commitment to share in the cost of post-listing reviews.
- A levy (perhaps 1% of sales) on manufacturers, to be pooled and used for anonymous reviews.

- A fee for listing, although this would have to be managed carefully to avoid any perception of conflict of interest.

RECOMMENDATION 3

Drugs found to be harmful should be delisted (removed from the Formulary) immediately.

Out of concern for how long it took for Canada and Ontario to take action on Avandia, Council members agreed that where there is accumulated evidence of harmful effects, delisting should be immediate.

The Council considered a range of approaches to delisting. It organized its discussion along the following lines:

- Cases where harmful effects are demonstrated clinically after a drug is listed;
- Cases of multiple drugs for same therapy ('me too' drugs);
- Drugs or self-monitoring technologies that have variable effectiveness depending on the therapeutic needs of the individual patients;
- Drugs that have been on the Formulary for a long time and may now be less effective than newer drugs.

RECOMMENDATION 4

The implementation of a delisting decision must be preceded by an appropriate notice period and adequate education of health professionals, patients and the general public.

Council members agreed that delisting should be a thoughtful decision and that education must include the reasons for delisting, as well as alternatives available (alternative drugs or alternative funding mechanisms where warranted, including patient-funding).

Should a manufacturer cease production or distribution in Ontario, for reasons of delisting or otherwise, the effects on the health practitioners and on patients would be the same, therefore the same conditions should apply.

RECOMMENDATION 5

The contractual agreement required for listing a drug on the Formulary should include a commitment from the manufacturer to give adequate notice before ceasing production or distribution of the drug in Ontario.

This recommendation emerged from a discussion of situations in which a manufacturer can simply remove a drug from the market on the basis that it is no longer profitable. Council members were concerned that this gives manufacturers the upper hand in decisions and wanted to ensure that the Ministry as well as the public were informed in advance so that appropriate alternatives could be identified.

RECOMMENDATION 6

If for clinical reasons a patient cannot benefit from an alternative drug after delisting of a harmful drug, he/she could remain eligible for funding of the delisted drug under EAP.

Council members recognized that removing a drug from the Formulary could be difficult for those patients accustomed to taking it and worked hard to consider ways to reduce any disruptions that might result.

This recommendation relates to a situation in which a patient may need ongoing access to a drug whose status on the Formulary has changed. It is also intended to address a situation like Avandia where a patient may want to continue to take the drug in spite of its potential for harm.

To ensure that such patients are fully aware of the possibilities and also contribute to available information, Council members suggested that there be an informed-consent agreement signed by both patient and physician, to ensure that patients are appropriately notified of the potential risks of certain drugs and that they are provided with information about adverse effects.

Council members also wondered whether it was appropriate to delist a drug only if an appropriate alternative was available. This, too, may warrant further discussion.

RECOMMENDATION 7

Any new listing agreements should require full disclosure by the manufacturer of all trial results (positive and negative) related to the use of that drug).

The quality of the evidence is an essential component of good decision-making. Council members agreed that Ministry must demand complete transparency from manufacturers. To ensure this, it should make transparency a condition of listing.

Clinical trials are an important part of the information required in the Health Canada approval and OPDP listing process. However, it is widely known that the results of clinical trials are not always reported in their entirety and tend to focus more on the evidence that is positive. Furthermore, harmful effects may only be revealed once the drug is in use in the general population (as with Avandia).

Council members agreed that full disclosure and comprehensive evidence are required – both through broader clinical trials and through release of both positive and negative studies - before releasing a drug into the general population.

In addition to the need for full disclosure, the Council agreed on the importance of collecting evidence on an ongoing basis, both to feed the review process and so that there is an overall collective sense of adverse effects related to a drug. This relates to the matter of informed consent and gathering of information referred to in the preceding recommendation.

The Council had agreed, in its discussion of drugs for rare diseases, that all observations on the use of a drug should become part of the bank of knowledge that can support continuous improvement of treatment for patients using that drug. This applies equally with respect to

information regarding adverse effects.

Council members also wanted to ensure that Health Canada advisories – an important source of alert for the Ontario health authorities – are issued quickly so as not to delay the delisting in Ontario of a harmful drug.

RECOMMENDATION 8

In cases where the effectiveness of a drug or self-monitoring device varies with the severity of symptoms, strategic adaptation of the limited-use/exceptional access categories should be considered.

This comes out of the diabetes test strips case and consideration that some people may benefit more than others from a drug or drug product. Council members felt that it may be possible to adapt current processes related to Limited Use or Exceptional Access to allow access for those who would benefit.

The use of some self-monitoring technologies was the subject of considerable discussion. As outlined in the case study section of this report, test strips for diabetes are widely used in Ontario. Self-monitoring is very important for newly diagnosed individuals; however, as their condition becomes better understood, it may no longer be necessary to continue testing with the same frequency. The current categories in the Formulary (general use/limited use/EAP) do not allow for "gradations" of eligibility. A population-based approach, such as a "graduated" formula for limited use, might help in minimizing administrative complexity.

RECOMMENDATION 9

The Ministry of Health and Long-Term Care should open discussions with Health Canada specifically about discharging its approval authority and its responsibility for prompt advisories on problematic drugs.

This recommendation emerged from information provided to the Council about overlapping areas of jurisdiction between Health Canada and the provinces, as well as concerns about the length of time it took to take action on Avandia at both federal and provincial levels. The Council agreed that, in situations which would benefit from discussions between Health Canada and the provinces related to approvals and advisories on problematic drugs, MOHLTC should demonstrate leadership and take initiative.

RECOMMENDATION 10

Council should, in future sessions, consider other issues related to updating and modernizing the Ontario Drug Benefit Formulary.

Council members found that there was not enough time to consider adequately the many issues related to listing and delisting of drugs on the Formulary.

They raised a number of suggestions that might be explored in future sessions:

- Limiting the number of 'me too' drugs in a class

- Possibly limiting the overall number of drugs on the Formulary
- Instituting a "one-on, one-off" condition whereby a manufacturer would be involved in choosing to remove one of its drugs from the Formulary in order to add another
- Setting conditions that must be met in order that delisted drugs be eligible for grandparenting (i.e. continued access after delisting for those formerly using a now delisted drug)
- Creating strategies for reporting of adverse reactions by different medical professions
- Education – determining best ways to share health information with health professionals, patients and the public
- Providing security of information to allay any privacy concerns
- Analyzing patient want vs. patient need
- Using a more strategic approach to existing types of access - for example, considering a population-based approach for certain categories such as Test strips

Council members look forward to an opportunity to examine some of these more closely and to contribute their advice.

8.0 CONCLUSION

The Formulary will continue to play a pivotal role in the provision of the right medication for the right patient at the right time.

The Ontario Citizens' Council accepted the challenge of responding to the question:

Under what conditions or situations, should the Executive Officer of the Ontario Public Drug Programs consider delisting or limiting the use of drug products on the Ontario Formulary?

The discussion of the Council was rich and substantive. The Council offers its recommendations to the Executive Officer as ways to update the Ontario Drug Benefit Formulary. It also suggests that the OPDP itself present any forthcoming changes to the Formulary as important ways to modernize and streamline the Formulary to better serve the people of Ontario by making it more efficient and effective.

APPENDIX 1

MEMBERS OF THE ONTARIO CITIZENS' COUNCIL

Benita Baker
Nigel Berrisford
Shelley Blidner
Jeff Bondett
Louise Bourgault
Beverly Browne
Donna Edwards
Jane Ewing (not present)
Prem Lachhman
Mike Malesevich (not present)
Sherry Marshall
Debbie Marson
Dorothy Modritsch
Robert Moore
Josephine Quercia (not present)
Bruce Raymond
Abe Schwartz
Sharon Smith
Andrea Segal
Theresa Tasse
Gary Wasserman
Larry Westlake
Carol Ann Wilson
Craig Wolverton

APPENDIX 2

AGENDA
MANAGING THE DRUG FORMULARY
SECOND MEETING – CITIZENS' COUNCIL

Toronto Marriott Downtown Eaton Centre Hotel
525 Bay Street, Toronto, ON
April 15-17, 2011

FRIDAY, APRIL 15	
5:30 PM	**Check in and Light Supper**
6:30 PM	**Welcome and Introduction**
7:45 PM	**Introducing the Topic – Managing the Drug Formulary** ***Presenter: Diane McArthur***
8:00 PM	**Overview - the Ontario Drug Benefit Formulary** ***Presenter: Gerald Evans***
8:30 PM	**Questions / Answers**
9:00 PM	**Adjourn**

SATURDAY, APRIL 16	
8:00 AM	**Breakfast and Late Registration**
9:00 AM	**Agenda review and Questions / Answers**
9:30 AM	**Exploring issues related to the Formulary** ***Presenters:*** 1. Managing the Formulary & the Suitcase **– Jeff Hoch** 2. Why we need to remove drugs from the formulary **– Mona Sabarwhal** 3. Why a broad range of options should be available on the Formulary for some, or a particular, indication(s), or why the Formulary may already be too restrictive **– Carter Thorne**
10:00 AM	**Questions / Answers**
10:30 AM	**Break**
10:50 AM	**Introduction to Case Studies** *1.* The Harm/Benefit Ratio - ***Presenter: Baijuh Shah*** *2.* The Cost/Benefit Ratio - ***Presenter: Tara Gomes*** *3.* When is Enough Enough? - ***Presenter: Muhammad Mamdani***
12:00 PM	**Questions / Answers**
12:15 PM	**Lunch**
1:00 PM	**World Café discussion of three case studies**

	Round 1
2:15 PM	**Round 2**
3:15 PM	**Break**
3:30 PM	**Round 3**
4:30 PM	**Review and Reflections of the Day**
4:45 PM	**Wrap-up**
5:00 PM	**Adjournment**

SUNDAY, APRIL 17	
8:00 AM	**Breakfast**
8:30 AM	**Morning Check-in and Questions / Answers**
8:45 AM	**Where Are We? Overview**
10:15 AM	**Break**
10:30 AM	**Round Table: Field Testing Our Advice** ***Respondents: Diane McArthur and Mona Sabarwhal***
11:30 AM	**Lunch**
12:15 PM	**Clarifying Council Advice**
1:45 PM	**Preparing the Citizens' Council report**
2:30 PM	**Wrap-up**
3:00 PM	**Adjournment**

APPENDIX 3

BIOGRAPHIES OF PRESENTERS

Diane McArthur is Assistant Deputy Minister and Executive Officer of Ontario Public Drug Programs, appointed in June 2010. Ms. McArthur has been the Assistant Deputy Minister responsible for seniors' issues within the Government of Ontario, and Executive Coordinator of Health and Social Policy in the Cabinet Office of the Government of Ontario.

In her latter capacity, she supported the policy decision-making processes of the Cabinet committee that deals with health, social services, health promotion, francophone, women's, and seniors' issues; and was responsible for broader public sector labour relations.

Ms. McArthur has held progressively more senior positions in several ministries since joining the Government of Ontario as a Management Intern in 1989. She has extensive experience in human resources health policy and planning for health provider training, education, supply and distribution initiatives, data and health information planning and analysis, health care provider negotiations, rural health policy, labour relations and service delivery restructuring.

Ms. McArthur has a Bachelor of Public Relations degree from Mount Saint Vincent University in Halifax and a Master of Business Administration degree from the University of Ottawa.

Dr. Gerald Evans is an Associate Professor in the Departments of Medicine, Microbiology and Immunology, Pathology and Molecular Medicine at Queen's University. Dr. Evans is also an Infectious Diseases Specialist at Kingston General Hospital and Hotel Dieu Hospital in Kingston, Ontario. He has an active clinical practice in infectious diseases and HIV care, and has published many articles and guidelines on the management of infectious diseases.

Dr. Evans is Chair of the Committee to Evaluate Drugs and is President of the Association for Medical Microbiology and Infectious Disease Canada.

Jeffrey S. Hoch, PhD holds several positions. He is a Research Scientist in the Centre for Research on Inner City Health at St. Michael's Hospital. He is also Associate Professor in the Department of Health Policy Management and Evaluation at University of Toronto, Director of the Pharmacoeconomics Research Unit for Cancer Care Ontario.

He is also Co-Director at the Canadian Centre for Applied Research in Cancer Control (ARCC) - Advancing knowledge in health economics, ethics and policy.

Jeffrey Hoch received his PhD degree in health economics from the Johns Hopkins School of Public Health. Dr. Hoch also holds a Masters degree in Economics from Johns Hopkins University and a Bachelor of Arts degree in Quantitative Economics and Decision Sciences from

the University of California at San Diego.

Dr. Hoch has taught Health Economics and Economic Evaluation classes in Canada and throughout the world. Dr. Hoch is pursuing research on how to make health economics more useful to decision makers. Special interests include health services research related to cancer, mental health and other health issues affecting poor and vulnerable populations. Dr. Hoch is an award-winning teacher and is the recipient of a Career Scientist Award from the Ontario Ministry of Health and Long-Term Care.

Mona Sabharwal is the inaugural executive director of the pan-Canadian Oncology Drug Review (pCODR).

Ms. Sabharwal has worked in drug technology assessment and formulary management, in both British Columbia and Ontario, for more than 15 years. Before joining pCODR, she was the Senior Manager for Drug Programs Management with the Ontario Ministry of Health and Long-Term Care. In this role, she had operational oversight of the drug submission and evaluation process for Ontario's seven public drug programs.

During her time at the Ministry, Ms. Sabharwal was a key participant in the early development of pCODR and led operations for its precursor, the interim Joint Oncology Drug Review (iJODR). She was also instrumental in Ontario's development of a new and innovative evaluation framework for Drugs for Rare Diseases, which was implemented in 2008. In 2010, she spear-headed and launched Ontario's patient-evidence submission process, a formal process to systematically solicit patient-centred perspectives on new drug therapies.

Ms. Sabharwal is a registered pharmacist with experience in both community and hospital pharmacies. She has also conducted practice-based research focused on finding concrete ways to improve the delivery of pharmacist-based professional services. She obtained both her Bachelor of Science degree in Pharmacy and her Doctor of Pharmacy degree from the University of Toronto.

Carter Thorne is on the Consultant Staff at Southlake Regional Health Centre in Newmarket, Ontario, Chief of the Division of Rheumatology and Director of The Arthritis Program. He is sought for his expertise in developing Outcome Based clinical Programs, not only in Arthritis Care, but also Shared Care in a Comprehensive Musculoskeletal Program, Wound Management and NeuroRehab/Stroke Care. He is on the Steering committee of CARE, a European based project, addressing and identifying best practices in 'non-pharmacologic management of arthritis'.

He is active in Clinical Research as Principal Investigator with The Arthritis Program Research Group Inc. As part of a strategic interest in identifying 'Best Practices', he has established an Early Arthritis Clinic, collaborating with a national initiative (CATCH - of which he is Operations Director), and an Osteoporosis Intervention Clinic. He sits on the Steering and Scientific

Committee of the Ontario Biologic Research Initiative, a collaborative attempt to describe and disseminate outcomes and best practices in the management of Rheumatoid Arthritis. He is working with other Canadian Rheumatologists who have established the Canadian Rheumatology Research Consortium of which he is a Founding Member and currently Secretary-Treasurer. He is a founding member of the Ontario Rheumatology Association and Past-President (2006-10). He is also Vice President/President-elect of the Canadian Rheumatology Association.

Tara Gomes is an assistant professor at the Leslie Dan Faculty of Pharmacy at the University of Toronto, and an epidemiologist and the Project Research Lead at the Ontario Drug Policy Research Network based at the Institute for Clinical Evaluative Sciences. In this role she works closely with the Ontario Public Drug Program to develop, conduct and report policy-relevant studies in the areas of drug utilization, adherence, costs and safety.

Muhammad Mamdani is Director of the Applied Health Research Centre, St. Michael's Hospital. He is also Associate Professor in the Faculty of Medicine: Department of Health Policy Management and Evaluation and Faculty of Pharmacy at the University of Toronto.

He holds a Master of Public Health degree from Harvard University and a Master of Arts degree in Economics from Wayne State University, Detroit.

Baijuh Shah is a staff physician in the Division of Endocrinology at Sunnybrook Health Sciences Centre. He is also an assistant professor in the Department of Medicine at the University of Toronto and a Scientist at the Institute for Clinical Evaluative Sciences. Dr. Shah received his medical degree and completed post-graduate training in internal medicine and endocrinology, all at the University of Toronto. He then completed a PhD in Clinical Epidemiology from the University of Toronto. His research focuses on quality of care and outcomes for patients with diabetes, with particular interest in diabetes in pregnancy and in care for ethnic, immigrant and aboriginal populations.

APPENDIX 4

CASE STUDY MATERIAL

FORMULARY MANAGEMENT

The purpose of this session of the Citizens' Council is to better understand the values and principles that Ontarians believe should guide the Executive Officer and government as they consider how to best manage the Formulary of drugs paid for by the Ontario Public Drug Programs.

The key question the Citizens' Council is being asked to discuss is:

Under what conditions or situations should the Executive Officer consider delisting (removing) or limiting the use of drug products on the Ontario Formulary?

There are three case studies – each illustrated with a particular drug, intended to help Councillors think through the range of issues affecting formulary decisions. Through the case studies, the Council hopes to identify the values and principles that the Council members think government should consider as they make decisions about potential changes to how the drug Formulary is managed.

The three case studies are:

1. The Harm/Benefit Ratio: The Example of Avandia
2. The Cost/Benefit Ratio: The Example of Diabetes Test Strips
3. When is Enough Enough? The Example of 'Me Too' Drugs

The case studies have been developed to promote thoughtful discussion on a current and challenging issue. Council members will be able to work through them with others and talk together about which values, principles and other factors they would like to see reflected in the government's decision making.

For each case study, consideration will be given to the following questions:

- What are the concerns - what key problems does this case study illuminate?
- What values and principles are at play here?
- What are some options for addressing these concerns?
- Based on this case study, what factors, if any, should be taken into account when making a decision to limit/reduce the range of drugs available?

These case studies will be supported by presentations and there will be good opportunities to ask questions of presenters and also to talk with fellow members of the Citizens' Council.

What we are looking for, in our discussions this weekend, is a good sense of what you collectively value and why, so that this advice can be provided clearly and cogently to Diane McArthur and the Ministry. We hope that, whatever the outcome, you have a good discussion and come away with a better understanding about what is involved in making these challenging decisions.

CASE 1 - THE HARM/BENEFIT RATIO

The OPDP is increasingly faced with situations where information on a particular drug changes. In some cases, this information changes what was previously known about the harm and the benefit of the drug. Avandia is such a drug.

Overview of Avandia

Avandia (rosiglitazone) is an antidiabetic drug in the thiazolidinedione class of drugs. It works as an insulin sensitizer, by binding to the PPAR receptors in fat cells and making the cells more responsive to insulin. It is marketed by the pharmaceutical company GlaxoSmithKline (GSK) as a stand-alone drug (Avandia) and in combination with metformin (Avandamet) or with glimepiride (Avandaryl).

Public Reimbursement of Avandia in Ontario

In 2007, Avandia was listed as a General Benefit under the ODB Program.

In 2005/06, Avandia was the second most requested drug under the Exceptional Access Program (EAP, formerly known as the Individual Clinical Review mechanism). In that year, 13,764 requests for coverage were received of which 63.3% were approved, resulting in ODB expenditures of $12.4 million.

In January 2007, Avandia was listed as a General Benefit with therapeutic notes on the Ontario Drug Benefit (ODB) Formulary as part of a listing agreement between the Ministry and the manufacturer.

The US FDA's Labelling Review: 2007

In May 2007, the U.S. Food and Drug Administration (FDA) issued a warning about potentially severe cardiovascular complications associated with Avandia. Some reviewers concluded that Avandia caused more deaths than Actos (pioglitazone), another drug for the same indication, and recommended Avandia be taken off the market.

The FDA appointed an independent panel of experts from the Endocrine and Metabolic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee to review the cardiovascular ischemic/thrombotic (heart-related and blood clot related) risks of the thiazolidinediones, the class of drugs in which Avandia belongs, with a particular focus on Avandia. The FDA panel disagreed with the assertion that Avandia should be taken off the market, and instead proposed significant restrictions to its use. On July 30, 2007 those experts strongly advised the FDA to add new safety warnings to these diabetes drugs, while keeping them on the market, as they concluded that the benefits outweighed the risks.

On August 14, 2007 FDA officials confirmed that the manufacturer of Avandia (and Actos) will add "Black Box" warnings (the strongest form of warning) to their labelling - emphasizing that the drugs may cause or worsen heart failure in certain patients.

In November 2007, the FDA required that this warning be expanded to include an increased risk for heart attacks and death.

Canadian Advisories: 2007

In November 2007, Health Canada announced new usage restrictions for Avandia (and other Avandia-containing products), following their review of information available on cardiovascular (heart-related) safety. As a result, the consumer and prescriber sections of the official Canadian Product Monographs for Avandia-containing products were updated and include the new usage restrictions as follows:

- Avandia is no longer approved for use alone to treat type 2 diabetes, except when metformin use is contraindicated or not tolerated
- Avandia is no longer approved for use with a sulfonylurea drug (such as glyburide), except when metformin is contraindicated or not tolerated
- Avandia should not be used if the patient has heart failure, or has experienced heart failure in the past
- Patients who are taking Avandia, especially those with underlying heart disease, or those who are at high risk of heart attack or heart failure, should talk to their doctor about the benefits and risks of continuing Avandia therapy

On December 11, 2007, a new Canadian study focusing on Ontario residents aged 65 or older treated with at least one oral diabetic medication was released by the Institute for Clinical Evaluative Sciences (ICES). According to the study, drugs such as Avandia increase the risk of heart failure, heart attacks and death.

Change in Funding Status in Ontario: 2009

A new funding agreement was negotiated with GlaxoSmithKline and an announcement on the listing change was made on May 6, 2009.

Effective June 1, 2009, Avandia would only be available for funding through the Exceptional Access Program (EAP). These changes have been prompted by product labelling changes approved by Health Canada and multiple warnings issued by the manufacturer. Specifically, these warnings suggest that Avandia and Actos can cause congestive heart failure or make it worse in certain high risk patients; neither drug should be used for patients with any stage of heart failure. Increased risk of fracture has also been seen in patients receiving Avandia and Actos, particularly women. Data on the myocardial ischemic risks of Avandia and Actos remain inconclusive; however, use of either agent in patients with acute myocardial ischemia could increase the risk of heart failure and is not recommended.

Patients will be urged to discuss the current labelling and warnings with their physicians to determine appropriateness for ongoing use.

Patients currently being treated with Avandia would continue to have coverage with no interruption in therapy. EAP approvals would not be required for patients who received a claim for Avandia in the 12 months prior to the listing change.

Dangers Associated with Avandia

Researchers from Toronto's Institute for Clinical Evaluative Sciences (ICES) have indicated that people taking Actos for Type 2 diabetes are 23 per cent less likely to be hospitalized for heart failure and 14 per cent less likely to die than people taking Avandia.

ICES estimated that for every 120 people taking Avandia rather than Actos for a year, one more person would be hospitalized with heart failure. And for every 269 people who took Avandia rather than Actos for the same period, one person would die. This may seem comparatively marginal, however these results are significant when one considers that 1.17 million prescriptions for Avandia were filled in Canada in 2006. In 2008, due largely to the revelation of safety issues around Avandia, that figure had dropped to 690,000.

CASE 2 - THE COST/BENEFIT RATIO

The OPDP is sometimes faced with situations where information on a particular drug or drug product changes. In some cases, this information changes what was previously known about the costs and benefits of the drug. Diabetes (Blood Glucose) Test Strips are an example of this situation.

What Are Diabetes Test Strips?

About 2.5 million Canadians have diabetes (or diabetes mellitus in medical terms). There are three distinct forms of diabetes: gestational diabetes is a temporary condition that occurs during pregnancy; type 1 diabetes, usually diagnosed in children, occurs when the pancreas is unable to produce insulin; type 2 diabetes occurs when the pancreas does not produce enough insulin or the body does not effectively use the insulin it produces. About 90 per cent of people with diabetes have type 2.

Diabetes Test Strips are used for determining the approximate concentration of glucose in the blood. It is a key element of the self monitoring of blood glucose (SMBG) by people with diabetes or hypoglycemia (low blood sugar). Hypoglycemia is a life-threatening condition with effects that can range from mild dysphoria to more serious issues such as seizures, unconsciousness, and (rarely) permanent brain damage or death.

A small drop of blood, obtained by pricking the skin with a lancet (tiny sharp pin), is placed on a disposable test strip that is read by a meter that calculates the blood glucose level. A primary goal of the management of type 1 diabetes and type 2 diabetes is achieving closer-to-normal levels of glucose in the blood for as much of the time as possible, guided by SMBG several times a day.

For patients treated with insulin, the use of test strips up to 3 or more times daily is recommended. However, there are no clear guidelines regarding how often test strips should be used in patients with diabetes who are not being treated with insulin.

Test strips fall into the category of medical devices (from a Health Canada perspective). However, in many Canadian jurisdictions, test strips are covered on drug plans the same way that drugs are covered, so they are functionally classified as drugs by the way they are listed and managed.

What Is The Problem?

Despite the current widespread use of blood glucose test strips in patients with type 1, type 2, and gestational diabetes, there is uncertainty regarding the benefits of SMBG. Recent evidence suggests the practice has a limited clinical benefit in many patients.

In some publicly funded drug plans in Canada, and in Ontario in particular, blood glucose test strips are among the top five classes in total expenditure. Government expenditures on SMBG test strips in Ontario for fiscal 2009/10 were approximately $126 million. Use of SMBG test strips has been increasing dramatically over the past 12 years in Ontario. The province has experienced a 250% increase in the number of elderly patients with diabetes who are receiving SMBG strips, with an overall rise in annual costs of $67.7 million rise from 1997 to 2008. Over the next 5 years, this trend is expected to continue, and if no restrictions are placed on reimbursement, the MOHLTC can expect to spend roughly half a billion dollars on SMBG test strips for Ontarians with diabetes during that period.

Despite this increasing use and associated costs, approximately 80% of test strip use is by patients who do not meet the recently published recommendations by the Canadian Agencies for Drugs and Technologies in Health (CADTH). Despite evidence of no clear clinical benefit, test strips were dispensed to 30% of patients who use no drug therapy to control their diabetes. As well, 60% of patients treated with oral glucose-lowering drugs which are not known to induce hypoglycemia were given blood glucose test strips.

Evidence suggests that there is a lack of clinically relevant improvement in a number of diabetes-related outcomes with test strips in diabetic patients who are not treated with insulin. These patients see very little improvement in rates of glycemic control, body weight, quality of life, diabetes-related complications and mortality. There is even some suggestion of harm, as a number of patients report increased discomfort, inconvenience and worsening of depression scores accompanying use of test strips.

What Are The Benefits Of SMBG Test Strips?

The benefits include a reduction in the rate of occurrence and severity of long-term complications from hyperglycemia for patients as well as a reduction in the short-term, potentially life-threatening complications of hypoglycemia.

It should be noted that despite evidence that test strips may not improve glycemic control in patients not requiring insulin, the self-monitoring associated with them may promote patient engagement and improved awareness of the presence of diabetes.

CASE 3 - WHEN IS ENOUGH ENOUGH?

The OPDP has many drugs on the Formulary that perform the same function. These are known as "me-too" drugs. How should we be thinking about the ratio between choice and cost?

What Is A 'Me Too' Drug?

Modern drug discovery can be a long process with a significant period of drug development before clinical trials. Competing manufacturers often find themselves developing related chemical compounds at the same time. The compounds are characterized by small chemical differences that could, in some cases, translate to meaningful clinical differences.

The first product to emerge in a new class of drugs is usually viewed (and described as) a "blockbuster". Subsequent compounds made by other manufacturers or generic manufacturers are often referred to as "me too" drugs. These drugs are almost never directly compared in a head-to-head fashion, and therapeutic equivalence is often presumed.

Can "Me Too" Drugs Be an Asset?

While there may be only slight differences between "me too" drugs and the earlier products, it is argued that these products can be beneficial to the overall market for a particular drug. Proponents argue that "me too" products offer valuable therapeutic options for physicians and create competition, thereby improving the quality and lowering the costs of drug therapy.

The original product in a class of drugs defines the baseline value for treatment with a particular drug. Subsequent products in the same class need to offer either better clinical outcomes than the original product, lower cost, or both, in order to compete with the original product.

In many cases, the introduction of additional drugs into a class can provide added value for healthcare providers by lowering the cost of treatment and introducing an element of cost competition into the market for a particular drug.

Can 'Me Too' Drugs Be A Liability?

Detractors of "me too" products argue that there are often only trivial differences between market latecomers and the original products. Most "me too" products offer only minor variations on pharmaceuticals already in the market with little therapeutic value and an arguable impact on price competition.

It is also argued that "me too" pharmaceuticals are often introduced into the market with less clinical experience than the original product, and the potential to reap cost savings from such drugs could provoke healthcare providers to promote the use of the drugs before their safety has been adequately established.

Other arguments have been made that "me too" drugs do little to introduce price competition and value into the market. Rather than lowering the price of treatment by providing the product to a share of the overall market at a lower price, the aggressive marketing associated with these products can actually expand the overall size of the market for a particular class of drugs, thereby increasing the overall cost.

APPENDIX 5

WORLD CAFÉ OVERVIEW

ONTARIO CITIZENS' COUNCIL
MINISTRY OF HEALTH AND LONG-TERM CARE
SECOND MEETING

Facilitators: Miriam Wyman and Jacquie Dale

Over the past few years, World Café has become a simple practice that enables rich new combinations of insight, innovation, ideas and emotional connection. It is an intentional way to create a living network of conversations about questions that matter.
The format is flexible and adapts to many different circumstances.

This small group format entails having four or five people at a conversation cluster, and enables each voice to be heard. Instructions will be given to participants to then engage in an informal way bringing a spirit of curiosity and desire to hear others' ideas.

Questions posed to participants in this format focus on intention and attention to what really counts. Open ended questions work best, for example:

- "What could a good school also be?" rather than "What problems do we have in our school system?"
- Thinking of yourself as an agent of change, remember a time when something you did shifted the status quo. Share this with one other person at your table. Then ask: What would you attempt if you knew you could not fail?
- What's missing that, if it were present, would empower you to act on what you want in your work?

The opportunity to express views, meet new people whose perspectives are different, move between tables, and enjoy the setting are the hallmarks of World Café dialogue. The cross-pollination of ideas among participants greatly enhances the richness of knowledge and shared understanding.

Often hosts kick off the Café conversation by explaining the process and assumptions, then set up three rounds of conversations of about 30 minutes each. After these conversations, there is usually a period of sharing discoveries and insights with the whole group. Upon completing one round of conversation, one person agrees to remain at the table as a host while others travel to new tables carrying the core ideas, insights and questions of their initial group. Table hosts welcome their new guests, share high points of their initial conversation.

World Café uses paper to cover the tables and people are encouraged to make their ideas visible through words and pictures. This helps the host and others to literally see what others mean. The guests then connect their ideas and insights, or offer entirely different perspectives.

For the third round of conversations, people may return to their home group for a new question to deepen the inquiry or to synthesize their discoveries.

At every World Café, people are encouraged to listen together for the emerging patterns, collective wisdom and surprising realizations. The conversation of the whole at the conclusion of the table conversations enables reflection, recognition of shared understanding and awareness of collective learning.

After presentations by health professionals, the deliberations were conducted in a format referred to as "World Café", a system designed to ensure that by rotating among three groups, all Council members were given a maximum opportunity to have their individual opinions heard. The system was most effective and resulted in the Council framing the recommendations that close the attached Report.

Managing the Drug Formulary is a daunting task, even during affluent times, but to meet the many demands upon the Formulary management during the present "financially challenging" times makes the task even more difficult.

The Council appreciates the candour with which the Ministry's Public Drug Programs health professionals shared their experiences and frustrations. They were invaluable.

Not surprisingly, the Council's deliberations led to as many questions as answers regarding the Formulary. Accordingly, it is the belief of the Council that at least one more session should be devoted to this overwhelmingly important subject.

Respectfully

Gerri Gershon, Chair
Ontario Citizens' Council
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