Appendix

Response Letter from
Ministry of Health and Long-Term Care

Ministry of Health and Long-Term Care

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Ontario

August 26, 2009

Mr. André Marin
Ombudsman of Ontario
Ombudsman Ontario
483 Bay Street
10th Floor South Tower
Toronto ON M5G 2C9

Dear Mr. Marin:

Thank you for the opportunity to respond to your review of the funding of Avastin (bevacizumab) as outlined in the preliminary report "Investigation into the Ministry of Health and Long-Term Care's decision-making around the funding of Avastin for colorectal cancer patients", dated August 2009.

We respectfully submit that one of the Government's key principles as outlined in the *Transparent Drug System for Patients Act* (TDSPA), 2006 which amended the *Ontario Drug Benefit Act* (ODBA) was to enshrine in legislation that drug funding decisions are based in evidence. The Government, through the Transparent Drug System for Patients Act, devolved the authority to make funding decisions under the Ontario Public Drug Programs (OPDP) to the newly created Executive Officer role. The Executive Officer has the mandate to make decisions based on evidence, cost-effectiveness and overall budget impact.

The ministry's Committee to Evaluate Drugs has an important role in this process. As background, the Committee to Evaluate Drugs (CED), formerly the Drug Quality and Therapeutics Committee, was established in 1968 to provide independent, specialized advice to the Ministry of Health and Long-Term Care on drug-related matters. The Committee provides essential advice to the Executive Officer and the Minister of Health and Long-Term Care through its rigorous, evidence-based review of drug products, and subsequent recommendations concerning which drug products to fund. The Committee's role is focused on reviewing clinical and cost-effectiveness evidence, and not on the pricing and listing negotiations with pharmaceutical companies. It is the express role of the Executive Officer and her staff to determine the need for and engage in negotiations with pharmaceutical companies with respect to pricing and listing agreements. This approach is routinely implemented by OPDP.

For oncology products, the Executive Officer relies on the advice of up to 20 individual clinical experts, from the Committee to Evaluate Drugs (CED) and its joint CED/Cancer Care Ontario (CCO) subcommittee. The Executive Officer also considers the advice of external clinical experts and highly qualified staff within the Ontario Public Drug Programs Division and Cancer Care Ontario to interpret evidence on the clinical benefit and cost-effectiveness of each drug submitted for funding.

The funding decision for Avastin considered the clinical evidence, cost-effectiveness evidence, the Program in Evidence Based Care disease site guidelines, clinical opinions from the CED, CED-CCO, and medical experts, as well as the overall budget impact. The ministry also considered the manufacturer's own submissions, as well as the status of funding and rationale for funding in other provinces.

The CED recommended not to fund Avastin for the treatment of colorectal cancer. The main concern was that Avastin was not cost-effective in combination with an irinotecan-based chemotherapy regimen; in addition, the Committee was concerned about the lack of cost-effectiveness data with respect to Avastin in combination with oxaliplatin. Clinical and cost-effectiveness advice was provided by committee members, members of the oncology Disease Site Group (DSG), and CCO. The clinical experts engaged in these discussions were

individuals who have extensive experience in treating colorectal cancer and are well informed of the evidence regarding the use of Avastin.

There were four key randomized controlled studies that were used to support the evidence based guidelines published by the Disease Site Group. These guidelines form the base of evidence that was discussed at the CED/CCO Subcommittee and the CED. Recognizing that the studies used various doses of Avastin and compared it to various chemotherapy regimens in different groups of patients, the CED relied on the advice of oncology experts to explain how the product would be used in clinical practice, particularly since the standard of care (FOLFIRI – combination chemotherapy containing infusional 5-fluorouracil, folinic acid and irinotecan) was not a direct comparator within any of the studies. This is particularly concerning to the CED since it is difficult to extrapolate the results of the studies to patients in Ontario since the treatment regimens are different. Each study reviewed by the Committees had differing lengths of times to progression free survival and outcome status for patients.

The pharmacoeconomic analysis indicated that the incremental cost-effectiveness ratio for Avastin was $151,000 per quality-adjusted life year (QALY) when compared to the standard of care containing irinotecan based combination chemotherapy. QALY calculations are used to compare increase in cost with increased health benefit (in same natural units, e.g., years of survival). QALY is a standard indicator used globally when assessing the funding of drug therapy. The Committee typically considers a range of $40 - $60,000 QALY as an acceptable range. The concept of QALY has been written about extensively and this range is consistent with many other jurisdictions. Therefore, Avastin was 3 times the traditionally acceptable cost-effectiveness range. Based on discussions with CCO, clinicians and pharmacoeconomic experts, it was estimated that the incremental expenditures for Avastin would be in the range of $45 to $50 million annually.

Recommendations 1 and 2

The final funding decision took into consideration clinical, cost-effective and budget impact information noted above, as well as experience from British Columbia which was funding the product at that time. As noted in your report British Columbia funded Avastin based on a cap of 16 cycles and it is our understanding that at that time the majority of patients receiving Avastin were under the cap. Therefore, due to the high cost of this product and poor cost-effectiveness, the Ministry decided to set a cap for funding at 16 weeks.

Recognizing that clinical and cost-effectiveness evidence changes over time and that funding decisions are based on the best available clinical and cost-effectiveness evidence at the point of that decision, manufacturers and representatives of the DSG are aware that new information can be submitted to the ministry for review by the CED and its subcommittee. The ministry has always been and will continue to be willing to review new evidence. In our ongoing discussions with Roche Canada, we have requested that they submit any new evidence related to the criteria for funding Avastin in first-line therapy. There is reference in the preliminary report that the Head of the DSG refers to availability of newer outcome data. Neither the manufacturer nor the DSG has submitted new information for consideration by the ministry.

On May 21st, 2009, the ministry met with Roche Canada to discuss, among other things, the funding of Avastin. The ministry followed up with a subsequent meeting on June 15, 2009 to discuss the Avastin cycle cap issue. The spirit of the ministry's willingness to review the funding of Avastin is characterized in the first paragraph of the letter from Roche Canada, "It is encouraging to see the Ministry's willingness to look at how this issue might be resolved so that patients can receive appropriate care for their metastatic colorectal cancer."

As follow-up to both the May 21st, 2009 and June 15th, 2009 meetings, the ministry requested additional data from Roche Canada. More specifically, Roche provided statistics with respect to duration of treatment of Avastin in B.C., Quebec, and Ontario. The average duration of treatment in Ontario was 9.1 cycles, and the median duration of treatment was 8 cycles.

Until such time as we receive and review any new evidence, the ministry intends to continue funding to a cap of 16 cycles – this is based on cost-effectiveness and overall affordability within a limited drug budget. Avastin's cost-effectiveness ratio of $151,000 –almost triple the 'acceptable' range – is simply not cost-effective. As you will appreciate, the cap on funding allows more people to receive Avastin: admittedly this is a difficult decision to make but we think it is better that more people have some access to this expensive drug than for none to have access at all.

We have developed a compassionate review policy that is posted on the ministry's website for products funded under the Ontario Public Drug Programs. The ministry will work with CCO to finalize a similar policy that has been under development for oncology products. In the meantime, and until the policy has been finalized, physicians may submit requests for their patients according to the compassionate review policy; the ministry will consider funding if the patient's clinical circumstances meet the criteria for funding as detailed in the compassionate review policy.

Recommendation 3

While the ministry has publicly communicated the funding criteria for Avastin and communicated the rationale for same to the oncologist community through Cancer Care Ontario, we recognize that the detailed rationale for funding Avastin has not been posted. We commit to posting this as soon as possible.

The ministry communicated to hospitals and clinicians through CCO that funding was available and that communication included information on the criteria and conditions for funding. Consistent with the CCO mandate, staff from CCO also met with the Disease Site Group (DSG) to explain the criteria for funding. The communications from the ministry and CCO were proactive to explain the decision. It our understanding that there were no objections to this approach at that time. For the reasons described above, the ministry did not disclose the full details of the agreement with the clinicians due to confidentiality restrictions within the agreement but the details on the clinical criteria for funding and 16 cycles limit were fully disclosed.

The ministry does monitor expenditures under the New Drug Funding Program as part of its normal budget forecasting and tracking process. Furthermore, we communicate regularly with CCO to obtain budget information and details on utilization as required. As an operational service agency of Government, it is part of CCO's mandate to monitor and manage the expenditures under the Program, including expenditures of Avastin. We will discuss with CCO their monitoring of drug expenditures under the New Drug Funding Program. Additionally, the ministry requested Roche Canada to do an analysis.

Recommendation 4

As for the suggestion to report quarterly, the ministry is prepared to report back to the Ombudsman on a biannual basis over a two-year period regarding our progress.

In closing, we believe that the report contains statements that mischaracterize information and/or comments provided by ministry staff to Ombudsman staff; we also believe that some information and/or comments provided by CED members and other experts require additional context in order to be fully understood. We would be pleased to identify specific instances should that be helpful in your investigation.

Sincerely,

Original signed by John McKinley, A/Deputy Minister

Ron Sapsford
Deputy Minister