



Common Drug Review *Patient Group Input Submissions*

Denosumab (Xgeva) for the Prevention of skeletal-related events due to bone metastases from solid tumours.

Patient group input submissions were received from the following patient groups. Those with permission to post are included in this document.

Canadian Cancer Survivor Network— permission granted to post.

Rethink Breast Cancer — permission granted to post.

The Canadian Breast Cancer Network — permission not granted to post.

CADTH received patient group input for this review on or before June 16, 2015

CADTH posts all patient input submissions to the Common Drug Review received on or after February 1, 2014 for which permission has been given by the submitter. This includes patient input received from individual patients and caregivers as part of that pilot project.

The views expressed in each submission are those of the submitting organization or individual; not necessarily the views of CADTH or of other organizations. While CADTH formats the patient input submissions for posting, it does not edit the content of the submissions.

CADTH does use reasonable care to prevent disclosure of personal information in posted material; however, it is ultimately the submitter's responsibility to ensure no personal information is included in the submission. The name of the submitting patient group and all conflict of interest information are included in the posted patient group submission; however, the name of the author, including the name of an individual patient or caregiver submitting the patient input, are not posted.

Canadian Cancer Survivor Network

Section 1 — General Information

Name of the drug	Xgeva (denosumab)
Name of the patient group	Canadian Cancer Survivor Network
Name of the primary contact for this submission:	[REDACTED]
Position or title with patient group	[REDACTED]
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1.1 Submitting Organization

The Canadian Cancer Survivor Network (CCSN) is a national network of patients, families, survivors, friends, community partners, funders and sponsors who have come together to take action to promote the very best standards of care, whether it be early diagnosis, timely treatment and follow-up care, support for cancer patients, or issues related to survivorship or quality of end of life care. CCSN works to connect patients, survivors and other stakeholder groups with decision makers and the wider community to engage in discussion and to act on evidence-based best practices to alleviate the medical, emotional, financial and social costs of cancer and encourage research on ways to overcome barriers to optimal cancer care for survivors in Canada.

1.2 Conflict of Interest Declarations

Conflict of Interest Declaration: In 2015, CCSN has received contributions from: Amgen; Astellas; Bayer; Boehringer Ingelheim; BristolMyersSquibb; Eisai; Janssen; Lilly; Merck; Novartis.

Section 2 — Condition and Current Therapy Information

2.1 Information Gathering

The information to complete section 2 was obtained through a survey which received 12 responses; half of the respondents (6) had experience with Xgeva.

2.2 Impact of Condition on Patients

The impact of bone metastases from solid tumours included sleeping problems – insomnia (8 of 12); weakness (7 of 12); living with uncertainty (half); bone pain (4 of 12); spinal compression (3 of 12); fractures, weight loss – loss of appetite, panic attacks, depression (2 of 12); HCM (1 of 12). Conditions

which were most difficult to control were bone pain (9 of 12); weakness (8 of 12); fractures (half); sleeping problems – insomnia (half); spinal compression (4 of 12).

2.3 Patients' Experiences With Current Therapy

Current therapy for the eight patients who responded to this question included radiation (3 of 8); surgery (2 of 8); Zometa (1 of 8); Xgeva (7 of 8); clinical trial (1 of 8).

It was clear from the additional comments patients made that most were trying varied treatments to stability their bone metastases. Comments included:

“Hormone blocker then chemo, using extensive naturopathic methods and radical diet change. Now about to start Abiraterone as PSA has risen to 30.”

“GemCarbo – active chemotherapy; stage IV metastatic patient.”

“Zytiga, prednisone and calcium, Vitamin D.”

“ADT (Eligard), Xtandi, had radiation in past but failed as cancer progressed.”

Treatment side effects identified by the 11 patients who responded to this question included: fatigue (10 of 11); muscle weakness (7 of 11); bone pain (6 of 11); joint pain (6 of 11); anemia (3 of 11); rash of eczema (3 of 11); nausea and vomiting (1 of 11); shortness of breath (1 of 11).

The most difficult for patients to deal with were fatigue, muscle weakness, and joint pain.

Of 11 patients who answered the question about whether they had problems accessing treatment, two replied that their problem related to travel costs associated with getting treatment, one had issues related to supplies or administration, and one experienced financial hardship related to cost.

Two of 10 who stated that there were needs in their current therapy that were not being met. When asked what issues they would hope a new drug would address to manage bone metastases, 9 responded stop disease progression; 6 responded better able to control symptoms; 5 responded reduce side effects from current medications; and 3 responded ease of use. One comment added was “obviously want to stop my bone mets from getting worse and having fractures.”

2.4 Impact on Caregivers

Please note that no caregivers responded to our survey.

Section 3 — Information about the Drug Being Reviewed

3.1 Information Gathering

Please see 2.1.

3.2 What Are the Expectations for the New Drug or What Experiences Have Patients Had With the New Drug?

Six patients indicated experience with Xgeva. When asked what issues are better managed on Xgeva than on their previous therapy, 4 responded ease of use; 3 responded better able to control symptoms; 3 responded stop disease progression; 2 responded reduction in side effects from current medication or treatment; and one responded that there was no difference.

Comments included:

“I have fewer bone mets, and therefore, less pain.”

“Metastatic areas on my bone scan seem to be stabilized.”

“Don’t have as much bone pain.”

“I do not have the digestive issues I experienced with the oral biophosphinates.”

“I do not have to wait for two hours before after using Xgeva, as I did with oral bone mets treatments.”

“Once a month injection is very tolerable.”

Adverse effects reported were:

“Flu-like symptoms, additional fatigue, short-term bone and muscle pain/stiffness.”

“No adverse effects other than fatigue and loss of strength. The latter probably has more to do with hormone therapy (Zoladex) than Denosumab.”

“Sore jaw.”

When asked what expectations they had for their long-term health and well-being as a result of taking Xgeva, patients responded:

“Control of my bone mets and symptoms related thereto.”

“Several more years of life pain free.”

“ Less bone problems.”

“Hopefully my bone mets won’t get worse.”

“No spinal compression or fractures.”

“Hopefully stops cancer progression and allows bone growth. Strengthens bones to prevent future fractures.”

From this small sample of patients, half of whom were taking Xgeva, patients reported that this drug was easier to use, reduced side effects, increased the ability control symptoms, and reduced disease progression.

Rethink Breast Cancer

Section 1 — General Information

Name of the drug	Xgeva - Denosumab (Drug Plan Submission)
Name of the patient group	Rethink Breast Cancer
Name of the primary contact for this submission:	[REDACTED]
Position or title with patient group	[REDACTED]
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Website	www.rethinkbreastcancer.com
Permission is granted for CADTH to post this submission	Yes

1.1 Submitting Organization

Launched in 2001, Rethink Breast Cancer™ is the first-ever, Canadian breast cancer charity to bring bold, relevant awareness to the 40s and under crowd; foster a new generation of young and influential breast cancer supporters; infuse sass and style into the cause; and, most importantly, respond to the unique needs of young (or youngish) women going through it.

Rethink is not a membership based organization. We have a Board of Directors, Scientific Advisory Committee and Young Women's Network that guide us at the national level.

1.2 Conflict of Interest Declarations

Roche
 Novartis
 Amgan
 Allergan
 Genomic Health
 Astra Zeneca
 Pfizer

Section 2 — Condition and Current Therapy Information

2.1 Information Gathering

The following information was collected by Rethink Breast Cancer (Rethink)

1. 2012 Metastatic Breast Cancer Patient and Caregiver Survey: An online survey was distributed to patients living with metastatic breast cancer and their caregivers. No patients surveyed had experience with the treatment under review. Survey questions comprised of a combination of scoring options and free form commentary. Patients were contacted through the membership databases of Canadian Breast Cancer Network (CBCN) and Rethink Breast Cancer (Rethink).
71 patients participated in the survey
16 caregivers participated in the survey
2. Breast Cancer: Economic Impact and Labour Force Re-entry. Canadian Breast Cancer Network, 2010
3. Input from Rethink Breast Cancer's Scientific Advisory Committee

2.2 Impact of Condition on Patients

Metastatic breast cancer is the spread of cancerous cell growth to areas of the body other than where the cancer first formed, and is often more severe. It is most commonly spread to the bones, but can include the lungs, liver, brain and bones. Current treatment options for metastatic breast cancer are only effective at prolonging progression-free disease, and most cases of advanced disease will progress and symptoms will worsen. Patients with a diagnosis of metastatic breast cancer understand the limitations of current treatment options, and seek to live their remaining months and years with the best possible quality of life that they can achieve.

The physical impact of metastatic breast cancer -How the disease presents itself through symptoms, how it progresses, and how it is experienced varies by patient, but many effects of metastatic breast cancer represent a significant or debilitating impact on their quality of life. In the 2012 Metastatic Breast Cancer Patient and Caregiver Survey (2012 Survey), patients were asked what impact **cancer related symptoms** had on their quality of life:

- 54% of patients reported that **fatigue** resulted in a significant or debilitating impact, and 40% reported some or moderate impact;
- 39% of patients reported that **insomnia** resulted in a significant or debilitating impact, and 46% reported some or moderate impact;
- 37% of patients reported that **pain** resulted in a significant or debilitating impact, and 44% reported some or moderate impact;
- 31% of patients reported that **problems concentrating** resulted in a significant or debilitating impact, and 59% reported some or moderate impact;
- 26% of patients reported that **depression** resulted in a significant or debilitating impact, and 53% reported some or moderate impact

Other physical symptoms that were identified by patients include: early menopause, mood swings, loss of appetite, neuropathy, loss of balance, incontinence, and skin bruising.

The social impact of metastatic breast cancer

The impact of this disease spreads across all aspects of a patient's life, restricting an individual's employment and career, ability to care for children and dependents, and their ability to be social and

meaningfully participate in their community. When asked in the 2012 Survey what kind of **impact living with metastatic breast cancer** has had on their quality of life:

- Among those who were employed, 71% of patients identified significant restrictions to **their ability to work**;
- Among those with children or dependents, 21% identified significant restrictions and 53% some or moderate restrictions to **their caregiving responsibilities**;
- 49% of patients identified significant restrictions and 38% identified some or moderate restrictions to their ability to **exercise**;
- 42% of patients identified significant restrictions and 42% identified some or moderate restrictions to their ability to **pursue hobbies and personal interests**;
- 41% of patients identified significant restrictions and 41% identified some or moderate restrictions to their ability to **participate in social events and activities**;
- 31% of patients identified significant restrictions and 46% identified some or moderate restrictions to their ability to **volunteer**;
- 25% of patients identified significant restrictions and 43% identified some or moderate restrictions to their ability to **self-manage other chronic diseases or health issues**.
- 22% of patients identified significant restrictions and 52% identified some or moderate restrictions to their ability to spend time with loved ones.

Other experiences identified by patients: guilt, the feeling of being a burden on caregivers, fear of death, poor body image, not knowing what functionality will be lost, fear of impact of the cancer and the loss of a parent on children, not knowing what will happen to children, the loss of support of loved ones, marital stress/loss of fidelity and affection from husband.

2.3 Patients' Experiences With Current Therapy

The goals of current therapy

The goals of current treatment options for metastatic breast cancer include controlling the progression of the disease (extending life), and reducing cancer-related symptoms (extending or stabilising quality of life). Treatment options and effectiveness vary among type of cancer, location of cancer, and how symptoms are experienced.

Patient willingness to tolerate treatment side effects

In the 2012 survey, when asked what level of side effects and how much impact on one's quality of life would be worth extending progression-free disease by six months, the message sent by patients was that this assessment can only be determined by an individual patient, in this circumstance.

When asked to rate how much impact different symptoms of cancer and cancer treatment would be considered tolerable:

- Almost two-thirds of patients indicated that when it comes to **fatigue, nausea, depression, problems with concentration, memory loss, diarrhea and insomnia**, some or a moderate impact on one's quality of life would be considered acceptable, and approximately one quarter of patients indicated that a strong or debilitating impact would be considered acceptable.
- 70% of patients indicated that when it comes to **pain**, some or a moderate impact on one's quality of life would be considered acceptable, and 27% of patients indicated that a strong or debilitating impact would be considered acceptable.

Based on comments provided in the open-ended portion of the survey section, patients made two observations that put limitations on this statistical data:

1. Some patients felt they did not understand the wording of the question.
2. Some patients did not feel that they had the capacity to respond to a hypothetical question of this nature.

“My preference is for access to lots of treatments so I can live for long time. Less side effects are preferable, but if there is no option I will put up with symptoms of treatment in order to live longer.” – Patient

“Not all patients suffer the same way. [...] It was a difficult task to answer that question.” – Patient

Patient willingness to tolerate risk

When asked in the 2012 survey about their willingness to tolerate risk with a new treatment:

- 34% were willing to accept serious risk with treatment if it would control the disease
- 45% were willing to accept some risk with treatment
- 21% were very concerned and felt less comfortable with serious risks with treatment

The financial burden of treating and managing breast cancer

The financial burden associated with living with breast cancer extends far beyond any loss of income during a temporary or permanent absence from employment. In addition to the loss of income during illness, breast cancer patients can incur substantial costs associated with treatment and disease management.

Research on the financial impact of breast cancer on patients identified the following:ⁱ

- 80% of breast cancer patients report a financial impact due to their illness.
- Patients who are self-employed frequently do not have health care coverage that will cover the cost of treatment for the breast cancer, nor medication and alternative treatments such as massage, acupuncture and nutritional counselling to manage side effects.
- Many patients are not eligible for their corporate health care plan, or face confusing and time-consuming application processes to access corporate or government assistance plans.
- 44% of patients have used their savings, and 27% have taken on debt to cover costs.
- Compared to other types of cancer, breast cancer results in higher out of pocket expenses related to devices and family care costs, and has a higher perceived financial burden among patients. Examples of common costs include:
 - childcare when ill, when receiving clinic-based clinics, and when travelling to receive treatment in another community or region;
 - Parking costs during treatment and medical appointments; and
 - Transportation and accommodation costs when patients must travel to receive treatment in another community or region.

These findings were consistent with the responses in the 2012 Survey:

- Nearly one third of patients indicated that the **cost of medication, the cost of alternative treatments (i.e. massage, physiotherapy, etc.) to manage symptoms and side effects, and the time required to travel to treatment** had a significant or debilitating impact on their quality of life.
- 24% of patients indicated that the **costs associated with travel** had a significant or debilitating impact on their quality of life, and 41% of patients indicated that it had some or moderate impact on their quality of life.

Other barriers that were mentioned include: not qualifying for insurance at work, inability to change employers due to loss of insurance, and the prohibitive cost of new treatment options.

“Many of the next step treatments are very expensive [and not covered by government programs] and it is a HUGE struggle to get [coverage]. [...] When dealing with an incurable disease the last thing you want to have to do is spend time on a letter writing campaign to argue about whether or not you should receive the drugs [recommended by your physician]. At about \$1500.00 a week, I don't know many who can afford that.” - Patient

Patient access to local resources and supports during treatment

When living with cancer, many patients experience significant barriers and challenges around availability of health care services and quality childcare in their community. In response to 2012 Survey questions about the availability of supports such as childcare, transportation, and alternative treatments in their community:

- Among patients with children or other dependents, 53% indicated that there is minimal or no access to appropriate care for their loved ones when they are experiencing debilitating symptoms related to their cancer, and 40% identified barriers to accessing quality care during cancer treatment.
- 26% of patients indicated that there are minimal or no transportation options in their community when they seek treatment and support for symptoms, and 18% indicated a serious lack of adequate transportation options to access cancer treatment. One patient indicated that in a rural community, it is difficult to get to the hospital in the winter months.

2.4 Impact on Caregivers

While they provide loving support, caregivers experience a significant negative impact on their quality of life. In response to the 2012 Survey, caregivers reported experiencing a number of symptoms of stress, as well as a negative impact on their ability to continue their daily routines, responsibilities, and self-care for personal health issues.

The physical impact of caregiving for someone with metastatic breast cancer

Among the participants of the survey:

- 77% of caregivers indicated that **anxiety, fatigue, and problems with concentration** had a negative impact on their quality of life;
- 67% of caregivers indicated that **depression and insomnia** had a negative impact on their quality of life; and
- 55% of caregivers indicated that **memory loss and physical pain** such as muscle tension had a negative impact on their quality of life.

The social and financial impact of caregiving for someone with metastatic cancer

All caregivers reported that their role has resulted in a negative impact on their personal, social, and professional lives. Among the participants of the 2012 Survey:

- 100% of caregivers identified restrictions to their employment, their ability to pursue personal interests and hobbies, their ability to travel, and their ability to exercise. One respondent indicated that there was a clear impact on his or her ability to fulfill his job responsibilities and negatively impacted on his or her career progression.;
- 89% of caregivers identified restrictions to their ability to participate in social events and activities;
- 75% of caregivers identified restrictions to their ability to volunteer;
- 67% of caregivers identified restrictions to their ability to spend time with loved ones; and

- 44% of caregivers identified restrictions to their ability to care for children and dependents.

“I do not want to be a burden on my family. I would not want my family to decline/lose good opportunities in their careers & restrict them in anyway on my behalf/condition.” – Patient

Section 3 — Information about the Drug Being Reviewed

3.1 Information Gathering

The following information was collected by Rethink Breast Cancer (Rethink)

1. Key informant interviews: Online/telephone interview was conducted with five patients that have direct experience with the treatment under review.
2. Input from Rethink Breast Cancer’s Scientific Advisory Committee

3.2 What Are the Expectations for the New Drug or What Experiences Have Patients Had With the New Drug?

Impact on patients

By reducing the risk of developing skeletal-related events in patients with bone metastases from breast cancer, this treatment can improve a patient’s quality of life. When living with no or with minimal cancer-related symptoms, and with minimal side effects from the treatment, patients are able to reduce the impact of cancer on their ability to care for children and dependents, continue with their employment and earn income, spend time with loved ones and participate in their life in a meaningful way by engaging in social activities, travelling, maintaining friendships, and pursuing personal interests.

Value to patients

The value to patients of extending the time that their cancer is progression-free cannot be overestimated. Patients living with metastatic breast cancer are aware that their advanced disease will progress with worsening symptoms until death, and embrace opportunities to try new treatment, even if benefits may be as little as a six month extension of progression-free disease. It is also very important for patients to have quality of life when receiving treatment for metastatic disease. Patients that we speak to on a regular basis acknowledge the importance to have the energy to attend the children’s activities and to spend time with family and friends. A number of patients express concern over the costs of the treatment, indicating that new treatments often come with high costs which must be covered by patients out of pocket, or which require lengthy processes for public and private insurance to secure approval for the expense.

All five patients we spoke to have very positive experiences taking XGEVA. For four out of five patients XGEVA is being used as a 1st line therapy. One patient as a 2nd line of therapy. The 2nd line patient had a terrible reaction to the previous therapy and has no adverse effects taking XGEVA. She finds the injection much easier than IV (previous method). One patient interviewed said, “I am in and out of the hospital within 10 minutes - it is a simple subcutaneous injection that I do not find at all painful and doesn’t leave me with any bruising, swelling, etc after.”

None of the patients surveyed have experienced adverse side effects from XGEVA. The women only had positives things to say about the treatment. It has helped with their quality of life and has kept their bone metastases stable.

“I have been on Xgeva for about a year now, since my diagnosis of stage IV breast cancer with metastases to my vertebrae (February 2014). Since beginning my cancer treatments CT scans continue to show further healing in my spine. Prior to beginning treatment, I was unable to lift my son out of his crib - today, I am running and rebounding and downhill skiing without any pain or discomfort.” ~XGEVA patient

“I have gone from extreme pain in my back, to basically none at all.” ~ XGEVA patient

“I am not living with pain, which allows me to remain active which I believe will also have a positive impact on my long-term health.” ~ XGEVA patient

One patient experienced no evidence of metastases of her bones after taking XGEVA for three years. Her most recent bone scan came back as no evidence of disease. She attributes XGEVA to “saving her life.”

For these women, quality of life is extremely important. XGEVA is giving them the opportunity to go back to daily activities before their diagnosis of bone metastases.

“It’s given me back mobility to carry on with life and do activities - back to being where I used to - aerobics, housework. I have a 10 year old & can keep up to her.” ~ XGEVA patient

“I love Xgeva, actually. :-) Everyone should have access to it.”~ XGEVA patient

i Janet Dunbrack, Breast Cancer: Economic Impact and Labour Force Re-entry. Canadian Breast Cancer Network, 2010

Canadian Breast Cancer Network

Section 1 — General Information

Name of the drug	Xgeva/Denosumab (Drug Plan Submission) Prevention of skeletal-related events due to bone metastases from solid tumours
Name of the patient group	The Canadian Breast Cancer Network
Name of the primary contact for this submission:	██████████
Position or title with patient group	██
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Website	www.cbcn.ca
Permission is granted for CADTH to post this submission	No

The patient group has not granted permission to post its patient input submission. As announced in [CDR Update — Issue 99](#), when permission is not granted, CADTH will post on its website that a patient submission was received, but it was not posted at the request of the submitter.

The patient input that was provided in this submission, along with all other patient input received for this drug, is included in the summary of patient input that is contained in the posted *CDR Clinical Review Report*.