MYELOMA CANADA
MAKING MYELOMA MATTER

InfoSheet

GENERIC DRUGS IN CANADA

What are generic drugs, or 'generics'?

Generic drugs are pharmaceutically equivalent (bioequivalent) copies of brand name drugs. Compared to their brand name counterparts, generic drugs:

- are created to have no significant difference in terms of safety, efficacy, mode of administration, quality, and expected behaviour in the body;
- contain identical medicinal ingredients;
- may have different non-medicinal ingredients.

To be available for sale in Canada, a generic drug must be approved for sale by Health Canada and must demonstrate bioequivalence to its brand name counterpart.

- **Bioequivalence means that there is no significant difference between the generic and brand name drug in how:**
  - quickly medicinal ingredients are absorbed;
  - quickly medicinal ingredients reach a certain level in the blood (bioavailability);
  - the generic drug acts in the body and that it's as safe and effective as its brand name counterpart.

Innovative brand name drugs are usually protected by national and international patents, as well as data protection requirements (period of market exclusivity). Generic drugs can only be sold after these protections expire.

- **More than one generic version of the same brand name drug may be available**.

How are generic drugs tested and reviewed?

Companies who have created/developed a generic drug and want to sell it in Canada must complete a generic drug submission for review by Health Canada.

- **Generic companies conduct studies with human volunteers to ensure that the pharmaceutical bioequivalence of a generic drug to its brand name version are met.**
  - The two drugs are taken by different groups of people at the same dose and in the same way (i.e., oral, injection);
  - For each group, level(s) of the medicinal ingredient(s) in the blood are measured at specific timepoints to calculate the drugs' bioavailability.
  - Results and data from the studies are provided in the generic drug submission. This includes information of the generic drug compared to the brand name drug, i.e.: what the body does to a drug as the drug moves through and out of the body (i.e., absorption, bioavailability, distribution, metabolism, and excretion).

- The generic drug submission must also contain information on how the drug will be made (i.e., processes, ingredients with amounts and specifications) and tested (i.e., during manufacture, before being distributed or sold).

How are generic drug submissions reviewed?

Generic drug submissions go through a very similar review process as brand name drug submissions by scientists in the Health Products and Food (HPFB) Branch of Health Canada.

- **The HPFB review process includes a thorough evaluation of the submitted information, and:**
  - may sometimes include external consultants and advisory committees;
  - evaluates the safety, efficacy and quality data to determine potential benefits and risks of the generic drug;
  - reviews information about the drug that will be provided to healthcare professionals and patients (e.g., drug label and product brochure).

What tests are used to diagnose and monitor AL amyloidosis?

Prompt initial assessments are crucial for the diagnosis of AL amyloidosis. The most common tests used to diagnose the disease include:

- Blood tests:
  - **Serum free light chain assay** - measures normal and abnormal light chains
  - **Complete blood count** - measures red blood cells, white blood cells, and platelets
- 24-hour measurement of urine protein
- Bone marrow biopsy: Looks for and quantifies abnormal plasma cells
- Heart biomarkers (BNP, NT-proBNP), kidney function (creatinine clearance), and liver function tests
- Heart-specific tests (e.g., echocardiogram, electrocardiogram, heart MRI)
- Tissue biopsy: Removal and examination of some tissue from the affected organ(s). This is used to identify - or type - the amyloid protein affecting the tissues and/or organs. Results often take longer but are key to diagnosing the disease.

The same tests are used to monitor for disease relapse.

How is AL amyloidosis treated?

Treatments for AL amyloidosis are similar to those for multiple myeloma. Newly diagnosed AL amyloidosis patients may benefit from:

- treatment with a combination of drugs called CyBorD (cyclophosphamide, bortezomib [Velcade], dexamethasone);
- daratumumab (Darzalex) in combination with CyBorD (may not be available in all provinces/territories);
- high-dose therapy and autologous stem cell transplantation. (See Myeloma Canada's *High-dose Therapy and Autologous Stem Cell Transplantation InfoGuide* on Myeloma Canada's website, myeloma.ca, under Resources.)

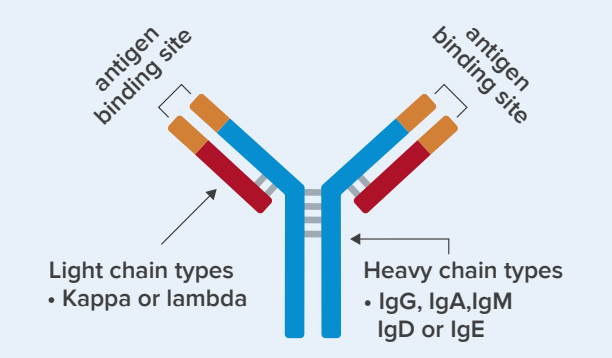
At relapse, new amyloid protein fibre deposits build-up in tissues and/or organs. Treatment should be individualized based on previous therapies and potential side effects. Relapsed AL amyloidosis may be treated with the same combination of drugs as before or a different combination of drugs.

Supportive care treatments can be given alongside AL amyloidosis treatment to control or alleviate the symptoms and complications of the disease, as well as any side effects that may result from the treatment itself.

Where do amyloid protein fibres come from?

Healthy plasma cells produce a variety of antibodies (proteins known as *immunoglobulins*) that circulate in the blood and are critical to the body's immune system function. (See Figure 1)

Figure 1. Structure of an antibody (immunoglobulin)



In AL amyloidosis, abnormal plasma cells:

- overproduce unstable immunoglobulin light chain fragments that circulate in the blood;
- produce abnormal immunoglobulins that have no useful function.

Unstable immunoglobulin light chain (e.g., kappa or lambda) fragments can misfold or "become sticky" and link together to form amyloid protein fibres.

Can amyloid protein fibre deposits be broken down by the body?

Amyloid protein fibre deposits, or protein fibres, are broken down extremely slowly (months to years) by the body.

Can amyloid protein fibre deposits be broken down by treatment?

Treatments for AL amyloidosis cannot effectively break down amyloid protein fibre deposits.

Treatment can:

- kill abnormal plasma cells to prevent new deposits from forming;
- allow for effective disease control, symptom reduction, and improved quality of life;
- result in periods of remission where the disease is not active or causing symptoms.

Over time, AL amyloidosis will likely become active again (disease relapse).

Myeloma Canada publications are reviewed by patients and healthcare professionals prior to publication. Thank you to Dr Victor H. Jimenez-Zepeda for his insights. IS_AL_01/2022_1