Important Safety Information
Bacitracin for Injection (50,000 IU per vial) – Risk of Nephrotoxicity and Anaphylactic Reactions

2020/12/21

Audience
Healthcare professionals including pediatricians, infectious disease specialists, surgeons, critical care physicians, emergency physicians, pharmacists, nurses, and intensive care unit (ICU) and emergency room (ER) medical staff.

Key messages

- **Serious cases of nephrotoxicity and hypersensitivity, including allergic contact dermatitis and/or anaphylaxis, have been reported in patients treated with bacitracin for injection following intramuscular and local administration.**
- **Bacitracin for injection products are now contraindicated in patients with impaired renal function, including those taking nephrotoxic drugs.**
- **Healthcare professionals are advised to:**
  - **evaluate renal function before initiating treatment with bacitracin for injection products, daily during therapy, and after treatment has stopped.**
  - **not use bacitracin for injection products concurrently with other nephrotoxic drugs.**
  - **not exceed the recommended daily dose. Maintain fluid intake and urinary output at proper levels to avoid nephrotoxicity.**
  - **discontinue bacitracin for injection products if nephrotoxicity or hypersensitivity reactions occur.**
- **Healthcare professionals are reminded that bacitracin for injection products are NOT indicated as an irrigation solution for intraoperative prophylaxis nor for pre-soaking of medical devices or implants prior to surgery.**
- **Health Canada is working with the manufacturers of bacitracin for injection products to update the Canadian Product Monographs to further strengthen the information about nephrotoxicity and to include information about anaphylactic reactions.**

What is the issue?

Health Canada recently conducted a safety review and found there may be a link between the use of bacitracin for injection products and the risk of nephrotoxicity and hypersensitivity, including allergic contact dermatitis and/or anaphylaxis. Cases of nephrotoxicity and serious hypersensitivity, including allergic contact dermatitis and/or anaphylaxis, have also been reported when these products are used outside of their authorized indications. Health Canada is working with the manufacturers to update the Canadian Product Monographs for all bacitracin for injection products to further strengthen the information about nephrotoxicity and to include information about anaphylactic reactions.

Products affected

Brand/Product Name	Dosage Form and Strength	Manufacturer	Drug Identification Number (DIN)
BACIJECT	Powder for Solution, 50,000 IU/ vial	SteriMax Inc.	02245571
BACITRACIN USP	Powder for Solution, 50,000 IU/ vial	Pfizer Canada ULC	00030708
BACITRACIN FOR INJECTION*	Powder for Solution, 50,000 IU/ vial	Fresenius Kabi Canada Ltd.	02255820
BACITRACIN FOR INJECTION, USP*	Powder for Solution, 50,000 IU/ vial	Auro Pharma Inc.	02491109

*This product has been authorized for sale, but it is not marketed in Canada at this time.

Background information

Bacitracin for injection products are indicated for intramuscular use in the treatment of infants with pneumonia and empyema caused by staphylococci shown to be susceptible to the drug.

Bacitracin solutions, applied locally in the form of compresses or instillations, may be used once or twice daily in secondarily infected wounds, ulcers, pyodermas and other superficial skin infections and in superficial infections of the eye caused by bacitracin-susceptible organisms. Bacitracin solutions may be instilled into the nasal cavities or administered by inhalation as an aerosol in the treatment of bacitracin-susceptible infections of the upper and lower respiratory tract. In severe or extensive infections, appropriate antibacterial therapy should be given in addition to local treatment with bacitracin.

Health Canada conducted a safety review and concluded that there may be a link between the use of bacitracin for injection products and the risk of nephrotoxicity and serious hypersensitivity, including allergic contact dermatitis and/or anaphylaxis. This safety review was triggered by the United States Food and Drug Administration (U.S. FDA) Drug Safety Communication dated January 31, 2020. In that communication, the FDA requested all current U.S. manufacturers of bacitracin for injection to voluntarily withdraw their product from the U.S. market. The FDA review determined that U.S. healthcare professionals no longer use bacitracin for

injection, and considered the availability of other approved, effective treatments that do not have the same serious risks, including nephrotoxicity and anaphylactic reactions. Health Canada's review did not include non-prescription bacitracin-containing products marketed as ointments since no safety concerns for these products were identified in the U.S. FDA's Drug Safety Communication.

Bacitracin for injection products are now contraindicated in patients with impaired renal function, including those taking nephrotoxic drugs.

To further minimize risks in Canada, Health Canada, in collaboration with the manufacturers of bacitracin for injection products, will update the *Contraindications*, *Warnings and Precautions (*including *the Serious Warnings and Precautions Box), and Consumer Information* sections of the Canadian Product Monographs for all bacitracin for injection products. These updates will strengthen statements regarding the risk of nephrotoxicity, including kidney failure, and include information about serious hypersensitivity, including allergic contact dermatitis and/or anaphylaxis, in patients exposed to bacitracin.

Health Canada will also work with the manufacturers of bacitracin for injection products to collect information on utilization of these products and physician awareness of these risks in Canada. After reviewing this information, Health Canada will determine if further measures are needed to mitigate the risks.

Information for consumers
Bacitracin for injection products are prescription drugs used to treat:

- infants with pneumonia and accumulation of pus in the chest (empyema) caused by staphylococci, a type of bacteria, when administered by injection into the muscle.
- infected wounds, ulcers, large painful skin sores, and other surface skin and eye infections, when applied locally in form of compresses or drops.
- upper and lower respiratory tract infections, when applied as nasal drops or administered by aerosol inhalation.

Bacitracin for injection products have been associated with side effects such as serious kidney damage, including kidney failure (a condition where the kidneys become unable to filter waste products from the blood), and serious allergic reactions. Before and during treatment, patients should have blood tests done to check their kidney function.

Patients need to seek immediate medical attention if they experience signs of:

- **kidney damage, including kidney failure** such as back and abdominal pain, change in the colour of urine (pale or dark), decrease in amount of urine produced, nausea, pain or discomfort when urinating, swelling of the legs and ankles, tiredness, weight gain; or
- **allergic reactions** such as difficulty breathing or swallowing, feeling sick to the stomach or vomiting, hives, itchy skin, rash, skin blisters, swelling of the tongue or throat.

Patients should discuss any questions or concerns about this information with their healthcare professional.

Information for healthcare professionals
Bacitracin for injection products are NOT indicated as an irrigation solution for intraoperative prophylaxis nor for pre-soaking of medical devices or implants prior to surgery. Anaphylactic reactions and nephrotoxicity can occur when bacitracin is used in this manner.

Bacitracin for injection products are now contraindicated in patients with impaired renal function, including those taking nephrotoxic drugs.

Healthcare professionals are advised before prescribing or administering bacitracin for injection products to:

- ensure that patients are not hypersensitive to the drug or any ingredient in the formulation or component of the primary container.
- determine that patients do not have impaired renal function and/or are not taking nephrotoxic drugs.

Healthcare professionals are also advised that:

- serious hypersensitivity, including anaphylaxis and/or allergic contact dermatitis, in patients exposed to bacitracin following intramuscular and local administration may occur following the first dose. If hypersensitivity reactions occur, the drug should be discontinued.
- close monitoring of renal function is recommended in patients treated with bacitracin. Glomerular and tubular kidney function must be evaluated and checked before commencement of therapy, as well as during and after treatment. Bacitracin should be used only where adequate laboratory facilities are available and when constant supervision of the patient is possible. The recommended daily dose should not be exceeded and fluid intake and urinary output maintained at proper levels to avoid kidney toxicity. If renal toxicity occurs, the drug should be discontinued.
- concurrent use of other nephrotoxic drugs should be avoided.
- bacitracin may cause renal failure due to tubular and glomerular necrosis due to high systemic absorption. Intramuscular use should be restricted to infants with *Staphylococcal pneumonia* and empyema due to organisms shown to be susceptible to bacitracin.

Action taken by Health Canada
Health Canada, in collaboration with manufacturers of bacitracin for injection products, is working to update the Canadian Product Monographs to further strengthen information about the risk of nephrotoxicity, including kidney failure, and include information about serious hypersensitivity, including allergic contact dermatitis and/or anaphylaxis.

Health Canada is communicating this important safety information to healthcare professionals and Canadians via the Recalls and Safety Alerts Database (https://healthycanadians.gc.ca/recall-alert-rappel-avis/index-eng.php) on the

Healthy Canadians Web Site. This communication will be further distributed through the MedEffect™ e-Notice email notification system as well as social media channels including LinkedIn and Twitter.

Report health or safety concerns

Health Canada's ability to monitor the safety of marketed health products depends on healthcare professionals and consumers reporting adverse reactions and medical device incidents. Any case of nephrotoxicity, hypersensitivity, anaphylactic reaction or other serious or unexpected side effects in patients receiving bacitracin for injection should be reported to the appropriate manufacturer (see "Products affected") or Health Canada.

SteriMax Inc., 2770, Portland Drive, Oakville, ON, L6H 6R4 Phone: 1-800-881-3550 Fax: 1-877-546-7667 E-mail: pv@sterimaxinc.com	Pfizer Canada ULC 17300 Trans-Canada Highway, Kirkland, QC H9J 2M5 Phone: 1-866-723-7111 Fax: 1-855-242-5652
Auro Pharma 3700 Steeles Avenue West, Suite 402, Woodbridge, ON, L4L 8K8 Phone: 905-856-8063; Ext.: 238 Fax: 905-856-8094 Email: pvteam@auropharma.ca	Fresenius Kabi Canada Ltd. 165 Galaxy Boulevard Suite 100, Toronto, ON, M9W 0C8 Phone: 1-877-779-7760 Email: Canada_Vigilance@fresenius-kabi.com

To correct your mailing address or fax number, contact the appropriate MAH.

You can report any suspected adverse reactions associated with the use of health products to Health Canada by:

- Calling toll-free at 1-866-234-2345; or
- Visiting MedEffect™ Canada's Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax.

For other health product inquiries related to this communication, contact Health Canada at:

Marketed Health Products Directorate
E-mail: hc.mhpd-dpsc.sc@canada.ca
Telephone: 613-954-6522
Fax: 613-952-7738

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SteriMax Inc. DocuSigned by: Ritesh Acharya er 16, 2020 | 1:38:47 PM F3EB2DA650A245F... Ritesh Acharya, M. Pharm Executive Vice President, Scientific Affairs SteriMax Inc., Oakville, ON	***Pfizer Canada ULC*** DocuSigned by: 6, 2020 | 2:44:32 PM MST D62C6DFD49824FC... Vratislav Hadrava M.D., Ph.D. Vice President & Medical Director Pfizer Canada ULC
Auro Pharma Inc. DocuSigned by: December 17, 2020 | 1:08:49 PM EST Dr. Rana Harb, Ph.D Vice President, Technical Affairs, RA, QA & PV Auro Pharma Inc., Woodbridge, ON	***Fresenius Kabi Canada Ltd.*** DocuSigned by: December 18, 2020 | 8:37:26 AM EST 63E55950FDCA4EF... Barbara Bednarek Director, Regulatory Affairs Fresenius Kabi Canada Ltd., Toronto, ON