INFORMATION ON ZOLEDRONIC ACID

- Zoledronic acid is an intravenous bisphosphonate which has been proven to be effective in reducing the risk of hip, spine and other fractures. It reduces fracture risk by approximately 50% within one year of initiation.[1-2]

- It is typically given at a dose of 5 mg once a year. One study in women with osteopenia who were at high risk for fracture (many of whom had suffered prior fractures), demonstrated that zoledronic acid 5 mg given at 18 months intervals can also be effective.[3]

- Zoledronic acid must be infused over no less than 15 minutes. For patients with eGFRs less than 45 mg/min, it may be safer to infuse over 30 minutes. Patients should be advised to be well hydrated on the day of their infusion. It is recommended to drink two full cups of fluid before and two full cups after the infusion.

- To ensure that zoledronic acid will be safe for the patient, some screening blood work will be needed prior to each dose.

- Absolute contraindications include hypocalcemia and eGFR < 35 mL/min. Relative contraindications include loop diuretics, NSAIDs (particularly if they have affected renal function), longer term diabetes (especially if not well controlled) and congestive heart failure. A documented 25 hydroxyvitamin D value ≥ 75 recently or within the last few months prior to the infusion is strongly recommended.

- One in 3 patients will experience an acute phase reaction following the very first dose of zoledronic acid. This will consist of low-grade fever, arthralgias, myalgias and fatigue that can last up to 5 days or so. This can be managed with antipyretics. The acute phase reaction typically does not recur with subsequent doses.

- More serious, but extremely rare, complications include acute renal dysfunction (typically only in patients with poor renal function in the first place), osteonecrosis of the jaw (ONJ) and atypical femoral fractures, the latter two more so after prolonged exposure.

- In Nova Scotia, osteoporosis doses of zoledronic acid are usually administered in infusion clinics.

- Like other bisphosphonates, the duration of treatment must be monitored and drug holidays considered where advisable.
    - If using once a year zoledronic acid, the recommendation is for at least 3 doses at one year interval, but should be continued for 6 doses or longer for patients with severe osteoporosis or at very high risk for fractures (e.g., older patients, patients with prior hip or vertebral fractures, patients who suffer a fracture during the first 3 years on treatment, patients on prednisone)
    - The single published study using zoledronic acid every 18 months was limited to a course of 4 doses over a 6-year period.[3]
    - If a drug holiday is offered, the recommendation is typically for a 3-year drug holiday, starting from the date of the first “missed” dose.

STEPS WHEN YOU ARE ORGANIZING A ZOLEDRONIC ACID INFUSION:

For the purpose of this exercise, we are using the generic zoledronic acid formulation with DIN 02422433 because it is the generic formulation that has been the most consistently available to Nova Scotia pharmacies.

- Ensure the patient's screening blood work indicates it will be safe to proceed. There should be a check of serum calcium and eGFR within the month prior to the infusion and a check of 25-hydroxyvitamin D within a few months prior to the infusion (assuming the dose of vitamin D has remained stable).
- Prescribe the zoledronic acid. Specify generic formulation with DIN 02422433 with NO SUBSTITUTION.
- Fill out the infuZe Program enrollment form (attached separately). If the appointment is face-to-face, the patient must sign the consent form. If this is a virtual/phone appointment, you can specify on the form that you have received verbal consent from the patient.
- The patient will be contacted by the infuZe centre within a few days to arrange an appointment for their infusion.
- INSTRUCTIONS TO GIVE TO YOUR PATIENT:
  - Inform them that zoledronic acid is usually not kept in stock at the pharmacy and that it may take up to 3 days for the pharmacy to receive it.
  - Give them the phone number of the infuZe centre (1-877-767-2260) just in case. If they have not been contacted within 7-10 days, ask them to phone the infuZe centre. The aim is to get the infusion shortly after their screening blood work, but within about one month of their screening blood work at the latest.
  - Remind them to bring their zoledronic acid vial with them when they go for their infusion appointment.
  - There will be no charge for the infusion services (it's included in the cost of the medication itself provided the correct infusion enrollment form for the generic formulation that was prescribed has been filled out and signed).
  - Instruct them to drink lots of fluids on the day of their infusion: at least 2 full cups before and 2 full cups after the infusion. Additionally, instruct them to cancel their infusion should a situation occur that might lead to dehydration around the time of their infusion (e.g., unexpected gastro, etc.).

- *SRx Health Solutions* is a specialized pharmacy that provides in-home injection/infusion services. This can be a practical solution for many patients including those who are housebound. This service is available in certain geographic regions of Nova Scotia. There may a charge to the patient (not always). Should your patient prefer this route, fax your prescription to *SRx Health Solutions* at 833-666-0564. They will usually coordinate the rest.

- Generic zoledronic acid is open access on the Nova Scotia Seniors' Pharmacare Program. Just like for alendronate and risedronate, there is no need to fill out any forms.

- For any further information, please consult the zoledronic acid product monograph.

REFERENCES:

1. Black DM, Delmas PD, Eastell R, et al. Once-yearly zoledronic acid for treatment of postmenopausal osteoporosis. N Engl J Med 2007; 356(18): 1809-22.
2. Boonen S, Reginster JY, Kaufman JM, et al. Fracture risk and zoledronic acid therapy in men with osteoporosis. N Engl J Med 2012; 367(18): 1714-23.
3. Reid IR, Horne AM, Mihov B, et al. Fracture prevention with zoledronate in older women with osteopenia. N Engl J Med 2018; 379(25): 2407-16.

Prepared by Dr. Diane Theriault, MD, FRCPC, CCD July 2023

infuZe Infusion Enrollment Form

PHYSICIAN INFORMATION (please print clearly)

Name:		*Email:*
Address:		
Telephone:	*After Hours Emergency Number:*	*Fax:*

I confirm that this patient qualifies for treatment of Zoledronic Acid Injection, Solution for Intravenous Infusion, 5mg/100 ml IV, over no less than 15 minutes, in accordance with the Product Monograph and any contraindications, warning and precautions described therein.

Date: (dd/mm/yyyy)	*Physician Signature:*

PATIENT INFORMATION (please print clearly)

Name:	*DOB: (dd/mm/yyyy)*	☐ *Male* ☐ *Female*
Address:		
Home Telephone:	*Work Phone:*	*Email (optional):*
Caregiver (if applicable):		

PRESCRIPTION INFORMATION

Infuse Zoledronic Acid for Injection 5 mg/100 ml by IV, over no less than 15 minutes, once yearly.

Prescriber Certification:

- *This prescription represents the original of the prescription drug order.*
- *The addressee is the only intended recipient and there are no others.*
- *The original prescription will be invalidated, securely filed and not transmitted elsewhere at another time.*

PATIENT CONSENT (to be completed by the patient)

I, _____ (patient name/on behalf of), understand the services offered by Coverdale Infusion Clinic Inc. My physician has explained the purpose and expected benefit of Zoledronic Acid Injection 5 mg/100mL. I authorize my physician to disclose my personal health information for the infusion program and prescription to Coverdale Infusion Clinic Inc. and its authorized representatives. I authorize the collection, use and disclosure of my personal information. I authorize Coverdale Infusion Clinic Inc. and its authorized representatives using my personal information solely for the dispensing and administering of Zoledronic Acid Injection 5 mg/100mL.

I understand that I may arrange to access the personal information held by Coverdale Infusion Clinic Inc. and may rectify any deficient information, by contacting Coverdale Infusion Clinic Inc. in writing at Coverdale Infusion Clinic Inc., 2848 Main Street, Hillsborough, NB E4H 2Y7, Attn: Privacy Officer. I understand that I may revoke this consent at any time by writing to Coverdale Infusion Clinic Inc. at the address above. I can obtain a copy of Coverdale Infusion Clinic Inc.'s privacy policies by calling 1-877-767-2260 and asking for the Privacy Officer.

Date: (dd/mm/yyyy)	*Patient/POA Signature:*

POWER OF ATTORNEY INFORMATION (if applicable)

Name:	*Telephone:*
Address:	*Email:*

Please send completed form by fax **1-877-905-6146** or email **infuZe@drreddys.com**

To reorder the Infusion Enrollment Form tear pad, please call us at 1-877-767-2260