Regimen Reference Order – BRST – zoledronic acid (Adjuvant)

To order this therapy in ARIA, refer to ADDITIONAL INFORMATION

Planned Course: **Every 3 months for 2 years (8 doses)**
OR
Every 6 months for 3* years (6 doses) (*see Additional Information)

Indication for Use: **Breast Cancer Adjuvant**

CVAD: At Provider's Discretion

Proceed with treatment if:

- ***Calcium equal to or greater than 2.15 mmol/L***
- ***Creatinine clearance equal to or greater than 30 mL/minute****

  *** For patients with Creatinine clearance between 30 and 60 mL/min, dose adjustments for renal dysfunction should be applied according to table below* ***Recommended Dose Adjustments for zoledronic acid***

  ❖ **Contact Physician if parameters not met**

Note: Reporting of albumin-corrected calcium has been discontinued. See ADDITIONAL INFORMATION

SEQUENCE OF MEDICATION ADMINISTRATION

Pre-treatment Requirements

Drug	Dose	CCMB Administration Guideline
Not Applicable		

Treatment Regimen – BRST – zoledronic acid (Adjuvant)

Establish primary solution 500 mL of: normal saline

Drug	Dose	CCMB Administration Guideline
zoledronic acid	4 mg; adjust dose for renal dysfunction (see table below)	IV in normal saline 100 mL over 15 minutes

In the event of an infusion-related hypersensitivity reaction, refer to the **'Hypersensitivity Reaction Standing Order'**

REQUIRED MONITORING

All Doses

- Serum creatinine, calcium and albumin within 21 days prior to each zoledronic acid dose as per Physician Orders
- Recent patient weight (no more than 3 months prior to zoledronic acid dose)

Recommended Support Medications

Drug	Dose	CCMB Administration Guideline
calcium carbonate*	1250 mg** (500 mg elemental calcium)	Orally twice daily at physician's discretion (providing 1000 mg elemental calcium per day)
cholecalciferol (vitamin D3)*	1000 International Units**	Orally once daily at physician's discretion

* May not be recommended in the presence of hypercalcemia
** Daily calcium and vitamin D requirements should account for both dietary sources and supplements

DISCHARGE INSTRUCTIONS

- Patient should advise dentist/hygienist that they are receiving zoledronic acid
- Ensure patient is given appointment for next dose

ADDITIONAL INFORMATION

- zoledronic acid can cause osteonecrosis of the jaw
- All **new patients** will start on zoledronic acid every 3 months for 2 years total duration
- For patients receiving zoledronic acid every 6 months, the optimal duration is 3 years as per the Breast DSG. Treatment up to 5 years is permitted after agreement between patient and prescriber
- zoledronic acid can cause deterioration in renal function and hypocalcemia. Close monitoring of renal function and calcium level is recommended with each dose
- Dose adjustments for renal dysfunction should be applied according to table below *Recommended Dose Adjustments for zoledronic acid*
- In Manitoba, total serum calcium (reported as Calcium in ARIA) is the recommended test for monitoring calcium levels
- zoledronic acid can cause deterioration in renal function and hypocalcemia. Close monitoring of renal function and calcium level is recommended with each dose
- In a patient with reported low calcium, further interpretation of calcium level may be considered by **direct ionized calcium** determination at the prescriber's discretion, when clinically indicated. See Appendix A *Recommended Assessment of Hypocalcemia prior to zoledronic acid*
- In the presence of **hypocalcemia in a patient who is asymptomatic**, is recommended to order direct ionized calcium to confirm normocalcemia or hidden hypocalcemia (asymptomatic but associated with high cardiovascular risk and poor prognosis)
- **ARIA ordering**: Support protocol is available under **zoledronic acid ADJ** in the "Breast Cancer" folder

Recommended Dose Adjustments for zoledronic acid

Creatinine clearance (mL/minute)	zoledronic acid dose
Greater than or equal to 60	4 mg
50 to 59.9	3.5 mg
40 to 49.9	3.3 mg
30 to 39.9	3 mg
Less than 30	Not recommended

Creatinine clearance should be calculated based on actual body weight (ABW)
Patient's dose should be adjusted based on recommended doses above.

Contact physician if:

a) Calcium is less than 2.15 mmol/L **OR**
b) Creatinine clearance less than 30 mL/minute

Consideration should be given to discontinuing zoledronic acid in the presence of persistent renal deterioration, defined as greater than 90 micromol/L increase in baseline serum creatinine from the time of zoledronic acid initiation.

Creatinine Clearance (Cockcroft-Gault Formula)

$$GFR = \frac{N \times (140 - \text{age in years}) \times ABW\ (kg)}{\text{serum creatinine in micromol/L}} = \_\_\_\_\_\ mL/min$$

N = 1.04 in females

N = 1.23 in males

The estimated creatinine clearance is based on limited evidence. Sound clinical judgment and interpretation of the estimation are required, because this equation may not be appropriate for some patient populations (for example, acute renal failure).

APPENDIX A

Recommended Assessment of Hypocalcemia prior to zoledronic acid

Calcium level	Patient assessment/ clinical setting	Further interpretation of calcium recommended
Low (total serum calcium below 2.15 mmol/L)	**Symptomatic** (patient has symptoms of hypocalcemia)	**No -** No further interpretation required; use total serum calcium results. **Delay zoledronic acid**
	Asymptomatic (patient has no symptoms of hypocalcemia)	**Yes - Direct Ionized calcium*** is recommended to confirm either normocalcemia or hidden hypocalcemia (asymptomatic but associated with high cardiovascular risk and poor prognosis)

***Note:** Direct ionized calcium requires collection in a separate anaerobic tube (normal range 1.17 to 1.32)