SACT PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

Bisphosphonates in Myeloma (Multiple Myeloma)

PROTOCOL REF: MPHABMMM
(Version No. 1.0)

Approved for use in:

- Myeloma (to prevent or manage bone disease)

Dosage:

Drug	Dose	Route	Frequency
Zoledronic Acid	**Dependent on renal function**	IV infusion	Day 1 only of a 28 day cycle
Or if creatinine clearance <30mL/min:			
Pamidronate	**30mg**	IV Infusion	Day 1 only of a 28 day cycle

Continue for 2 years from start of myeloma treatment. Can be continued longer if clinically relapsed disease within the 2 years or deriving significant benefit.

Administration:

Patient must be counselled on the following:

- Maintain good oral hygiene, undergo routine dental check-ups, and immediately report any oral symptoms such as dental mobility, pain or swelling, or non-healing of sores or discharge during treatment with bisphosphonates.
- Report any thigh, hip or groin pain and any patient presenting with such symptoms should be evaluated for an incomplete femur fracture. Also report any ear pain or discharge.
- Maintain adequate hydration

Emetogenic risk:

Not applicable.

Supportive treatments:

Adcal D_3 1 twice daily (or equivalent)

Extravasation risk:

Zoledronic Acid: Not vesicant

Pamidronate: Not vesicant

Refer to the CCC policy for the 'Prevention and Management of Extravasation Injuries'

Dosing in renal and hepatic impairment:

	Creatinine Clearance (mL/min)	Zoledronic acid Dose
Renal	≥60	4mg
	50 – 59	3.5mg
	40 – 49	3.3mg
	30 – 39	3.0mg
	<30	Switch to Pamidronate 30mg

Hepatic	Zoledronic Acid	Limited clinical data in significant impairment. No recommendation made.
	Pamidronate	Limited clinical data in significant impairment. Use with caution.

Interactions:

Please refer to the SPC for details regarding drug interactions.

Treatment schedule:

Day	Drug	Dose	Route	Diluent and rate
1	**Zoledronic Acid**	**Dependent on renal function**	**IV**	Sodium Chloride 0.9% 100mL over 15 minutes
	Or			
	Pamidronate	**30mg**	**IV**	Sodium Chloride 0.9% 250mL over 120minutes

Main toxicities:

Hypocalcaemia, hypophosphataemia, renal impairment, bone pain

Zoledronic Acid / Pamidronate	
Common	Hypocalcaemia, hypophosphataemia, renal impairment, headache, conjunctivitis, bone pain, anaemia, nausea, vomiting, decreased appetite, fever, flu-like symptoms
Uncommon	Osteonecrosis of the jaw, atypical femoral fractures, arthritis, hypokalaemia, hypomagnesaemia, acute renal failure, chest pain, muscle cramps, dyspnea, diarrhoea, constipation, abdominal pain

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6	Ongoing
Informed Consent	X							
Clinical Assessment	X							As clinically indicated or at the end of treatment
Dental examination	X						X	Every 6 months
Vitamin D	X							Every 12 months
U&E & LFTs, Magnesium and adjusted calcium	X	X	X	X	X	X	X	Every Cycle
CrCl (Cockcroft and Gault)	X	X	X	X	X	X	X	Every cycle
Height & Weight recorded	X	X	X	X	X	X	X	Every cycle

Dose Modifications and Toxicity Management:

Haematological toxicity:

No dose modifications required.

Non- Haematological toxicity:

See previous section regarding **Dosing in Renal and Hepatic Impairment**.

Calcium & Vitamin D Levels

	Adjusted Calcium (mmol/L)	Treatment
Adjusted Calcium Levels	≥2.6 (High)	Give bisphosphonate as per protocol, omit Adcal D_3
	2.20 – 2.60 (Normal)	Give bisphosphonate as per protocol
	<2.20 (Low)	**OMIT** bisphosphonate, double the dose of Adcal D_3 (2 twice daily) for 3 days and then revert to normal dose (1 twice daily)

Vitamin D deficiency should be corrected prior to initiating bisphosphonate treatment and levels checked annually. If vitamin D deficiency occurs during treatment add in supplementation as per table below.

	Vitamin D (nanomol/L)	Treatment
Vitamin D Levels	26 - 50	Colecalciferol 800 units daily (contained within supportive Adcal D_3, or as separate colecalciferol if hypercalcaemia)
	≤25	Colecalciferol 20,000 units once daily for 15 days and then once a month*

*Vitamin D levels should be re-checked after 6 months and supplementation adjusted as required.

Serious adverse events including osteonecrosis of the jaw and atypical femoral fractures have been reported with bisphosphonate use. Please contact the responsible consultant if the patient reports pain in the jaw, dental issues or recent bone fractures.

References:

1. https://www.medicines.org.uk/emc Zoledronic Acid
2. https://www.medicines.org.uk/emc Disodium Pamidronate
3. BNF available via: https://bnf.nice.org.uk/
4. NICE: CG35 Myeloma: diagnosis and management. Published date: Feb 2016 (updated Oct 2018)
5. Treatment of Vitamin D Deficiency in Adults. Pan Mersey Guideline v1.11. Feb 2018. Available via: https://www.panmerseyapc.nhs.uk/media/2146/vitamind_adult.pdf

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Version History

		Author name and designation	Summary of main changes
		Jennifer Gibson	V1.0