BNSSG Shared Care Guidance
Please complete all sections

Section 1: Heading

Drug	Leuprorelin (Prostap)
Amber ***three months***	
Indication	• Treatment of pre and peri-menopausal women with advanced breast cancer suitable for hormonal manipulation. • Adjuvant treatment of endocrine-responsive early stage breast cancer in both pre- and peri-menopausal women. Indicated for those at higher risk of disease recurrence. Leuprorelin is used in combination with tamoxifen or an aromatase inhibitor, • Indicated for preservation of ovarian function in pre-menopausal women with neoplastic disease undergoing chemotherapy treatment that can cause premature ovarian insufficiency. (Licensed indication for **monthly leuprorelin only).**

Section 2: Treatment Schedule

Usual dose and frequency of administration *(Please indicate if this is licensed or unlicensed and any relevant dosing information)*	11.25mg every 3 months or 3.75mg monthly
Route and formulation	Pre-filled syringe for subcutaneous injection
Duration of treatment	First three months of treatment are carried out in BHOC and then to be taken over by the patient's GP. The recommended total duration for adjuvant endocrine treatment in early stage breast cancer is up to 5-10 years. For advanced breast cancer treatment is usually continued until disease progression or unacceptable toxicity.

Section 3: Monitoring

Please give details of any tests that are required before or during treatment, including frequency, responsibilities (please state whether they will be undertaken in primary or secondary care), cause for adjustment and when it is required to refer back to the specialist.

Baseline tests - where appropriate

Prior to commencing Leuprorelin, premenopausal status should be confirmed by blood concentrations of oestradiol, LH and FSH within the reference ranges for premenopausal women. Please note these results can be difficult to interpret post chemotherapy or if the patient is already on tamoxifen.

NB: Treatment with leuprorelin must be initiated at least 4 weeks before starting aromatase inhibitor treatment.

Bone mineral density should be assessed before starting treatment with leuprorelin, particularly in women who have additional risk factors for osteoporosis. These patients should be closely monitored and treatment for, or prophylaxis of, osteoporosis should be initiated when appropriate

If the patient is to be considered for therapy with an aromatase inhibitor, it is important to confirm adequate ovarian suppression (gonadotrophin analogue- induced menopause) by serial assessment of circulating FSH and estradiol 3-4 months following commencement of leuprorelin and repeated at 12 months. Measurements should be repeated annually thereafter, to avoid a rebound increase in circulating oestrogen caused by the aromatase inhibitor.

NB: Circulating FSH levels are lowered in response to gonadotrophin analogue-induced ovarian suppression unlike natural menopause where FSH levels are elevated.

The risk of musculoskeletal disorders (including joint or musculoskeletal pain) when a GnRH agonist is used in combination with either an aromatase inhibitor or tamoxifen is approximately 89% with the aromatase inhibitor and approximately 76% with tamoxifen.

Premenopausal women with breast cancer receiving GnRH agonist in combination with either an aromatase inhibitor or tamoxifen should have regular monitoring of cardiovascular risk factors (i.e. lipid profile and systolic blood pressure). Premenopausal women receiving leuprorelin in combination with either an aromatase inhibitor or tamoxifen should also have regular monitoring of risk factors for diabetes with blood glucose monitoring on a regular basis and appropriate anti-diabetic treatment initiated, if appropriate, according to national guidelines.

Development or aggravation of diabetes may occur, therefore diabetic patients may require more frequent monitoring of blood glucose during treatment.

Subsequent tests - where appropriate *(Please indicate who takes responsibility for taking bloods and interpreting results)*

Test	Frequency	Who by	Action/management
FSH	3-4 months after treatment initiation. Repeat at 12 months and monitor annually.	Consultant Oncologist	If patient is on combination therapy with an aromatase inhibitor.

Estradiol	3-4 months after treatment initiation. Repeat at 12 months and monitor annually.	Consultant Oncologist	As above

Section 4: Side Effects

Please list only the most pertinent side effects and management. Please provide guidance on when the GP should refer back to the specialist. For everything else, please see BNF or SPC.

Side effects and management	The most frequently reported side effects are the result of oestrogen deficiency. • hot flushes • mood swings including depression (occasionally severe) • vaginal dryness • insomnia • headache • joint and musculoskeletal pain. All side effects to initially be managed with lifestyle advice and/or the appropriate medication. Oestrogen levels return to normal after treatment is discontinued. The induced hypo-estrogenic state results in a small loss in bone density over the course of treatment, some of which may not be reversible. The extent of bone demineralisation due to hypo-estrogenaemia is proportional to time, therefore may be frequently seen after 5 years of treatment. Hypertension has been reported as a targeted adverse event at a very common frequency with GnRH agonist in combination with either exemestane or tamoxifen. Suggest monitoring of BP/ CV risk assessment especially for those with pre-existing HTN or cardiac issues.
Referral back to specialist	If side effects are problematic. If symptoms of worsening metastatic disease arise.

Section 5: Other Issues

(e.g. Drug Interactions, Contra-indications, Cautions, Special Recommendations)

Please list only the most pertinent action for GP to take (For full list please see BNF or SPC)

Issues	No official interaction studies have been performed. (EMC 2020) Since androgen deprivation treatment may prolong the QT interval, the concomitant use of leuprorelin with medicinal products known to prolong the QT interval or medication likely to induce Torsade de pointes should be carefully evaluated. Examples of which include: quinidine, disopyramide, amiodarone, sotalol, dofetilide, ibutilide, antiarrhythmic medicinal products, methadone, moxifloxacin and antipsychotics.
Reminder to ask patient about specific problems	Any of the side effects mentioned previously, diabetic control if relevant.

Section 6: Advice to the patient

Advice for prescribing clinician to inform patient

1. Warn patient/and family of side effects
2. Discuss the monitoring required if they are at risk of CV events or have diabetes.

Section 7: Generic principles of shared care for SECONDARY CARE

Please do not amend.

Core responsibilities

1. Initiating treatment and prescribing for the length of time specified in **section 1.**
2. Undertaking the clinical assessment and monitoring for the length of time specified in **section 1** and thereafter undertaking any ongoing monitoring as detailed in **section 3.**
3. Communicate details of the above in 1 and 2 to GP within the first month of treatment. This information should be transferred in a timely manner.
4. Refer patients to GP and provide information of further action where appropriate e.g. if blood test is due.
5. To provide advice to primary care when appropriate.
6. Review concurrent medications for potential interaction prior to initiation of drug specified in **section 1.**
7. Stopping treatment where appropriate or providing advice on when to stop.
8. Reporting adverse events to the MHRA.
9. Reminder to ask patients about particular problems see **section 5.**

Section 8: Generic principles of shared care for PRIMARY CARE

Please do not amend.

Core responsibilities

1. Responsible for taking over prescribing after the length of time specified in **section 1.**
2. Responsible for any clinical assessment and monitoring if detailed in **section 3** after the length of time specified in **section 1.**
3. Review of any new concurrent medications for potential interactions.
4. Reporting adverse events to the MHRA.
5. Refer for advice to specialist where appropriate.
6. Reminder to ask patients about particular problems see **section 5.**

Section 9: Contact Details

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Section 10: Document Details

Date prepared	5.8.2020
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Section 11: Collaboration

All shared care protocols should be BNSSG wide where possible. Specialists in any one discipline are encouraged to collaborate across the health community in preparing shared care guidance. Please give details

1. Click here to enter details

Section 12: References

Please list references

1. Takeda 2020, Prostap 3 DCS 11.25 mg Powder and Solvent for Prolonged-release Suspension for Injection in Pre-filled syringe. Electronic Medicines Compendium. Online: https://www.medicines.org.uk/emc/product/4651/smpc#INTERACTIONS
2. National Institute for Health and Care Excellence. (NG101) Early and locally advanced breast cancer: diagnosis and management. Online: https://www.nice.org.uk/guidance/ng101
3. Regan MM, Francis PA, Pagani O, et al. Absolute improvements in freedom from distant recurrence with adjuvant endocrine therapies for premenopausal women with hormone receptor-positive (HR+) HER2-negative breast cancer (BC): Results from TEXT and SOFT. J Clin Oncol 36, 2018 (suppl; abstr 503).
4. Burstein et al, 2016. Adjuvant Endocrine Therapy for Women With Hormone Receptor–Positive Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update on Ovarian Suppression. Journal of Clinical Oncology34, no. 14(May 10, 2016)1689-1701