PROSTAP SR DCS/ PROSTAP 3 DCS leuprorelin acetate depot injection 3.75mg/ 11.25mg PRESCRIBING INFORMATION FOR UNITED KINGDOM. Refer to Summaries of Product Characteristics (SmPC) before prescribing.

Presentation: Prostap SR DCS: leuprorelin acetate 3.75mg powder, equivalent to 3.57mg base, powder and solvent for prolonged-release suspension for injection in pre-filled syringe with safety device. **Prostap 3 DCS:** leuprorelin acetate 11.25mg equivalent to 10.72mg base, powder and solvent for prolonged-release suspension for injection in pre-filled syringe with safety device. **Indications: Prostap SR DCS /Prostap 3 DCS:** As treatment in pre- and perimenopausal women with advanced breast cancer suitable for hormonal manipulation; As adjuvant treatment in combination with tamoxifen or an aromatase inhibitor, of endocrine responsive early stage breast cancer in pre- and perimenopausal women at higher risk of disease recurrence (young age, high grade tumour, lymph node involvement). In women who have received chemotherapy, premenopausal status must be confirmed after completion of chemotherapy. **Prostap SR DCS** also indicated for preservation of ovarian function in pre-menopausal women with neoplastic disease undergoing chemotherapy treatment that can cause premature ovarian insufficiency. Prostap SR DCS is not a replacement for standard fertility-preservation methods. Treatment with a GnRH analogue should be proposed after careful evaluation, in each case, of the benefit/risk profile. Prostap 3 DCS should not be used for preservation of ovarian function. **Dosage and administration:** Prostap DCS should be prepared, reconstituted and administered only by healthcare professionals familiar with these procedures. Advanced breast cancer: **Prostap SR DCS:** 3.75 mg administered as a single subcutaneous injection every month. **Prostap 3 DCS**: 11.25 mg as a single subcutaneous injection every 3 months. Early breast cancer: **Prostap SR DCS:** 3.75 mg administered as a single subcutaneous injection every month in combination with tamoxifen or an aromatase inhibitor. **Prostap 3 DCS:** 11.25 mg as a single subcutaneous injection every 3 months in combination with tamoxifen or an aromatase inhibitor. In women receiving chemotherapy, commence leuprorelin after completion of chemotherapy, once pre-menopausal status has been confirmed. Recommended leuprorelin treatment duration for adjuvant treatment in combination with other hormonotherapy is up to 5 years. In combination with aromatase inhibitor for advanced and early breast cancer: Initiate leuprorelin treatment at least 6-8 weeks before aromatase inhibitor treatment and with a minimum of two injections of Prostap SR DCS (with an interval of 1 month between) or a minimum of one injection of Prostap 3 DCS. During treatment with an aromatase inhibitor, leuprorelin must not be interrupted. Preservation of ovarian function: **Prostap SR DCS:** 3.75 mg administered as a single subcutaneous or intramuscular injection. Patients should receive this dose 2 weeks before starting chemotherapy to allow time to achieve suppression of the sex hormone levels and then continue with monthly administration of Prostap SR for the duration of the chemotherapy treatment. Injection site should be varied periodically. Prostap 3 DCS should not be used for preservation of ovarian function.

Contraindications: hypersensitivity to the active substance; any of the excipients or to synthetic GnRH or GnRH-derivatives; lactation; pregnancy; undiagnosed abnormal vaginal bleeding. In the pre- and perimenopausal breast cancer setting: Initiation of aromatase inhibitor treatment before adequate ovarian suppression with leuprorelin has been achieved.

Warnings and precautions: aggravation of diabetes may occur; more frequent blood glucose monitoring recommended in diabetic patients. Hepatic dysfunction and jaundice with elevated liver enzyme levels reported; close observation recommended. Spinal fractures, paralysis, hypotension, worsening of depression have been reported. Patients at high risk for metabolic or cardiovascular diseases should be appropriately monitored. Postmarketing reports of seizures have been reported, and in those with or without a history of epilepsy, seizure disorders or risk disorders for seizures. Advanced and early breast cancer: In order to ensure adequate ovarian suppression in pre- and perimenopausal women, administer leuprorelin for at least 6-8 weeks prior to commencement of an aromatase inhibitor and on schedule without interruption throughout aromatase inhibitor treatment to avoid rebound increases in circulating estrogens in premenopausal women. Following chemotherapy and before commencement of leuprorelin, confirm premenopausal status by blood concentrations of estradiol and FSH, to avoid unnecessary treatment in the event of chemotherapy-induced menopause. Following commencement of leuprorelin and prior to aromatase inhibitor treatment, confirm ovarian suppression by assessment of circulating FSH and estradiol and repeat every 3 months during combination treatment. Discontinue aromatase inhibitors within 1 month of the last Prostap SR DCS administration and within 3 months of the last Prostap 3 DCS administration. Check relevant safety information of co-administered products. Assess bone mineral density before starting treatment and monitor and treat for osteoporosis when appropriate. Risk of musculoskeletal disorders when a GnRH agonist is used in combination with either an aromatase inhibitor or tamoxifen. Hypertension has been reported. Monitor cardiovascular risk factors, blood pressure, hyperglycaemia and diabetes regularly in premenopausal women with breast cancer receiving

GnRH in combination with exemestane or tamoxifen. Monitor patients with depression or depression history. Patients should notify physician if regular menstruation persists. **Interactions:** no studies performed. Carefully evaluate use with medicines that prolong QT interval or induce Torsade de pointes. **Fertility, pregnancy and lactation:** breastfeeding: should not be used. Patients should see their physician if they suspect a pregnancy. Discontinue treatment if patient becomes pregnant whilst on treatment. **Undesirable effects:** adverse events occurring most frequently with Prostap SR DCS and Prostap 3 DCS are associated with hypo-estrogenism. Most frequently reported are hot flushes, mood swings including depression (occasionally severe), and vaginal dryness. Oestrogen levels return to normal after treatment is discontinued. Very Common (≥1/10): insomnia, headache (occasionally severe), hot flush. Common (≥1/100 to <1/10): weight fluctuation, mood altered depression, parathesiae, dizziness, nausea, arthralgia, muscle weakness, breast tenderness, breast atrophy, vulvovaginal dryness, oedema peripheral, injection site reactions. Other serious undesirable effects: pituitary haemorrhage following initial administration in patients with pituitary adenoma, glucose tolerance abnormal, which may affect diabetic control, anaemia, thrombocytopenia, leucopenia, hypersensitivity reactions (including rash, pruritus, urticaria and rarely, wheezing or interstitial pneumonitis, anaphylactic reactions), paralysis, seizure, pulmonary embolism, jaundice, spinal fracture, interstitial lung disease and vaginal haemorrhage. Refer to the SmPC for details on full side effect profile and interactions. **UK Basic NHS Price: Prostap SR DCS:** £75.24; **Prostap 3 DCS** £225.72. **Legal Classification:** POM. **Marketing Authorisation (MA)**: **Prostap SR DCS:** 16189/0012; **Prostap 3 DCS**: 16189/0013. **Name and address of MA holder:** Takeda UK Ltd, 1 Kingdom Street, London, W2 6BD, United Kingdom. **PI approval code:** pi-01224. **Date of preparation:** January 2021.

Adverse events should be reported to the Medicines and Healthcare products Regulatory Agency. Reporting forms and information can be found at: www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Takeda at: AE.GBR-IRL@takeda.com.