

# Benefits of less frequent injections in advanced prostate cancer

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Leuporelin is indicated for the palliative treatment of advanced prostate cancer (APC) and is available as 1, 3, 4 and 6-monthly injections. There are advantages of longer leuporelin injection intervals in the treatment of APC.

Across all injection intervals, efficacy is similar and the majority of patients achieve testosterone suppression and normalisation of prostate-specific antigen. Treatment is well tolerated. Six-monthly leuporelin injections are less costly to the healthcare system than the shorter interval injections.

**E**ven though there is a trend towards earlier detection of prostate cancer, unfortunately, many men are not diagnosed until it has progressed to the later stage, known as advanced prostate cancer (APC). Hormone therapy, also called androgen deprivation therapy, can slow or stop the growth of prostate cancer by stopping the production of testosterone, which prostate cancer cells usually depend on for growth.

More than 80% of men with APC benefit from this treatment, reflected by reduced serum prostate-specific antigen (PSA) levels.<sup>1</sup> A rise in PSA levels following initial prostate cancer treatment can indicate cancer recurrence.<sup>2</sup>

There are two main approaches to hormone therapy: a surgical procedure to remove the testicles (orchidectomy) or

medication to 'switch off' testosterone. Leuporelin is used for palliative treatment of APC and is available as 1, 3, 4 and 6-monthly injections. Are there advantages of giving leuporelin injections less frequently to patients with APC?

A review of long-acting injections for APC in the US<sup>3</sup> found there were no differences between the injection intervals based on efficacy. However, they did find differences in the availability of long-acting formulations, dosage forms, administration techniques, ease of preparation, storage and handling.<sup>3</sup>

Efficacy, in terms of serum testosterone suppression and normalisation of PSA, has been shown to be similar for 1, 3, 4 and 6-month injection intervals (*Table 1*). More common adverse events of hot flushes and fatigue seem to be similar with a slight increase in the proportions of moderate hot flushes with longer interval injections.

A study by Tunn found Italian urologists choose 6-monthly leuporelin injections because of the longer dosing interval (90%), small injection volume of  $\leq 0.5$  ml (20%) and short needle size of pre-filled syringe (15%).<sup>4</sup>

The interval between injections affects the number of consultations with a healthcare practitioner. In addition, the Pharmaceutical Benefits Scheme (PBS) listing for longer interval injection products (3, 4 and 6-monthly) is for one

injection and one repeat. This means that 3-monthly injections require two scripts a year, while 6-monthly injections require just one script per year. The less frequent injection means patients have fewer trips to the pharmacy and doctor.

An economic analysis in nine European countries showed monthly leuporelin injections was the most expensive treatment option, whereas 6-monthly injections offered cost savings.<sup>5</sup> The savings stemmed primarily from reduced resource utilisation (ie fewer visits required for less frequent injections). The savings were greatest in countries with the highest costs associated with visits (Belgium and Portugal), but cost savings could still be achieved in the country with the lowest visit reimbursement level (Poland). The size of savings was directly related to costs of treatment visits.<sup>5</sup>

A similar economic analysis using costs in Australia found the common 4-monthly leuporelin injections (34% of patients) and 3-monthly injections (45% of patients) were more costly when compared with 6-monthly injections (\$142 and \$260 per year respectively; *Table 1*). Monthly injections cost \$1161 more per year when compared to 6-monthly injections (*Table 1*). Significant savings to the healthcare system of \$1.8 million per year could be achieved by converting 1, 3 and 4-monthly injection patients to 6-monthly injections (*Table 1*).

**Table 1. Comparison of leuprorelin treatment by injection interval**

	1-monthly	3-monthly	4-monthly	6-monthly
Strength	7.5 mg	22.5 mg	30 mg	45 mg
PBS repeats	5	1	1	1
Mean serum testosterone at 28 days (SD) <sup>5,7-9</sup>	6.1 (4.3)	10.1 (0.7)	12.4 (0.8)	12.3 (2.1)
Mean PSA levels at 28 days (SD) <sup>5,7-9</sup>	3.2 (1.2)	1.7 (0.5)	1.3 (0.3)	1.2 (0.3)
Drug cost per script*	\$420.54	\$1108.97	\$1451.54	\$2124.19
Administration frequency per year	12	4	3	2
Drug cost per year	\$5046.48	\$4435.88	\$4354.62	\$4248.38
Costs per administration <sup>†</sup>	\$36.30	\$36.30	\$36.30	\$36.30
Total administration cost	\$435.60	\$145.20	\$108.90	\$72.60
Total cost per year	\$5482.08	\$4581.08	\$4463.52	\$4320.98
Difference from 6-monthly injections	\$1161	\$260	\$142	
PBS leuprorelin scripts in 2013 <sup>‡</sup>	3660	15,641	8804	3079
Patients treated with formulation <sup>§</sup>	305	3910	2934	1540
Savings per year	\$354,105	\$1,016,665	\$419,657	

\*Drug Cost March 2014 PBS book, Schedule of Pharmaceutical Benefits, [www.pbs.gov.au/publication/schedule/2015/04/2015-04-01-general-schedule.pdf](http://www.pbs.gov.au/publication/schedule/2015/04/2015-04-01-general-schedule.pdf); <sup>†</sup>Administration cost MBS schedule item 23; <sup>‡</sup>2013 PBS script counts from the Medicare Australia Website, [http://medicarestatistics.humanservices.gov.au/statistics/mbs\\_item.jsp](http://medicarestatistics.humanservices.gov.au/statistics/mbs_item.jsp); <sup>§</sup>Number of patients was estimated by dividing the number of scripts by the number of administrations per year  
PBS, Pharmaceutical Benefits Scheme; PSA, Prostate-specific antigen

Market research of 200 European men with prostate cancer<sup>4</sup> found maintaining lifestyle during treatment was important for the majority (83%). Sixty-eight per cent preferred 6-monthly injections over 1 or 3-monthly injections and nearly half (with 81% aged  $\leq 70$  years of age) believed a 6-monthly injection could improve their quality of life.<sup>6</sup>

There are some advantages to giving shorter interval leuprorelin injections. Some patients do need regular PSA measurement to monitor for leuprorelin-resistance disease. If patients visit their GPs more than once every 3–4 months, the cost savings for the longer interval might not be as large.

Overall, the advantages of longer injection intervals include minimal disruption to patient lifestyle during treatment and a decreased cost to the healthcare system. However, longer durations between injections may mean patients are assessed less frequently by a medical practitioner. The final choice should therefore be discussed with the

patient, taking the risks and benefits of longer injection intervals into account.

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