NHS Tayside Drug & Therapeutics Committee

Local Protocol for the use of Exenatide Injection (Byetta®)

1.	**New medicine name:** Exenatide 5 or 10 micrograms solution for injection, prefilled pen
2.	**Licensed indication(s):** Treatment of type 2 diabetes mellitus in combination with metformin and/or sulphonylureas in patients who have not achieved adequate glycaemic control on maximally tolerated doses of these oral therapies.
3.	**Scottish Medicines Consortium advice:** Exenatide (Byetta®) is accepted for restricted use within NHS Scotland for the treatment of type 2 diabetes mellitus in combination with metformin and/or sulphonylureas in patients who have not achieved adequate glycaemic control on maximally tolerated doses of these oral therapies. It has shown non-inferiority to two insulin regimens with which it has been compared and has a beneficial effect on weight. It is restricted to use as an alternative to insulin in patients who have failed treatment on metformin and/or sulphonylureas and in whom insulin would be the next treatment option. **Medicines Advisory Group advice:** Restricted to patients for whom glitazones are unsuitable. GPs may prescribe under the direction of the diabetic clinic.
4.*	**Prescriber details:** Prescribed by GPs on the recommendation of the diabetic clinic.
5.*	**Criteria for patient selection:** Patients who have failed to achieve glycaemic control on metformin and/or sulphonylureas and in whom glitazones are unsuitable (eg due to heart failure, hepatic impairment or where rapid glycaemic control is required) and who would otherwise move to insulin therapy.
6.	**Administration details:** Therapy should be initiated at 5 micrograms exenatide per dose, administered twice daily, for at least one month in order to improve tolerability. The dose of exenatide can then be increased to 10 micrograms twice daily to further improve glycaemic control. Doses higher than 10 micrograms twice daily are not recommended. Each dose should be administered sc in the thigh, abdomen or upper arm at any time within the 60-minute period before the morning and evening meal (or two main meals of the day at least six hours apart) and should **not** be administered after a meal.
7.	**Contra-indications:** Hypersensitivity to exenatide or excipients.
8.	**Side-effects/cautions:** Exenatide should not be used in type 2 diabetes patients who require insulin therapy due to beta cell failure. The incidence of gastrointestinal side effects is common, 33-57% of patients experienced nausea and 9-17% experiencing vomiting in clinical studies. When exenatide is added to sulphonylurea therapy, a reduction in the dose of sulphonylurea should be considered to reduce the risk of hypoglycaemia. The concurrent use of exenatide with insulin, nateglinide, repaglinide, or acarbose has not been studied. Whilst limited experience of concurrent use with glitazones exists, this is currently unlicensed. There is no experience in children and adolescents below 18 years.

	Exenatide may reduce the extent and rate of absorption of some oral medicines. Patients receiving oral medicines with a narrow therapeutic range or those requiring careful clinical monitoring should be followed closely. Oral medicines dependent on threshold concentrations eg contraceptives or antibiotics should be taken at least one hour before exenatide. Increased INR has been reported during concomitant use with warfarin. Exenatide should be used with caution in the elderly. No dosage adjustment is necessary in patients with mild renal impairment, in patients with moderate impairment, dose escalation from 5 micrograms to 10 micrograms should proceed conservatively. Exenatide is not recommended in patients with end-stage renal disease or severe renal impairment. No dosage adjustment is necessary in patients with hepatic impairment.
9.*	**Monitoring - response to treatment:** The dose of exenatide does not need to be adjusted on a day-by-day basis depending on self-monitored glycaemia. However, blood glucose self-monitoring may become necessary to adjust the dose of sulphonylureas.
10.*	**Monitoring – treatment safety:** Patients receiving oral medicines with a narrow therapeutic range or those requiring careful clinical monitoring should be followed closely (see 8. above).
11.*	**Written by:** Tayside Medicines Unit **Date:** June 2007 **Approved by:** Dr Geraldine Brennan **Date:** June 2007
12.*	**Review date:** June 2008

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