Exenatide Immediate-Release –twice daily (Byetta®)

N.B. Please ensure that the correct preparation of exenatide is selected from GP Prescribing Systems.

Prescribing Information Sheet – Updated November 2020

This document provides general prescribing information on the use of Exenatide twice Daily. For the most up to date information, consult the summary of product characteristics

For information on place in therapy, prescribing and monitoring requirements and responsibilities, please see the 'Overarching Shared Care Guideline for the use of Glucagon-like peptide 1 (GLP 1) agonists.' Document.

Licensed Indications	Immediate-release exenatide (Byetta®) is indicated for treatment of type 2 diabetes mellitus in combination with: - metformin - sulphonylureas - thiazolidinediones - metformin and a sulphonylurea - metformin and a thiazolidinedione in adults who have not achieved adequate glycaemic control on maximally tolerated doses of these oral therapies. Immediate-release exenatide (Byetta®) is also indicated as adjunctive therapy to basal insulin with or without metformin and/or pioglitazone in adults who have not achieved adequate glycaemic control with these medicinal products.
Drug dose	**Adult patients 18 years and over:** • Initially 5 micrograms twice daily for at least 1 month, then increased if necessary up to 10 micrograms twice daily, dose to be taken within 1 hour before 2 main meals (at least 6 hours apart). Immediate-release exenatide **should not** be administered after a meal. • If an injection is missed, the treatment should be continued with the next scheduled dose. • Doses higher than 10 micrograms twice daily are not recommended. **Counselling** If a dose is missed, continue with the next scheduled dose—do not administer after a meal. Some oral medications should be taken at least 1 hour before or 4 hours after exenatide injection—consult product literature for details. Patients or their carers should be told how to recognise signs and symptoms of pancreatitis and advised to seek prompt medical attention if symptoms such as abdominal pain, nausea, and vomiting develop.

	Added to other hypoglycaemic agents When immediate-release exenatide is added to existing metformin and/or pioglitazone therapy, the current dose of metformin and/or pioglitazone can be continued as no increased risk of hypoglycaemia is anticipated, compared to metformin or pioglitazone alone. When immediate-release exenatide is added to sulphonylurea therapy, a reduction in the dose of sulphonylurea should be considered to reduce the risk of hypoglycaemia. When immediate-release exenatide is used in combination with basal insulin, the dose of basal insulin should be evaluated. In patients at increased risk of hypoglycaemia reducing the dose of basal insulin should be considered. The dose of immediate-release exenatide does not need to be adjusted on a day-by-day basis depending on self-monitored glycaemia. Blood glucose self-monitoring is necessary to adjust the dose of sulphonylurea or insulin, particularly when Byetta therapy is started and insulin is reduced. A stepwise approach to insulin dose reduction is recommended.
Drug modifications in Special Populations	**Elderly** • Immediate-release exenatide should be used with caution and dose escalation from 5 mcg to 10 mcg should proceed conservatively in patients >70 years. The clinical experience in patients >75 years is very limited. **Renal impairment** • Use with caution if eGFR 30–50 mL/minute/1.73 m^2 (dose escalation from 5 mcg to 10 mcg should proceed conservatively); avoid if eGFR less than 30 mL/minute/1.73$m^{2.}$. Do not use in patients with end stage renal disease. **Hepatic impairment** • No dosage adjustment is necessary in patients with hepatic impairment.
Administration details	• Immediate-release exenatide (Byetta®) should be given by **subcutaneous injection** administered in the thigh, abdomen, or upper arm. • If exenatide and basal insulin are both prescribed, they should be administered as two separate injections. • Injection site should be rotated. • Immediate-release exenatide (Byetta®) must **not** be administered intravenously or intramuscularly.
Formulations	Injection, exenatide 250 micrograms/mL, 5 microgram/dose prefilled pen (60 doses), 10 microgram/dose prefilled pen (60 doses).
Contra-indications/ Cautions	**Contraindications -** ketoacidosis; severe gastro-intestinal disease; renal disease (not recommended in severe or end stage) **Cautions -** elderly; pancreatitis (see below); may cause weight loss greater than 1.5 kg weekly. **Pancreatitis** Severe pancreatitis (sometimes fatal), including haemorrhagic or necrotising pancreatitis, has been reported rarely. Patients or their carers should be told how to recognise signs and symptoms of pancreatitis and advised to seek prompt medical attention if

	symptoms such as abdominal pain, nausea, and vomiting develop; discontinue permanently if pancreatitis is diagnosed. Exenatide should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. Exenatide is not a substitute for insulin. Diabetic ketoacidosis has been reported in insulin-dependent patients after rapid discontinuation or dose reduction of insulin. The Clinical experience in patients with moderate renal impairment is very limited. Clinicians should refer to the current electronic BNF or Summary of Product Characteristics (SPC's) for full details.
Side effects	Clinicians should refer to the Summary of Product Characteristics (SPC) and current electronic BNF for full details. The most frequent adverse reactions were mainly gastrointestinal related (nausea, vomiting and diarrhoea). The most frequently reported single adverse reaction was nausea which was associated with the initiation of treatment and decreased over time. Patients may experience hypoglycaemia when immediate-release exenatide is used with a sulphonylurea. Most adverse reactions associated with immediate-release exenatide were mild to moderate in intensity. Since immediate-release exenatide has been marketed, acute pancreatitis has been reported with a frequency not known and acute renal failure has been reported uncommonly. **MHRA warning (June 2019)** – GLP-1 receptor agonists: reports of diabetic ketoacidosis when concomitant insulin was rapidly reduced or discontinued. Report all suspected reactions to established drugs that are serious, medically significant, or result in harm to the MHRA using the yellow card scheme. http://yellowcard.mhra.gov.uk/
Drug Interactions	The effect of immediate-release exenatide to slow gastric emptying may reduce the extent and rate of absorption of orally administered medicinal products. Patients receiving medicinal products of either a narrow therapeutic ratio or medicinal products that require careful clinical monitoring should be followed closely. These medicinal products should be taken in a standardised way in relation to immediate-release exenatide injection. If such medicinal products are to be administered with food, patients should be advised to, if possible, take them with a meal when immediate-release exenatide is not administered. For oral medicinal products that are particularly dependent on threshold concentrations for efficacy, such as antibiotics, patients should be advised to take those medicinal products at least 1 hour before immediate-release exenatide injection. Gastroresistant formulations containing substances sensitive for degradation in the stomach, such as proton pump inhibitors, should be taken at least 1 hour before or more than 4 hours after immediate-release exenatide injection. Clinicians should refer to the Summary of Product Characteristics (SPC) and current electronic BNF for full details.

Pregnancy and breast feeding	Pregnancy There are no adequate data from the use of exenatide in pregnant women. Studies in animals have shown reproductive toxicity. The potential risk for humans is unknown. Exenatide should not be used during pregnancy and the use of insulin is recommended. Breast-feeding It is unknown whether exenatide is excreted in human milk. Exenatide should not be used if breast-feeding.
Effects on ability to drive and use machines	Exenatide has minor influence on the ability to drive and use machines. When exenatide is used in combination with a sulphonylurea or a basal insulin, patients should be advised to take precautions to avoid hypoglycaemia while driving and using machines.
Storage	Before use, exenatide should be stored in a refrigerator (2 °C - 8 °C). Once opened and in use it has a shelf-life of 30 days. Exenatide should be stored below 25 °C and the cap should be placed onto the pen when not in use in order to protect the medication from light.

References:-

1. Summary of Product Characteristics for Byetta® (Exenatide), accessed 30/10/20.
2. eBNF, accessed 30/10/20.
3. Drug Safety Update, MHRA, June 2019