

BYETTA  (exenatide)

ABBREVIATED PRESCRIBING INFORMATION

Presentation Synthetic exenatide solution for injection in a pre-filled pen. Each dose contains 5 micrograms (μg) in 20 millilitres, or 10 μg in 40 millilitres. Also contains metacresol.

Uses Byetta is indicated for treatment of Type 2 diabetes mellitus in combination with metformin, sulphonylureas, thiazolidinediones, or combinations of metformin and a sulphonylurea or metformin and a thiazolidinedione in patients who have not achieved adequate glycaemic control on maximally tolerated doses of these oral therapies.

Dosage and Administration Initiate at 5 μg exenatide per dose, administered twice daily (BD), for at least one month. The dose can then be increased to 10 μg BD. Doses higher than 10 μg BD are not recommended. Byetta can be administered at any time within the 60-minute period before the morning and evening meal (or two main meals of the day, approximately 6 hours or more apart). Byetta **should not** be administered after a meal. If an injection is missed, the treatment should be continued with the next scheduled dose. Each dose should be administered as a subcutaneous injection in the thigh, abdomen, or upper arm. When Byetta is added to existing metformin and/or thiazolidinedione therapy, the current dose of metformin and/or thiazolidinedione can be continued as no increased risk of hypoglycaemia is anticipated. When Byetta is added to sulphonylurea therapy, a reduction in the dose of sulphonylurea should be considered to reduce the risk of hypoglycaemia. The dose of Byetta does not need to be adjusted depending on daily self-monitored glycaemia. Blood glucose self-monitoring may be necessary to adjust the dose of sulphonylureas. **Elderly:** Byetta should be used with caution, and dose escalation from 5 μg to 10 μg should proceed conservatively in patients >70 years. **Renal or hepatic impairment:** No dosage adjustment is necessary in patients with mild renal impairment (creatinine clearance 50-80ml/min) or hepatic impairment. In patients with moderate renal impairment (creatinine clearance 30-50ml/min), dose escalation from 5 μg to 10 μg should proceed conservatively. Not recommended for use in patients with end-stage renal disease or severe renal impairment (creatinine clearance <30ml/min). **Children and adolescents:** The safety and effectiveness of exenatide have not been established in patients under 18 years of age.

Contra-indications Hypersensitivity to the active substance or to any of the excipients.

Warnings and Special Precautions Do not use in patients with Type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis, or Type 2 diabetes patients who require insulin therapy due to beta cell failure. Intravenous or intramuscular injection is not recommended. Not recommended for use in patients with end-stage renal disease or severe renal impairment (creatinine clearance <30ml/min). Clinical experience in patients with moderate renal impairment is very limited. There have been rare, spontaneously reported events of altered renal function, including increased serum creatinine, renal impairment, worsened chronic renal failure, and acute renal failure, sometimes requiring haemodialysis. Some of these events occurred in patients receiving pharmacological agents known to affect renal function/hydration status, including angiotensin converting enzymes inhibitors, angiotensin-II antagonists, non-steroidal anti-inflammatory medicinal products, and diuretics. Not recommended in patients with severe gastro-intestinal disease. There have been rare, spontaneously reported events of acute pancreatitis. Patients should be informed of the characteristic symptom of acute pancreatitis: persistent, severe abdominal pain. Resolution of pancreatitis has been observed with supportive treatment but very rare cases of necrotizing or hemorrhagic pancreatitis and/or death have been reported. If pancreatitis is suspected, Byetta and other potentially suspect medicinal products should be discontinued. Treatment with Byetta should not be resumed after pancreatitis has been diagnosed. The concurrent use of Byetta with insulin, D-phenylalanine derivatives, meglitinides, or alpha-glucosidase inhibitors has not been studied and cannot be recommended. Experience in patients with BMI ≤ 25 is limited. Weight loss greater than 1.5 kg per week has been observed in approximately 5% of clinical trial patients treated with exenatide. Weight loss of this rate may have harmful consequences. When Byetta was used in combination with a sulphonylurea, the incidence of hypoglycaemia was increased over that of placebo in combination with a sulphonylurea. To reduce the risk of hypoglycaemia associated with the use of a sulphonylurea, reduction in the dose of sulphonylurea should be considered.

Interactions Patients receiving orally administered medicinal products of either a narrow therapeutic ratio or that require careful clinical monitoring should be followed closely. If such medicinal products are to be administered with food, they should be taken with a meal when Byetta is not administered. Oral medicinal products that are dependent on threshold concentrations for efficacy should be taken at least 1 hour before Byetta injection. Gastro-resistant 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 Byetta injection. **HMG CoA reductase inhibitor:** Lovastatin AUC and C_{max} were decreased and T_{max} was delayed when Byetta (10 μg BD) was administered concomitantly with a single dose of lovastatin (40mg). Concomitant use of Byetta and HMG CoA reductase inhibitors was not associated with consistent changes in lipid profiles. Lipid profiles should be monitored regularly. **Digoxin, lisinopril, and warfarin:** A delay in T_{max} of about 2 hours was observed when digoxin, lisinopril, or warfarin was administered 30 minutes after exenatide. No clinically relevant effects on C_{max} or AUC were observed. Increased INR has been reported during concomitant use of warfarin and Byetta. INR should be closely monitored during initiation and dose increase of Byetta therapy in patients on warfarin and/or cumarol derivatives.

Pregnancy and Lactation Byetta should not be used during pregnancy and the use of insulin is recommended. Byetta should not be used if breast-feeding.

Driving, etc No studies on the effects on the ability to drive and use machines have been performed. When Byetta is used in combination with a sulphonylurea, avoid hypoglycaemia while driving and using machines.

Undesirable Effects Adverse Reactions Reported From Phase 3 Studies
Very common: Hypoglycaemia (with metformin and a sulphonylurea), hypoglycaemia (with a sulphonylurea), nausea, diarrhoea, vomiting.
Common: Decreased appetite, headache, dizziness, dyspepsia, abdominal pain, gastro-oesophageal reflux disease, abdominal distension, hyperhidrosis, feeling jittery, asthenia, weight decreased.
Uncommon: Acute pancreatitis. Injection site reactions have been reported. Patients may develop anti-exenatide antibodies following treatment with Byetta. These patients tend to have more injection site reactions (eg, skin redness, itching).
Spontaneously Reported Adverse Reactions (Frequency Not Known)
Anaphylactic reaction (very rarely), dehydration, generally associated with nausea, vomiting and/or diarrhoea (some reports associated with elevation of serum creatinine), dysgeusia, somnolence, eructation, constipation, flatulence, altered renal function, alopecia (rarely), macular rash, papular rash, pruritus, urticaria, angioneurotic oedema, INR ratio increased with concomitant warfarin (some reports associated with bleeding). *For full details of these and other side-effects, please see the Summary of Product Characteristics, which is available at <http://emc.medicines.org.uk>.*

Legal Category POM

Marketing Authorisation Numbers

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Basic NHS Cost

£68.24 per pack of 5 μg (1 pen), £68.24 per pack of 10 μg (1 pen)

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Full Prescribing Information is Available From

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**Adverse events should be reported.
Reporting forms and information can be
found at www.yellowcard.gov.uk.**

**Adverse events should also be reported
to Eli Lilly and Company Limited
(Tel No 0870 240 1125).**