***Amber with Guidance**= To be initiated and titrated to a stable dose in secondary care with follow up prescribing and monitoring by primary care where deemed appropriate.*

Barnsley Hospital NHS NHS Foundation Trust

South West Yorkshire Partnership NHS NHS Foundation Trust

NHS Barnsley Clinical Commissioning Group

# **Tresiba®** (insulin degludec 100units/ml FlexTouch pen & cartridge and 200units/ml FlexTouch pen)

## *Prescribe by brand name*

Please see the full Summary of Product Characteristics (www.medicines.org.uk/emc/) and the BNF (www.medicinescomplete.com/mc/bnf/current/) for more information.

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| **Background Information** | Insulin degludec (Tresiba®) is a new long acting basal insulin analogue for the management of diabetes mellitus.<br><br>Tresiba is available as:<br><br>• **Tresiba FlexTouch 100 units/mL** (solution for injection in pre-filled pen)<br>• **Tresiba FlexTouch 200 units/mL** (solution for injection in pre-filled pen)<br>• **Tresiba Cartridge 100 units/mL** (solution for injection in cartridge)<br><br>As Tresiba is available in two strengths, there is a potential risk of medication errors. However the manufacturer has minimised this risk by clearly differentiating the pack design of the two products and only making the 200units/ml strength available in a pre-filled pen. For both pre-filled pens, the **needed dose is dialed in units**.<br><br>The dose steps, however, differ between the two strengths of Tresiba.<br><br>• **With Tresiba FlexTouch 100 units/mL and Tresiba Cartridge 100 units/ml**, a dose of 1–80 units per injection, in steps of 1 unit, can be administered.<br><br>• **With Tresiba FlexTouch 200 units/mL** a dose of 2–160 units per injection, in steps of 2 units, can be administered. The dose is provided in half the volume of 100 units/mL basal insulin products.<br><br>The **dose counter shows the number of units** regardless of strength and **no** dose conversion should be done when transferring a patient to a new strength.<br><br>Other long acting insulin's available on the formulary are insulin glargine (Lantus, Toujeo & Abasaglar) and insulin detemir (Levemir).<br><br>NHS Never Event: Overdose of insulin due to abbreviations or incorrect device (January 2018)<br>• The words 'unit' or 'international units' should not be abbreviated<br>• Specific insulin administration devices should always be used to measure insulin i.e. Insulin syringes and pens.<br>• Insulin should **not** be withdrawn from an insulin pen or pen refill and then administered using a syringe and needle. |
| **BNF therapeutic class** | Long-acting insulin's. |
| **Indication** | Tresiba® is licensed for the treatment of diabetes mellitus in adults, adolescents and children from the age of 1 year. |
| **Dosage and administration** | Tresiba® is a basal insulin licensed for once-daily subcutaneous administration at any time of the day, preferably at the same time every day. It has a duration of action beyond 42 hours within the therapeutic dose range.<br><br>In type 1 diabetes mellitus, Tresiba must be combined with short-/rapid-acting insulin to |

cover mealtime insulin requirements.

In patients with type 2 diabetes mellitus, Tresiba can be administered alone or in any combination with oral antidiabetic medicinal products, GLP-1 receptor agonists and bolus insulin.

Tresiba® is to be dosed in accordance with the individual patient's needs. It is recommended to optimise glycaemic control via dose adjustment based on fasting plasma glucose.

On occasions when administration at the same time of the day is not possible, Tresiba® allows for flexibility in the timing of insulin administration. A minimum of 8 hours between injections should always be ensured.

Patients, who forget a dose, are advised to take it upon discovery and then resume their usual once-daily dosing schedule.

Transfer from other insulin medicinal products
Close glucose monitoring is recommended during the transfer and in the following weeks. Doses and timing of concurrent rapid-acting or short-acting insulin products or other concomitant antidiabetic treatment may need to be adjusted.

*Patients with type 2 diabetes mellitus*
For patients with type 2 diabetes taking once-daily basal, basal-bolus, premix or self-mixed insulin therapy, changing the basal insulin to Tresiba can be done unit-to-unit based on the previous basal insulin dose followed by individual dosage adjustments.

A dose reduction of 20% based on the previous basal insulin dose followed by individual dosage adjustments should be considered when
- transferring to Tresiba from twice-daily basal insulin
- transferring to Tresiba from insulin glargine (300 units/mL)

*Patients with type 1 diabetes mellitus*
For patients with type 1 diabetes a dose reduction of 20% based on the previous basal insulin dose or basal component of a continuous subcutaneous insulin infusion regimen should be considered with subsequent individual dosage adjustments based on the glycaemic response.

Use of Tresiba in combination with GLP-1 receptor agonists in patients with type 2 diabetes mellitus
When adding Tresiba to GLP-1 receptor agonists, the recommended daily starting dose is 10 units followed by individual dosage adjustments.

When adding GLP-1 receptor agonists to Tresiba, it is recommended to reduce the dose of Tresiba by 20% to minimise the risk of hypoglycaemia. Subsequently, dosage should be adjusted individually.

Dosing in Special Populations

Elderly patients (≥ 65 years old): In the elderly, progressive deterioration of renal function may lead to a steady decrease in insulin requirements.

Renal impairment: In patients with renal impairment, insulin requirements may be diminished due to reduced insulin metabolism.

Hepatic impairment: In patients with hepatic impairment, insulin requirements may be diminished due to reduced capacity for gluconeogenesis and reduced insulin metabolism.

Paediatric population: Tresiba® can be used in adolescents and children from the age of 1.

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| | Pregnancy: There is no clinical experience with use of Tresiba in pregnant women. Animal reproduction studies have not revealed any difference between insulin degludec and human insulin regarding embryotoxicity and teratogenicity.<br><br>Breast-feeding: There is no clinical experience with Tresiba during breast-feeding. In rats, insulin degludec was secreted in milk; the concentration in milk was lower than in plasma. It is unknown whether insulin degludec is excreted in human milk. No metabolic effects are anticipated in the breast-fed newborn/infant. |
| **Cautions and Contraindication** | **Cautions**<br><br>Hypoglycaemia<br>- Omission of a meal or unplanned strenuous physical exercise may lead to hypoglycaemia.<br>- Hypoglycaemia may occur if the insulin dose is too high in relation to the insulin requirement.<br>- In children, care should be taken to match insulin doses (especially in basal-bolus regimens) with food intake and physical activities in order to minimise the risk of hypoglycaemia.<br>- Patients whose blood glucose control is greatly improved (e.g. by intensified insulin therapy) may experience a change in their usual warning symptoms of hypoglycaemia and must be advised accordingly. Usual warning symptoms may disappear in patients with long-standing diabetes.<br>- Concomitant illness, especially infections and fever, usually increases the patient's insulin requirement. Concomitant diseases in the kidney, liver or diseases affecting the adrenal, pituitary or thyroid gland may require changes in the insulin dose.<br>- As with other basal insulin products, the prolonged effect of Tresiba may delay recovery from hypoglycaemia.<br><br>Hyperglycaemia<br>- Administration of rapid-acting insulin is recommended in situations with severe hyperglycaemia.<br>- Inadequate dosing and/or discontinuation of treatment in patients requiring insulin may lead to hyperglycaemia and potentially to diabetic ketoacidosis.<br><br>Combination of pioglitazone and insulin medicinal products<br>- Cases of cardiac failure have been reported when pioglitazone was used in combination with insulin, especially in patients with risk factors for development of cardiac failure.<br>- If the combination is used, patients should be observed for signs and symptoms of heart failure, weight gain and oedema.<br>- Pioglitazone should be discontinued if any deterioration in cardiac symptoms occurs.<br><br>Avoidance of medication errors<br>- Patients must be instructed to always check the insulin label before each injection to avoid accidental mix-ups between Tresiba® and other insulin products.<br>- Patients must visually verify the dialed units on the dose counter of the pen.<br>- Therefore, the requirement for patients to self-inject is that they can read the dose counter on the pen.<br>- Patients who are blind or have poor vision must be instructed to always get help/assistance from another person who has good vision and is trained in using the insulin device.<br><br>**Contraindications**<br><br>Hypersensitivity to the active substance or to any of the excipients. |
| **Adverse Drug Reactions** | The safety profile of Tresiba® is similar to insulin's in general.<br><br>Immune system disorders: |

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| | Hypersensitivity, Urticaria – Rare (≥ 1/10,000 to < 1/1,000)<br><br>Metabolism and nutrition disorders:<br>Hypoglycaemia – Very Common (≥ 1/10)<br><br>Skin and subcutaneous tissue disorders:<br>Lipodystrophy – Uncommon (≥ 1/1,000 to < 1/100)<br><br>General disorders and administration site conditions:<br>Injection site reactions – Common (≥ 1/100 to < 1/10)<br>Peripheral oedema – Uncommon (≥ 1/1,000 to < 1/100) |
| **Monitoring** | There are no specific monitoring requirements for Tresiba® other than the routine monitoring undertaken for all insulin's. |
| **Interactions** | A number of medicinal products are known to interact with glucose metabolism.<br><br>The following substances may reduce the insulin requirement:<br>• Oral anti–diabetic medicinal products, GLP-1 receptor agonists, monoamine oxidase inhibitors (MAOI), beta-blockers, angiotensin converting enzyme (ACE) inhibitors, salicylates, anabolic steroids and sulphonamides.<br><br>The following substances may increase the insulin requirement:<br>• Oral contraceptives, thiazides, glucocorticoids, thyroid hormones, sympathomimetics, growth hormone and danazol.<br><br>Beta-blockers may mask the symptoms of hypoglycaemia.<br><br>Octreotide/lanreotide may either increase or decrease the insulin requirement.<br><br>Alcohol may intensify or reduce the hypoglycaemic effect of insulin. |

## Contact names and details

| Contact Details | Telephone number | Email |
|---|---|---|
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| Gillian Turrell<br>Medicines Information Pharmacist | 01226 432857 | gilliansmith2@nhs.net |

## References


1. Summary of Product Characteristics. Tresiba®. May 2017. Novo Nordisk Limited. Available at: https://www.medicines.org.uk/emc/product/7936/smpc (Accessed 20th October 2020).
2. British National Formulary. Available at: www.medicinescomplete.com/mc/bnf/current (Accessed 20th October 2020).


## Development Process

*This Amber-G guideline has been subject to consultation and endorsement by the Area Prescribing Committee on 16th December 2020.*