Formulary decision guide: Trurapi® ▼ (insulin aspart 100 units/ml)

Commissioned by Sanofi Ltd

Guidelines in practice

Key points

- Trurapi is indicated for the treatment of diabetes mellitus in adults, adolescents, and children aged 1 year and above[1]
- In a head-to-head study involving patients with type 1 diabetes mellitus (T1DM), Trurapi demonstrated similar pharmacokinetic exposure profiles and glucodynamic potency to the originator product, NovoRapid[2]
- In a head-to-head study involving patients with T1DM and type 2 diabetes mellitus (T2DM), similar efficacy and safety results were observed for the biosimilar, Trurapi, and the originator product, NovoRapid[3]
- Trurapi is available in the SoloSTAR® pen, the most prescribed disposable insulin pen wordwide[4]
- Trurapi NHS list price is 30% less than the originator for pre-filled pens and the cartridges.[5]

Product name

Trurapi® ▼ (insulin aspart 100 units/ml)

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information

Indications

- Trurapi is indicated for the treatment of diabetes mellitus in adults, adolescents, and children aged 1 year and above.[1]

Dosage

- The dose of Trurapi is individual and determined in accordance with the needs of the patient[1]
- Trurapi should normally be used in combination with intermediate-acting or long-acting insulin[1]
- Blood glucose monitoring and insulin dose adjustments are recommended to achieve optimal glycaemic control[1]
- The individual insulin requirement in adults and children is usually between 0.5 and 1.0 unit/kg/day—in a basal-bolus treatment regimen 50%–70% of this requirement may be provided by Trurapi and the remainder by intermediate-acting or long-acting insulin[1]
- Adjustment of dose may be necessary if patients undertake increased physical activity, change their usual diet, or during concomitant illness.[1]

Similarity

- Similar pharmacokinetic (PK) and pharmacodynamic (PD) profiles have been demonstrated between Trurapi and the originator product (NovoRapid)[2]
- A head-to-head study in patients with type 1 (T1DM) and type 2 diabetes mellitus (T2DM) demonstrated similar efficacy, tolerability, and safety profile for Trurapi and the originator[3]
- No dose conversion is necessary due to 1:1 dosing between Trurapi and the originator[3]
- When transferring from other insulin medicinal products, adjustment of the Trurapi dose and the dose of the basal insulin may be necessary; Trurapi has a faster onset and a shorter duration of action than soluble human insulin
- Close glucose monitoring is recommended during the transfer and in the initial weeks thereafter.

Efficacy

- In 597 patients with T1DM or T2DM treated for 26 weeks, there was similar glycaemic control between Trurapi and the originator regarding:[3]
  - reduction in HbA1c from baseline (least square [LS] mean difference Trurapi vs. NovoRapid: 0.08% [95%CI -0.192–0.039])
  - change in fasting blood glucose from baseline to week 26 (-0.49 mmol/l Trurapi vs -0.17 mmol/l NovoRapid)
  - proportion of patients achieving HbA1c target of <7% at week 26 (16.6% Trurapi vs. 14.5% NovoRapid)
  - change in self-measured plasma glucose, including postprandial glucose excursions.

Safety profile

- In 597 patients with T1DM or T2DM treated for 26 weeks, there was similar glycaemic control between Trurapi and the originator regarding:[3]
  - the percentage of patients with at least one episode of hypoglycaemia (regardless of category) during the 26-week treatment period
  - the small proportion of patients reporting severe hypoglycaemia (4.0% Trurapi vs. 3.4% NovoRapid)
  - the percentage of patients reporting any treatment-emergent adverse event (TEAE) (51.8% Trurapi vs. 49.3% NovoRapid) or serious TEAE (8.3% Trurapi vs. 6.1% NovoRapid)
  - the incidence and prevalence of anti-insulin aspart antibodies.

Device

- Trurapi is available in the SoloSTAR® pen, the most prescribed disposable insulin pen wordwide[4]
- Trurapi will be available to be prescribed in prefilled SoloStar pens and cartridges to be used in the AllStar and Junior Star insulin pens from mid July 2021.

Savings to the NHS

- NHS England's targets for the adoption of best-value biologics are:[6]
  - 90% of new patients starting on the best-value biologic (including biosimilars) within 3 months of guidance becoming available
  - 80% of applicable existing patients switched to the best-value biologic within 12 months
- Trurapi NHS list price is 30% less than the originator for pre-filled pens and the cartridges.[5]

References

1. Sanofi. *Insulin aspart Sanofi 100 units/ml solution for injection in cartridge—summary of product characteristics*. April 2021.
2. Kapitza C, et al. *Diabetes Technol Ther* 2020; **22** (4); 278–284.
3. Garg S et al. *Diabetes Technol Ther* 2020; **22** (2): 85–95.
4. Data on file - IQVIA Worldwide Disposable Insulin Pen Usage in 2020, MAT-GB-2101762(v1.0).
5. Data on File, MAT-GB-2101599 April 2021
6. PharmaPhorum. *Breaking policies and perceptual barriers: biosimilars.* Available at: www. deep-dive.pharmaphorum.com/magazine/market-access-2020/breaking-policy-and-perceptual-barriers-biosimilars/ (accessed May 2021)

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Insulin Trurapi® ▼ (insulin aspart 100 units/mL)

Formulary decision guide: Trurapi® ▼ (insulin aspart 100 units/ml)

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Prescribing Information:

Trurapi ▼ (Insulin aspart 100 units/ml)

Please refer to the Summary of Product Characteristics (SmPC) before prescribing.

Presentation: Trurapi 100 units/ml solution for injection in a cartridge or in a pre-filled pen, each containing 3ml of solution for injection, equivalent to 300 units insulin aspart.

Indication: The treatment of diabetes mellitus in adults, adolescents and children aged 1 year and above.

Dosage and Administration: Trurapi is a rapid-acting insulin analogue, normally used in combination with intermediate-acting or long-acting insulin. The dosage should be determined by the physician in accordance with individual patient needs. Blood glucose monitoring and insulin dose adjustments are recommended to achieve optimal glycaemic control. The individual insulin requirement in adults and children is usually 0.5–1.0 unit/kg/day. In a basal-bolus treatment regimen 50–70% of this requirement may be provided by Trurapi and the remainder by intermediate-acting or long-acting insulin. Adjustment of dose may be necessary if patients undertake increased physical activity, change their usual diet or during concomitant illness (see Precautions and Warnings). *Transfer from other insulin medicinal products:* When transferring from other insulin medicinal products, adjustment of the Trurapi and basal insulin dose may be necessary as Trurapi has a faster onset and a shorter duration of action than soluble human insulin. When injected subcutaneously into the abdominal wall, the onset of action will occur within 10–20 minutes of injection. The maximum effect is exerted 1–3 hours after the injection with duration of action of 3–5 hours. Method of administration: Trurapi is administered subcutaneously by injection in the upper arms, thighs, buttocks or abdomen. Injection sites should always be rotated within the same region in order to reduce the risk of lipodystrophy and cutaneous amyloidosis. Subcutaneous injection in the abdominal wall ensures a faster absorption than other injection sites and faster onset of action of insulin aspart is maintained regardless of the injection site. The duration of action will vary according to the dose, injection site, blood flow, temperature and level of physical activity. Due to the faster onset of action, insulin aspart should generally be given immediately before a meal. When necessary insulin aspart can be given soon after a meal. *Trurapi in cartridges*: only suitable for subcutaneous injections from a specified type of reusable pen. *Trurapi in pre-filled pen*: only suitable for subcutaneous injections and patients must visually verify the dialled units on the dose counter of the pen. Therefore, the requirement for patients to self-inject is that they can read the dose counter on the pen. 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.

Special Populations: Elderly patients and renal/hepatic impairment: Trurapi can be used in elderly patients and patients with renal or hepatic impairment; glucose monitoring should be intensified and dose adjusted on an individual basis. Paediatric population: Trurapi can be used in adolescents and children aged 1 year and above in preference to soluble human insulin when a rapid onset of action might be beneficial, for example, in the timing of the injections in relation to meals. The safety and efficacy in children below 1 year of age have not been established.

Contraindications: Hypersensitivity to insulin aspart or to any of the excipients.

Precautions and Warnings: Traceability: The name and the batch number of the administered product should be clearly recorded to improve the traceability. Hyperglycaemia: Inadequate dosing or discontinuation of treatment, especially in type 1 diabetes, may lead to hyperglycaemia and diabetic ketoacidosis (which is potentially lethal). The first symptoms usually develop gradually over a period of hours or days. Hypoglycaemia: Care should be taken to match insulin doses (especially in basal-bolus regimens) with food intake, physical activities, and current blood glucose level to minimise the risk of hypoglycaemia (especially in children). Hypoglycaemia may occur if the insulin dose is too high in relation to the insulin requirement and in case of hypoglycaemia or if hypoglycaemia is suspected Trurapi must not be injected. After stabilisation of patient's blood glucose adjustment of the dose should be considered. Patients whose blood glucose control is greatly improved may experience a change in their usual warning symptoms of hypoglycaemia, and usual warning symptoms may disappear in patients with longstanding diabetes, so patients should be advised accordingly. Hypoglycaemia in rapid-acting insulin analogues may occur earlier after an injection when compared with soluble human insulin and since Trurapi should be administered immediately in relation to a meal, the rapid onset should be considered in patients with concomitant diseases or treatment where a delayed absorption of food might be expected. Concomitant illness usually increases the patient's insulin requirements and concomitant diseases in the kidney, liver or affecting the adrenal, pituitary or thyroid gland can require changes in the insulin dose. When patients are transferred between different types of insulin medicinal products, the early warning symptoms of hypoglycaemia may change or become less pronounced than those experienced with their previous insulin. Transfer from other insulin medicinal products: Should be done under strict medical supervision. If dose adjustment is needed, it may occur with the first dose or during the first few weeks or months. Close glucose monitoring is recommended during the transfer and in the initial weeks thereafter. Injection site reactions (including lipodystrophy and cutaneous amyloidosis): As with any insulin therapy, injection site reactions may occur and include pain, redness, hives, inflammation, bruising, swelling and itching. Continuous rotation of the injection site within a given area reduces the risk of developing these reactions and these usually resolve in a few days to a few weeks. Continuous rotation of the injection site also reduces the risk of developing lipodystrophy and cutaneous amyloidosis. Blood glucose monitoring is recommended after the change in the injection site due to risk of hypoglycaemia, and dose adjustment of antidiabetic medications may be considered. On rare occasions, injection site reactions may require discontinuation of insulin aspart. Combination with pioglitazone: 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 heart failure. Pioglitazone should be discontinued if any deterioration in cardiac symptoms occurs. Medication errors: Patients must be instructed to always check the insulin label before each injection to avoid accidental mix-ups between Trurapi and other insulin products. Insulin antibodies: Insulin administration may cause insulin antibodies to form, which in rare cases may necessitate adjustment of the insulin dose to correct a tendency to hyper- or hypoglycaemia. Travel: Patients should seek physician advice before travelling to different time zones as this may mean that the insulin and meals may be taken at different times. Sodium: This medicinal product contains less than 1 mmol sodium (23mg) per dose, i.e. essentially "sodium free".

Interactions: Several medicinal products are known to interact with the glucose metabolism. Substances that may reduce insulin requirements: Oral antidiabetic medicinal products, monoamine oxidase inhibitors (MAOI), betablockers, angiotensin converting enzyme (ACE) inhibitors, salicylates, anabolic steroids and sulphonamides. Substances that may increase insulin requirements: Oral contraceptives, thiazides, glucocorticoids, thyroid hormones, sympathomimetics, growth hormone and danazol. Other potential interactions of note: Octreotide/lanreotide may either increase or decrease the insulin requirement. Beta-blockers may mask the symptoms of hypoglycaemia. Alcohol may intensify or reduce the hypoglycaemic effect of insulin.

Pregnancy and Breast-Feeding: Pregnancy: It is essential to maintain good control of the insulin-treated (insulindependent or gestational diabetes) patient throughout pregnancy and intensified blood glucose control and monitoring of pregnant women with diabetes are recommended throughout pregnancy and when contemplating pregnancy. Data from two randomised controlled clinical trials do not indicate any adverse effect of insulin aspart on pregnancy or on the health of the fetus/newborn when compared to human insulin. Breastfeeding: There are no restrictions on treatment with Trurapi during breast-feeding, but the dose may need to be adjusted.

Adverse Reactions: Adverse reactions observed in patients using Trurapi are mainly due to the pharmacologic effect of insulin. Hypoglycaemia is the most frequent adverse reaction and may occur if the insulin dose is too high in relation to the insulin requirement. *Uncommon (≥1/1,000 to <1/100):* urticaria, rash, eruptions, refraction disorders, diabetic retinopathy, injection site reactions such as lipodystrophy and oedema that can be reduced by continuous rotation of the injection site. *Rare (≥1/10,000 to <1/1,000):* Peripheral neuropathy (painful neuropathy). *Very rare (<1/10,000):* anaphylactic reactions which can potentially be life threatening. *Frequency not known:* cutaneous amyloidosis. Special populations: The frequency, type and severity of adverse reactions observed in the paediatric population, elderly patients and patients with renal or hepatic impairment do not indicate any differences to the broader experience in the general population. Please see SmPC for full details of the adverse reactions.

Legal Category: POM

Marketing Authorisation (MA) Holder: Sanofi, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK.

GB List price and MA numbers: Trurapi 100 units/ml solution for injection in cartridge 5 x 3ml: £19.82 – PLGB 04425/0885. Trurapi 100 units/ml solution for injection in prefilled pen 5 x 3ml: £21.42 – PLGB 04425/0886.

Further information is available from: Medical Information, Sanofi, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK. ukmedicalinformation@ sanofi.com

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Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Sanofi Tel: 0800 090 2314. Alternatively, send via email to UK-drugsafety@sanofi.com