PCDS consensus statement: A strategy for managing the supply shortage of the GLP-1 RAs Ozempic and Trulicity

In recent days, the PCDS has been made aware of GLP-1 receptor agonist shortages in the UK. Due to increased global use, manufacturers are currently unable to produce enough to meet demand. This is not a consequence of any safety or quality-related concern. While they are trying to address this, stock remains very low. Therefore, the PCDS proposes a strategy to ensure that, where supply is limited, people with diabetes can be safely switched to alternative agents within the GLP-1 RA class.

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In recent days, the PCDS has been made aware of GLP-1 receptor agonist shortages in the UK. Due to increased global use, manufacturers are currently unable to produce enough to meet demand. The PCDS is aware that there is very limited supply.

On 30 September, the Department of Health and Social Care issued medicine supply notifications for Ozempic (s/c semaglutide) and Trulicity (s/c dulaglutide):

Ozempic:

- Ozempic 1 mg solution for injection is **out of stock** until week commencing 17 October 2022. Thereafter, **supply will only be available for existing patients** until January 2023.
- Ozempic 0.5 mg solution for injection remains available but can only support a partial uplift in demand. Check with local pharmacy teams; in regions where there is stock of the 0.5 mg dose, temporary reduction to this dose may be considered.

Trulicity:

- Supplies of Trulicity 0.75 mg, 1.5 mg, 3 mg and 4.5 mg solution for injection devices are limited until January 2023. **Supply will only be available for existing patients.**

Alternative oral and parenteral GLP-1 receptor agonists remain available. This situation is not due to any manufacturing quality issue or regulatory action.

The situation is rapidly changing. Although it has been stated that supplies of Ozempic 1 mg will be available for existing patients from the week commencing 17 October, the PCDS accepts the **possibility that supply issues may persist up to or even beyond January 2023**. Therefore, we propose the following strategy to ensure that, where supply is limited, people with diabetes can be safely initiated on or switched to alternative agents within the GLP-1 RA class.

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PCDS consensus advice

- There should be **no new initiations of Ozempic or Trulicity**.
- For patients currently being prescribed **Ozempic**, **if supply is an ongoing issue**:
  - ➤ Where patients contact practices unable to obtain their prescription, they should be directed to clinicians with knowledge and competence to prescribe alternative agents.

    However, where possible, we recommend a proactive approach as follows:
  - ➤ **Step 1:** Perform a search to identify all individuals being prescribed Ozempic.
  - ➤ **Step 2:** Notify these individuals of the drug shortage (see ***Box 1*** for an example letter/text, which can be adapted to suit the processes and capacity of the practice).
  - ➤ **Step 3:** Where there is no available supply of Ozempic 1 mg, to avoid exacerbating supply issues, **do not prescribe 2×0.5 mg pens** (this is also an unlicensed use). We advise switching to one of the three options in ***Table 1***, following discussions with the person living with diabetes and considering their needs and preferences.
- For patients currently being prescribed **Trulicity**:
  - ➤ At the time of writing, Eli Lilly & Co. have indicated they will maintain sufficient supply of Trulicity for existing patients. **People with diabetes who are already taking Trulicity can be titrated up to higher doses**.
  - ➤ If the situation changes and supply becomes a problem, we advise following the strategy above and switching to one of the three options in ***Table 1***.

Note that the alternative agents may have different effects in terms of glycaemic-lowering, weight loss and cardiovascular protection. As per NICE NG28 recommendations, measure HbA_{1c} levels every 3–6 months (tailored to individual needs) until HbA_{1c} is stable on unchanging therapy.

Table 1. Options for initiating GLP-1 receptor agonists or switching from Ozempic (subcutaneous semaglutide) to an alternative GLP-1 receptor agonist owing to supply issues.

	Option 1: Rybelsus (oral semaglutide)	Option 2: Victoza (liraglutide)	Option 3: Byetta or Bydureon (exenatide)
Drug description	Once daily oral tablet Available in three doses: 3 mg (starter dose), 7 mg and 14 mg (maintenance doses)	Once daily subcutaneous injection Prefilled, multi-use, disposable pen containing 18 mg liraglutide, allowing delivery of three dose strengths: 0.6 mg, 1.2 mg and 1.8 mg	**Byetta:** Twice daily subcutaneous injection Prefilled, multi-use disposable pens (available in 5 µg and 10 µg doses) **Bydureon:** Once weekly subcutaneous injection Prefilled, single-use, disposable pen: dose 2 mg
How to initiate if GLP-1 RA naïve or to make the switch if on Ozempic 0.25mg	Start at a dose of 3 mg once daily for 1 month, then increase to 7 mg once daily for at least 1 month if tolerated. Based on individual need, dose may be increased to 14 mg once daily	Start at 0.6 mg once daily and increase to 1.2 mg once daily after 1 week	**Byetta:** Initiate at 5 µg twice daily for at least 1 month. Dose can then be increased to 10 µg twice daily **Bydureon:** 2 mg once weekly (no dose titration needed)
How to if already on Ozempic 0.5 mg or 1.0 mg	Start at a dose of 7 mg once daily, titrating up to 14 mg once daily after 1 month if tolerated. To cut down on general practice workload, consider issuing an acute prescription for the 7 mg tablets and a repeat prescription for the 14 mg (14 mg is equivalent in HbA_{1c}-lowering efficacy to Ozempic 0.5 mg). Some people may wish to start on 14 mg straight away.	Start at a dose of 1.2 mg once daily for at least 1 week (note the 1.8 mg dose is not usually recommended due to cost)	**Byetta:** Start at 10 µg twice daily, to be taken within 1 hour before two main meals (at least 6 hours apart) **Bydureon:** start at 2 mg once weekly
Dose adjustment needed in renal/hepatic impairment?	Avoid in end-stage renal disease and caution in hepatic impairment	Avoid in end-stage renal disease and in severe hepatic impairment	Avoid if eGFR <30 mL/min/1.73 m^2 and caution with Byetta if eGFR 30–50 mL/min/1.73 m^2
Do I need to prescribe needles?	No	Yes – we recommend 4 mm 32-gauge needle. Consider revisiting good injection technique	Yes – we recommend 4 mm 32-gauge needle. Consider revisiting good injection technique
Key points for person with diabetes	Ensure people are aware of the special administration instructions (see ***Box 2***).	This is a daily injection not a weekly injection	The pen devices may mean a person needs support to use appropriately when initiating
Summary of Product Characteristics	SPC Rybelsus	SPC Victoza	SPC Byetta SPC Bydureon
Patient Information Leaflets	PIL Rybelsus	PIL Victoza	PIL Byetta PIL Bydureon
Supply requirements for 1 month	One pack of 30 tablets	Two 3 mL prefilled pens Note: must be refrigerated to 2–8°C when stored; can be used for 1 month if kept below 30°C)	**Byetta:** One pen (30 days) Note: store in refrigerator at 2–8°C. Once in use, store below 25°C **Bydureon:** One pack of four prefilled pens Note: store in refrigerator at 2–8°C. Can be kept at room temperature but not exceeding 30°C for up to 4 weeks if needed

Note: These alternative agents have different effects in terms of glycaemic-lowering, weight loss and cardiovascular protection. As per NICE NG28 recommendations, measure HbA_{1c} levels every 3–6 months (tailored to individual needs) until HbA_{1c} is stable on unchanging therapy.

Box 1. Example letter/text to be sent to a person living with diabetes who is being prescribed Ozempic.

From our records, we believe that you are currently taking Ozempic (semaglutide) injections for type 2 diabetes.

We regret to inform you that there are significant disruptions in the supply chain of this medication, which may affect your ability to continue therapy in the short term. These shortages may last until January 2023.

We would like to offer you alternative therapy to bridge this gap in supply and ask that you please contact the surgery to discuss at your earliest convenience.

Thank you.

Box 2. Special administration instructions for Rybelsus (oral semaglutide).

Rybelsus tablets should be swallowed whole (not split, crushed, or chewed) and taken with a sip of water (up to 120 mL) on an empty stomach upon waking.

Patients should wait at least 30 minutes before eating or drinking or taking other oral medicines, as this affects absorption and may reduce the glucose-lowering effect.

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Missed doses

If a dose of Rybelsus is missed, the missed dose should be skipped and the next dose should be taken the following day.

For those taking levothyroxine

No other medicines should be taken at the same time as Rybelsus. This may be a challenge for those people also taking levothyroxine, as this drug should also be taken on an empty stomach, preferably before breakfast or the first meal of the day. We therefore suggest that the Rybelsus is taken as described above and the levothyroxine is taken before bed, provided this is several hours after a meal.

Rybelsus may increase the absorption of levothyroxine, and thyroid function should be periodically monitored and the thyroxine dose adjusted as required.