Record of the Diabetes Advisory Committee Meeting held on 17 October 2022

Diabetes Advisory Committee records are published in accordance with the Terms of Reference for the Pharmacology and Therapeutics Advisory Committee (PTAC) Specialist Advisory Committees 2021.

Note that this document is not necessarily a complete record of the Diabetes Advisory Committee meeting; only the relevant portions of the meeting record relating to Diabetes Advisory Committee discussions about an application or Pharmac staff proposal that contain a recommendation are generally published.

The Diabetes Advisory Committee may:

(a) recommend that a pharmaceutical be listed by Pharmac on the Pharmaceutical Schedule and the priority it gives to such a listing;

(b) defer a final recommendation, and give reasons for the deferral (such as the supply of further information) and what is required before further review; or

(c) recommend that Pharmac decline to list a pharmaceutical on the Pharmaceutical Schedule.

Pharmac Advisory Committees make recommendations, including priority, within their therapeutic groups of interest.

The record of this Advisory Committee meeting will be reviewed by PTAC at an upcoming meeting.

Specialist Advisory Committees and PTAC may differ in the advice they provide to Pharmac, including recommendations' priority, due to the committees' different, if complementary, roles, expertise, experience, and perspectives.

Pharmac is not bound to follow the recommendations made below. Applications are prioritised by Pharmac against other funding options and progressed accordingly. The relative priority of any one funding choice is dependent on a number of factors, including (but not limited to) the recommendation of PTAC and/or Specialist Advisory Committees, the mix of other applications being assessed, the amount of funding available, the success of commercial negotiations and/or the availability of clinical data.

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1. Attendance

Present
Diana McNeill
Esko Wiltshire
Helen Lunt
Karen MacKenzie
Kate Smallman
Nic Crook
Rinki Murphy
Sean Hanna
Tim Stokes

Apologies
Bruce King
Elizabeth Dennett

2. The role of Specialist Advisory Committees and records of meetings

2.1. This meeting record of the Diabetes Advisory Committee is published in accordance with the Terms of Reference for the Pharmacology and Therapeutics Advisory Committee (PTAC) and Specialist Advisory Committees 2021, available on the Pharmac website at https://pharmac.govt.nz/assets/2021-Specialist-Advisory-Committee-Terms-of-Reference.pdf. The Terms of Reference describe, *inter alia*, the establishment, activities, considerations, advice, and the publication of such advice of Specialist Advisory Committees and PTAC.

2.2. Conflicts of Interest are described and managed in accordance with section 7.2 of the PTAC Terms of Reference.

2.3. The Diabetes Advisory Committee is a Specialist Advisory Committee of Pharmac. The Diabetes Advisory Committee and PTAC and other Specialist Advisory Committees have complementary roles, expertise, experience, and perspectives. The Diabetes Advisory Committee and other Specialist Advisory Committees may therefore, at times, make recommendations for treatments for diabetes mellitus that differ from PTAC's, including the priority assigned to recommendations, when considering the same evidence. Likewise, PTAC may, at times, make recommendations for treatments for diabetes mellitus that differ from the Diabetes Advisory Committee's, or Specialist Advisory Committees may make recommendations that differ from other Specialist Advisory Committees'.

2.4. Pharmac considers the recommendations provided by both the Diabetes Advisory Committee and PTAC and any other relevant Specialist Advisory Committees when assessing applications for treatments for diabetes mellitus.

3. Dulaglutide Supply Issue – Monday, 17 October 2022

Application

3.1. The Committee noted a paper from Pharmac staff seeking clinical advice to help manage a current supply issue with dulaglutide (a GLP-1 receptor agonist, funded as per SA2065). The Committee noted Pharmac sought advice on the health need of those who may be affected by the dulaglutide supply issue, eligibility criteria to target supply, and possible alternative treatments.

Recommendation

3.2. The Advisory Committee recommended, in the context of supply issues, that the priority should be to ensure that dulaglutide remains available for patients already initiated on treatment. The Committee considered that this was because supply interruptions can provide additional barriers for those becoming established on the treatment and may pose as a barrier to their continuation of treatment over the long term.

3.3. The Advisory Committee recommended that new initiations on dulaglutide should be restricted to those with the highest health need, who meet the current funding criteria but for whom there are no, or minimal funded alternatives. The Committee considered that this would be those patients who require assistance (eg. a carer) to administer their medications (for example paediatric patients, patients with neurocognitive, neuromuscular or physical disabilities); and those patients who have severe renal disease (eGFR <30ml/min/1.73m^2). The Advisory Committee considered the Special Authority could be amended as follows (additions in bold):

Initial application from any relevant practitioner. Approvals valid without further renewal unless notified for applications meeting the following criteria:

1. Either

1.1 Patient requires assistance of a carer or health care professional to administer their medications (for example paediatric patients, patients with neurocognitive, neuromuscular or physical disabilities) such that they require a once weekly injectable; or

1.2 Patient has severe renal disease (eGFR <30ml/min/1.73m2); and

2 All of the following:

2.1 Patient has type 2 diabetes; and

2.2 Any of the following:

2.2.1 Patient is Māori or of any Pacific ethnicity*; or

2.2.2 Patient has pre-existing cardiovascular disease or risk equivalent (see note a)*; or

2.2.3 Patient has an absolute 5-year cardiovascular disease risk of 15% or greater according to a validated cardiovascular risk assessment calculator*; or

2.2.3 Patient has a high lifetime cardiovascular risk due to being diagnosed with type 2 diabetes during childhood or as a young adult*; or

2.2.5 Patient has diabetic kidney disease (see note b)*; and

2.3 Target HbA1c (of 53 mmol/mol or less) has not been achieved despite the regular use of at least one blood-glucose lowering agent eg metformin, vildagliptin, or insulin) for at least 3 months.

Notes: * Criteria intended to describe patients at high risk of cardiovascular or renal complications of diabetes.

a) Pre-existing cardiovascular disease or risk equivalent defined as: prior cardiovascular disease event (ie angina, myocardial infarction, percutaneous coronary intervention, coronary artery bypass grafting, transient ischaemic attack, ischaemic stroke, peripheral vascular disease), congestive heart failure or familial hypercholesterolaemia.

b) Diabetic kidney disease defined as: persistent albuminuria (albumin:creatinine ratio greater than or equal to 3 mg/mmol, in at least two out of three samples over a 3-6 month period) and/or eGFR less than 60 mL/min/1.73m2 in the presence of diabetes, without alternative cause

3.4. The Advisory Committee recommended that, within the context of supply issues, if another GLP-1 agonist was to be funded that it should be funded with the same Special Authority criteria that applies to dulaglutide at present, as follows (additions to current dulaglutide criteria shown in **bold**):

Initial application from any relevant practitioner. Approvals valid without further renewal unless notified for applications meeting the following criteria:

Either:
1. Patient has previously received an initial approval for **either** an SGLT-2 inhibitor **or GLP-1 agonist**; or
2. All of the following:
    2.1 Patient has type 2 diabetes; and
    2.2 Any of the following:
        2.2.1 Patient is Māori or of any Pacific ethnicity*; or
        2.2.2 Patient has pre-existing cardiovascular disease or risk equivalent (see note a)*; or
        2.2.3 Patient has an absolute 5-year cardiovascular disease risk of 15% or greater according to a validated cardiovascular risk assessment calculator*; or
        2.2.4 Patient has a high lifetime cardiovascular risk due to being diagnosed with type 2 diabetes during childhood or as a young adult*; or
        2.2.5 Patient has diabetic kidney disease (see note b)*; and
    2.3 Target HbA1c (of 53 mmol/mol or less) has not been achieved despite the regular use of at least one blood-glucose lowering agent eg metformin, vildagliptin, or insulin) for at least 3 months.

Notes: * Criteria intended to describe patients at high risk of cardiovascular or renal complications of diabetes.
    a) Pre-existing cardiovascular disease or risk equivalent defined as: prior cardiovascular disease event (ie angina, myocardial infarction, percutaneous coronary intervention, coronary artery bypass grafting, transient ischaemic attack, ischaemic stroke, peripheral vascular disease), congestive heart failure or familial hypercholesterolaemia.
    b) Diabetic kidney disease defined as: persistent albuminuria (albumin:creatinine ratio greater than or equal to 3 mg/mmol, in at least two out of three samples over a 3-6 month period) and/or eGFR less than 60 mL/min/1.73m2 in the presence of diabetes, without alternative cause

3.5. In making these recommendations, the Advisory Committee considered the health needs of the different type-2 diabetes patient populations, the suitability of the alternative medications that may impact on use to the person, whānau, and health workforce.

Discussion

Māori Impact Statement

3.6. The Committee considered that type 2 diabetes disproportionally affects Māori. The Committee considered that there was a high proportion of Māori patients on dulaglutide, and it was important to ensure that supply interruptions did not impact those established on the treatment, as this could pose as a barrier to their continuation of treatment over the long term.

Background

3.7. The Committee noted that dulaglutide 1.5 mg per 0.5 ml prefilled pen for injection is a GLP-1 agonist indicated for the improvement of glycaemic control in adults with type 2 diabetes mellitus. The Committee noted that the approved dose of dulaglutide is 1.5 mg subcutaneously, once weekly. The Committee noted that dulaglutide is the only GLP-1 agonist that is funded by Pharmac and that it was awarded sole subsidised supply status as a result of the 2020 request for proposals for diabetes agents, and was funded from 1 September 2021 after Medsafe consent was granted.

3.8. The Committee noted that Pharmac funds other agents used for glycaemic control including insulin, vildagliptin, metformin, empagliflozin, and sulphonylureas.

3.9. The Committee noted that the supplier of dulaglutide has indicated that there are supply issues with dulaglutide due to unanticipated increases in global demand for GLP-1 receptor agonists and a supply issue of another Supplier's GLP-1 receptor agonist (semaglutide). The Committee noted that this may mean New Zealand experiences constrained supply until mid-2023. The Committee noted that the supplier of dulaglutide has committed to maintaining supplies of dulaglutide at levels that will support existing patients already initiated on treatment, and that the supplier considered that, while the supply situation remains dynamic, existing patients should be able to fill their dulaglutide prescriptions without interruption.

3.10. The Committee noted that Pharmac staff sought advice on the health need of those who may be affected by the dulaglutide supply issue, eligibility criteria to target supply, and possible alternative treatments.

3.11. The Committee considered that type 2 diabetes disproportionally affects Māori and Pacific people.

3.12. The Committee noted that according to dispensing data, a total of 14,814 patients have accessed dulaglutide since the listing date (up to 9 October 2022) with 344,594 injections dispensed. The Committee noted that 44% of this patient group identifies as Māori or Pacific ethnicity. The Committee noted that, since the start of funding for dulaglutide, uptake has been rapid with an approximate increase of 2,000 patients per month. The Committee considered that it was unclear if initiations of dulaglutide would continue to increase at this rate, and for how long.

Discussion

3.13. The Committee noted that Pharmac funds other agents used for glycaemic control including insulin, vildagliptin, metformin, empagliflozin, and sulphonylureas. However, the Committee considered that a supply issue with dulaglutide was disruptive to clinical care and expressed frustration that the Supplier was unable to supply enough stock for New Zealand to meet ongoing demand.

3.14. The Committee considered possible mitigations to alleviate the supply issue, including removing stat dispensing, amending the current restrictions and adding renewal criteria.

3.14.1. The Committee noted that the current Special Authority criteria for dulaglutide is currently targeted towards those who are at the highest risk of developing diabetes-related complications and who would receive the most health benefit from treatment with dulaglutide.

3.14.2. The Committee noted that currently dulaglutide is dispensed in 3-monthly amounts. The Committee considered that altering this to 1-monthly dispensing may alleviate some pressure on the stock of dulaglutide in the very short term, but that this would not have a significant impact in the longer term.

3.14.3. Members highlighted that they were aware, anecdotally, of patients being prescribed higher doses of dulaglutide to assist with additional glucose and weight lowering benefits. The Committee considered that, according to dispensing data, that this number was small at present (~5% of patients), and

that adding a dosing restriction would be unlikely to impact on demand substantially at this stage. However, the Committee considered that this may require careful monitoring and formal review in the coming months.

3.14.4. The Committee noted that dulaglutide is used long-term but considered it likely that some patients who are prescribed dulaglutide will continue to fill their prescriptions without following up with their GP or healthcare provider to assess the benefit from their treatment. The Committee considered that this may mean that some patients are taking dulaglutide unnecessarily, without benefit, or have stopped taking it due to serious or intolerable adverse gastrointestinal effects. The Committee considered that although cessation of dulaglutide for these patients would slightly alleviate the pressure on the current stock of dulaglutide, the addition of renewal criteria or a requirement for follow-up would put significant pressure on healthcare providers and would not be feasible.

3.14.5. The Committee considered that reducing the impact on existing patients who have recently initiated on dulaglutide should be the priority, as supply interruptions can provide additional barriers for those who have become established on treatment and may pose as a barrier to their continuation of treatment over the longer term. The Committee considered that patients who have already initiated treatment with dulaglutide should continue to receive the GLP-1 agonist without interruption and that temporarily restricting the Special Authority criteria would be an appropriate mechanism to achieve this. The Committee considered that this should be a temporary measure that is rescinded once confidence in the supply of dulaglutide is restored.

3.15. The Committee considered that there are a small number of high-risk patients, for whom currently funded clinical alternatives are not appropriate, that should be able to initiate treatment on dulaglutide throughout the duration of the supply issue.

3.15.1. The Committee considered that for patients who require assistance (eg from a carer) to administer their medications (eg paediatric patients, patients with neurocognitive, neuromuscular or physical disabilities), once weekly injections with dulaglutide are more suitable for glycaemic control than other funded alternatives. In addition, the Committee noted that Pharmac was exploring securing supply of liraglutide, administered via daily injection, and considered that a daily injection would have an impact on carer burden and health resource, if a nurse was required. The Committee was uncertain what the size of this patient group would be but considered it would likely be small (<400 patients per year).

3.15.2. The Committee considered that there is another small group of patients for whom there are no suitable funded alternatives; those with severe renal disease (eGFR <30ml/min/1.73m2). The Committee considered that use of empagliflozin is not Medsafe approved for use in patients with eGFR <30ml/min/1.73m2, and therefore considered that dulaglutide was a necessary treatment option for this patient group. The Committee considered that this group could be approximately 50 patients per year.

3.16. The Committee considered that allowing access to these high-risk groups of patients as well as for those who are currently initiated on dulaglutide would not greatly increase the number of patients being prescribed dulaglutide.

3.17. The Committee noted that Pharmac was exploring supply of a number of other GLP-1 receptor agonists as alternative agents to dulaglutide and sought the Committee's advice on this.

3.17.1. The Committee emphasised the need to suspend the sole supply of dulaglutide and secure supply of an alternative GLP-1 receptor agonist, should this be possible, given the high health need of eligible people and the length of time the supply issue with dulaglutide could continue for.

3.17.2. The Committee noted that there are global supply issues with the injectable semaglutide at this time and that supply of semaglutide would be unlikely.

3.17.3. The Committee noted that there are two presentations of the GLP-1 receptor agonist exenatide, a twice-daily injection (Brand name Byetta) exenatide and a extended-release injectable suspension formulated as a single-use autoinjector administered once-weekly (Brand name Bydureon).The Committee noted that Byetta was not available in sufficient quantities and Bydureon was not Medsafe approved but may be worth exploring as a potential option.

3.17.4. The Committee considered lixisenatide, was a GLP-1 receptor agonist administered once daily. The Committee noted that Medsafe approval for this had lapsed.

3.17.5. The Committee considered liraglutide (Victoza), was Medsafe approved for glycaemic control in patients with type 2 diabetes mellitus and is administered once daily.

3.18. The Committee considered that the most preferable, and likely available, alternative to dulaglutide for new patients not yet initiated on a GLP-1 agonist would be liraglutide or oral semaglutide, however, noted that oral semaglutide was not Medsafe approved. The Committee considered that the once daily preparation in a titratable pen would be easy for patients to use who do not need full doses, and that the once daily preparation may be easier to tolerate for those patients who have experienced gastrointestinal side effects from dulaglutide.

3.19. Should Pharmac be able to secure supply of liraglutide, the Committee considered that the eligibility criteria for liraglutide should be the same as the current criteria for dulaglutide. The Committee considered that the uptake of liraglutide would be high, due to the secondary weight-loss benefits which are thought to be superior to dulaglutide. The Committee considered, however, that once daily injections may not be tolerable or suitable for some patients and estimated that the population taking liraglutide would be approximately 25% less than that of dulaglutide due to this.

3.20. The Committee considered there could be a strong clinical desire to use liraglutide in higher than Medsafe approved doses to assist with weight management. The Committee considered that should Pharmac fund liraglutide, for the same indication as dulaglutide, that Pharmac may need to consider adding a dose restriction to minimise the risk of dose creep. The Committee noted that the Medsafe approved maximum dose of liraglutide (Victoza) for glycaemic control was 1.8mg daily and that a majority of patients would who are initiated on liraglutide would titrate up to 1.8mg per day. The Committee considered there would be a small percentage of patients who would not be able to tolerate the side effects associated with higher doses that would remain on a 1.2mg per day dosing regimen.

3.21. The Committee considered that should Pharmac fund liraglutide in the context of the dulaglutide supply issues, and once the supply of dulaglutide is resumed in full, that patients may prefer to change from liraglutide to the once weekly dulaglutide. The Committee emphasised that any switching between GLP-1 receptor agonists, as a result of the dulaglutide supply issue situation, should be guided by clinician and patient choice rather than by the imposition of funding restrictions.

3.22. The Committee noted that Pharmac sought advice on whether there were any other alternatives, apart from GLP-1 agonists it was aware of, that it could explore.

3.22.1. The Committee considered that tirzepatide would be desirable. The Committee noted that the FDA had approved tirzepatide for type 2 diabetes in May 2022 and that it is currently reviewing tirzepatide for obesity under the fast-track review process.

3.22.2. Members also considered that low calorie diet meal replacements such as Optifast, would help with weight loss which may in turn help with glycaemic control. However, Members considered that this better considered via a funding application as there would be other patient groups, apart from those who meet the eligibility criteria for dulaglutide, that would also want funded access