15.4 HEALTH TECHNOLOGY ASSESSMENT ADVICE FOR NHSSCOTLAND

On 11 January 2016 the Scottish Medicines Consortium (SMC) advised that albiglutide (Eperzan®) is accepted for restricted use within NHSScotland for treatment of type 2 diabetes mellitus in adults to improve glycaemic control in combination with other glucose-lowering medicinal products including basal insulin, when these, together with diet and exercise, do not provide adequate glycaemic control.

SMC restriction: an alternative once weekly glucagon-like peptide-1 (GLP-1) agonist for use in combination with oral anti-diabetic agents as a third-line pre-insulin treatment option.

This SMC advice takes account of the benefits of a Patient Access Scheme (PAS) that improves the cost-effectiveness of albiglutide. This advice is contingent upon the continuing availability of the PAS in NHS Scotland or a list price that is equivalent or lower.

Albiglutide is also indicated for adults with type 2 diabetes mellitus to improve glycaemic control as monotherapy when diet and exercise alone does not provide adequate glycaemic control in patients for whom use of metformin is considered inappropriate due to contraindications or intolerance. SMC has not reviewed albiglutide in this indication and cannot recommend its use within NHSScotland.

On 13 October 2014 SMC advised that alogliptin (Vipidia®) is accepted for restricted use within NHSScotland in adults aged 18 years and older with type 2 diabetes mellitus to improve glycaemic control in combination with other glucose-lowering medications including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control.

SMC restriction: dual therapy

- In combination with metformin, when metformin alone, together with diet and exercise does not provide adequate glycaemic control in patients for whom the addition of a sulfonylurea is inappropriate.
- In combination with a sulfonylurea, when sulfonylurea alone, together with diet and exercise does not provide adequate glycaemic control in patients for whom the addition of metformin is inappropriate due to contra-indications or intolerance.

SMC cannot recommend the use of alogliptin as single therapy or triple therapy as the company's submission related only to its use in dual therapy.

On 13 October 2014 SMC advised that alogliptin plus metformin combination tablet (Vipdomet®) is accepted for restricted use within NHSScotland in the treatment of adult patients aged 18 years and older with type 2 diabetes mellitus:

- as an adjunct to diet and exercise to improve glycaemic control in adult patients, inadequately controlled on their maximal tolerated dose of metformin alone, or those already being treated with the combination of alogliptin and metformin.
- in combination with pioglitazone (i.e. triple combination therapy) as an adjunct to diet and exercise in adult patients inadequately controlled on their maximal tolerated dose of metformin and pioglitazone.
- in combination with insulin (i.e. triple combination therapy) as an adjunct to diet and exercise to improve glycaemic control in patients when insulin at a stable dose and metformin alone do not provide adequate glycaemic control.

SMC restriction: to use in patients for whom this fixed dose combination of alogliptin and metformin is an appropriate choice of therapy and only when the addition of a sulphonylurea to metformin monotherapy is not appropriate.

Alogliptin/metformin is licensed for use in triple combination therapy with pioglitazone or as add-on to insulin. The manufacturer's submission related only to the use of alogliptin/ metformin in dual therapy, therefore SMC cannot recommend the use of alogliptin/ metformin in triple therapy with either pioglitazone or insulin.

On 9 June 2014 SMC advised that canagliflozin (Invokana®) is accepted for restricted use within NHSScotland in adults aged 18 years and older with type 2 diabetes mellitus to improve

glycaemic control as add-on therapy with other glucose-lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control.

SMC restriction: to use in the following situations:

- dual therapy in combination with metformin
- triple therapy in combination with metformin plus standard of care
- add-on to insulin therapy in combination with insulin plus standard of care.

Canagliflozin is also licensed for use as monotherapy. The manufacturer's submission related only to the use of canagliflozin as add-on therapy with other glucose-lowering medicinal products. SMC cannot recommend the use of canagliflozin as monotherapy.

On 12 January 2015 SMC advised that canagliflozin plus metformin (Vokanamet®) is accepted for restricted use within NHSScotland in adults aged 18 years and older with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycaemic control:

- in patients not adequately controlled on their maximally tolerated doses of metformin alone
- in patients on their maximally tolerated doses of metformin along with other glucose-lowering medicinal products, including insulin, when these do not provide adequate glycaemic control
- in patients already being treated with the combination of canagliflozin and metformin as separate tablets.

SMC restriction: use in patients for whom a combination of canagliflozin and metformin is an appropriate choice of therapy.

Canagliflozin in combination with metformin has been shown to be bioequivalent to canagliflozin and metformin administered separately and canagliflozin administered twice daily has been shown to provide similar exposure to the equivalent dose administered once daily.

On 14 January 2013 SMC advised that dapagliflozin (Forxiga®) is accepted for restricted use within NHSScotland in adults aged 18 years and older with type 2 diabetes mellitus to improve glycaemic control in combination with other glucose-lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control.

SMC restriction: Dapagliflozin is restricted to use as dual therapy in combination with metformin, when metformin alone with diet and exercise does not provide adequate glycaemic control and a sulphonylurea is inappropriate.

The submitting companies did not present a sufficiently robust economic analysis to gain acceptance by SMC for use in addition to insulin in patients who have inadequate glycaemic control.

Dapagliflozin is also licensed for use as monotherapy when diet and exercise alone do not provide adequate glycaemic control in patients for whom use of metformin is considered inappropriate due to intolerance. The manufacturers' submission related only to the use of dapagliflozin when used as dual therapy in combination with either metformin or insulin. SMC cannot recommend the use of dapagliflozin as monotherapy.

On 10 March 2014 SMC advised that dapagliflozin (Forxiga®) is accepted for restricted use within NHSScotland in adults aged 18 years and older with type 2 diabetes mellitus to improve glycaemic control in combination with other glucose-lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control.

SMC restriction: In combination with insulin, when insulin with diet and exercise, does not provide adequate glycaemic control.

Dapagliflozin is also licensed for use as monotherapy when diet and exercise alone do not

provide adequate glycaemic control in patients for whom use of metformin is considered inappropriate due to intolerance. The companies' submission related only to the use of dapagliflozin when used in combination with insulin. SMC cannot recommend the use of dapagliflozin as monotherapy. SMC has previously accepted dapagliflozin for restricted use in combination with metformin.

On 7 July 2014 SMC advised that dapagliflozin (Forxiga®) is accepted for restricted use within NHSScotland in adults aged 18 years and older with type 2 diabetes mellitus to improve glycaemic control as add-on combination therapy in combination with other glucose-lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control.

SMC restriction: in triple therapy in combination with metformin and sulphonylurea, as an alternative to a dipeptidyl peptidase-4 (DPP-4) inhibitor.

SMC has previously accepted dapagliflozin for use:

- as dual therapy in combination with metformin, when metformin alone with diet and exercise does not provide adequate glycaemic control and a sulphonylurea is inappropriate
- in combination with insulin, when insulin with diet and exercise, does not provide adequate glycaemic control.

Dapagliflozin is also licensed for use as monotherapy but the company's resubmission did not relate to its use in this setting. SMC cannot recommend the use of dapagliflozin as monotherapy.

On 11 August 2014 SMC advised that dapagliflozin plus metformin (Xigduo®) is accepted for restricted use within NHSScotland in adults aged 18 years and older with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycaemic control:

- in patients inadequately controlled on their maximally tolerated dose of metformin alone
- in combination with other glucose-lowering medicinal products, including insulin, in patients inadequately controlled with metformin and these medicinal products
- in patients already being treated with the combination of dapagliflozin and metformin as separate tablets.

SMC restriction: to use in patients for whom a combination of dapagliflozin and metformin is an appropriate choice of therapy ie

- when metformin alone does not provide adequate glycaemic control and a sulphonylurea is inappropriate
- in combination with insulin, when insulin and metformin does not provide adequate control
- in combination with a sulphonylurea, when a sulphonylurea and metformin does not provide adequate control.

Dapagliflozin in combination with metformin has been shown to be bioequivalent to dapagliflozin and metformin administered separately and dapagliflozin administered twice daily has been shown to provide similar exposure to the equivalent dose administered once daily.

On 8 August 2016 SMC advised that insulin degludec (Tresiba®) is accepted for use within NHSScotland.for treatment of diabetes mellitus in adults.

Insulin degludec is also indicated for the treatment of diabetes mellitus in adolescents and children from the age of one year. The holder of the marketing authorisation has not made a submission to SMC regarding this indication and as a result SMC cannot recommend its use within NHSScotland.

On 12 October 2015 SMC advised that insulin degludec/liraglutide (Xultophy®) is accepted for restricted use within NHSScotland for treatment of adults with type 2 diabetes mellitus to

improve glycaemic control in combination with oral glucose-lowering medicinal products when these alone or combined with a GLP-1 receptor agonist or with basal insulin do not provide adequate glycaemic control.

SMC restriction: for use in patients who are uncontrolled on basal insulin analogues (glycosylated haemoglobin [HbA1c] >7.5% [59mmol/mol]) and for whom a GLP-1 receptor agonist is appropriate as an add-on intensification therapy to basal insulin to obtain glucose control.

On 9 August 2004 SMC advised that insulin detemir is accepted for restricted use within NHSScotland for the treatment of diabetes mellitus.

Its use should be targeted on patients attempting to achieve better hypoglycaemic control as there may be some benefit related to a reduced intra-individual variation in glycaemic profile for insulin detemir compared with established insulins. It appears to be cost-effective from the base-case of economic modelling, but this is limited by the degree of extrapolation involved and the associated width of the confidence intervals.

On 7 March 2016 SMC advised that insulin detemir (Levemir®) is accepted for restricted use within NHSScotland for treatment of diabetes mellitus in adults, adolescents and children aged 1 year and above in patients unable to achieve good glycaemic control with established insulins.

On 11 January 2016 SMC advised that dulaglutide (Trulicity®) is accepted for restricted use within NHSScotland in adults with type 2 diabetes mellitus to improve glycaemic control as add-on therapy in combination with other glucose-lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control.

SMC restriction: as part of a triple therapy in patients with inadequate glycaemic control on two oral anti-diabetic drugs, as an alternative glucagon-like peptide 1 (GLP-1) agonist option.

Dulaglutide is also indicated for adults with type 2 diabetes mellitus to improve glycaemic control as monotherapy when diet and exercise alone do not provide adequate glycaemic control in patients for whom the use of metformin is considered inappropriate due to intolerance or contraindications. SMC has not reviewed dulaglutide in this indication and cannot recommend its use within NHSScotland.

On 13 October 2014 SMC advised that empagliflozin (Jardiance®) is accepted for restricted use within NHSScotland for treatment of type 2 diabetes to improve glycaemic control in adults as add-on combination therapy in combination with other glucose–lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control.

SMC restriction: to use in the following situations:

- dual therapy in combination with metformin, when a sulphonylurea is inappropriate
- triple therapy in combination with metformin plus standard of care
- add-on to insulin therapy in combination with insulin plus standard of care.

Empagliflozin is also indicated as monotherapy in patients who cannot tolerate metformin. SMC cannot recommend the use of empagliflozin as monotherapy as the company's submission did not include evidence of cost-effectiveness in this setting.

On 12 October 2015 SMC advised that empagliflozin/metformin (Synjardy®) is accepted for restricted use within NHSScotland in adults aged 18 years and older with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycaemic control:

- in patients inadequately controlled on their maximally tolerated dose of metformin alone
- in patients inadequately controlled with metformin in combination with other glucose-lowering medicinal products, including insulin
- in patients already being treated with the combination of empagliflozin and metformin as separate tablets.

SMC restriction:

- for use in patients for whom this fixed dose combination of empagliflozin and metformin is considered appropriate

for use as dual therapy (empagliflozin and metformin) when a sulphonylurea is inappropriate.

On 9 July 2007 SMC advised that exenatide (Byetta®) is accepted for restricted use within NHSScotland for the treatment of type 2 diabetes mellitus in combination with metformin and/or sulphonylureas in patients who have not achieved adequate glycaemic control on maximally tolerated doses of these oral therapies.

On 7 March 2011 SMC advised that exenatide (Byetta®) is accepted for restricted use within NHSScotland for treatment of type 2 diabetes mellitus in combination with thiazolidinediones with or without metformin in patients who have not achieved adequate glycaemic control on maximally tolerated doses of these oral therapies.

SMC restriction: restricted to use in combination with metformin and a thiazolidinedione as a third-line pre-insulin treatment option.

Exenatide has previously been accepted by SMC for restricted use for the treatment of type 2 diabetes mellitus in combination with metformin and/or sulphonylureas in patients who have not achieved adequate glycaemic control on maximally tolerated doses of these oral therapies.

On 16 January 2012 SMC advised that exenatide once weekly (Bydureon®) is accepted for restricted use within NHSScotland for treatment of type 2 diabetes mellitus in combination with:

- metformin
- sulphonylurea
- thiazolidinedione
- metformin and sulphonylurea
- metformin and thiazolidinedione

in adults who have not achieved adequate glycaemic control on maximally tolerated doses of these oral therapies.

SMC restriction: Exenatide once weekly is restricted to use as a third line treatment option. The economic case for exenatide once weekly for second line use in combination with metformin in place of a sulphonylurea has not been made.

On 11 June 2012 SMC advised that exenatide (Byetta®) is accepted for use within NHSScotland as adjunctive therapy to basal insulin with or without metformin and/or pioglitazone in adults with type 2 diabetes who have not achieved adequate glycaemic control with these agents.

On 8 April 2013 SMC advised that insulin glargine (Lantus) is accepted for restricted use within NHSScotland for treatment of diabetes mellitus in adults, adolescents and children aged 2 years and above in patients in whom treatment with an insulin analogue is appropriate.

In patients with type 2 diabetes it should be restricted to those who suffer from recurrent episodes of hypoglycaemia or require assistance with their insulin injections.

On 7 September 2015 SMC advised that insulin glargine 300 units/mL (Toujeo®) is accepted for restricted use within NHSScotland for treatment of type 1 or type 2 diabetes mellitus in adults aged 18 years and above in whom treatment with an insulin analogue is appropriate.

In patients with type 2 diabetes it should be restricted to those who suffer from recurrent episodes of hypoglycaemia or require assistance with their insulin injections.

Insulin glargine 300 units/mL (Toujeo®) has similar efficacy but is not bioequivalent to insulin glargine 100 units/mL (Lantus®) and therefore not interchangeable without dose adjustment. At doses that provide comparable glycaemic control, Toujeo® is available at a similar cost to Lantus®.

On 16 January 2012 SMC advised that linagliptin film-coated tablet (Trajenta®) is accepted for restricted use within NHSScotland for the treatment of type 2 diabetes mellitus to improve glycaemic control in adults.

As monotherapy:

- in patients inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to intolerance, or contra-indicated due to renal impairment.

As combination therapy:

- in combination with metformin when diet and exercise plus metformin alone do not provide adequate glycaemic control
- in combination with a sulphonylurea and metformin when diet and exercise plus dual therapy with these medicinal products do not provide adequate glycaemic control.

SMC restriction: in combination therapy with metformin when diet and exercise plus metformin alone does not provide adequate glycaemic control in patients for whom the addition of a sulphonylurea is inappropriate.

SMC cannot recommend the use of linagliptin as monotherapy or in combination with metformin and a sulphonylurea as the company's submission related only to its use in combination with metformin.

On 11 February 2013 SMC advised that linagliptin (Trajenta®) is accepted for restricted use within NHSScotland for the treatment of type 2 diabetes mellitus to improve glycaemic control in adults.

As monotherapy:

- in patients inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to intolerance, or contraindicated due to renal impairment.

As combination therapy:

- in combination with a sulphonylurea and metformin when diet and exercise plus dual therapy with these medicinal products does not provide adequate glycaemic control
- in combination with insulin with or without metformin, when this regimen alone, with diet and exercise, does not provide adequate glycaemic control.

SMC restriction: as monotherapy in patients for whom both metformin and sulphonylureas are inappropriate due to contraindications or intolerance; as combination therapy with a sulphonylurea and metformin when diet and exercise plus dual therapy does not provide adequate glycaemic control.

SMC is unable to recommend the use of linagliptin in combination with insulin as the economic case has not been demonstrated.

On 11 February 2013 SMC advised that linagliptin plus metformin tablets (Jentadueto®) is accepted for restricted use within NHSScotland for treatment of adult patients with type 2 diabetes mellitus:

- as an adjunct to diet and exercise to improve glycaemic control in adult patients inadequately controlled on their maximal tolerated dose of metformin alone, or those already being treated with the combination of linagliptin and metformin
- in combination with a sulphonylurea (i.e. triple combination therapy) as an adjunct to diet and exercise in adult patients inadequately controlled on their maximal tolerated dose of metformin and a sulphonylurea.

SMC restriction: to use in patients for whom a combination of linagliptin and metformin is an appropriate choice of therapy and these fixed-doses are considered appropriate.

On 11 May 2015 SMC advised that linagliptin (Trajenta®) is accepted for use within NHSScotland for the treatment of type 2 diabetes mellitus to improve glycaemic control in

adults in combination with insulin with or without metformin, when this regimen alone, with diet and exercise, does not provide adequate glycaemic control.

SMC has previously accepted linagliptin for restricted use as monotherapy in combination with metformin, and in combination with a sulphonylurea and metformin. This now extends the advice to include its use in combination with insulin.

On 8 June 2015 SMC advised that llinagliptin plus metformin combination tablets (Jentadueto®) is accepted for restricted use within NHSScotland for the treatment of adult patients with type 2 diabetes mellitus in combination with insulin (ie triple combination therapy) as an adjunct to diet and exercise to improve glycaemic control when insulin and metformin alone do not provide adequate glycaemic control.

SMC restriction: to use in patients for whom a combination of linagliptin and metformin is an appropriate choice of therapy and the fixed doses are considered appropriate.

On 7 December 2009 SMC advised that liraglutide (Victoza) is accepted for restricted use within NHSScotland for the treatment of adults with type 2 diabetes mellitus to achieve glycaemic control:

- in combination with metformin or a sulphonylurea, in patients with insufficient glycaemic control despite maximal tolerated dose of monotherapy with metformin or sulphonylurea
- in combination with metformin and a sulphonylurea or metformin and a thiazolidinedione in patients with insufficient glycaemic control despite dual therapy.

SMC restriction: liraglutide is restricted to use as a third-line antidiabetic agent.

The economic case for second-line use, added to metformin in place of a sulphonylurea, has not been demonstrated.

On 11 May 2015 SMC advised that liraglutide (Victoza®) is accepted for use within NHSScotland for the treatment of adults with type 2 diabetes mellitus to achieve glycaemic control in combination with basal insulin when this, together with diet and exercise, does not provide adequate glycaemic control.

Liraglutide has previously been accepted for restricted use as a third line antidiabetic agent for use in combination with oral antidiabetic agents. This now extends the advice to include its use in combination with insulin.

On 12 September 2016 SMC advised that in the absence of a submission from the holder of the marketing authorisation, liraglutide (Victoza®) is not recommended for use within NHSScotland as monotherapy for the treatment of adults with type 2 diabetes mellitus to achieve glycaemic control when diet and exercise alone do not provide adequate glycaemic control in patients for whom use of metformin is considered inappropriate due to intolerance or contraindications.

The holder of the marketing authorisation has not made a submission to SMC regarding this product in this setting. As a result SMC cannot recommend its use within NHSScotland.

On 12 October 2015 SMC advised that insulin degludec/liraglutide (Xultophy®) is accepted for restricted use within NHSScotland for treatment of adults with type 2 diabetes mellitus to improve glycaemic control in combination with oral glucose-lowering medicinal products when these alone or combined with a GLP-1 receptor agonist or with basal insulin do not provide adequate glycaemic control.

SMC restriction: for use in patients who are uncontrolled on basal insulin analogues (HbA1c >7.5% (59 mmol/mol)) and for whom a GLP-1 receptor agonist is appropriate as an add-on intensification therapy to basal insulin to obtain glucose control.

On 9 September 2013 SMC advised that lixisenatide (Lyxumia®) is accepted for restricted use within NHSScotland as treatment of adults with type 2 diabetes mellitus to achieve glycaemic control in combination with oral glucose-lowering medicinal products and/or basal insulin when these, together with diet and exercise, do not provide adequate glycaemic control.

SMC restriction: to use in patients for whom a GLP-1 agonist is appropriate, as an alternative

to existing GLP-1 agonists.

On 12 September 2005 SMC advised that pioglitazone (Actos®) is accepted for restricted use within NHSScotland as monotherapy for type 2 diabetes mellitus patients in whom consideration is otherwise being given to commencing insulin therapy. It is not recommended as monotherapy for any other group of patients.

On 12 March 2007 SMC advised that pioglitazone (Actos®), as triple therapy in combination with metformin and a sulphonylurea, is accepted for restricted use within NHSScotland for the treatment of patients (particularly overweight patients) with insufficient glycaemic control despite dual oral therapy and where patients are unable or unwilling to take insulin. It should be initiated and monitored only by physicians experienced in the treatment of diabetes mellitus who will be able to identify and manage patients who might benefit.

On 10 September 2007 SMC advised that pioglitazone (Actos®) is accepted for use within NHSScotland in combination with insulin in type 2 diabetes mellitus patients with insufficient glycaemic control on insulin for whom metformin is inappropriate because of contraindications or intolerance.

On 11 September 2006 SMC advised that pioglitazone 15 mg/metformin 850 mg hydrochloride (Competact) is accepted for restricted use in NHSScotland for the treatment of type 2 diabetes mellitus. It should be used for overweight patients who are unable to achieve sufficient glycaemic control at their maximally tolerated doses of oral metformin alone. It is restricted to patients who cannot be treated with a sulphonylurea in combination with metformin.

This combination product costs the same as equivalent doses of the individual constituent preparations and offers a more convenient, though less flexible, dosing regimen.

On 9 December 2013 SMC advised that saxagliptin (Onglyza®) is accepted for restricted use within NHSScotland in adult patients aged 18 years and older with type 2 diabetes mellitus to improve glycaemic control as triple oral therapy in combination with metformin plus a sulphonylurea when this regimen alone, with diet and exercise, does not provide adequate glycaemic control.

On 10 March 2014 SMC advised that in the absence of a submission from the holder of the marketing authorisation saxagliptin (Onglyza®) is not recommended for use within NHSScotland as monotherapy in adult patients aged 18 years and older with type 2 diabetes mellitus to improve glycaemic control inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to contraindications or intolerance.

The holder of the marketing authorisation has not made a submission to SMC regarding this product in this indication. As a result SMC cannot recommend its use within NHSScotland.

On 10 November 2014 SMC advised that saxagliptin (Onglyza®) is accepted for use within NHSScotland in adult patients aged 18 years and older with type 2 diabetes mellitus to improve glycaemic control as combination therapy with insulin (with or without metformin), when this regimen alone, with diet and exercise, does not provide adequate glycaemic control.

The manufacturer's submission related only to the use of saxagliptin in combination with insulin (with or without metformin). SMC cannot recommend the use of saxagliptin as monotherapy.

On 10 June 2013 SMC advised that saxagliptan + metformin (Komboglyze) is accepted for restricted use within NHSScotland as an adjunct to diet and exercise to improve glycaemic control in adult patients aged 18 years and older with type 2 diabetes mellitus who are inadequately controlled on their maximally tolerated dose of metformin alone or those already being treated with the combination of saxagliptin and metformin as separate tablets.

SMC restriction: use in patients for whom a combination of saxagliptin and metformin is an appropriate choice of therapy and only when the addition of sulphonylureas to metformin monotherapy is not appropriate.

Saxagliptin/metformin is also licensed for use in combination with insulin for the treatment of type 2 diabetes. The manufacturer's submission related only to the use of saxagliptin and

metformin in combination therefore SMC cannot recommend the use of saxagliptin/metformin in combination with insulin.

On 13 January 2014 SMC advised that saxagliptin plus metformin (Komboglyze®) is accepted for use within NHSScotland in combination with a sulphonylurea (i.e. triple combination therapy) as an adjunct to diet and exercise to improve glycaemic control in adult patients aged 18 years and older with type 2 diabetes mellitus when the maximally tolerated dose of both metformin and the sulphonylurea does not provide adequate glycaemic control.

On 8 October 2007 SMC advised that sitagliptin (Januvia®) is accepted for restricted use within NHSScotland for treatment of patients with type 2 diabetes mellitus to improve glycaemic control in combination with metformin when diet and exercise, plus metformin, do not provide adequate glycaemic control. It should be restricted to use in patients only when the addition of sulphonylureas is not appropriate, and represents an alternative to other agents such as thiazolidinediones.

On 13 October 2008 SMC advised that sitagliptin (Januvia®) is accepted for use within NHSScotland for patients with type 2 diabetes mellitus to improve glycaemic control in combination with a sulphonylurea when diet and exercise plus maximal tolerated dose of a sulphonylurea alone do not provide adequate glycaemic control and when metformin is inappropriate due to contraindications or intolerance; or in combination with a sulphonylurea and metformin when diet and exercise plus dual therapy with these agents do not provide adequate glycaemic control.

Sitagliptin is also licensed for use in combination with thiazolidinediones. The manufacturer's submission related only to the use of sitagliptin in combination with sulphonylureas with or without metformin. SMC cannot recommend the use of sitagliptin in combination with thiazolidinediones.

On 12 July 2010 SMC advised that sitagliptin (Januvia) is accepted for restricted use within NHSScotland as monotherapy, to improve glycaemic control in patients with type 2 diabetes mellitus who are inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to contraindications or intolerance.

SMC restriction: to patients for whom both metformin and sulphonylureas are inappropriate due to contraindications or intolerance.

The health economic case was demonstrated only for a sub-population of patients within the licensed indication.

The licensed indication for sitagliptin has also recently been extended to include use in triple combination therapy with metformin plus thiazolidinediones and use as add-on therapy to insulin. The manufacturer's submission related only to the use of sitagliptin as monotherapy Therefore SMC cannot recommend the use of sitagliptin in combination with metformin plus thiazolidinediones or as add-on therapy to insulin.

On 7 September 2015 SMC advised that sitagliptin (Januvia®) is accepted for use within NHSScotland for treatment of type 2 diabetes mellitus to improve glycaemic control in adults as add-on to insulin (with or without metformin) when diet and exercise plus stable dose of insulin do not provide adequate glycaemic control.

SMC has previously accepted sitagliptin for use in combination with a sulphonylurea (with or without metformin), and for restricted use with metformin and as monotherapy. This now extends the advice to include its use in combination with insulin.

On 10 May 2010 SMC advised that sitagliptin 50 mg and metformin hydrochloride 1,000 mg (Janumet® 50/1,000) is accepted for restricted use within NHSScotland as an adjunct to diet and exercise to improve glycaemic control in patients with type 2 diabetes mellitus inadequately controlled on their maximal tolerated dose of metformin alone, or those already being treated with the combination of sitagliptin and metformin.

SMC restriction: restricted to use in patients for whom a combination of sitagliptin and metformin is an appropriate choice of therapy and only when the addition of sulphonylureas to metformin monotherapy is not appropriate. Sitagliptin represents an alternative to other agents such as thiazolidinediones.

On 9 August 2010 SMC advised that sitagliptin plus metformin (Janumet® 50/1,000) is accepted for use within NHSScotland in combination with a sulphonylurea (ie triple combination therapy) as an adjunct to diet and exercise in patients inadequately controlled on their maximal tolerated dose of metformin and a sulphonylurea.

Sitagliptin/metformin is also licensed for use in triple combination therapy with a thiazolidinedione or as add-on to insulin. The manufacturer's submission related only to the use of sitagliptin/metformin in combination with a sulphonylurea, therefore SMC cannot recommend the use of sitagliptin/metformin in triple therapy with either a thiazolidinedione or insulin.

On 12 October 2009 SMC advised that vildagliptin (Galvus®) is accepted for use within NHSScotland for the treatment of type 2 diabetes mellitus as dual oral therapy in combination with a sulphonylurea, in patients with insufficient glycaemic control despite maximal tolerated dose of a sulphonylurea or for whom metformin is inappropriate due to contraindications or intolerance.

Vildagliptin is also licensed for use in combination with metformin or thiazolidinedione drugs for the treatment of type 2 diabetes. SMC has already issued advice on use in combination with metformin. As this submission from the manufacturer related only to the use of vildagliptin in combination with a sulphonylurea, SMC cannot recommend the use of vildagliptin in combination with thiazolidinedione drugs.

On 14 January 2013 SMC advised that vildagliptin (Galvus®) is accepted for restricted use within NHSScotland for treatment of type 2 diabetes mellitus in adults as monotherapy in patients inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to contraindications or intolerance.

SMC restriction: for use in patients for whom both metformin and sulphonylureas are inappropriate due to contraindications or intolerance.

On 13 May 2013 SMC advised that in the absence of a submission from the holder of the marketing authorisation vildagliptin (Galvus®) is not recommended for use within NHSScotland for treatment of type 2 diabetes mellitus in adults in combination with insulin (with or without metformin) when diet and exercise plus a stable dose of insulin do not provide adequate glycaemic control.

The holder of the marketing authorisation has not made a submission to SMC regarding this product in this indication. As a result SMC cannot recommend its use within NHSScotland.

On 9 December 2013 SMC advised that vildagliptin (Galvus®) is accepted for restricted use within NHSScotland for treatment of type 2 diabetes mellitus in adults as triple oral therapy in combination with a sulphonylurea and metformin when diet and exercise plus dual therapy with these medicinal products do not provide adequate glycaemic control.

On 13 May 2013 SMC advised that in the absence of a submission from the holder of the marketing authorisation vildagliptin/metformin hydrochloride (Eucreas®) is not recommended for use within NHSScotland for treatment of type 2 diabetes mellitus:

- in combination with a sulphonylurea (i.e. triple combination therapy) as an adjunct to diet and exercise in patients inadequately controlled with metformin and a sulphonylurea
- in triple combination therapy with insulin as an adjunct to diet and exercise to improve glycaemic control in patients when insulin at a stable dose and metformin alone do not provide adequate glycaemic control.

The holder of the marketing authorisation has not made a submission to SMC regarding this product in these indications. As a result SMC cannot recommend its use within NHSScotland.