Drug	Manufacturer	Date Advice Issued	Indication	SMC advice
Biguanides				
Metformin (Glucophage SR®)	Merck Serono Ltd	12 Oct 2009	Type 2 diabetes	**ADVICE:** following a 2nd resubmission: **Metformin hydrochloride prolonged release tablets (Glucophage SR®)** are accepted for restricted use for the treatment of type 2 diabetes mellitus in adults, particularly in overweight patients, when dietary management and exercise alone does not result in adequate glycaemic control. This new formulation appears to have similar short-term efficacy to immediate-release metformin. Evidence of improved gastrointestinal tolerability is not convincing and the prolonged-release formulation is more expensive than the immediate-release formulation. It is restricted to use in patients who are intolerant of immediate release metformin and in whom the prolonged release tablet allows the use of a dose of metformin not previously tolerated or in patients for whom a once-daily preparation offers a clinically significant benefit. http://www.scottishmedicines.org.uk/smc/7003.html
Metformin hydrochloride (Glucophage SR®) 500 mg/1000 mg Powder for Solution	Merck Serono Ltd	12 April 2010	Type 2 diabetes	**ADVICE:** following an **abbreviated** submission **Metformin powder for oral solution (Glucophage®)** is accepted for restricted use within NHS Scotland. Licensed indication under review: the treatment of type 2 diabetes mellitus, particularly in overweight patients, when dietary management and exercise alone does not result in adequate glycaemic control: – In adults, metformin may be used as monotherapy or in combination with other oral anti-diabetic agents or insulin; – In children, from 10 years of age and adolescents, metformin may be used as monotherapy or in combination with insulin. A reduction of diabetic complications has been shown in overweight type 2 diabetic adult patients treated with metformin as first-line therapy after diet failure. SMC restriction: Use is restricted to patients who are unable to swallow the solid dosage formulation. There is a price premium relative to metformin immediate release tablets but a saving

				compared to an existing formulation of metformin oral solution. http://www.scottishmedicines.org.uk/smc/8027.html
DPP-4 inhibitors				
Saxagliptin 5 mg (Onglyza®)	Bristol-Myers Squibb	08 Mar 2010	Type 2 diabetes	**ADVICE**: following a full submission **Saxagliptin (Onglyza®)** is accepted for restricted use within NHS Scotland in adult patients with type 2 diabetes mellitus as add-on combination therapy with metformin, when metformin alone, with diet and exercise, does not provide adequate glycaemic control. It is restricted to use in patients only when the addition of sulphonylureas is not appropriate, and represents an alternative to other agents such as thiazolidinediones. Efficacy, as assessed by measurement of HbA1c, is comparable to another dipeptidyl peptidase-4 inhibitor. It appears to have minimal effect on body weight. Saxagliptin is also licensed for use in combination with sulphonylureas or thiazolidinedione drugs for the treatment of type 2 diabetes. The manufacturer's submission related only to the use of saxagliptin in combination with metformin. SMC cannot recommend the use of saxagliptin in combination with sulphonylureas or thiazolidinediones. http://www.scottishmedicines.org.uk/smc/7320.html
Sitagliptin (Januvia®) monotherapy	Merck Sharp & Dohme Ltd	12 July 2010	Type 2 diabetes	**ADVICE:** following a full submission **Sitagliptin (Januvia®)** is accepted for restricted use within NHS Scotland. Licensed indication under review: 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. Sitagliptin met the pre-defined efficacy criterion for non-inferiority versus metformin in a study of treatment naïve patients. It appears to have minimal effect on body weight. 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. http://www.scottishmedicines.org.uk/SMC_Advice/Advice/607_10_sitagliptin_Januvia_100mg_tablets/sitagliptin__Januvia__monotherapy
Sitagliptin (Januvia®)	Merck Sharp & Dohme Ltd	13 Oct 2008	Type 2 diabetes	**ADVICE**: following a full submission **Sitagliptin (Januvia®)** is accepted for use within NHS Scotland 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. When added to a sulphonylurea with or without metformin, sitagliptin had a modest beneficial effect on glycated haemoglobin (HbA1c) levels. Sitagliptin is also licensed for use in combination with thiazolidinedione drugs. 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. http://www.scottishmedicines.org.uk/smc/5854.html
Sitagliptin 100 mg tablets (Januvia®)	Merck Sharp & Dohme Ltd	8 Oct 2007	Type 2 diabetes	**ADVICE:** following a full submission: **Sitagliptin (Januvia®)** is accepted for restricted use within NHS Scotland 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. Efficacy, as assessed by measurement of HbA1c, is similar to sulphonylurea and thiazolidinedione drugs added at this stage in therapy. It appears to have minimal effects on body weight. http://www.scottishmedicines.org.uk/smc/5358.html
Vildagliptin (Galvus®)	Novartis	12 Oct 2009	Type 2 diabetes	**ADVICE:** following a full submission **Vildagliptin (Galvus®)** is accepted for use within NHS Scotland 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. When added to a sulphonylurea, vildagliptin had a modest beneficial effect on glycated haemoglobin (HbA1C). 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. http://www.scottishmedicines.org.uk/smc/7002.html
Vildagliptin (Galvus®)	Novartis	07 April 2008	Type 2 diabetes	**ADVICE**: following a full submission **Vildagliptin (Galvus®)** is accepted for restricted use within NHS Scotland for the treatment of type 2 diabetes mellitus as dual oral therapy in combination with metformin, in patients with insufficient glycaemic control despite maximal tolerated dose of monotherapy with metformin. It is restricted to use in patients only when the addition of sulphonylureas is not appropriate, and represents an alternative to other agents such as thiazolidinediones. Efficacy, as assessed by measurement of glycated haemoglobin (HbA1c), is similar to thiazolidinedione drugs added at this stage in therapy. It appears to have minimal effect on body weight. Vildagliptin is also licensed for use in combination with sulphonylureas or thiazolidinedione drugs for the treatment of type 2 diabetes. The manufacturer's submission related only to the use of vildagliptin in combination with metformin. SMC cannot recommend the use of vildagliptin in combination with these agents. http://www.scottishmedicines.org.uk/smc/5473.html
GLP-1 receptor agonists				
Liraglutide (Victoza®)	Novo Nordisk	07 Dec 2009	Type 2 diabetes	**ADVICE:** following a full submission **Liraglutide (Victoza®)** is accepted for restricted use within NHS Scotland. Licensed indication under review: **Liraglutide** 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. Five randomised controlled studies have demonstrated efficacy of liraglutide against relevant comparators in terms of the primary endpoint, change from baseline in glycated haemoglobin (HbA1c) after 26 weeks of treatment. **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. For full detailed advice, please refer to: http://www.scottishmedicines.org.uk/smc/7159.html
Exenatide (Byetta®)	Eli Lilly & Company Ltd	7 Mar 2011	Type 2 diabetes	**ADVICE:** following a full submission **Exenatide (Byetta®)** is accepted for restricted use within NHS Scotland. Indication under review: 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. The addition of exenatide to a thiazolidinedione alone or in combination with metformin modestly improved glycaemic control compared with placebo in studies up to 26 weeks, but was associated with nausea and vomiting in some patients. 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. http://www.scottishmedicines.org.uk/SMC_Advice/Advice/684_11_exenatide_Byetta/exenatide_Byetta
Exenatide 5 or 10 micrograms, solution for injection, prefilled pen (Byetta®)	Eli Lilly & Company Ltd	9 July 2007	Type 2 diabetes	**ADVICE**: following a full submission **Exenatide (Byetta®)** is accepted for restricted use within NHS Scotland 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. It has shown non-inferiority to two insulin regimens with which it has been compared and

				has a beneficial effect on weight. It is restricted to use as an alternative to insulin in patients who have failed treatment on metformin and/or sulphonylureas and in whom insulin would be the next treatment option. http://www.scottishmedicines.org.uk/smc/5206.html
Thiazolidinediones				
Pioglitazone 15 mg, 30 mg and 45 mg tablets (Actos®)	Takeda UK Ltd	10 Sep 2007	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	**ADVICE**: following a full submission **Pioglitazone (Actos®)** is accepted for use within NHS Scotland 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. It improved glycaemic control when added to insulin in the relevant patient population. http://www.scottishmedicines.org.uk/smc/5317.html
Pioglitazone 15 mg, 30 mg and 45 mg tablets (Actos® triple therapy)	Takeda UK Ltd	12 Mar 2007	Type 2 diabetes	**ADVICE:** following a full submission **Pioglitazone (Actos®),** as triple therapy in combination with metformin and a sulphonylurea, is accepted for restricted use within NHS Scotland 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. http://www.scottishmedicines.org.uk/smc/5209.html
Pioglitazone (Actos®)	Takeda	12 Sep 2005	Type 2 diabetes mellitus	**ADVICE:** following a re-submission **Pioglitazone (Actos®)** is accepted for restricted use within NHS Scotland as monotherapy for

			patients for whom metformin is inappropriate	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. It is one of two peroxisome proliferator-activated receptor-g agonists marketed in the UK for this indication. Its use should be restricted to patients who have already experienced severe hypoglycaemia or patients in whom metformin and sulphonylureas are contra-indicated or not tolerated. http://www.scottishmedicines.org.uk/smc/2237.html
Combined formulation medicines				
Sitagliptin/ Metformin (Janumet® 50/1000)	Merck Sharp and Dohme Ltd	10 May 2010	Type 2 diabetes	**ADVICE:** following an **abbreviated** submission **Sitagliptin 50 mg and metformin hydrochloride 1000 mg (Janumet® 50/1000):** is accepted for restricted use within NHS Scotland. **Licensed indication under review:** 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. Efficacy of sitagliptin when added to metformin, as assessed by measurement of HbA1c, is similar to sulphonylurea and thiazolidinedione drugs added at this stage in therapy. It appears to have minimal effects on body weight. http://www.scottishmedicines.org.uk/SMC_Advice/Advice/492_08_sitagliptin_metformin_Janumet/sitagliptin_metformin__Janumet_
Sitagliptin plus metformin (Janumet® 50/1000)	Merck Sharp and Dohme Ltd	9 Aug 2010	In combination with a sulphonylurea (ie, triple combination therapy) as an adjunct to diet	**ADVICE:** following an **abbreviated** submission **Sitagliptin plus metformin (Janumet® 50/1000)**: is accepted for use within NHS Scotland. **Licensed indication under review:** In combination with a sulphonylurea (i.e., triple combination therapy) as an adjunct to diet and exercise in patients inadequately controlled on their maximal tolerated dose of metformin and a sulphonylurea. For patients in whom triple combination therapy with metformin, a sulphonylurea and sitagliptin is appropriate it has the potential to reduce the pill burden at no additional cost.

			and exercise in patients inadequately controlled on their maximal tolerated dose of metformin and a sulphonylurea.	When added to a sulphonylurea with metformin, sitagliptin has shown a modest effect on glycated haemoglobin (HbA1c) levels. Note that a lower dose of the sulphonylurea may be required to reduce the risk of hypoglycaemia. 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. http://www.scottishmedicines.org.uk/SMC_Advice/Advice/627_10_sitagliptin_plus_metformin_Janumet_50_1000/627_10_sitagliptin_plus_metformin_Janumet_50_1000
Vildagliptin/ Metformin (Eucreas®)	Novartis	07 July 2008	Type 2 diabetes	**ADVICE:** following an **abbreviated** submission **Vildagliptin 50 mg/metformin hydrochloride 850 mg film coated tablets and vildagliptin 50 mg/metformin hydrochloride 1000 mg film coated tablets (Eucreas® 50 mg/850 mg and 50 mg/1000 mg)** are accepted for restricted use within NHS Scotland for the treatment of type 2 diabetes mellitus patients who are unable to achieve sufficient glycaemic control at their maximally tolerated dose of oral metformin alone or who are already treated with the combination of vildagliptin and metformin as separate tablets. The addition of vildagliptin to metformin is restricted to use in patients only when the addition of sulphonylureas is not appropriate, and represents an alternative to other agents such as thiazolidinediones. Efficacy, as assessed by measurement of glycated haemoglobin (HbA1c), is similar to thiazolidinedione drugs added at this stage in therapy. It appears to have minimal effect on body weight. http://www.scottishmedicines.org.uk/smc/5915.html
Pioglitazone 15 mg/ Metformin 850 mg hydrochloride (Competact®)	Takeda UK Ltd	11 Sep 2006	Type 2 diabetes	**ADVICE:** following an **abbreviated** submission **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. http://www.scottishmedicines.org.uk/smc/4881.html

Insulins				
Insulin glulisine (Apidra®)	Sanofi-Aventis	10 Nov 2008	Adolescents and children with diabetes	**ADVICE:** following an **abbreviated** submission **Insulin glulisine (Apidra®)** is accepted for restricted use within NHS Scotland for the treatment of adolescents and children, 6 years or older with diabetes mellitus, where treatment with insulin is required and for whom the use of a short-acting insulin analogue is appropriate. Insulin glulisine has a similar efficacy to other short-acting insulins in reducing glycated haemoglobin and a similar pharmacokinetic profile to at least one other insulin analogue. It is restricted to use in patients where soluble human insulin is inappropriate. The Scottish Medicines Consortium has previously accepted this product for restricted use for this indication in adults. http://www.scottishmedicines.org.uk/smc/4429.html
Insulin glulisine (Apidra® Solostar)	Sanofi-Aventis	07 April 2008	Treatment of adult patients with diabetes mellitus	**ADVICE:** following an **abbreviated** submission **Onsulin glulisine 100 units/ml solution for injection in a pre-filled pen (Apidra® Solostar)** is accepted for restricted use within NHS Scotland for the treatment of adult patients with diabetes mellitus in whom treatment with this insulin analogue is appropriate and in whom the use of a pre-filled pen offers advantages over a pen and cartridge device. Insulin glulisine has similar efficacy to other short-acting insulins in reducing glycated haemoglobin and a similar pharmacokinetic profile to at least one other insulin analogue. It is restricted to use in patients where regular human insulin is inappropriate. http://www.scottishmedicines.org.uk/smc/5691.html
Insulin glulisine for subcutaneous injection 100 units/ml (Apidra®)	Sanofi Aventis	11 Sep 2006	Diabetes mellitus	**ADVICE:** following a full submission **Insulin glulisine (Apidra®)** is accepted for restricted use within NHS Scotland for the treatment of adult patients with diabetes mellitus in whom treatment with a short-acting insulin analogue is appropriate. Insulin glulisine has similar efficacy to other short-acting insulins in reducing glycated haemoglobin and a similar pharmacokinetic profile to at least one other insulin analogue. It is restricted to use in patients where regular human insulin is inappropriate. http://www.scottishmedicines.org.uk/smc/4911.html

Insulin lispro (Humalog® KwikPen)	Lilly UK	13 Oct 2008	For adults and children with diabetes mellitus who require insulin for the maintenance of normal glucose homeostasis	**ADVICE**: following an **abbreviated** submission **Insulin lispro (Humalog® KwikPen)** is accepted for use within NHS Scotland for the treatment of adults and children with diabetes mellitus who require insulin for maintenance of normal glucose homeostasis, and for the initial stabilisation of diabetes mellitus. It may be used in patients for whom treatment with this short-acting insulin analogue is appropriate. http://www.scottishmedicines.org.uk/smc/6193.html
Insulin lispro (Humalog® Mix25, Mix50 KwikPen)	Lilly UK	13 Oct 2008	For patients with diabetes mellitus who require insulin for the maintenance of normal glucose homeostasis.	**ADVICE**: following an **abbreviated** submission **Insulin lispro (Humalog® Mix25 KwikPen) and insulin lispro (Humalog® Mix50 KwikPen)** are accepted for use within NHS Scotland for the treatment of patients with diabetes mellitus who require insulin for maintenance of normal glucose homeostasis, for whom treatment with this biphasic insulin analogue is appropriate. http://www.scottishmedicines.org.uk/smc/6194.html
Insulin glargine (Lantus® Solostar)	Sanofi-Aventis	07 April 2008	For the treatment of adults, adolescents and children of 6 years and above with diabetes mellitus, where treatment with insulin is required.	**ADVICE:** following an **abbreviated** submission **Insulin glargine 100 units/ml solution for injection in a pre-filled pen (Lantus® SoloStar)** is accepted for restricted use in the treatment of adults, adolescents and children of 6 years or above with diabetes mellitus, where treatment with insulin is required. It may be used in patients in whom treatment with this insulin analogue is appropriate and in whom the use of a pre-filled pen offers advantages over a pen and cartridge device. The use of insulin glargine should be targeted on patients with Type I diabetes who are at risk of or experience unacceptable frequency and/or severity of nocturnal hypoglycaemia on attempting to achieve better hypoglycaemic control during treatment with established insulins. It is also acceptable as a once daily insulin therapy for patients who require carer administration of their insulin. In patients with type 2 diabetes it should be restricted to those who suffer from recurrent episodes of hypoglycemia or require assistance with their insulin injections. http://www.scottishmedicines.org.uk/smc/5690.html
Insulin glargine (Lantus®)	Aventis	04 Oct 2002	Diabetes mellitus	**ADVICE:** recommended for restricted use within the NHS Scotland. **Insulin glargine** is an acceptable treatment for patients with diabetes mellitus. Pending

				further studies, its use should be targeted on patients who are at risk or experience unacceptable frequency and/or severity of nocturnal hypoglycaemia on attempting to achieve better hypoglycaemic control during treatment with established insulins. It is also acceptable as a once daily insulin therapy for patients who require carer administration of their insulin. At present the evidence does not support its routine use in patients with type 2 diabetes unless they suffer from recurrent episodes of hypoglycemia or require assistance with their insulin injections. http://www.scottishmedicines.org.uk/smc/1838.html
Insulin detemir, 100 U/ml solution for injection via InnoLet device (Levemir® in InnoLet)	Novo Nordisk Ltd	13 Aug 2007	Diabetes mellitus	**ADVICE**: following an **abbreviated** submission **Insulin detemir (Levemir®) for injection via the InnoLet® device** is accepted for restricted use within NHS Scotland for treatment of diabetes mellitus in patients for whom insulin detemir is an appropriate choice of insulin and who have poor visual acuity and dexterity problems. The Scottish Medicines Consortium has previously advised that insulin detemir should be restricted to 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. http://www.scottishmedicines.org.uk/smc/5273.html
Insulin detemir (Levemir®)	Novo Nordisk Ltd	13 June 2005	Children and adolescents with diabetes mellitus	**ADVICE:** following an **abbreviated** submission **Insulin detemir** is accepted for restricted use in Scotland in the treatment of children and adolescents with diabetes mellitus. The licence has been extended to include these patient groups and the restriction reflects similar advice from the Scottish Medicines Consortium (August 2004) when insulin detemir was reviewed as a new product for adult patients only. http://www.scottishmedicines.org.uk/smc/2185.html
Insulin detemir (Levemir®)	Novo Nordisk Ltd	09 Aug 2004	Diabetes mellitus	**ADVICE:** following a full submission. **Insulin detemir** is accepted for restricted use within NHS Scotland for the treatment of diabetes mellitus. Insulin detemir is an acceptable basal insulin for patients with 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. http://www.scottishmedicines.org.uk/smc/2048.html
Biphasic insulin aspart 30 (NovoMix 30®)	NovoNordisk	06 June 2003	Diabetes mellitus	**ADVICE:** following a resubmission. Recommended for general use within NHS Scotland. In trials of 12 weeks duration, **biphasic insulin aspart** has demonstrated similar effects on HbA1c levels to biphasic human insulin 30 and biphasic insulin lispro Mix 25. Biphasic insulin aspart 30 has demonstrated similar effects to its competitor insulins and therefore is an effective treatment for diabetes at broadly similar costs. http://www.scottishmedicines.org.uk/smc/1804.html
Medicines for cardiovascular indications				
Olmesartan medoximil / amlodipine besilate (Sevikar®)	Daiichi Sankyo UK Ltd	12 Oct 2009	treatment of essential hypertension	**ADVICE:** following an **abbreviated** submission **Olmesartan medoxomil/amlodipine as besilate (Sevikar®)** is accepted for use in NHS Scotland for treatment of essential hypertension in patients whose blood pressure is not adequately controlled on olmesartan medoxomil or amlodipine monotherapy. In patients for whom concomitant use of these medicines is appropriate it allows administration of a single tablet at a lower or modestly increased cost compared to the individual components (depending on dose). Angiotensin receptor blockers are an alternative to ACE inhibitors where these are not tolerated. This fixed dose combination is one of many options for the treatment of hypertension, many of which are less expensive. http://www.scottishmedicines.org.uk/smc/7000.html
Amlodipine besylate/valsartan (Exforge®)	Novartis Pharmaceuticals UK Ltd	12 March 2007	For patients whose blood pressure is not adequately controlled on amlodipine or valsartan monotherapy.	**ADVICE:** following an **abbreviated** submission **Amlodipine/valsartan (Exforge®)** is accepted for use in NHS Scotland for patients whose blood pressure is not adequately controlled on amlodipine or valsartan monotherapy. In patients for whom concomitant use of these medicines as a fixed dose combination is appropriate it allows administration of a single tablet at no greater cost than valsartan (Diovan®) alone. Angiotensin receptor blockers are an alternative to ACE inhibitors where these are not tolerated. This fixed dose combination is one of many options for the treatment of

				hypertension, many of which are less expensive. http://www.scottishmedicines.org.uk/smc/5175.html
Ezetimibe/ Simvastatin (Inegy®)	Merck Sharp & Dohme/Schering Plough Ltd	13 June 2005	Hypercholesterolaemia and Homozygous Familial Hypercholesterolaemia	**ADVICE:** following an **abbreviated** submission **Ezetimibe/simvastatin** (InegyP®P) is accepted for restricted use in NHS Scotland only for patients who have failed to achieve target cholesterol levels after titration and optimisation of statin monotherapy and where the combination of ezetimibe 10mg and simvastatin 20mg, 40mg or 80mg is appropriate. This reflects advice on ezetimibe issued by the Scottish Medicines Consortium in September 2003 (61/03) and is based on the combined tablets being priced at approximately the same level as the individual ingredients. http://www.scottishmedicines.org.uk/smc/2186.html
Ezetimibe (Ezetrol®)	Merck Sharp & Dohme Ltd/Schering Plough Ltd	08 Sep 2003	Primary hypercholesterolaemia	**ADVICE:** Recommended for restricted use within NHS Scotland **Ezetimibe** may be considered in combination with a statin for patients who have failed to reach target cholesterol levels despite treatment with titrated/optimised statins alone. It may also be considered as monotherapy where statins are inappropriate or poorly tolerated. http://www.scottishmedicines.org.uk/smc/1925.html
Clopidogrel 75mg tablets (Plavix®)	Sanofi-Aventis/ Bristol Myers-Squibb	13 August 2007	ST-segment elevation myocardial infarction (STEMI)	**ADVICE**: following a full submission **Clopidogrel (Plavix®)** is accepted for restricted use within NHS Scotland for patients with ST segment elevation acute myocardial infarction (MI), in combination with aspirin, in medically treated patients eligible for thrombolytic therapy. The addition of short-term treatment with clopidogrel to long-term low dose aspirin has improved the patency rate of the infarct related artery as well as clinical endpoints. Treatment with clopidogrel in these patients is restricted to continuation for 4 weeks. http://www.scottishmedicines.org.uk/smc/5263.html
Clopidogrel (Plavix®)	Sanofi-Synthelabo and Bristol-Myers-Squibb	08 Mar 2004	Prevention of atherothrombotic events in acute coronary syndrome	**ADVICE:** following a full submission. **Clopidogrel (Plavix®)** is accepted for restricted use within NHS Scotland for the treatment of acute coronary syndrome (without ST-segment elevation) in combination with aspirin. It should be initiated only during an inpatient stay and only in patients in whom a diagnosis of acute coronary syndrome is confirmed with ECG changes or raised cardiac enzymes/markers. The maximum benefit appears within 3 months of starting treatment and

				the available information suggests that there is loss of benefit on stopping treatment. Benefits are greatest in patients with a high Thrombosis In Myocardial Infarction (TIMI) riskscore (5 – 7). http://www.scottishmedicines.org.uk/smc/1997.html
Nebivolol tablets 5mg (Nebilet®)	A Menarini Pharmaceuticals UK	13 Aug 2007	Chronic heart failure	**ADVICE**: following a re-submission **Nebivolol (Nebilet®)** is accepted for use within NHS Scotland for the treatment of stable mild and moderate chronic heart failure (CHF) in addition to standard therapies in elderly patients ≥70 years. Compared to placebo, nebivolol, added to standard therapy, was associated with improved left ventricular function and a reduction in a composite endpoint combining all cause mortality and cardiovascular hospitalisation rates in elderly patients with chronic heart failure. There are no direct comparisons with other beta-blockers that are available at a lower acquisition cost. http://www.scottishmedicines.org.uk/smc/5259.html
Nebivolol tablets 5mg (Nebilet®)	Menarini Pharmaceuticals UK SRL	11 Sep 2006	Stable mild and moderate chronic heart failure	**ADVICE**: following a full submission **Nebivolol (Nebilet®)** is not recommended for use within NHS Scotland for the treatment of stable mild and moderate chronic heart failure (CHF) in addition to standard therapies in elderly patients ³70 years. Nebivolol, added to standard therapy, was associated with improved left ventricular function and a reduction in a composite endpoint combining all cause mortality and cardiovascular hospitalisation rates in elderly patients with chronic heart failure. There is no comparison with other beta-adrenoceptor blockers. Cost effectiveness relative to other beta-adrenoceptor blockers in common use in chronic heart failure has not been demonstrated. http://www.scottishmedicines.org.uk/smc/5037.html
Perindopril (Coversyl arganine) 2.5 mg 5 mg 10 mg tablets	Servier Laboratories	09 June 2008	Treatment of hypertension	**ADVICE:** following an **abbreviated** submission **Perindopril arginine (Coversyl Arginine) 2.5 mg, 5 mg, 10 mg tablets** are accepted for use in NHS Scotland for the treatment of essential hypertension. The 2.5mg and 5mg tablets are also accepted for treatment of symptomatic heart failure. This advice relates to patients for whom perindopril is an appropriate choice of therapy. These preparations are also licensed for the reduction of risk of cardiac events in patients

				with a history of myocardial infarction and/or revascularisation, however this indication has not been reviewed by SMC. The arginine salt replaces a tert-butylamine salt previously available and the 2.5 mg, 5 mg and 10 mg arginine tablets are equivalent to the 2mg, 4mg and 8mg tert-butylamine tablets in terms of the content of perindopril base. Caution is therefore required when prescribing perindopril as the two salts are not dose equivalent. Generic preparations of the tert butylamine salt are available at a lower cost than the proprietary preparations of perindopril. http://www.scottishmedicines.org.uk/smc/5830.html
Perindopril in combination with indapamine (Coversyl plus) 5 mg/1.25 mg tablet	Servier Laboratories	09 June 2008	Treatment of essential hypertension	**ADVICE:** following an **abbreviated** submission **Perindopril arginine 5 mg and indapamide 1.25 mg tablet (Coversyl Arginine Plus ®)** is accepted for use in NHS Scotland for the treatment of essential hypertension in patients whose blood pressure is not adequately controlled on perindopril alone and for whom this combination is an appropriate choice of therapy. The 5mg perindopril arginine in this formulation is equivalent in terms of the content of perindopril base to the 4mg perindopril tert-butylamine contained in the formulation previously available. After review of a full submission, SMC issued advice on 8th September 2003 that the previously available formulation of perindopril, indapamide (Coversyl PlusÒ) was recommended for general use within NHS Scotland. It produces a modest reduction in blood pressure in patients with essential hypertension uncontrolled by perindopril alone. http://www.scottishmedicines.org.uk/smc/5831.html
Perindopril/ Indapamide (Coversyl Plus®)	Servier Laboratories	08 Sep 2003	Hypertension	**ADVICE:** Recommended for general use within NHS Scotland **Perindopril, indapamide (Coversyl Plus®)** produces a modest reduction in blood pressure in patients with essential hypertension uncontrolled by perindopril alone. A daily dose of one tablet is almost cost-neutral compared with individual drug preparations. http://www.scottishmedicines.org.uk/smc/1924.html
Telmisartan (Micardis®)	Boehringer Ingelheim Ltd	9 May 2010	Hypertension and heart failure	**ADVICE:** In the absence of a submission from the holder of the marketing authorisation **Telmisartan (Micardis)**, is not recommended for use within NHSScotland for use in cardiovascular prevention (to reduce cardiovascular morbidity in patients with manifest atherothrombotic cardiovascular disease history of coronary heart disease, stroke, or

				peripheral arterial disease) or type 2 diabetes mellitus with documented target organ damage. The holder of the marketing authorisation has not made a submission to SMC regarding this product in this indication. As a result we cannot recommend its use within NHSScotland.
Telmisartan/ hydrochlorothiazide (MicardisPlus®)	Boehringer Ingleheim	09 May 2003	Essential hypertension	**ADVICE**: Recommended for restricted use within NHS Scotland. **Telmisartan / hydrochlorothiazide (MicardisPlus®)** has efficacy similar to the antihypertensive effects of the individual constituents added together in the treatment of essential hypertension. No increased costs are associated with this product compared with telmisartan (Micardis®) alone. Angiotensin II receptor antagonists are an alternative to ACE inhibitors where these are not tolerated. http://www.scottishmedicines.org.uk/smc/1813.html
Medicines for neuropathic pain				
Pregabalin (Lyrica®)	Pfizer Ltd	11 May 2009	Peripheral neuropathic pain	**ADVICE:** following a second resubmission **Pregabalin (Lyrica®)** is accepted for restricted use within NHS Scotland for the treatment of peripheral neuropathic pain in adults. The clinical evidence of efficacy in patients with peripheral neuropathic pain who are refractory to treatment was based on open-label, uncontrolled, non-randomised studies, with small patient numbers and different methodologies. Pregabalin is restricted to use in patients who have not achieved adequate pain relief from, or have not tolerated, conventional first and second line treatments for peripheral neuropathic pain. Treatment should be stopped if the patient has not shown sufficient benefit within 8 weeks of reaching the maximally tolerated therapeutic dose. http://www.scottishmedicines.org.uk/smc/6677.html
Duloxetine 30 mg and 60 mg capsules (Cymbalta®)	Eli Lilly and Company Limited/Boehringer Ingelheim	11 Sep 2006	Diabetic peripheral neuropathic pain in adults	**ADVICE:** following a full submission **Duloxetine (Cymbalta®)** is accepted for restricted use for the treatment of diabetic peripheral neuropathic pain in adults**.** Duloxetine relieved peripheral neuropathic pain compared with placebo in patients with diabetes. It is restricted to initiation by prescribers experienced in the management of diabetic peripheral neuropathic pain as 2nd or 3rd line therapy. http://www.scottishmedicines.org.uk/smc/4989.html