## Biguanides

<table>
<thead>
<tr>
<th>Drug</th>
<th>Manufacturer</th>
<th>Date Advice Issued</th>
<th>Indication</th>
<th>SMC advice</th>
</tr>
</thead>
</table>
| **Metformin** (Glucophage SR®)             | Merck Serono Ltd  | 12 Oct 2009       | Type 2      | **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.  
[Link](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      | **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
**Advice from the Scottish Medicines Consortium relevant to SIGN 116 – Management of Diabetes (correct at 26 April 2011)**

Compared to an existing formulation of metformin oral solution.

http://www.scottishmedicines.org.uk/smc/8027.html

### DPP-4 inhibitors

<table>
<thead>
<tr>
<th><strong>Saxagliptin</strong>&lt;sup&gt;5 mg&lt;/sup&gt; (Onglyza®)</th>
<th>Bristol-Myers Squibb</th>
<th>08 Mar 2010</th>
<th>Type 2 diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ADVICE:</strong> following a full submission</td>
<td></td>
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</tr>
<tr>
<td><strong>Saxagliptin (Onglyza®)</strong> 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.</td>
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<tr>
<td><a href="http://www.scottishmedicines.org.uk/smc/7320.html">http://www.scottishmedicines.org.uk/smc/7320.html</a></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Sitagliptin</strong>&lt;sup&gt;monotherapy&lt;/sup&gt; (Januvia®)</th>
<th>Merck Sharp &amp; Dohme Ltd</th>
<th>12 July 2010</th>
<th>Type 2 diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ADVICE:</strong> following a full submission</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sitagliptin (Januvia®)</strong> 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</td>
<td></td>
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</tr>
<tr>
<td><a href="http://www.scottishmedicines.org.uk/smc/7320.html">http://www.scottishmedicines.org.uk/smc/7320.html</a></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### 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 metformin plus thiazolidinediones or as add-on therapy to insulin.  

http://www.scottishmedicines.org.uk/smc/5358.html
Advice from the Scottish Medicines Consortium relevant to SIGN 116 – Management of Diabetes (correct at 26 April 2011)

| 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 |

<table>
<thead>
<tr>
<th>GLP-1 receptor agonists</th>
</tr>
</thead>
</table>

| 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 |
Advice from the Scottish Medicines Consortium relevant to SIGN 116 – Management of Diabetes (correct at 26 April 2011)

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Manufacturer</th>
<th>Date</th>
<th>Type of Diabetes</th>
<th>Advice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liraglutide</td>
<td>Eli Lilly &amp; Company Ltd</td>
<td>5th Mar 2011</td>
<td>Type 2 diabetes</td>
<td>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. <strong>Restriction:</strong> 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: <a href="http://www.scottishmedicines.org.uk/smc/7159.html">http://www.scottishmedicines.org.uk/smc/7159.html</a></td>
</tr>
<tr>
<td>Exenatide (Byetta®)</td>
<td>Eli Lilly &amp; Company Ltd</td>
<td>6th Mar 2011</td>
<td>Type 2 diabetes</td>
<td>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. <strong>SMC restriction:</strong> 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. <a href="http://www.scottishmedicines.org.uk/SMC_Advice/Advice/684_11_exenatide_Byetta/exenatide_Byetta">http://www.scottishmedicines.org.uk/SMC_Advice/Advice/684_11_exenatide_Byetta/exenatide_Byetta</a></td>
</tr>
<tr>
<td>Exenatide 5 or 10 micrograms, solution for injection, prefilled pen (Byetta®)</td>
<td>Eli Lilly &amp; Company Ltd</td>
<td>9 July 2007</td>
<td>Type 2 diabetes</td>
<td>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</td>
</tr>
</tbody>
</table>
Advice from the Scottish Medicines Consortium relevant to SIGN 116 – Management of Diabetes (correct at 26 April 2011)

Thiazolidinediones

<table>
<thead>
<tr>
<th>Pioglitazone 15 mg, 30 mg and 45 mg tablets (Actos®)</th>
<th>Takeda UK Ltd</th>
<th>10 Sep 2007</th>
<th>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.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pioglitazone (Actos®)</td>
<td>Takeda UK Ltd</td>
<td>12 Mar 2007</td>
<td>Type 2 diabetes</td>
</tr>
<tr>
<td>Pioglitazone (Actos®)</td>
<td>Takeda</td>
<td>12 Sep 2005</td>
<td>Type 2 diabetes mellitus</td>
</tr>
</tbody>
</table>

**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 (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®)** is accepted for restricted use within NHS Scotland as monotherapy for 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
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-γ 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

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Manufacturer</th>
<th>Date</th>
<th>Indication</th>
<th>Advisory</th>
</tr>
</thead>
</table>
| Sitagliptin/ Metformin (Janumet® 50/1000) | Merck Sharp and Dohme Ltd | 10 May 2010 | Type 2 diabetes | 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. |  
| 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 | 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. |
Advice from the Scottish Medicines Consortium relevant to SIGN 116 – Management of Diabetes (correct at 26 April 2011)

<table>
<thead>
<tr>
<th>Medicine Type</th>
<th>Manufacturer</th>
<th>Date</th>
<th>Condition</th>
<th>ADVICE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vildagliptin/ Metformin (Eucreas®)</td>
<td>Novartis</td>
<td>07 July 2008</td>
<td>Type 2 diabetes</td>
<td>following an abbreviated submission</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>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.</td>
</tr>
<tr>
<td>Pioglitazone 15 mg/ Metformin 850 mg hydrochloride (Competact®)</td>
<td>Takeda UK Ltd</td>
<td>11 Sep 2006</td>
<td>Type 2 diabetes</td>
<td>following an abbreviated submission</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pioglitazone 15 mg/metformin 850 mg hydrochloride (Competact®) is accepted for restricted use in NHS Scotland 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.</td>
</tr>
</tbody>
</table>
### 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 |
<table>
<thead>
<tr>
<th>Drug</th>
<th>Manufacturer</th>
<th>Date</th>
<th>Population</th>
<th>ADVICE: following an abbreviated submission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin lispro (Humalog® KwikPen)</td>
<td>Lilly UK</td>
<td>13 Oct 2008</td>
<td>For adults and children with diabetes mellitus who require insulin for the maintenance of normal glucose homeostasis</td>
<td><strong>Insulin lispro (Humalog® KwikPen)</strong> 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. <a href="http://www.scottishmedicines.org.uk/smc/6193.html">http://www.scottishmedicines.org.uk/smc/6193.html</a></td>
</tr>
<tr>
<td>Insulin lispro (Humalog® Mix25, Mix50 KwikPen)</td>
<td>Lilly UK</td>
<td>13 Oct 2008</td>
<td>For patients with diabetes mellitus who require insulin for the maintenance of normal glucose homeostasis.</td>
<td><strong>Insulin lispro (Humalog® Mix25 KwikPen) and insulin lispro (Humalog® Mix50 KwikPen)</strong> 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. <a href="http://www.scottishmedicines.org.uk/smc/6194.html">http://www.scottishmedicines.org.uk/smc/6194.html</a></td>
</tr>
<tr>
<td>Insulin glargine (Lantus® Solostar)</td>
<td>Sanofi-Aventis</td>
<td>07 April 2008</td>
<td>For the treatment of adults, adolescents and children of 6 years and above with diabetes mellitus, where treatment with insulin is required.</td>
<td><strong>Insulin glargine 100 units/ml solution for injection in a pre-filled pen (Lantus® SoloStar)</strong> 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. <a href="http://www.scottishmedicines.org.uk/smc/5690.html">http://www.scottishmedicines.org.uk/smc/5690.html</a></td>
</tr>
<tr>
<td>Insulin glargine (Lantus®)</td>
<td>Aventis</td>
<td>04 Oct 2002</td>
<td>Diabetes mellitus</td>
<td><strong>Insulin glargine</strong> is an acceptable treatment for patients with diabetes mellitus. Pending</td>
</tr>
</tbody>
</table>
Advice from the Scottish Medicines Consortium relevant to SIGN 116 – Management of Diabetes (correct at 26 April 2011)

| 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®)** 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/1838.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 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/5273.html

http://www.scottishmedicines.org.uk/smc/2185.html
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

| Medicine                                      | Manufacturer                       | Date          | Condition                          | ADVICE: following a resubmission.  
|-----------------------------------------------|------------------------------------|---------------|------------------------------------|---------------------------------  
| Biphasic insulin aspart 30 (NovoMix 30®)      | NovoNordisk                        | 06 June 2003  | Diabetes mellitus                  | 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 medoxomil/amlopidine besilate      | Daiichi Sankyo UK Ltd              | 12 Oct 2009   | treatment of essential hypertension| **ADVICE:** following an *abbreviated* submission  
*Olmesartan medoxomil/amlopidine 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 amlopidine 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
| Drug | Manufacturer | Approval Date | Indication | Advice
|------|--------------|--------------|-----------|---------
| Ezetimibe/ Simvastatin (Inegy®) | Merck Sharp & Dohme/Scher ing Plough Ltd | 13 June 2005 | Hypercholester olaemia and Homozygous Familial Hypercholester olaemia | **ADVICE:** following an **abbreviated** submission. Ezetimibe/simvastatin (Inegy®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](http://www.scottishmedicines.org.uk/smc/2186.html)
| Ezetimibe (Ezetrol®) | Merck Sharp & Dohme Ltd/Schering Plough Ltd | 08 Sep 2003 | Primary hypercholester olaemia | **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](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](http://www.scottishmedicines.org.uk/smc/5263.html)
| Clopidogrel (Plavix®) | Sanofi-Synthelabo and Bristol- Myers-Squibb | 08 Mar 2004 | Prevention of atherothrombot ic 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...
Advice from the Scottish Medicines Consortium relevant to SIGN 116 – Management of Diabetes *(correct at 26 April 2011)*

<table>
<thead>
<tr>
<th>Medication</th>
<th>Manufacturer</th>
<th>Date</th>
<th>Condition</th>
<th>ADVICE:</th>
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<tr>
<td>Nebivolol tablets 5mg</td>
<td>A Menarini Pharmaceuticals UK</td>
<td>13 Aug 2007</td>
<td>Chronic heart failure</td>
<td>following a re-submission <strong>Nebivolol</strong> <em>(Nebilet®)</em> 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. <a href="http://www.scottishmedicines.org.uk/smc/1997.html">http://www.scottishmedicines.org.uk/smc/1997.html</a></td>
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<tr>
<td>Nebivolol tablets 5mg</td>
<td>Menarini Pharmaceuticals UK SRL</td>
<td>11 Sep 2006</td>
<td>Stable mild and moderate chronic heart failure</td>
<td>following a full submission <strong>Nebivolol</strong> <em>(Nebilet®)</em> 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 ≥70 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. <a href="http://www.scottishmedicines.org.uk/smc/5259.html">http://www.scottishmedicines.org.uk/smc/5259.html</a></td>
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| Perindopril (Coversyl arginine) 2.5 mg 5 mg 10 mg tablets | Servier Laboratories | 09 June 2008 | Treatment of hypertension | 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](http://www.scottishmedicines.org.uk/smc/5830.html)

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<th>Advice</th>
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| 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-butyamine 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 Plus®) 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](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](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.

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<tr>
<td>Telmisartan/hydrochlorothiazide (MicardisPlus®)</td>
<td>Boehringer Ingleheim</td>
<td>09 May 2003</td>
<td>Essential hypertension</td>
<td><strong>ADVICE:</strong> 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. <a href="http://www.scottishmedicines.org.uk/smc/1813.html">http://www.scottishmedicines.org.uk/smc/1813.html</a></td>
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**Medicines for neuropathic pain**

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<th>Date of Approval</th>
<th>Indication</th>
<th>Advice</th>
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</thead>
</table>
| 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](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](http://www.scottishmedicines.org.uk/smc/4989.html) |