Lincolnshire NHS

Prescribing and Clinical Effectiveness Bulletin

Volume 2; Number 1 **January 2008**

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This bulletin has been created specifically to convey details of decisions taken at the Prescribing and Clinical Effectiveness Forum (PACEF) to all stakeholders across the Lincolnshire Healthcare Community in both primary and secondary care. Steps will be taken to ensure the widest possible distribution across Lincolnshire PCT and within United Lincolnshire Hospitals Trust and Lincolnshire Partnership Trust. Both paper and electronic copies will be circulated initially with a view to evolving into complete electronic distribution as soon as we are confident that all key stakeholders can access E-mail. There are also plans to make all bulletins, guidelines, formularies, new product assessments, care pathways and other PACEF publications available through the LPCT website.

SUMMARY OF PACEF DECISIONS: JANUARY UPDATE

Drug	Indication	Traffic Light Status
Co-proxamol 32.5mg/325mg tablets	**Unlicensed analgesic**	**RED-RED Unlicensed prescribing must be reserved for the small number of patients unresponsive or intolerant to alternatives**
Ezetimibe (Ezetrol)	**Lipid regulating agent licensed for primary hypercholesterolaemia, homozygous familial hypercholesterolaemia and homozygous sitosterolaemia**	**GREEN Subject to restrictions detailed below. N.B. The simvastatin/ezetimibe combination tablet (Inegy) is prohibitively expensive and is designated RED-RED**
Grazax tablets	**Grass pollen induced rhinitis and conjunctivitis diagnosed with a positive**	**RED-RED (Exceptional cases may be approved through the**

	skin prick test and/or specific IgE test	**Exceptional Cases Committee)**
Insulin glargine (Lantus)	**Diabetes mellitus**	**GREEN (Both the OptiSet and SoloStar pens are approved for use)**
Insulin glulisine (Apidra)	**Diabetes mellitus**	**GREEN (Both the OptiSet and SoloStar pens are approved for use)**
Lenalidomide (Revlimid)	**For use in combination with dexamethasone for the treatment of multiple myeloma in patients who have received at least one prior therapy.**	**RED-RED**
Omalizumab (Xolair)	**Severe persistent allergic asthma**	**RED Subject to NICE restrictions**
Rivastigmine Transdermal Patch (Exelon)	**Symptomatic treatment of mild to moderately severe Alzheimer's dementia**	**AMBER (N.B. NICE restrictions preclude the use of rivastigmine in the treatment of mild AD) Shared care requirements apply.**

RED-RED: This signifies that a product is **not recommended** for prescribing in **both** primary and secondary care. All new products are classified as RED-RED pending assessment by PACEF.
RED: This signifies that a product has been approved for use within ULHT and/or LPT **only** and has **no role in primary care**.
AMBER: This signifies that a drug has been approved for use in primary care **subject to specialist initiation; a shared care guideline (SCG) may also be required**. The main purpose of the SCG will be to clearly define both specialist and GP responsibilities. Not all AMBER drugs that require SCGs are currently covered by formal documents; in the coming months PACEF will be working to rectify this.
GREEN: This signifies a product that is **approved for initiation in either primary or secondary care**. Specialist initiation and shared care guidelines are not considered necessary.

NEW DRUG ASSESSMENTS

LENALIDOMIDE CAPSULES (REVLIMID)

Lenalidomide (Revlimid) is a structural analogue of thalidomide licensed for use in combination with dexamethasone for the treatment of multiple myeloma in patients who have received at least one prior therapy. The molecule has been developed in an attempt to optimise the established anti-cancer activity of thalidomide, while at the same time minimising toxicity. The two placebo controlled double blind trials, used to support the license application, demonstrated the efficacy of lenalidomide in extending the time to progression of multiple myeloma compared to placebo. In theory, the efficacy of the lenalidomide/ dexamethasone regime should significantly prolong remissions and improve overall survival, however there is currently no data to quantify the impact of lenalidomide on quality of life and early assessments of cost-effectiveness suggest a particularly high Cost per QALY. Equally there are no studies that directly compare lenalidomide with established treatments such as thalidomide or the recently NICE approved bortezomib; it is therefore difficult to

define its role in the current treatment of multiple myeloma. The average annual cost is approx £35,322 per patient, approximately £3,500 more per annum than bortezomib (Velcade).

PACEF Recommendation:
PACEF were concerned about the paucity of relevant comparative data and the potentially poor cost-effectiveness of lenalidomide. Further guidance is awaited from the Trent Cancer Network. NICE have also announced that lenalidomide will be reviewed as part of their 15th wave of appraisals. Pending further guidance, both local and national, lenalidomide is designated RED-RED.

RIVASTIGMINE TRANSDERMAL PATCH (EXELON)

The rivastigmine transdermal patch is a new formulation of an established acetylcholinesterase inhibitor licensed for the symptomatic treatment of mild to moderately severe Alzheimer's dementia (AD). The IDEAL study demonstrates equivalent efficacy between the maximum licensed oral dose of rivastigmine (12mg per day) and the maximum licensed transdermal dose (10cm^2 patch). Comparative safety data from the same study reveals the improved tolerability of the patch, particularly a reduced incidence of nausea (7% of patients on the patch compared to 23% on capsules) and vomiting (6% compared to 17%). The cost of treatment with rivastigmine patches is comparable to oral capsules and cheaper than treatment with oral solution.

PACEF Recommendation:

PACEF acknowledge that rivastigmine transdermal patches offer an alternative for patients who would benefit from an acetylcholinesterase inhibitor, but who are unable to tolerate side effects linked to peak plasma levels of oral therapies (such as nausea and vomiting). The formulation is designated AMBER subject to the prescribing restrictions on the prescribing of treatments for AD published by NICE in TA111 (2007) (see *PACE Bulletin* Vol 1 No 6 (November 2007)). The use of the patch should be restricted to those for whom rivastigmine is considered an appropriate therapy and the patch an appropriate formulation.

GRAZAX TABLETS

Grazax is the first oral vaccine licensed for the treatment of grass pollen induced rhinitis and conjunctivitis in adult patients with clinically relevant symptoms who have been diagnosed with a positive skin prick test and/or a specific Immunoglobulin E (IgE) test to grass pollen. It is formulated as a once daily fast melting sublingual tablet containing standardised allergen extract of Timothy grass pollen.

The GT-08 study, the most significant of the clinical trials, involved 634 pts aged between 18 and 65 with at least a two year history of significant grass pollen induced allergic rhinoconjunctivitis, a positive prick test to IgE and a FEV_1 higher than 70% of predicted value. Patients were randomised to either Grazax or placebo and self-scored their response in terms of symptom scores and use of rescue medication (such as desloratadine, budesonide nasal spray or oral prednisolone). The results showed a statistically significant improvement in symptom scores and reduced use of rescue medication, although the rating scales used were based on the individual patient's evaluation of the severity of their symptoms and could be open to bias. The clinical significance of these findings remains uncertain. Other studies such as GT-02

and GT-07 have delivered less impressive results; an extension study to GT-08 is underway designed to determine the benefits of more prolonged Grazax treatment up to three years with a further two years follow-up.

For optimum results, Grazax should be taken daily for 16 weeks prior to the grass pollen season (in the UK normally late May to August) and continuously thereafter for a total of three years; some efficacy may be obtained if taken 2 to 3 months before the season starts. There is a high incidence of local oral reactions following administration, although, in general, the product appears to be well tolerated. There have been no reports of anaphylaxis, although angioedema and bronchospasm may occur in less than 1% of patients.

A cost comparison reveals the high cost of Grazax in comparison to other treatments:

Drug	**Daily dose range**	**Cost (£)pa**
Grazax tabs	**Once daily**	**£877.50**
Loratadine tabs	10mg daily	£12.86
Cetirizine tabs	10mg daily	£5.58
Beclometasone nasal spray	1 spray each nostril twice daily	£34.56
Sodium cromoglicate 2% eye drops	1 drop each eye four times a day	£25.61
Triamcinolone 40mg/ml	Single dose	£1.96
Pollinex	Course s/c injections	£320

Pollinex subcutaneous therapy provides a possible alternative to Grazax, although there is an associated need for frequent clinic visits (normally for 8 to 16 weeks) and a greater risk of anaphylactic reactions during treatment. In addition, Grazax contains allergens to only one type of grass and therefore will not be suitable for other grass and tree pollen allergies, whereas Pollinex contains grass and rye pollens; there is also a separate Pollinex formulation containing tree pollen allergens.

PACEF Recommendation:
PACEF remain unconvinced of the clinical and cost-effectiveness of Grazax in comparison to lower cost alternatives such as subcutaneous therapy. As a result of this, Grazax remains RED-RED. It is recognized that there may be a limited role for the agent in adults (aged 18 to 65) who have not responded to optimal doses of conventional treatment for seasonal rhinitis and conjunctivitis and who are deemed unsuitable for subcutaneous therapy. Such patients must have a positive skin prick test or IgE test for grass pollen, specifically Timothy grass. In these circumstances, a specialist wishing to initiate therapy will need to first gain approval from the Exceptional Cases Committee (ESC). If the ESC approve Grazax for use in a specific patient this will be subject to specialist initiation and appropriate shared care arrangements.

NEW DELIVERY SYSTEM ASSESSMENT

LANTUS SOLOSTAR AND APIDRA SOLOSTAR INSULIN PENS

Sanofi-Aventis have recently introduced a new design of pre-filled pen for insulin glargine (Lantus) and insulin glulisine (Apidra) known as the SoloStar.
These pens offer the following advantages over the existing OptiSet pen:

- They allow for the dose to be set in steps of 1 unit compared to that of 2 units with the OptiSet pen.
- They allow for a maximum dose of 80 units compared to that of 40 units for the OptiSet pen.
- The two pens are produced in different colours which make it easier for patients to identify the correct device. OptiSet pens for the two types of insulin are very similar in appearance resulting in a greater risk of inadvertent administration of the wrong dose or type of insulin.

The comparative costs of SoloStar and OptiSet pens are as follows:

Insulin Glargine

Product	Detail	Cost
Lantus SoloStar®	Pre filled pen	£42.00 5 x 3ml
Lantus OptiSet®	Pre-filled pen	£39.00 5x3ml

Insulin Glulisine

Product	Detail	Cost
Apidra SoloStar®	Pre-filled pen	£25.00 5 x 3ml
Apidra OptiSet®	Pre-filled pen	£29.54 5x3ml

PACEF Recommendation:
Both insulin glargine (Lantus) and insulin glulisine (Apidra) are designated GREEN. The AMBER status of all insulin analogues is to be reconsidered and amended to GREEN. Both the OptiSet and the SoloStar pens are approved for use.

PRODUCT WITHDRAWALS

CO-PROXAMOL UPDATE

At the end of 2007 all of the licenses for currently available co-proxamol products were cancelled. Only Meda Pharmaceuticals Ltd retain a marketing authorisation and will continue to market the product for unlicensed supply in 2008. **In the January 2008 *Drug Tariff*, the price of co-proxamol tablets was announced as £20.36 for 100; this compares to a pre-Christmas price of £2.79 for 100 and represents a seven-fold price increase.** Prescribers are reminded that this product must be reserved for the small number of patients unresponsive or intolerant to alternatives; any remaining prescribing of co-proxamol will be unlicensed and remain the responsibility of the prescriber.

PACEF Recommendation:
Any remaining co-proxamol patients should be reviewed as a matter of urgency and moved to alternative treatments wherever possible.

NICE UPDATE

NICE TECHNOLOGY APPRAISAL 131: INHALED CORTICOSTEROIDS FOR THE TREATMENT OF CHRONIC ASTHMA IN CHILDREN UNDER THE AGE OF 12 YEARS (NOVEMBER 2007)

The key recommendations are as follows:

- For children aged between 5 and 15 years, inhaled corticosteroids (ICSs) should be delivered using a **pressurised metered dose inhaler (pMDI) with an appropriate spacer device**. Other devices are advocated as second line alternatives. The same advice applies to children under 5 except that a face mask should also be used if necessary.
- For children under the age of 12 years with chronic asthma in whom treatment with an inhaled corticosteroid (ICS) is considered appropriate, the **least costly product** that is suitable for an individual child (within its marketing authorisation) is recommended.
- For children under the age of 12 years with chronic asthma in whom treatment with an ICS and long-acting beta-2 agonist (LABA) is considered appropriate, the **least costly product** that is suitable for an individual child (within its marketing authorisation) is recommended.

PACEF Recommendations:

Beclometasone dipropionate (BDP) is currently the recommended first choice ICS for children. This recommendation is based on the wide range of licensed inhaler devices available, known safety at recommended doses, no lower age limit for the generic pMDI and cost. A BDP pMDI plus a spacer device is the recommended first line device. There are four BDP pMDIs currently available including generics; they are similar in price (generic BDP, Filair, Beclazone and Clenil Modulite pMDIs). The recent withdrawal of Becotide pMDIs from the market has triggered price rises for generic BDP pMDIs that may be set to continue into 2008. This makes it difficult to specify a least costly device at this point in time. Only the lower 50 microgram and 100microgram strengths are licensed for use in children. Where a breath operated MDI is indicated, both Aerobec and Beclazone Easi-Breathe are appropriate alternatives; both are reasonably priced in comparison to BDP pMDIs. Dry powder devices such as Asmabec Clickhaler, Becodisks, Cyclocaps and Pulvinal are all more expensive than pMDIs and should not be routinely used first line. Qvar inhaler, Qvar Autohaler, Qvar Easi-Breathe and Easyhaler beclometasone are not licensed for use in children.

Of the alternative ICSs indicated for children, budesonide and fluticasone offer no convincing evidence of superiority to BDP in terms of either safety or efficacy. Clinically, the three drugs are interchangeable; budesonide is dose equivalent with BDP, fluticasone is equivalent to half the daily dose of BDP. Where budesonide is indicated, the pMDI plus spacer is recommended first line. This is likely to be more expensive than a BDP pMDI plus spacer. Where a budesonide DPI is indicated, the Easyhaler represents the least costly device. Where fluticasone is indicated, the pMDI (Flixotide Evohaler) plus spacer is recommended first line. This is likely to be more expensive than a BDP pMDI plus spacer. Where a fluticasone DPI is indicated, the Flixotide Accuhaler represents the least costly device.

Where a combination ICS/LABA device is indicated, a pMDI plus spacer is recommended first line; the Seretide pMDI is the only combination device currently available as a pMDI.

NICE TECHNOLOGY APPRAISAL 132: EZETIMIBE FOR THE TREATMENT OF PRIMARY (HETEROZYGOUS FAMILIAL AND NON-FAMILIAL) HYPERCHOLESTROLAEMIA (NOVEMBER 2007)

Ezetimibe (Ezetrol) is a cholesterol absorption inhibitor that blocks the intestinal absorption of dietary and biliary cholesterol and related plant sterols. Because of this different mode of action, it has a complementary effect when combined with statin therapy. Whereas doubling the dose of statin or switching to an alternative statin generally leads to further reduction in baseline LDL-C of approximately 6 to 8%, the addition of ezetimibe to statin therapy is likely to lead to greater incremental reductions in LDL-C concentrations. A meta-analysis performed by the NICE Assessment Group showed ezetimibe plus statin therapy reduces LDL-C by an additional 13.9% compared with statin therapy alone. At present, ezetimibe (Ezetrol) is only licensed for the treatment of primary (heterozygous-familial or non-familial) hypercholesterolaemia and NICE have only evaluated the drug within this context. Nonetheless, PACEF recognize that in many practices ezetimibe is increasingly prescribed both as monotherapy and in combination with statins in the primary and secondary prevention of coronary heart disease (CHD). With this in mind, we make some recommendations below relating to the use of ezetimibe within this context.

The key recommendations from TA 132 are as follows:

- Ezetimibe monotherapy is recommended as an option for the treatment of adults with primary (heterozygous-familial or non-familial) hypercholesterolaemia who would otherwise be initiated on statin therapy (as per NICE guidance TA 94 in adults with non-familial hypercholesterolaemia) but who are unable to do so because of **contra-indications** to initial statin therapy or **intolerance** to statin therapy.
- Ezetimibe, co-administered with initial statin therapy, is recommended as an option for the treatment of adults with primary (heterozygous-familial or non-familial) hypercholesterolaemia who have been initiated on statin therapy (as per NICE guidance TA 94 in adults with non-familial hypercholesterolaemia) when: (1) **serum total cholesterol (TC) or low-density lipoprotein cholesterol (LDL-C) concentration is not appropriately controlled** either after appropriate dose titration of initial statin therapy or because dose titration is limited by intolerance to initial statin therapy or (2) **consideration is being given to changing from initial statin therapy to an alternative statin.**
- Intolerance to initial statin therapy should be defined as the presence of clinically significant adverse effects from statin therapy that are considered to represent an unacceptable risk to the patient or may compromise compliance. **Adverse effects include: new onset muscle pain (often associated with levels of muscle enzymes in the blood indicative of muscle damage), significant GI disturbance or alterations of liver function tests (LFTs).**

PACEF Recommendations: Ezetimibe in the primary prevention of cardiovascular disease (CVD)

NICE TA 94 recommends statin therapy first line as part of the management strategy for the primary prevention of CVD in adults who have a 20% or greater 10-year risk of developing CVD. The statin of lowest acquisition cost is recommended first line (i.e. simvastatin). The draft NICE Lipid Modification Clinical Guideline did not recommend targets for TC or LDL-C for people treated with a statin for primary prevention. There are no clinical trials in primary prevention that have evaluated the relative and absolute benefits of cholesterol lowering to different TC and LDL-C targets. When using ezetimibe within the context of primary prevention, the drug should be restricted predominantly to those with intolerance to statins or a clear contra-indication. Where simvastatin 40mg is not tolerated, simvastatin 20mg or pravastatin 40mg is recommended as an alternative; where low cost generic statins are not tolerated branded agents should be considered. If intolerance to statins remains a problem, ezetimibe 10mg monotherapy seems a reasonable option. Only patients with exceptionally high lipid levels could justifiably receive combination simvastatin/ ezetimibe therapy within the primary prevention context. In most primary prevention patients, target chasing is unnecessary; similarly, the addition of ezetimibe to statin therapy to augment performance against targets is also unnecessary.

Statins are contra-indicated in active liver disease (or persistently abnormal LFTs), pregnancy and during breast feeding (ezetimibe is contra-indicated in breast feeding). Rosuvastatin is contra-indicated in renal impairment. There are a range of other situations where statins should be used with caution. These include: patients with a history of liver disease or with a high alcohol intake, hypothyroidism, abnormal LFTs, patients with risk factors for myopathy or rhabdomyolysis, porphyria. Where statins are contra-indicated, ezetimibe 10mg monotherapy should be considered first line.

PACEF Recommendations: Ezetimibe in the secondary prevention of CVD

Prescribers are reminded that current Department of Health recommended targets for secondary prevention are 5mmol/L (TC) and 3mmol/L (LDL-C). Within this context, ezetimibe combination therapy with a statin is recommended where: (1) serum TC or LDL-C concentration is not appropriately controlled either after appropriate dose titration of initial statin therapy or because dose titration is limited by intolerance to initial statin therapy or (2) consideration is being given to changing from initial statin therapy to an alternative statin.

The following table illustrates the comparative lipid lowering potential and the cost of ezetimibe in comparison to statins:

Percentage Reductions in LDL Cholesterol and Total Cholesterol

Statin	Daily Dose	28 day cost	Percentage reduction in LDL-C	Percentage reduction in total cholesterol
Atorvastatin	10mg	£18.03	37%	32%
Atorvastatin	20mg	£24.64	43%	36%
Atorvastatin	40mg	£28.21	49%	42%
Atorvastatin	80mg	£28.21	55%	47%
Pravastatin	10mg	£3.15	19-20%	14.7%
Pravastatin	20mg	£4.82	24%	17.2%
Pravastatin	40mg	£7.12	29%	29%
Rosuvastatin	5mg	£18.03	38%	33%
Rosuvastatin	10mg	£18.03	43%	37%
Rosuvastatin	20mg	£29.69	48%	40%
Simvastatin	10mg	£0.36	27-28%	20.3%
Simvastatin	20mg	£0.55	32-35%	25.7%
Simvastatin	**40mg**	**£1.39**	**37%**	**31%**
Simvastatin	80mg (or 2 x 40mg)	£4.91 (£2.62)	42%	35%
Ezetimibe	**10mg**	**£26.21**	**17-19%**	**12-13%**
Ezetimibe 10mg/simvastatin 20mg tablets (Inegy)	10mg/20mg	£33.42	51.5%	36.6%
Ezetimibe 10mg/simvastatin 40mg tablets (Inegy)	10mg/40mg	£38.98	54.8%	39.2%
Ezetimibe 10mg/simvastatin 80mg tablets (Inegy)	10mg/80mg	£41.21	61%	44%

From this we can draw a number of conclusions:
(1) Ezetimibe monotherapy is not as effective in terms of TC and LDL-C lowering as a low dose of simvastatin. If a patient cannot tolerate simvastatin 40mg, it is worth trying a lower dose of simvastatin, pravastatin or even a high cost branded agent before moving to ezetimibe.
(2) Where ezetimibe is prescribed in combination with a statin, simvastatin 40mg should be sufficient in most cases. Where components are prescribed separately, this combination is lower in cost than high dose atorvastatin (80mg) or rosuvastatin (20mg), comparable in potency and potentially better tolerated. Co-prescribing of high-cost high-potency statins with ezetimibe is prohibitively expensive and should be reserved for exceptional circumstances. Where exceptionally high TC or LDL-C reductions are required, a combination of ezetimibe and simvastatin 80mg should be considered.
(3) A fixed dose combination tablet containing ezetimibe and simvastatin is available (Inegy), but is significantly more expensive than separate components and should not be prescribed. Simvastatin/ezetimibe (Inegy) is

designated RED-RED. Ezetimibe prescribed as a separate component is designated GREEN (subject to the constraints detailed above).

NICE TECHNOLOGY APPRAISAL 133: OMALIZUMAB FOR SEVERE PERSISTENT ALLERGIC ASTHMA (NOVEMBER 2007)

Omalizumab is a monoclonal antibody that inhibits the binding of IgE to high-affinity receptors on the surface of mast cells and basophils. It prevents the release of pro-inflammatory mediators and reduces allergen-induced airway reactions. It is licensed for use as additional therapy in adult and adolescent patients (12 years and older) with severe persistent allergic asthma who have a positive skin test or in vitro reactivity to a perennial aeroallergen and who have reduced lung function (forced expiratory volume in 1 second, FEV1 < 80%) as well as frequent daytime symptoms or night-time awakenings and who have had multiple documented severe asthma exacerbations despite daily high-dose inhaled corticosteroids (ICS) plus a long-acting beta-2 agonist (LABA). The licensed indication also states that omalizumab should only be considered for patients with convincing IgE mediated asthma. Omalizumab is administered subcutaneously every 2 to 4 weeks. The dosage is determined by baseline IgE before the start of treatment and body weight.

The key recommendations in TA133 are as follows:

- **Omalizumab** is recommended, within its licensed indication, as an option for the **treatment of severe persistent allergic (Immunoglobulin E (IgE) mediated) asthma** as add-on therapy to optimised standard therapy, only in adults and adolescents (12 years and older) who have been identified as having severe unstable disease.
- Omalizumab add-on therapy should only be initiated if the patient fulfils the following criteria of severe unstable allergic asthma: (1) Confirmation of IgE mediated allergy to a perennial allergen by clinical history and allergy skin testing and (2) Either two or more severe exacerbations of asthma requiring hospital admission within the previous year, or three or more severe exacerbations of asthma within the previous year, at least one of which required admission to hospital, and a further two of which required treatment or monitoring in excess of the patient's usual regimen in an accident and emergency unit.
- Omalizumab add-on therapy should be **initiated** and **monitored** by a **physician experienced in both allergy and respiratory medicine in a specialist centre.**
- **Omalizumab add-on therapy should be discontinued at 16 weeks in patients who have not shown an adequate response to therapy.**

PACEF Recommendation:
Omalizumab is now designated RED subject to the restrictions detailed by NICE.

MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY (MHRA) : SAFETY UPDATES

Fibrates

Revised prescribing advice was issued by the MHRA in November 2007 following a review of long term efficacy and safety. The following key points have been highlighted:

- Fibrates should be considered as first-line therapy only in patients with isolated severe hypertriglyceridaemia.
- For patients with mixed hyperlipidaemia, fibrates may be used only when a statin or other effective treatments are contraindicated or not tolerated.
- In patients with primary hypercholesterolaemia, the use of gemfibrozil may be considered, but only when a statin or other effective treatments are contraindicated or not tolerated.
- Combination therapy with a statin or fibrate should be used with caution and only when benefits are expected to outweigh potential risks. The concomitant use of gemfibrozil with a statin should be avoided.

PACEF Recommendation
All patients currently prescribed gemfibrozil should be reviewed and if concurrent therapy with statins is identified, alternative treatment should be considered.

Rosiglitazone & Pioglitazone

The MHRA have issued revised advice on cardiovascular risk associated with rosiglitazone and pioglitazone:

- Rosiglitazone & pioglitazone should not be used in people with heart failure or a history of heart failure.
- The Incidence of heart failure is increased when either rosiglitazone or pioglitazone is combined with insulin
- People who are at particular risk of heart failure should start rosiglitazone or pioglitazone at the lowest available dose; any dose increases should be done gradually.
- Patients should be monitored closely during treatment for signs and symptoms of fluid retention, including weight gain or oedema.
- Treatment should be stopped if any deterioration in cardiac status occurs.
- Rosiglitazone might be associated with small increased risk of cardiac ischaemia and therefore should only be used in patients with current or previous cardiac ischaemia only after careful evaluation of risk.
- Clinical trials have recorded an increased risk of cardiac ischaemia for rosiglitazone combined with insulin. Therefore this combination should only be used in exceptional circumstances and under close supervision.

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