Greater East Midlands Commissioning Support Unit in association with
Lincolnshire Clinical Commissioning Groups, Lincolnshire Community Health Services,
United Lincolnshire Hospitals Trust and Lincolnshire Partnership Foundation Trust

Lincolnshire Prescribing and Clinical Effectiveness Bulletin

Volume 8; Number 13 **July 2014**

What's new this month?

- **Brimonidine tartrate 3mg/g gel (*Mirvaso*) is the first treatment to be licensed specifically for facial erythema in rosacea. Due to the temporary cosmetic nature of the treatment and the exceptionally high cost the product is designated RED-RED (see page 2).**
- **Sodium chloride 5% preservative free eye drops (*PF drops*) are designated AMBER without shared care and approved for inclusion in the *Lincolnshire Joint Formulary* for the temporary relief of corneal oedema. Sodium chloride 5% single use eye drops (*NaCl 5%*) are not approved for the same indication as they are higher cost; designation RED-RED (see page 5).**
- **Melatonin prolonged release tablets 2mg (*Circadin*) are approved for initiation by clinicians within LPFT and re-designated AMBER without shared care for the short-term (13 weeks) treatment of primary insomnia in patients aged 55 and over (see page 6).**
- **People who have been prescribed an adrenaline auto-injector (*Emerade*, *Epipen* or *Jext*) because of the risk of anaphylaxis should carry two with them at all times for emergency, on-the-spot use. After every use of an adrenaline auto-injector, an ambulance should be called (even if symptoms are improving), the individual should lie down with their legs raised and, if at all possible, should not be left alone. Prescribers should ensure that adrenaline auto-injectors are usually prescribed in quantities of two. Patients should ensure that pairs of auto-injectors are kept together rather than spread over two separate locations such as home and school. Where a school supply is necessary, two auto-injectors should be supplied, not one (see page 9).**
- **After a review of benefits and risks, the MHRA have concluded that the benefits of using any statin within licensed indications outweigh the risks in most patients. PACEF is in the process of reviewing the updated NICE Clinical Guideline on Lipid Modification and will be publishing updated local guidance in the Autumn. Until then, local prescribing guidance remains unchanged (see page 10).**

CONTENTS

SUMMARY OF PACEF DECISIONS: *JUNE 2014 UPDATE*

Drug	Indication(s)	Traffic Light and Joint Formulary Status
Brimonidine tartrate 3mg/g gel *(Mirvaso)* (Galderma)	Symptomatic treatment of facial erythema due to rosacea	RED-RED

Melatonin prolonged- release 2mg tablets *(Circadin)*	For the short-term treatment (13 weeks) of primary insomnia in patients aged 55 and over.	AMBER without shared care. Approved for inclusion in the *Lincolnshire Joint Formulary*
Melatonin prolonged-release 2mg tablets (Circadin) Melatonin 3mg tablets (*Bio-Melatonin*) Melatonin preparations (manufactured by Penn Pharmaceuticals)	Unlicensed use in children and adolescents with severe sleep problems linked to neurological or neuro-developmental disorders	AMBER subject to shared care guideline. Included in the *Lincolnshire Joint Formulary* for this indication.
All alternative imported melatonin preparations	Any indication	RED-RED except where all other options are unsuitable.
All melatonin preparations	Jet lag or sleep disturbance linked to shift working	RED-RED
Sodium chloride 5% single use eye drops (*NaCl 5%*) (Essential Pharmaceuticals)	For the temporary relief of corneal oedema.	RED-RED Not approved for inclusion in the *Lincolnshire Joint Formulary*
Sodium chloride 5% preservative free eye drops (*PF drops*) (Moorfields Pharmaceuticals)	For the temporary relief of corneal oedema.	AMBER without shared care. Approved for inclusion in the *Lincolnshire Joint Formulary*
Sodium chloride 5% single use eye Drops (unlicensed special)	Unlicensed	RED-RED
Voriconazole 50mg tablets and oral suspension 40mg/ml (*Vfend*)	For the treatment of invasive aspergillosis, candidaemia in non-neutropenic patients, fluconazole resistant serious invasive *Candida* infections caused by *Scedosporium* spp and *Fusarium* spp in patients with progressive possibly life-threatening infections.	RED Included in the *Lincolnshire Joint Formulary* for secondary and tertiary care use only

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. Back issues of the *PACE Bulletin* and other PACEF publications are available through the NHS in Lincolnshire website (www.lincolnshire.nhs.uk); follow the commissioning link to PACEF. Electronic copies of both the *PACE Bulletin* and our sister publication *PACE Shorts* (a short summary of the *PACE Bulletin*) are circulated to a wide readership via email. If you are not currently on our distribution list and wish to receive regular copies of PACEF publications please contact Sandra France on sandra.france@gemcsu.nhs.uk.

Google searching can be a quick and effective way of finding back numbers of the *PACE Bulletin* relevant to a specific topic of interest. Searchers are advised to use the official version of the *Bulletin* available from the NHS in Lincolnshire website rather than depend on a potentially unreliable draft or variant found through Google or an alternative search engine.

The *Lincolnshire Joint Formulary* is available on line and is fully searchable; it can be accessed at www.lincolnshirejointformulary.nhs.uk

NEW DRUG ASSESSMENTS

NEW DRUG ASSESSMENT: *BRIMONIDINE TARTRATE 3MG/G GEL (MIRVASO) FOR FACIAL ERYTHEMA OF ROSACEA*

Brimonidine tartrate 3mg/g gel (*Mirvaso*) is the first treatment to be licensed specifically for the treatment of facial erythema in rosacea. Due to the temporary cosmetic nature of the treatment and the exceptionally high cost the product is designated RED-RED.

Rosacea is a chronic relapsing disease of facial skin, characterised by recurrent episodes of facial flushing, persistent erythema, telangiectasia (fine, dilated blood

vessels), papules and pustules. For the symptoms of flushing and erythema (without papules and pustules) there is historically no effective treatment in primary care and management consists of lifestyle advice, including applying sunscreen and avoiding trigger factors.

Brimonidine tartrate 3mg/g gel (*Mirvaso*) holds a marketing authorisation for the symptomatic treatment of facial erythema due to rosacea in adults (i.e. those over 18); it is the first treatment to be authorised specifically for this indication. Alternative treatments (including short courses of oral tetracyclines, low dose erythromycin, topical formulations of metronidazole (*Metrogel*, *Metrosa*, *Rosiced*, *Rozex, Zyomet*) and azelaic acid 15% gel (*Finacea*)) tend to be authorised either for rosacea or for the topical treatment of papulopustular rosacea.

Supporting evidence for the use of brimonidine tartrate 3mg/g gel (*Mirvaso*) comes from two short-term (28 day) randomised placebo controlled trials. Both trials demonstrate that *Mirvaso* is more effective than vehicle gel alone at reducing erythema in people with a clinical diagnosis of rosacea and moderate to severe erythema. However, success rates (defined as a 2 grade reduction in the severity of erythema as defined by patients and clinicians) were only 25-30% with brimonidine gel compared to 10% with placebo. Some response (defined as 1 grade reduction in severity of erythema) was seen in 70% of the brimonidine gel group compared to a particularly strong placebo response of 30 to 40%. There are no published trials comparing *Mirvaso* with any pharmacologically active alternative. There is no long-term efficacy or safety data, although the manufacturer is promoting the product for on-going symptomatic treatment over a potentially long period. Brimonidine gel was found to act rapidly in trials (i.e. within 30minutes in 28% of patients with the effect partially maintained over a 12 hour period). The gel can be applied as required up to a maximum frequency of once daily.

Current treatment options for rosacea, such as oral tetracyclines, are primarily used for the reduction of inflammatory lesions, although some reduction in erythema may occur. Although effective when used short term, tetracyclines and other broad spectrum antibiotics carry with them the risk of increasing bacterial resistance, particularly if over used.

Adverse effects commonly associated with *Mirvaso* treatment include: erythema, pruritus and a burning sensation in the skin. Results from a longer term safety and efficacy study suggest that adverse effects do not worsen with longer treatment. As brimonidine is a highly selective alpha-adrenergic receptor agonist there is a potential for interaction with drugs affecting noradrenergic transmission (e.g. monoamine oxidase inhibitors, tricyclic antidepressants) and also in patients susceptible to the effects of alpha-adrenergic receptor agonists, such as those with cardiovascular disease, depression, cerebral or coronary insufficiency, Raynaud's phenomenon or orthostatic hypotension.

A cost comparison reveals that brimonidine 3mg/g gel (*Mirvaso*) is significantly higher in cost than any other alternative:

Drug	Authorised indication	Daily dose range	Cost (£) 28 days
Brimonidine 3mg/g gel (*Mirvaso*)	**Symptomatic treatment of facial erythema due to rosacea**	**Apply once daily**	**£33.69 (30g)**
Oral antibiotics			
Oxytetracyline 250mg tablets	Rosacea	500mg twice daily	£4.56
Tetracycline 250mg tablets	Rosacea	500mg twice daily	£9.84
Erythromycin 250mg tablets/capsules	Rosacea	500mg twice daily	£6.44
Doxycycline 100mg capsules	Unlicensed	100mg once daily	£3.68
Doxycycline 40mg MR capsules (*Efracea*)	Facial rosacea	40mg daily	£15.98
Other topical preparations			
Azelaic acid 15% gel (*Finacea*)	Papulopustular rosacea	Twice daily	£7.48 (30g)
Metronidazole 0.75% aqueous gel (*Metrogel*)	Acute inflammatory exacerbations of rosacea	Twice daily	£22.63 (40g)
Metronidazole 0.75% aqueous gel (*Metrosa*)	Acute inflammatory exacerbations of rosacea	Twice daily	£12.00 (30g) £19.90 (40g)
Metronidazole 0.75% cream (*Rosiced)*	Treatment of inflammatory papulo-pustules of rosacea	Twice daily	£7.50 (30g)
Metronidazole 0.75% aqueous gel (*Rozex)*	Treatment of inflammatory papules, pustules and erythema of rosacea	Twice daily	£6.60 (30g) £9.88 (40g)
Metronidazole 0.75% cream (*Rozex)*	Treatment of inflammatory papules, pustules and erythema of rosacea	Twice daily	£6.60 (30g) £9.88 (40g)
Metronidazole 0.75% gel (*Zyomet*)	Rosacea	Twice daily	£12.00 (30g)
Camouflagers			
Covermark foundation		Apply daily	£11.86(15ml)
Dermablend		Apply daily	£5.60 (12g)

<u>PACEF Recommendation</u>:

PACEF were concerned that the cosmetic relief offered by regular use of brimonidine tartrate 3mg/g gel (*Mirvaso*) would be likely to result in recurrent long-term use. This is problematic in the absence of long-term efficacy and safety data, In the comparative trials against placebo reviewed, the placebo gel performed particularly strongly and there are no comparative trails against any active comparator. *Mirvaso* is also exceptionally high cost in comparison to other products used in the treatment of rosacea. In the absence of more compelling comparative data and mindful of the exceptionally high cost, brimonidine tartrate 3mg/g gel (*Mirvaso*) is designated RED-RED.

<u>Reference</u>:
NICE Evidence Summary New Medicine, *Facial erythema of rosacea: brimonidine tartrate gel* (8th July 2014)

RAPID DRUG ASSESSMENT: *SODIUM CHLORIDE 5% PRESERVATIVE FREE EYE DROPS (PF DROPS AND NaCl 5%)*

Both Moorfields Pharmaceuticals and Essential Pharmaceuticals have launched preservative free formulations of sodium chloride 5% eye drops licensed for the temporary relief of corneal oedema.

Sodium Chloride 5% eye drops are used as a hypertonic agent to reduce swelling and discomfort in the treatment of corneal oedema. At this strength, sodium chloride acts by drawing fluid out of the cornea and must not to be confused with the lower strength 0.9% sodium chloride products used as lubricants in the treatment of dry eye.

Sodium chloride 5% preservative free eye drops (*NaCl 5%*) are manufactured by Essential Pharmaceuticals. A pack contains 20 unit doses for single use only. *PF* Sodium Chloride 5% preservative free eye drops are manufactured by Moorfield's Pharmaceuticals. This product comes in a 10ml multi-dose container known as the Ophthalmic Squeeze Dispenser (OSD). The OSD is an easy-to-use 10ml eye drop bottle designed to prevent microbial contamination of the sterile contents for up to 60 days after first use. A number of Moorfields preservative free eye drop preparations are now available in the OSD bottle. Moorfields previously manufactured a sodium chloride 5% preservative free eye drop with an expiry date of 7 days (one week) after opening if kept in the refrigerator. This was available as an unlicensed special at a cost of £21.14 for 10ml. Following re-launch in the OSD device the price will become £25.20 for 10ml.

A comparison of the cost of these two alternative products reveals that *PF* sodium Chloride 5% preservative free eye drops are significantly lower in cost than *NaCl5%*:

Product	**Cost (£) for 4 day course**
Sodium chloride 5% single use eye drops (*NaCl 5%*) (Essential Pharmaceuticals)	£73.58 for 20
PF Sodium chloride 5% preservative free eye drops (Moorfields Pharmaceuticals)*	£25.20 (10ml)

*PF drops will be included in the *Drug Tariff* from August 2014 at a price of £25.20. Until August they are still available from Moorfields priced £21.12.

PACEF Recommendation:

Standard MHRA and PACEF advice is that licensed medicines should always be selected in preference to unlicensed medicines, wherever a licensed product is available. As a result of this, sodium chloride 5% preservative free eye drops should no longer be prescribed or supplied as an unlicensed special. Of the two licensed products, *PF sodium chloride 5% preservative free eye drops* are preferred on grounds of cost; *NaCl 5%* single use eye drops should only be prescribed if *PF drops* are unavailable. Corneal oedema is a medical emergency that requires referral to an ophthalmologist for diagnosis and initiation of treatment. As a result of this, *PF sodium chloride 5% preservative free eye drops* are designated AMBER without shared care and approved for inclusion in the *Lincolnshire Joint Formulary*. Many patients require more than a 4 day course and may require treatment for weeks,

months or even indefinitely. Within this context, prescribers in primary care will be expected to prescribe. Sodium chloride 5% single use eye drops (*NaCl 5%*) are designated RED-RED and have not been included in the *Joint Formulary* although they should be prescribed in preference to an unlicensed special where genuinely supply difficulties with *PF drops* exist.

REVIEW: *MELATONIN PROLONGED RELEASE 2MG TABLETS (CIRCADIN)*

Melatonin prolonged release tablets 2mg (*Circadin*) are approved for initiation by clinicians within LPFT and re-designated AMBER without shared care for the short-term treatment of primary insomnia in patients aged 55 and over.

This is a review and update of a new drug assessment that originally appeared in *PACE Bulletin* Vol 2, No 13 (August 2008).

Melatonin prolonged release 2mg tablets (*Circadin*) are licensed as monotherapy for the short-term treatment of primary insomnia in patients aged 55 or over. Since it was first launched in 2008, the definition of short-term use has been extended from 2 to 4 weeks to 13 weeks. Primary insomnia (i.e. insomnia not connected with any underlying medical condition) accounts for 10-30% of the total number of cases of insomnia. Melatonin is a naturally occurring hormone which is produced by the pineal gland and associated with the control of circadian rhythms and sleep regulation. Natural production of melatonin decreases with age and may explain why older patients are more prone to suffer from insomnia.

Our original assessment reviewed the data from two randomised controlled trials that demonstrated small improvements in quality of sleep and 'morning awakeness' in patients taking melatonin prolonged release 2mg tablets compared to placebo. Both key trials were of short duration (three weeks) and had low patient numbers. Since then a 6 to 12 month open label placebo controlled study in 244 adults aged 18 to 80 years with primary insomnia has been published. This has extended the efficacy and safety data of melatonin up to 6 months and beyond and provides reassurance that there are no adverse effects when melatonin is withdrawn, such as rebound insomnia or sleep disturbances. A further randomized placebo controlled double blind study in 781 adults with primary insomnia aged 18 to 80 years has confirmed short and longer-term efficacy of melatonin, but has failed to correlate low melatonin production in the patient with good response to *Circadin.* There is still no published data comparing melatonin with any alternative hypnotic.

Alongside the developing evidence base supportive of the use of melatonin, safety issues and price changes have rendered the use of alternative hypnotics, particularly in the elderly, as increasingly problematic. Standard advice in the current *British National Formulary* is that:

> 'Benzodiazepines and the z-drugs should be avoided in the elderly, because the elderly are at greater risk of becoming ataxic and confused, leading to falls and injury'

A cost comparison of melatonin versus alternative hypnotics reveals the following:

Drug	Daily dose range	Cost (28 days)
Melatonin 2mg MR tablets (*Circadin*)	**2mg once daily 1-2 hours before bedtime**	**£14.36**
Temazepam 10mg tablets	10mg – 20mg at bedtime	£19.25
Temazepam 20mg tablets	10mg – 20mg at bedtime	£18.13
Zaleplon 5mg capsules (*Sonata)*	5mg at bedtime (elderly dose)	£6.24
Zaleplon 10mg capsules (*Sonata*)	10mg at bedtime	£7.52
Zopiclone 3.75mg tablets (generic)	3.75mg at bedtime (elderly dose)	£1.19
Zopiclone 7.5mg tablets (generic)	7.5mg at bedtime	£1.19
Zolpidem 5mg tablets (generic)	5mg at bedtime (elderly dose)	£1.50
Zolpidem 10mg tablets (generic)	10mg at bedtime	£1.53

PACEF Recommendation:

Since our last assessment, further placebo controlled trials have provided longer term safety and efficacy data supportive of the use of melatonin for longer periods of up to 13 weeks in the treatment of primary insomnia. Trial evidence confirms significantly better efficacy than placebo, good tolerability and no evidence of rebound insomnia or sleep disturbances following withdrawal. However, there is still no comparative data against commonly used alternative treatments such as benzodiazepines or z-drugs. Recent supply difficulties with temazepam 10mg and 20mg tablets and the resultant high prices mean that melatonin 2mg MR tablets (*Circadin*) are now lower in price than generic temazepam, although generic z-drugs such as zopliclone and zolpidem are still significantly lower in cost. Increasing concerns around the use of benzodiazepines and z-drugs in the elderly are resulting in some opinion leaders and guidelines advocating more prominent use of melatonin in the treatment of primary insomnia. As a result of this, melatonin prolonged release tablets 2mg (*Circadin*) are approved for initiation by clinicians within LPFT and re-designated AMBER without shared care within licensed indications (i.e. short-term relief of primary insomnia in patients 55 and over for up to 13 weeks). Non-pharmacological approaches to the treatment of insomnia are still advocated first line. Where a hypnotic is indicated, a short course (two to four weeks) of a low cost z drug is the preferred alternative in younger patients. Hypnotics should only be prescribed where insomnia is severe, disabling and subjecting the individual to extreme distress.

In addition, guidance on the use of melatonin for wider indications remains unchanged:

All melatonin formulations are designated RED-RED for jet lag and sleep restriction (e.g. due to shift work). PACEF acknowledge that there is a role for melatonin in the treatment of children and adolescents with severe sleep disturbances linked to neurological or neuro-developmental disorder. The MHRA have advised that, where possible*, Circadin*, the licensed formulation of melatonin should be used preferentially. Where the patient can swallow tablets

and a sustained release formulation is suitable, *Circadin* 2mg MR tablets should be prescribed. If the patient requires an immediate release formulation and can swallow tablets, Pharma-Nord *Bio-Melatonin* 3mg tablets should be prescribed (by brand name). This is a product which is a licensed medical product in its country of origin (Hungary) and is available with English language packaging. The MHRA have advised that this may be an appropriate second line choice if *Circadin* does not meet the clinical needs of the patient. Both of these formulations of melatonin are designated AMBER within the criteria specified.

MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY, *DRUG SAFETY UPDATE* (MAY 2014)

VORICONAZOLE: REMINDER OF RISK OF LIVER TOXICITY, PHOTOTOXICITY AND SQUAMOUS CELL CARCINOMA

Voriconazole (*Vfend*) is known to be associated with a risk of liver toxicity, phototoxicity, and squamous cell carcinoma of the skin. Liver function should be assessed before starting treatment with voriconazole and at least weekly during the first month of treatment. Patients should be advised to avoid sunlight exposure while taking voriconazole.

Advice for healthcare professionals:
The advice below applies to both adults and children taking voriconazole.

Liver toxicity

- Test liver function before starting treatment with voriconazole (specifically, aspartate transaminase [AST] and alanine transaminase [ALT] levels).
- Continue testing liver function at least weekly for the first month of treatment and monthly thereafter if there are no changes in the first week of treatment.
- Stop voriconazole if AST or ALT levels become markedly elevated, unless you consider the benefits of voriconazole treatment to outweigh the risk of liver toxicity in that individual.

Phototoxicity and squamous cell carcinoma

- Tell patients to avoid sunlight exposure while taking voriconazole. Advise patients to wear protective clothing and use sunscreen with a high sun protection factor if in sunlight.
- Refer patients with phototoxic reactions to a dermatologist and consider stopping voriconazole treatment.
- If voriconazole is continued despite a phototoxic reaction, check the skin frequently and thoroughly to detect and manage pre-cancerous lesions as early as possible.
- Stop voriconazole if pre-cancerous skin lesions or squamous cell carcinoma are identified. Note that patients may develop squamous cell carcinoma without a prior phototoxic reaction.

PACEF Comment
Voriconazole 50mg tablets and oral suspension (*Vfend*) are designated RED and use is restricted to secondary and tertiary care only. Voriconazole is indicated for the treatment of invasive aspergillosis, candidaemia in non-neutropenic patients, fluconazole resistant serious invasive *Candida* infections caused by *Scedosporium* spp and *Fusarium* spp in patients with progressive possibly life-threatening infections.

ADRENALINE AUTO-INJECTOR - ADVICE FOR PATIENTS

People who have been prescribed an adrenaline auto-injector (*Emerade*, *Epipen* or *Jext*) because of the risk of anaphylaxis should carry two with them at all times for emergency, on-the-spot use. After every use of an adrenaline auto-injector, an ambulance should be called (even if symptoms are improving), the individual should lie down with their legs raised and, if at all possible, should not be left alone.

Advice for healthcare professionals:

- Ensure that people with allergies and their carers have been trained to use the particular auto-injector that they have been prescribed. Injection technique varies between injectors.
- Encourage people with allergies and their carers to obtain and practice using a trainer device (available free from manufacturers' websites).

Advice to give to people with allergies and their carers:

- Carry two adrenaline auto-injectors at all times. This is particularly important for people who also have allergic asthma as they are at increased risk of a severe anaphylactic reaction.
- Use the adrenaline auto-injector at the first signs of a severe allergic reaction.
- Take the following actions immediately after every use of an adrenaline auto-injector:
    1. Call 999, ask for an ambulance and state "anaphylaxis", **even if symptoms are improving.**
    2. Lie flat with the legs raised in order to maintain blood flow. If you have breathing difficulties sit up to make breathing easier.
    3. Seek help immediately after using the auto-injector and if at all possible stay with the person while waiting for the ambulance.
    4. If the person does not start to feel better, the second auto-injector should be used 5 to 15 minutes after the first
- Check the expiry date of the adrenaline auto-injectors and obtain replacements before they expire. Expired injectors will be less effective.

PACEF Recommendation:
Prescribers should ensure that adrenaline auto-injectors are usually prescribed in quantities of two. Patients should ensure that pairs of auto-injectors are kept together rather than spread over two separate locations such as home and school. Where a school supply is necessary, two auto-injectors should be supplied, not one.

STATINS - BENEFITS AND RISKS

The benefits of using any statin within licensed indications outweigh the risks in most patients.

In the lead up to the imminent publication of the updated NICE Clinical Guideline on *Lipid Modification: cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease* (due July 2014), the MHRA have weighed into the debate on the benefits and risks of statin therapy, particularly mindful of the context within which NICE intend to recommend these treatments for a wider section of the population at lower levels of cardiovascular risk.

Key points are as follows:

- Evidence from large clinical trials shows that statins can reduce heart attacks and the need for bypass surgery, and can save lives in certain patient groups. Meta-analysis of randomised trial data shows that if patients with a 10-year cardiovascular risk of at least 20% take statins for 5 years, it would prevent at least 450 heart attacks, strokes, or vascular deaths per 10,000 treated patients.
- Large clinical trials also show that statins are generally well tolerated by most people who take them. However, these trials were generally aimed at establishing efficacy rather than safety and suspected side effects were not investigated as the main outcomes.
- Muscle-related problems are the most frequently reported side effect of statins. Incidences of statin side effects are estimated from trial data, cohort studies, published case reports and spontaneous report as:
    - mild muscle pain: 190 cases per 100,000 patient years
    - myopathy: 5 cases per 100,000 patient years
    - rhabdomyolysis: 1.6 cases per 100,000 patient years
- The risk of myopathy is increased with all statins and is known to be dose dependent. Myopathy risk also increases when certain medicines are used together with statins, either because both medicines can cause myopathy or because the second medicine increases the blood plasma concentration of the statin (mimicking the effects of a higher statin dose).
- Certain genetic profiles may increase the risk of statin-induced myopathy. Recent studies have highlighted that some people's genetic make-up may make them more prone to experiencing myopathy while taking certain statins.

Things to consider when prescribing statins

- Advise patients to seek prompt medical attention if they experience muscle problems while taking statins. Myopathy may not be clinically serious to start with, but can rarely progress to potentially fatal rhabdomyolysis.
- Review statin treatment if muscle problems occur. For some patients, stopping statin treatment may be appropriate. If statin treatment must be continued despite muscle problems, consider using a lower statin dose or switching to a different statin.
- Take into account the severity of the myopathy, the degree of hyper-cholesterolaemia, and the patient's medical history.

PACEF Comment:
PACEF have already reviewed a draft of the NICE Clinical Guideline on *Lipid Modification* and plan to review the final version in September. Local prescribing policy will remain unchanged until the results of that review are published in the *PACE Bulletin* in October.

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Stephen Gibson
Head of Prescribing and Medicines Optimisation GEM CSU

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