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 18 **October 2014**

What's new this month?

- **PACEF have agreed a new set of shared care principles that should be followed by specialist services wishing to initiate AMBER medicines and GPs approached to undertake shared care (see page 3).**
- **Considerable media interest was generated recently following the publication of a large scale review claiming that daily aspirin could significantly reduce cancer risk. PACEF were concerned about the overall quality of this review which resulted in the exclusion of certain key systematic reviews and the inclusion of poorer quality observational data. In addition, the quoting of relative risk reduction rather than absolute risk reduction tended to overemphasize the benefits and risks. Clinicians are advised to continue to prescribe aspirin as indicated for the secondary prevention of thrombotic, cerebrovascular or cardiovascular disease and following by-pass surgery. Patients prescribed aspirin monotherapy or dual antiplatelet therapy for stroke prevention in atrial fibrillation need to be reviewed with a view to discontinuing or changing therapy in accordance with NICE guidance. More robust evidence around the risks and benefits of prescribing aspirin to reduce the incidence of cancer and cancer related deaths in the general population is required before a change in practice can be justified (see page 4).**
- **Alprostadil 300 microgram in 100mg cream (*Vitaros*) for erectile dysfunction is designated RED for specialist use only. Subject to favourable audit results, PACEF will review this decision in six months' time. GPs should refuse all requests to prescribe *Vitaros* cream as the product is currently available only through secondary care (see page 5).**
- **Following a recent review by the European Medicines Agency, the MHRA has confirmed that there is no definite proven link between decreasing efficacy of emergency contraception and increasing body weight. As a result of this, emergency contraception (specifically levonorgestrel (*Levonelle 1500/ Upostelle*) and ulipristal (*EllaOne*)) can continue to be used to prevent unintended pregnancy in women of any weight or body mass index (see page 8).**
- **Denosumab injection (*Prolia*) is now supported by a shared care guideline, within licensed indications, developed by the Peterborough Hospitals. As a result of this, denosumab injection has been reclassified as AMBER with shared care for patients initiated on therapy from Peterborough. Elsewhere in the county, where shared care has yet to develop, denosumab injection remains RED (see page 9).**
- **Nitrofurantoin is now contraindicated in patients with an estimated glomerular filtration rate (eGFR) of less than 45 ml/min (see page 10).**
- **Following the recent review of serious cardiac adverse effects associated with domperidone and resultant changes to the marketing authorisation, domperidone is no longer available as an over the counter (OTC) product and can only be supplied on prescription (see page 11).**

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SUMMARY OF PACEF DECISIONS: *SEPTEMBER 2014 UPDATE*

Drug	Indication(s)	Traffic Light and Joint Formulary Status
Alprostadil 300microgram in 100mg cream *(Vitaros)*	Treatment of men over the age of 18 years with erectile dysfunction.	RED Approved for inclusion in the *Lincolnshire Joint Formulary*
Denosumab injection (*Prolia*) (Amgen)	For the treatment of postmenopausal osteoporosis in women at increased risk of fractures. For the treatment of bone loss associated with hormone ablation in men with prostate cancer at increased risk of fractures	AMBER where a shared care guideline is available (e.g. through Peterborough Hospitals); otherwise RED. Included in the *Lincolnshire Joint Formulary* for this indication.
Enzalutamide 40mg capsules (*Xtandi*)	For the treatment of adult men with metastatic castrate-resistant prostate cancer whose disease has progressed on or after docetaxel therapy.	RED Already approved for restricted use on the *Lincolnshire Joint Formulary* in accordance with the *National Cancer Drugs Fund List* for the treatment of castrate resistant metastatic prostate cancer.
Estradiol 10 microgram vaginal tablets (*Vagifem*)	Vaginal atrophy due to oestrogen deficiency in postmenopausal women	GREEN Approved for inclusion in the *Lincolnshire Joint Formulary* as a replacement for *Ortho-Gynest* pessaries (now withdrawn)
Finasteride tablets 5mg (generic)	Benign prostatic hyperplasia	GREEN Included in the *Lincolnshire Joint Formulary*
Ibuprofen 5% and 10% gel (*Fenbid*) (Amdipharm Mercury)	For backache, rheumatic and muscular pain, sprains, strains and neuralgia.	GREEN Ibuprofen 5% gel (*Fenbid*) is already included in the *Lincolnshire Joint Formulary.* Ibuprofen 10% gel (*Fenbid*) is approved for inclusion in the *Lincolnshire Joint Formulary.*
Ipilimumab intravenous infusion (*Yervoy*) (Bristol Myers Squibb)	For the treatment of advanced (unresectable or metastatic) melanoma in adults.	RED Approved by NICE for the treatment of previously treated and untreated advanced (unresectable or metastatic) melanoma. Approved for inclusion in the *Lincolnshire Joint Formulary* for both NICE approved indications.
Methotrexate pre-filled pen for subcutaneous injection 50mg/ml (*Metoject*)	Severe recalcitrant disabling psoriasis. Active rheumatoid arthritis in adults. Severe psoriatic arthritis in adults. Polyarthritic forms of severe active juvenile idiopathic arthritis when	RED. Approved for inclusion in the *Lincolnshire Joint Formulary.* Likely to be used by Healthcare at Home.

	response to NSAIDs has been inadequate.	
Prochlorperazine 5mg in 5ml liquid (generic)	Severe nausea, vomiting, vertigo, labyrinthine disorders.	GREEN Approved for inclusion in the *Lincolnshire Joint Formulary*

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

UPDATED SHARED CARE PRINCIPLES

Following a full review and in collaboration with United Lincolnshire Hospitals Trust and Lincolnshire Partnership Foundation Trust, PACEF have agreed the following principles to be followed on both sides of the primary-secondary care interface when new shared care arrangements are being agreed between specialists and the patient's GP:

(1) An approach must be made in writing to the GP or primary care based physician by the initiating specialist requesting participation in formal shared care around a specific medicine. As part of the communication, the GP should be signposted to the relevant shared care guideline either on the PACEF website (www.lincolnshire.nhs.uk) or the initiating Trust website.
(2) Wherever possible the invitation to shared care should be sent prior to the named treatment being initiated, although it is acknowledged that this is not always practical.
(3) Following receipt of a formal invitation to participate in shared care, the GP is requested to reply in writing (i.e. by letter or email) within two weeks stating whether or not they would be willing to enter into a shared care agreement.
(4) If shared care is agreed, there is an expectation that the specialist service will take responsibility for all of the specialist responsibilities stipulated in the shared care protocol (e.g. baseline checks, treatment initiation (if required) and dose titration (if necessary)).
(5) It is expected that all responsibility for monitoring the patient's condition, including any necessary biochemical monitoring such as regular blood tests, will remain with the specialist service until the GP formally takes over care, as specified within the protocol.
(6) Prior to the patient's care being transferred back to the GP and assuming specialist initiation of therapy, it is the responsibility of the hospital based service to ensure that the patient has sufficient supplies of medication. GPs should not feel pressured into accepting shared care responsibilities simply to help a patient who has run out of medication.
(7) The shared care protocol usually defines the point at which it is appropriate for a patient to be transferred back to the care of their GP; this varies but will normally be when the dose is stabilised and the patient has shown that they are tolerating and/or responding to the treatment. It is recognized that, in some cases, treatment will be initiated by the GP, subject to the GP accepting shared care responsibilities after initiation.

(8) When care is transferred back to the GP, details should be provided of any future appointments arranged for the patient by the specialist serviceI; the results of any investigations or monitoring that has not been previously communicated to the GP should also be shared.
(9) Shared care is not mandatory. However, PACEF approval of a shared care protocol signifies that the consensus view across the healthcare community is that shared care for the medicine in question is appropriate and that GP participation is strongly recommended. Nonetheless, individual clinicians will need to satisfy themselves that they are happy to accept prescribing responsibility for the medicine and that they are competent to fulfil the responsibilities defined in the shared care protocol before agreeing to take part. There may be occasions when the patient's GP feels that they are not able to agree to the proposed shared care. If this occurs, the GP is expected to contact the specialist service to explain the reasons behind the decision. It is expected that, where this situation arises, the specialist and the GP will work collaboratively to ensure that the needs of the patients are met.
(10) Any refusal to participate in PACEF approved shared care should be based on individual clinician concern around lack of personal competence in the use of a particular specialist medicine or the treatment of a complex condition. If specialist services encounter blanket refusal from a practice to participate in all shared care or specific PACEF approved shared care guidelines they are encouraged to report the problem to PACEF and the relevant Clinical Commissioning Group.
(11) Any approaches from specialists to initiate or accept shared care around a medicine that is not approved by PACEF for this purpose, should be reported in the first instance to Cathy Johnson, Interface Lead Pharmacist (cathy.johnson@gemcsu.nhs.uk). Shared care is never appropriate for a medicine that has been designated RED-RED or RED or for medicines that have not yet been evaluated by PACEF.

NEW TRIAL ASSESSMENT: *DOES DAILY ASPIRIN REDUCE CANCER RISK?*

A recent large scale review published in the *Annals of Oncology* caused something of the stir in the media when it concluded that daily aspirin taken over a period of 10 years significantly reduced the incidence of many different types of cancer as well as heart attack and stroke.

The researchers gathered evidence on the effects of aspirin on cancer risk and death from systematic reviews published between 2009 and 2012 as well as some individual studies on specific cancers. However, some recently conducted systematic reviews were excluded while some individual studies of variable design and quality (e.g. observational studies) were included. Evidence for aspirin's effect on cardiovascular disease came from a single large scale meta-analysis.

The researchers calculated that for average risk individuals aged 50 to 65 taking aspirin (75mg to 325mg daily) for 10 years there would be a relative risk reduction (RRR) of between 7% (women) and 9% (men) in the number of cancer, myocardial infarction and stroke events over a 15 year period and an overall 4% RRR in all deaths over a 20 year period. They estimated specific effects on individual cancer, heart attack and stroke incidence and deaths as follows:

	Incidence (RRR)	**Deaths (change in RR)**
Colorectal (bowel) cancer	30% reduction	35% reduction
Oesophageal cancer	25% reduction	45% reduction
Gastric cancer	25% reduction	30% reduction
Lung cancer	No reduction	10% reduction

Prostate cancer	5% reduction	10% reduction
Breast cancer	5% reduction	No reduction
Heart attack	18% reduction	5% reduction
Stroke	5% reduction	21% increase

The researchers claim that these benefits are not apparent until at least 3 years after starting aspirin, but may be sustained for several years after discontinuation. Increased relative risk in incidence and death associated with major (extracranial) bleeding, gastric bleeding and peptic ulcer are as follows:

	Incidence/ Deaths (change in RR)
Major (extracranial) bleeding	70% increase in incidence
Gastric bleeding	70% increase in deaths
Peptic ulcer	70% increase in deaths

PACEF Comment:
Considerable media interest was generated recently following the publication of a large scale review claiming that daily aspirin could significantly reduce cancer risk. PACEF were concerned about the overall quality of this review which resulted in the exclusion of certain key systematic reviews and the inclusion of poorer quality observational data. In addition, the quoting of relative risk reduction rather than absolute risk reduction tended to overstate the benefits and risks. Clinicians are advised to continue to prescribe aspirin as indicated for the secondary prevention of thrombotic, cerebrovascular or cardiovascular disease and following by-pass surgery. Patients prescribed aspirin monotherapy or dual antiplatelet therapy for stroke prevention in atrial fibrillation need to be reviewed with a view to discontinuing or changing therapy in accordance with NICE guidance. More robust evidence around the risks and benefits of prescribing aspirin to reduce the incidence of cancer and cancer related deaths in the general population is required before a change in practice can be justified.

References
Cuzick J et al, Estimates of benefits and harms of prophylactic use of aspirin in the general population, *Annals of Oncology* 00:1-10, 2014 doi:10.1093/annonc/mdu/225
Does long term aspirin prevent cancer? *British Medical Journal* 2010: 341: c7326.

NEW DRUG ASSESSMENT: *ALPROSTADIL 300 MICROGRAM IN 100MG CREAM (VITAROS)*

Alprostadil is an established second line treatment for erectile dysfunction used for the 25% of men who fail to respond to oral phosphodiesterase type 5 inhibitors. Until now, it has only been available as an intracavernosal injection (*Caverject*/*Viridal*) or as a pellet for urethral application (*MUSE*). *Vitaros* is a new cream based formulation of alprostadil. It is packaged in single doses of 300 microgram applied using an *AccuDose* container (similar in appearance to a syringe) to the tip off the penis within 5 to 30 minutes of attempted sexual intercourse.

PACEF reviewed the results of two phase 3 randomised double blind placebo controlled trials reported as a single integrated analysis. The results demonstrated a statistically significant improvement of all outcome measures of erectile dysfunction compared to placebo. There is a complete absence of comparative data against any active alternative treatment. As a result of this, it was impossible to reach any conclusion on the relative effectiveness of this alprostadil formulation in comparison to more established therapies.

The most commonly reported adverse effects with alprostadil cream were local to the penis and surrounding area including burning sensation, penile pain, genital discomfort and erythema. There is also a risk of prolonged erection lasting more than 4 hours (priapism). If this occurs, the manufacturer advises immediate treatment as it can result in penile tissue damage and permanent loss of potency. There have also been reports from trials of local reactions such as vulvo-vaginal burning sensation and vaginitis in female partners of the trial participants. The manufacturer recommends the use of a latex condom with this product to reduce local reactions in sexual partners.

Vitaros is contraindicated in those with orthostatic hypotension, myocardial infarction and syncope. It should not be used in those with conditions that predispose them to priapism and those with penile abnormalities. The product should not be used concurrently with anticoagulants, antihypertensive agents or sympathomimetics. There is also an enhanced risk of priapism if used concurrently with other treatments for erectile dysfunction.

At a cost of £10 per dose, *Vitaros* compares favourably with other alprostadil formulations, such as *MUSE* (£11.30 - £11.56 per dose) and intracavernosal injections (*Caverject* or *Viridal*) (£7.35 - £13.61 per dose).

In common with alprostadil pellets (*MUSE*), *Vitaros* cream requires storage in a refrigerator. It has a shorter expiry date at room temperature of 3 days compared to 14 days for the pellet.

Alprostadil cream (*Vitaros*) is covered by the current NHS prescribing restrictions for the management of erectile dysfunction and can only be prescribed on the NHS for certain categories of patient (see *Drug Tariff* Part VIIIB).

PACEF Recommendation:
Alprostadil 300 microgram in 100mg cream (*Vitaros*) for erectile dysfunction provides a less invasive method of administration than any other alprostadil formulation at a comparable price. Nonetheless, PACEF were concerned about the lack of comparative data with any other active alternative. As a result of this, the product has been designated RED and is approved for specialist use only for the next six months. Over this period, the product will be used by ULH urologists providing specialist erectile dysfunction services as a second line alternative after PDE5 inhibitors in accordance with British Society for Sexual Medicine guidelines. Subject to favourable audit results, PACEF will review this decision in six months' time. In the meantime, GPs should refuse all requests to prescribe *Vitaros* cream. The product is approved for use through the *Lincolnshire Joint Formulary*, but only available through secondary care.

NEW FORMULATION ASSESSMENT: *METHOTREXATE PRE-FILLED PEN FOR SUBCUTANEOUS INJECTION (METOJECT)*

To increase patient convenience and ease of use, Healthcare at Home are to introduce methotrexate in pre-filled pens for subcutaneous injection (*Metoject*). All patients are to be informed of this change in writing from Healthcare at Home.

PACEF Recommendation:
Methotrexate pre-filled pen for subcutaneous injection (*Metoject*) is designated RED and approved for inclusion in the *Lincolnshire Joint Formulary*. GPs are asked to ensure that specialist medicines are always recorded on the patient's Repeat Prescription List so that primary care prescribing is always cognisant of ongoing specialist therapy.

FORMULARY UPDATE

Finasteride 5mg tablets

Following an incorrect classification as AMBER on the *Joint Formulary*, finasteride 5mg tablets are confirmed as GREEN (see *PACE Bulletin*, Vol 5 No10 (May 2011)).

Prochlorperazine 5mg in 5ml liquid (generic)

Generic prochlorperazine 5mg in 5ml liquid is now a lower cost option per dose than prochlorperazine 3mg buccal tablets and has been approved for inclusion in the *Lincolnshire Joint Formulary*; designation GREEN.

Discontinuation of Ortho-Gynest (estriol) pessaries

In response to the discontinuation of *Ortho-Gynest*, estradiol pessaries (*Vagifem*) are approved for inclusion in *the Lincolnshire Joint Formulary* as a replacement; designation GREEN.

Ibuprofen 10% gel (Fenbid)

Both ibuprofen 5% and 10% gel (*Fenbid*) are now approved for inclusion in the *Lincolnshire Joint Formulary*; designation GREEN. *Fenbid* is the preferred low cost brand.

NICE TECHNOLOGY APPRAISAL 316: *ENZALUTAMIDE FOR METASTATIC HORMONE-RELAPSED PROSTATE CANCER PREVIOUSLY TREATED WITH A DOCETAXEL-CONTAINING REGIMEN* (JULY 2014)

Key Recommendation:

- Enzalutamide is recommended within its marketing authorisation as an option for treating metastatic hormone-relapsed prostate cancer in adults whose disease has progressed during or after docetaxel-containing chemotherapy, only if the manufacturer provides enzalutamide with the discount agreed in the patient access scheme.

PACEF Recommendation:
Enzalutamide (*Xtandi*) has a UK marketing authorisation for the treatment of adult men with metastatic castrate-resistant prostate cancer whose disease has progressed on or after docetaxel therapy. Enzalutamide 40mg capsules (*Xtandi*) are designated RED for specialist use only. The product is already approved for restricted use through the *Lincolnshire Joint Formulary* for the treatment of castrate resistant metastatic prostate cancer in accordance with the *National Cancer Drugs Fund List.*

NICE TECHNOLOGY APPRAISAL TA319: *IPILIMUMAB FOR PREVIOUSLY UNTREATED ADVANCED (UNRESECTABLE OR METASTATIC) MELANOMA* (JULY 2014)

Key Recommendation:

- Ipilimumab is recommended, within its marketing authorisation, as an option for treating adults with previously untreated advanced (unresectable or metastatic) melanoma, only if the manufacturer provides ipilimumab with the discount agreed in the patient access scheme.

PACEF Recommendation:
Ipilimumab (*Yervoy*) has a UK marketing authorisation for the treatment of advanced (unresectable or metastatic) melanoma in adults. Ipilimumab (*Yervoy*) intravenous infusion is designated RED for specialist use only. It is already available through the *Lincolnshire Joint Formulary* as a RED drug approved for use for previously treated advanced (unresectable or metastatic) melanoma as recommended by NICE TA 268.

MEDICINES AND HEALTHCARE REGULATORY AGENCY: *DRUG SAFETY UPDATE* (AUGUST 2014)

LEVONORGESTREL AND ULIPRISTAL REMAIN SUITABLE EMERGENCY CONTRACEPTIVES FOR ALL WOMEN, REGARDLESS OF BODY WEIGHT OR BODY MASS INDEX

Emergency contraceptives remain suitable for all women regardless of the woman's weight or body mass index (BMI). Emergency contraceptives should be used as soon as possible after unprotected sex or contraceptive failure to prevent unintended pregnancy.

Advice for healthcare professionals
Advice to give to women

- Use an emergency contraceptive as soon as possible after unprotected sex or contraceptive failure regardless of your weight or BMI.
- Emergency contraceptives should not be used to replace a regular contraceptive method.
- If your period is late or you have irregular bleeding after using an emergency contraceptive, use a pregnancy test.
- Speak to your doctor, nurse, or pharmacist if you have any concerns about emergency contraceptives.

PACEF Comment:
The conclusions of the European Medicine Agency (EMA) review of the efficacy of emergency contraceptives in women with a high body weight were reported in *PACE Bulletin* Vol 8 No 16 (September 2014). The published MHRA advice now supplements that guidance.

MEDICINES AND HEALTHCARE REGULATORY AGENCY: *DRUG SAFETY UPDATE* (SEPTEMBER 2014)

DENOSUMAB: MINIMISING THE RISK OF OSTEONECROSIS OF THE JAW; MONITORING FOR HYPOCALCAEMIA - UPDATED RECOMMENDATIONS

Denosumab is associated with a risk of osteonecrosis of the jaw (ONJ) and hypocalcaemia. Before starting denosumab treatment, a dental examination and appropriate preventive dentistry are now recommended to reduce the risk of ONJ. This applies to all patients considered for denosumab 120 mg for cancer and to patients with ONJ risk factors considered for denosumab 60 mg for osteoporosis. Patients should be advised to maintain good oral hygiene and report any oral symptoms. The risk of hypocalcaemia increases with the degree of renal impairment. Calcium levels should be monitored depending on the indication and patients told to report symptoms of hypocalcaemia.

Advice for healthcare professionals
Osteonecrosis of the jaw
The following precautions are now recommended to reduce the risk of ONJ:

Denosumab 120 mg (cancer indication)

- A dental examination and appropriate preventive dentistry before starting denosumab 120 mg are now recommended for all patients.
- Do not start denosumab 120 mg in patients with a dental or jaw condition requiring surgery, or in patients who have not recovered following oral surgery.

Denosumab 60 mg (osteoporosis indication)

- Check for ONJ risk factors before starting denosumab 60 mg. A dental examination and appropriate preventive dentistry are now recommended for patients with risk factors.

Tell all patients to maintain good oral hygiene, receive routine dental check-ups, and immediately report any oral symptoms such as dental mobility, pain, or swelling to a doctor and dentist.

Hypocalcaemia
Calcium levels should now be monitored as follows:

Denosumab 120 mg (cancer indication)

- Check calcium levels:
    - before the first dose
    - within two weeks after the initial dose
    - if suspected symptoms of hypocalcaemia occur.

Consider monitoring calcium levels more frequently in patients with risk factors for hypocalcaemia (e.g. severe renal impairment, creatinine clearance <30 ml/min).

Denosumab 60 mg (osteoporosis indication)

- Check calcium levels:
    - before each dose
    - within two weeks after the initial dose in patients with risk factors for hypocalcaemia (eg, severe renal impairment, creatinine clearance <30 ml/min)
    - if suspected symptoms of hypocalcaemia occur.

Tell all patients to report any symptoms of hypocalcaemia they experience to their doctor (e.g, muscle spasms, twitches or cramps, numbness or tingling in the fingers, toes, or around the mouth).

SHARED CARE UPDATE: *DENOSUMAB INJECTION (PROLIA) FOR PETERBOROUGH PATIENTS*

Prior to the publication of this *Drug Safety Update*, denosumab injection (*Prolia*) was approved for shared care by the Peterborough Hospitals Formulary and Medicines Management Committee. As a result of this, PACEF have agreed to change the Traffic

Light Status of denosumab injection (*Prolia*) to AMBER, within marketing authorisation, subject to a shared care guideline being in place (e.g. from Peterborough Hospitals). The shared care guideline will incorporate all key information included in the MHRA Drug Safety Update detailed above.

In areas of the county not served by the Peterborough Hospitals, the product remains RED pending the development of a shared care guideline. *Prolia* holds a UK marketing authorisation for

- the treatment of postmenopausal osteoporosis in women at increased risk of fractures.
- the treatment of bone loss associated with hormone ablation in men with prostate cancer at increased risk of fractures.

PACEF Comment
PACEF have approved denosumab injection (*Prolia*) as an AMBER drug with appropriate shared care in the area of Lincolnshire served by the Peterborough Hospitals. Where there is no shared care protocol in place, for example within ULH, all prescribing remains within the hospital and the product continues to be classed as RED for hospital use only. GPs participating in shared care with denosumab must ensure that calcium levels are checked prior to each dose and if symptoms of hypocalcaemia occur. Patients should be reminded of the importance of good oral hygiene and the need for regular dental check-ups. Where shared care is in place, all risk assessments for ONJ will be done by the specialist service prior to initiation of therapy.

NITROFURANTOIN NOW CONTRAINDICATED IN MOST PATIENTS WITH AN ESTIMATED GLOMERULAR FILTRATION RATE (eGFR) OF LESS THAN 45ML/MIN

Nitrofurantoin is now contraindicated in patients with an estimated glomerular filtration rate (eGFR) of less than 45 ml/min. However, a short course (3 to 7 days) may be used with caution in certain patients with an eGFR of 30 to 44 ml/min. Such patients should only be prescribed nitrofurantoin to treat lower urinary tract infection with suspected or proven multidrug resistant pathogens when the benefits of nitrofurantoin are considered to outweigh the risk of side effects. Lowering the eGFR threshold for this contraindication allows nitrofurantoin to be used in patients for whom it was previously not recommended.

Advice for healthcare professionals

- Nitrofurantoin is contraindicated in patients with an estimated glomerular filtration rate (eGFR) of less than 45 ml/min.
- Nitrofurantoin should not be used to treat sepsis syndrome secondary to urinary tract infection or suspected upper urinary tract infections
- A short course (3 to 7 days) may be used with caution in certain patients with an eGFR of 30 to 44 ml/min. Only prescribe to such patients to treat lower urinary tract infection with suspected or proven multidrug resistant pathogens when the benefits of nitrofurantoin are considered to outweigh the risks of side effects.
- Consider checking renal function when choosing to treat with nitrofurantoin, especially in the elderly.
- Closely monitor for signs of pulmonary, hepatic, neurological, haematological, and gastrointestinal side effects during treatment, as previously advised in the summary of product characteristics (see below).
- Consult official guidance on the appropriate use of antibiotics when prescribing nitrofurantoin.

DOMPERIDONE: RISK OF CARDIAC SIDE EFFECTS – NO LONGER AVAILABLE WITHOUT PRESCRIPTION

Following the recent review of serious cardiac adverse effects associated with domperidone and resultant changes to the marketing authorisation, domperidone is no longer available as an over the counter (OTC) product and can only be supplied on prescription.

Advice for healthcare professionals

- Domperidone must not be sold without prescription
- A recall has been issued for all non-prescription domperidone (*Motilium 10* and *Motilium Instants*)

Advice to give to patients

- If you have recently bought domperidone without a prescription and you wish to continue taking it, speak to your doctor or pharmacist at your next routine visit.
- If you wish to stop taking domperidone a healthcare professional can advise on suitable alternatives for nausea and vomiting.
- If you have been prescribed domperidone, there is no need to stop taking it. Speak to your doctor or pharmacist at your next routine visit if you have any heart problems or other concerns about the treatment.
- Talk to a doctor straight away if you experience dizziness, fainting, chest pain or a rapid, fluttering, or pounding heartbeat while taking domperidone.

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