

The Synapse

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Stop treatment in the event of severe and persistent diarrhoea. Caution in excessive reduction of blood pressure in patients with ischaemic cardiopathy of ischaemic cardiovascular disease. Caution in driving or operating machinery. Caution with patients with history of allergy and asthma. Not recommended in patients below 18 years of age. Excipients: Contains lactose and wheat starch. Interactions: Monitoring when used concomitantly with furosemide, lithium, products affected by serum potassium disturbances (eg digitalis glycosides, antiarrhythmics), calcium supplements or calcium sparing medicinal products. Possible interaction with digoxin, ibuprofen, St. John's wort, and rifampicin. Meals with high fat content substantially reduce absorption. Caution when used concomitantly with drugs that may increase potassium levels (eg potassium supplements, heparin sodium) and drugs that decrease potassium levels (eg corticosteroids, AGTH, amphotericin, carbamazepine, penicillin G, laxatives, salicylic acid derivatives, other kaliuretic diuretics). Caution if combined with other antihypertensives, curare derivatives, NSAIDs (especially in the elderly), digoxin, antidiabetic agents, allopurinol, amantadine, diazoxide, cytotoxic drugs, anticholinergic agents, cholestyramine and colestipol resins, vitamin D, calcium salts, pressor amines, antifungal medicines, and ciclosporin. Caution should be exercised on concomitant use with ketoconazole or other moderate P-gp inhibitors (ketoconazole, itraconazole, clarithromycin, erythromycin, amiodarone, telithromycin). Grapefruit juice. Alcohol. Adverse reactions: Common: Diarrhoea. For the aliskiren component, other reported adverse reactions include: Uncommon: Rash. Rare: Angioedema. Laboratory values: decrease in haemoglobin and haematocrit, increase in serum potassium. For the hydrochlorothiazide component, other reported adverse reactions include: Aplastic anaemia, bone marrow depression, neutropenia/agranulocytosis, haemolytic anaemia, leucopenia, thrombocytopenia, depression, sleep disturbances, restlessness, light-headedness, vertigo, paraesthesia, dizziness, transient blurred vision, xanthopsia, cardiac arrhythmias, postural hypotension, respiratory distress (including pneumonitis and pulmonary oedema), pancreatitis, anorexia, diarrhoea, constipation, gastric irritation, sialadenitis, loss of appetite, jaundice (intrahepatic cholestatic jaundice), anaphylactic reactions, toxic epidermal necrolysis, necrotizing angitis, vasculitis, cutaneous vasculitis, cutaneous lupus erythematosus-like reactions, reactivation of cutaneous lupus erythematosus, photosensitivity reactions, rash, urticaria, weakness, muscle spasm, interstitial nephritis, renal dysfunction, fever. Laboratory values: electrolyte imbalance, including hypokalaemia and hyponatraemia, hyperkalaemia, glycosuria, hyperglycaemia, increases in cholesterol and triglycerides. Legal Category: POM. Pack sizes: 7, 28 film-coated tablets. Marketing Authorisation Holder: Novartis Europharm Limited, Wimblehurst Road, Hove, East Sussex, RH12 5AB, United Kingdom. Marketing Authorisation Numbers: Rasilez HCT 300/12.5 mg - EU/1/06/491/041-060. Rasilez HCT 300/25 mg - EU/1/06/491/051-080. Please refer to Summary of Product Characteristics (SmPC) before prescribing. Full prescribing information is available on request from Novartis Pharma, P.O. Box 124, Valletta, VLT 1000, Malta. Tel +356 22983217. (2010-MF-RASHCT March 2010)

References: 1. Palinski P, Jung W, Shlyakhto E, et al. J Hum Hypertens. 2010; 24:93-103, published online 21 May 2009. 2. Villamil A, Chrysant SG, Calhoun D, et al. J Hypertens. 2007; 25:217-226

Editor's word

In this editorial I will focus on one of the biggest challenges which scientists are facing ... vaccines. Actually vaccines represent one of the most successful cost-effective medical advances of all time.

Nowadays recent advances in biotechnology (as well as the understanding of the inductive and effector components of immune responses) are invigorating the whole field of vaccinology. In fact other illnesses are now slowly but steadily becoming the new targets in this field, with the dual possibility of marketing either therapeutic vaccines (ex. oncology) or prophylactic vaccines (ex. HPV).

These new advances are basically based on either innovative antigens or the introduction of new adjuvants. We are already seeing several new plant-made vaccines being manufactured for veterinary purposes such as the Newcastle disease. However it is in this area that researchers are also eyeing what I call 'virgin platforms' ... the application of plant recombinant technology to the field of human medicine. The former has already brought about major advances in plant biology, allowing production of genetically modified (GM) plants. To be truthful, such progression has also meant headaches for key political champions ... just a few weeks ago we have seen uproars surrounding the decision of our European Commissioner for Health and Consumer Policy, John Dalli to lift a 13-year ban on the cultivation of a GM potato, called Amflora, to be used for starch by industry.

Nonetheless, such newer technologies have also enabled the development of noncrop plants (tobacco) to produce pharmaceutical molecules. This approach has major advantages in terms of speed, costs and safety. And this goes beyond the much advertised US creation of the lycopene-rich GM tomatoes which presumably protect

against prostatic cancer, way back in 2002 ... and six years later, the development by the Brits of the purple tomato, which is also rumoured to reduce cancer risk

However, an innovative application of plants as bioreactors is their use to express antigenic molecules to be administered as vaccines. Major potential advantages of producing immunogens in plant systems include the possibility of enabling the participation of less developed countries in pharmaceutical production, with an obvious emphasis on addressing local health issues. Examples of such scientific breakthrough are the recent production in tobacco of a H1N1 2009 vaccine based on the hemagglutinin (HA) protein and the initiation of clinical trials with a recombinant, plant-derived, idiosyncratic vaccine to treat B-cell lymphomas.

In case you are just saying ... Well, this is just an editorial for all its worth! ... scientists' grapevine has it that the next pandemic may quite likely be the Chikungunya virus. The virus, usually transmitted by Aedes aegypti mosquitoes, has now repeatedly been associated with a new vector, Ae. Albopictus (Asian Tiger Mosquito, seen in Malta during the past few weeks). Analysis of full-length viral sequences reveals an extremely rare phenomenon, known as evolutionary convergence. In virology, convergent mutations have been reported under the extreme selective pressure of antiviral therapy during the treatment of acute (ex. neuraminidase mutations of influenza virus) or chronic (ex. reverse-transcriptase/protease mutations of HIV) viral diseases. Apparently the selective pressure exerted on Mosquito-transmitted Chikungunya virus through the constraint of having to replicate in a new vector, is similar to that cited for antiviral therapy. And since the dispersal of the Asian Tiger Mosquito from Asia to Europe is largely the result of human activities

Published by Medical Portals Ltd.

The Professional Services Centre
Guzi Cutajar street
Dingli, Malta

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Printer - Europrint Ltd.

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(such as the commercial transportation of scrap car tyres), the adaptation of Mosquito-transmitted Chikungunya virus to the Asian Tiger Mosquito provides an incredible demonstration of how viruses can readily circumvent the impact of human interference on the ecosystem. Obviously this means that we are far from immune from future emerging arboviruses that infect humans.

Ian Ellul

Ian C Ellul



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PRESENTATION: Onbrez Breezhaler 150mcg and 300mcg inhalation powder hard capsules containing indacaterol maleate, and separate Onbrez Breezhaler inhaler. **INDICATIONS:** For maintenance bronchodilator treatment of airflow obstruction in adult patients with chronic obstructive pulmonary disease (COPD). **DOSAGE AND ADMINISTRATION:** Recommended dose is the inhalation of the content of one 150mcg capsule once a day, administered at the same time of the day each day, using the Onbrez Breezhaler inhaler. Capsules must not be swallowed. Dose should only be increased on medical advice. The inhalation of the content of one 300mcg capsule once a day has been shown to provide additional clinical benefit with regard to breathlessness, particularly for patients with severe COPD. Maximum dose is 300mcg once daily. No dose adjustment required in elderly patients, for patients with mild and moderate hepatic impairment or for patients with renal impairment. No data available for use in patients with severe hepatic impairment. No relevant use in the paediatric population. **CONTRAINDICATIONS:** Hypersensitivity to the active substance, to lactose or to any of the other excipients. **WARNINGS/PRECAUTIONS:** **Asthma:** ONBREZ BREEZHALER SHOULD NOT BE USED IN ASTHMA. **Paradoxical bronchospasm:** If paradoxical bronchospasm occurs Onbrez Breezhaler should be discontinued immediately and alternative therapy substituted. **Deterioration of disease:** Not indicated for treatment of acute episodes of bronchospasm, i.e. as rescue therapy. **Systemic effects:** Indacaterol should be used with caution in patients with cardiovascular disorders (coronary artery disease, acute myocardial infarction, cardiac arrhythmias, hypertension), in patients with convulsive disorders or thyrotoxicosis, and in patients who are unusually responsive to beta2-adrenergic agonists. **Cardiovascular effects:** Indacaterol may produce a clinically significant cardiovascular effect in some patients as measured by increases in pulse rate, blood pressure, and/or symptoms. ECG changes. In case such effects occur, treatment may need to be discontinued. **Hypokalaemia:** Beta2-adrenergic agonists may produce significant hypokalaemia in some patients, which has the potential to produce cardiovascular effects. In patients with severe COPD, hypokalaemia may be potentiated by hypoxia and concomitant treatment which may increase the susceptibility to cardiac arrhythmias. **Hyperglycaemia:** Inhalation of high doses of beta2-adrenergic agonists may produce increases in plasma glucose. Upon initiation of treatment with Onbrez Breezhaler plasma glucose should be monitored more closely in diabetic patients. During clinical studies, clinically notable changes in blood glucose were generally more frequent by 1-2% on Onbrez Breezhaler at the recommended doses than on placebo. Onbrez Breezhaler has not been investigated in patients with not well controlled diabetes mellitus. **Pregnancy and Lactation:** No data available from the use of indacaterol in pregnant women. Onbrez Breezhaler should only be used during pregnancy if the expected benefits outweigh the potential risks. Not known whether indacaterol / metabolites are excreted in human milk. A decision must be made whether to discontinue breast-feeding or discontinue Onbrez Breezhaler therapy, taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman. **INTERACTIONS:** Concomitant administration of other sympathomimetic agents may potentiate the undesirable effects of Onbrez Breezhaler. Onbrez Breezhaler should not be used in conjunction with other long-acting beta2-adrenergic agonists or medicinal products containing long-acting beta2-adrenergic agonists. Concomitant hypokalaemic treatment with methylxanthine derivatives, steroids, or non-potassium-sparing diuretics may potentiate the possible hypokalaemic effect of beta2-adrenergic agonists, therefore use with caution. Indacaterol should not be given together with beta-adrenergic blockers (including eye drops) as these may weaken or antagonise the effect of beta2-adrenergic agonists. Where required, cardioselective beta-adrenergic blockers should be preferred, although they should be administered with caution. Inhibition of the key contributors of indacaterol clearance, CYP3A4 and P-gp, does not raise any safety concerns given the safety experience of treatment with Onbrez Breezhaler. Indacaterol has not been shown to cause interactions with co-medications. **ADVERSE REACTIONS:** The most common adverse reactions with Onbrez Breezhaler are: nasopharyngitis, upper respiratory tract infection, sinusitis, diabetes mellitus and hyperglycaemia, headache, ischaemic heart disease, cough, pharyngolaryngeal pain, rhinorrhoea, respiratory tract congestion, muscle spasm, peripheral oedema. Uncommon: paraesthesia, atrial fibrillation and non-cardiac chest pain. Please refer to SmPC for a full list of adverse events for Onbrez Breezhaler. **LEGAL CATEGORY:** POM **PACK SIZES:** Onbrez Breezhaler 150mcg - carton containing 10 or 30 capsules and one Onbrez Breezhaler inhaler. Onbrez Breezhaler 300mcg - carton containing 30 capsules and one Onbrez Breezhaler inhaler. **MARKETING AUTHORISATION HOLDER:** Novartis Europharm Limited, Wimblehurst Road, Horsham, West Sussex, RH12 5AB, United Kingdom. **MARKETING AUTHORISATION NUMBERS:** EU/1/09/593/001, 002, 007. Please refer to Summary of Product Characteristics (SmPC) before prescribing. Full prescribing information is available on request from Novartis Pharma Services Inc, Representative Office P.O. Box 124, Valletta, VLT 1000 Malta. Tel: +356 22983217 2010-MT-01-ONB-16-Jun-2010

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References:
1. Cazzola M, Matera MG. Novel long-acting bronchodilators for COPD and asthma. *Br J Pharmacol*. 2008;155:291-296.
2. Novartis Europharm Ltd. Onbrez® (breezhaler®) Summary of Product Characteristics.

Issue Guide

Contributors



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Professor Albert Cilia-Vincenti MD FRCPath was Pathology Director to the Winchester & Eastleigh Healthcare Trust and Pathology Chairman, Malta Health Service. He served as London University Lecturer and was Pathology Head, University of Malta. He maintains an interest in nutritional and natural medicine and longevity, and also in wine. He is founding committee member of *il-Qatra*.



Dr Tanya Melillo Fenech MD MSc is a Public Health Specialist and Head of the Infectious Disease Prevention and Control Unit. She is mainly involved in influenza surveillance, pandemic preparedness and response, Chemical, Biological, Radiological and Nuclear (CBRN) preparedness and vector borne disease.



Dr Thomas Attard MD, FAAP, FACG is a consultant Paediatrician and Gastroenterologist at Mater Dei Hospital; he has trained at The Johns Hopkins and Creighton-UNMC SoM(US) and worked at UNMC-Omaha Children's Hospital since 2001. His research interests are Inflammatory Bowel Disease and Hereditary Polyposis Syndromes.

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Front Page

Adonis annua L. (Pheasant's eye, Ghajn is-Serduk)

Adonis annua L. is a scarce, annual, winter and spring flowering herbaceous plant which prefers disturbed ground.

Medicinal uses

It has been used in medicines as a diuretic, as a tonic to improve health, and as a cardiostimulant.

Photography: Guido Bonett ARPS AMPS
Reference: Lanfranco G. *Hxejjex medicinali u ohrajn fil-gzejjer*. Maltin. Media Centre Print; Malta. 1993.



European Society of Cardiology 2010 Clinical Practice Guidelines on Atrial Fibrillation

An Update on Classification and Pharmacotherapy

Abstract

The European Society of Cardiology guidelines published in 2010 offer an update on the previously published 2006 atrial fibrillation guidelines. The revisions are intended to optimize the understanding of the mechanisms of atrial fibrillation, and consequently the diagnosis and management of this common sustained cardiac arrhythmia, which afflicts up to 1-2% of the general population.

Ongoing research into the pathophysiology of atrial fibrillation and innovations in pharmacotherapy have forced a revised set of non-mandatory but advisory recommendations to guide clinicians and cardiologists along the challenging labyrinth which is atrial fibrillation management and diagnosis. The purpose of this synopsis is to highlight some of the most relevant changes included in the 2010 guidelines in so far as classification and pharmacotherapy of atrial fibrillation is concerned.

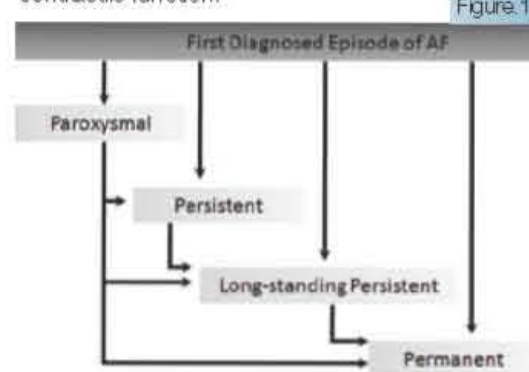
Atrial fibrillation, arrhythmia, heart failure, heart disease

Introduction

The European Society of Cardiology (ESC) guidelines published in 2010 offer an update on the previously published 2006 atrial fibrillation (AF) guidelines. The revisions are intended to optimize the understanding of the mechanisms of AF, and consequently the diagnosis and management of this common sustained cardiac arrhythmia, which afflicts up to 1-2% of the general population.¹

Mechanisms of Atrial Fibrillation

The structural remodeling that occurs in the ventricles and atria is the end result of many forms of structural heart disease. Within the atria this translates into proliferation and differentiation of fibroblasts into myofibroblasts and accumulation of surplus connective tissue with eventual fibrosis. These changes produce an electroanatomical substrate which is permissive to multiple small re-entrant circuits and which therefore permits the propagation of AF. Following the onset of AF, the atrial effective refractory period has been shown to shorten within the first days of its onset in addition to a disruption of the normal atrial contractile function.



AF clinical types

The diagram illustrates how a first diagnosed episode of AF may turn out to be any of the 4 clinical sub-types and how the AF categories are not mutually exclusive with patients having paroxysmal AF sometimes moving on to having persistent AF, so on and so forth.

AF=atrial fibrillation. Adapted from Camm AJ et al.¹

Clinical Types of AF

The 2010 ESC guidelines offer a modified nomenclature for classification of the AF clinical types (Figure

1). In particular the guidelines distinguish between:

- 1) First diagnosed AF: which represents the first ever episode of AF at the time of initial presentation irrespective of its duration or symptom severity.
- 2) Paroxysmal AF: representing AF which self-terminates within a maximum of 7 days (although in most cases self-termination occurs within the first 48 hours).
- 3) Persistent AF: representing non-self-terminating AF which either lasts longer than 7 days, or which requires pharmacological or electrical cardioversion before this time.
- 4) Long-standing Persistent AF: refers to persistent AF which has been present for ≥ 1 year before the implementation of a rhythm control strategy is contemplated.
- 5) Permanent AF: refers to established, accepted AF where both the patient and physician have opted not to pursue any rhythm control strategies.

Type and Severity of Symptoms

The 2010 guidelines place special emphasis on the presence and severity of AF-related symptoms and recommend tailoring the management of AF in such a way as to achieve maximum possible symptom relief. The European Heart Rhythm Association Score of AF-related symptoms² (Table 1) provides an unambiguous description of AF-related symptom severity.

Antithrombotic Management of AF

The CHADS₂ score (cardiac failure, hypertension, age, diabetes, stroke) risk index³ is recommended in these guidelines as a rapid and initial risk assessment tool for cerebrovascular events and transient ischaemic attacks in patients with non-valvular AF. Any patient having a score ≥ 2 will benefit from the use of chronic oral anticoagulant therapy (OAC) with a vitamin K antagonist (VKA), aiming to maintain a target international normalized ratio (INR) of 2.5, and a range of 2.0-3.0. The greatest limitation of the CHADS₂ score lies in its propensity for classifying a disproportionate number of patients within the 'grey-zone' of moderate risk for cerebrovascular events at a score of 1, thereby plunging many a physician into the much dreaded VKA-versus-aspirin conundrum.

The CHA₂DS₂-VASc score⁴ (Table 2) employs a more 'risk

Table 1

EHRA Class	Definition
EHRA Class I	No symptoms
EHRA Class II	Mild symptoms: Normal daily activity not affected
EHRA Class III	Severe symptoms: Normal daily activity affected
EHRA Class IV	Disabling symptoms: Normal daily activity discontinued

EHRA score of AF-related symptoms. Adapted from Kirchhof P et al.²

factor-based' approach to the categorization of patients with non-valvular AF and this scheme is the one most prominently campaigned for by the ESC. In patients with non-valvular AF, a CHA₂DS₂-VASc score of ≥ 2 would argue in favour of OAC therapy. One major risk factor would alone confer such a score, as would alternatively two cumulative clinically relevant but non-major risk factors. In either scenario, use of chronic OAC for thromboprophylaxis would be justified.

In summary, the guidelines recommend that with a CHADS₂ score ≥ 2 , chronic OAC therapy should be initiated, but in patients scoring a CHADS₂ of 0-1, a second more comprehensive risk scoring tool should be employed (CHA₂DS₂-VASc) to determine whether a subject benefits most from OAC as opposed to Aspirin or no antithrombotic therapy (Figure 2).

The HAS-BLED score⁵ (Table 3) is recommended as a simple bleeding risk score for AF patients, whereby a score ≥ 3 indicates high risk and calls for caution with the use of oral VKAs.

Long-term Control of Rate and Rhythm in AF

The 2010 guidelines underscore that ventricular rate control in AF is cardinal in all cases unless the heart rate during AF is naturally slow. Additionally rhythm control may be added on to rate control where the patient remains symptomatic despite adequate rate control; alternatively it may be deemed appropriate to choose rhythm control over rate control as the optimal management strategy based on factors such as younger age, symptomatology and higher activity levels. Broadly speaking, those younger patients with symptomatic paroxysmal AF in the absence of significant structural heart disease are usually earmarked for rhythm control. Conversely, patients with accepted permanent AF are usually scheduled to receive rate control with their designation changing to 'long-standing' persistent AF if a later trial of rhythm control is attempted.

A large body of evidence now exists⁶⁻¹² to dispel the archaic myth which made rhythm control the unchallenged prime end-point in AF management and which relegated rate control strategies to a lackluster division. This newly-found egalitarianism is fuelled by a new appreciation of the importance of patient-tailored therapy taking into consideration factors such as patient preference, level of physical activity and quality of life scores.

Recommended Drugs for Long-term Rate Control

• Beta-blockers

Particularly in patients with high adrenergic tone or angina in association with AF.

Recommended agents include: Metoprolol, Bisoprolol, Atenolol, Propranolol and Carvedilol.

• Non-dihydropyridine calcium channel blockers

Effective for acute and chronic rate control of AF. These drugs are to be avoided in patients with systolic heart failure in view of their negatively inotropic effect.

Recommended agents include: Verapamil and Diltiazem.

• Digoxin

Effective for heart rate control at rest but not during exercise. The potentially life-threatening adverse effects and propensity for drug interactions ascribed to digoxin dictates a cautious introduction in properly selected patient groups.

• Dronedronone

Perhaps one of the most noteworthy advances of the 2010 ESC guidelines is the inclusion of the recently approved dronedronone as an alternative rate controlling drug for

Table 2

Risk Factor	Attributable Score
Conjunctive heart failure/IV dysfunction	1
Hypertension	1
Age >75	2
Diabetes Mellitus	1
Stroke/TIA/systemic thrombo-embolism	2
Vascular disease	1
Age 65-74	1
Sex category (female sex)	1
Maximum score	9

CHA₂DS₂-VASc Scoring System.

Maximum possible score using the CHA₂DS₂-VASc Scoring System is 9.

Major risk factors are displayed inside dark grey cells.

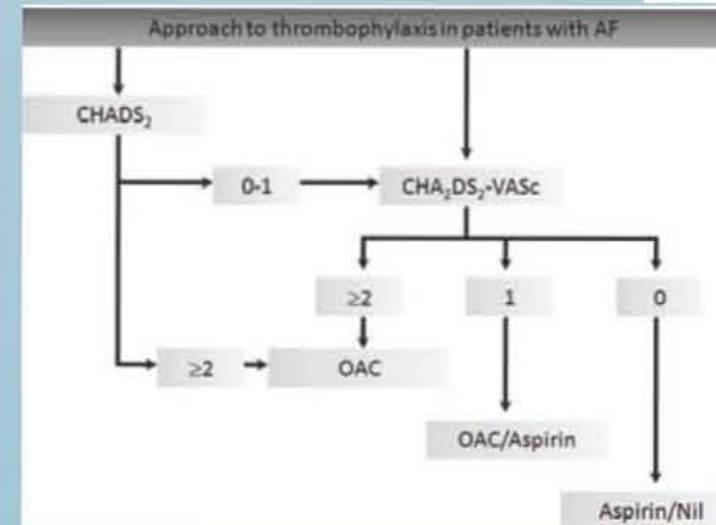
Clinically relevant non-major risk factors are displayed inside light grey cells.

Congestive heart failure is arbitrarily defined as left ventricular (LV) ejection fraction (EF) $\leq 40\%$.

Vascular disease encompasses any of: myocardial infarction, complex aortic plaque and peripheral artery disease.

LV=left ventricular; TIA=transient ischaemic attack.

Fig. 2



With a CHA₂DS₂-VASc score of 1, the recommendations are in favour of either OAC or aspirin 75-325mg daily. With a CHA₂DS₂-VASc score of 0, the recommendations are in favour of either aspirin 75-325mg daily or no antithrombotic therapy. Adapted from Camm AJ et al.¹

AF=atrial fibrillation; OAC=oral anticoagulation;

Table 3

Letter	Clinical Characteristic	Points Attributed
H	Hypertension	1
A	Abnormal Renal Function and/or Abnormal Liver Function	1
S	Stroke	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (age >65 years)	1
D	Drugs and/or Alcohol	1
	Maximum score	9

HAS-BLED score adapted from Pisters et al.⁵

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MULTAQ
Abbreviated Prescribing Information
PRESENTATION: MULTAQ[®] 400mg film-coated tablets contain 400 mg of dronedronone. INDICATIONS: MULTAQ[®] is indicated in adult clinically stable patients with a history of, or current non-permanent atrial fibrillation (AF) to prevent recurrence of AF or to lower ventricular rate. DOSAGE AND ADMINISTRATION: The recommended dose is 400 mg twice daily in adults. It should be taken as one tablet with the morning meal and one tablet with the evening meal. Grapefruit juice should not be taken together with MULTAQ. If a dose is missed, patients should take the next dose at the regular scheduled time and should not double the dose. Dose adjustments are not considered necessary in elderly patients with mild to moderate hepatic impairment or mild to moderate renal impairment. CONTRAINDICATIONS: Hypersensitivity to the active substance or to any of the excipients. 2nd or 3rd degree AV block or sick sinus syndrome (except when used with a pacemaker). Bradycardia <50bpm. Patients in unstable hemodynamic conditions including patients with symptoms of heart failure at rest or with minimal exertion (NYHA class IV and unstable class III patients). Co-administration with potent cytochrome P 450 (CYP) 3A4 inhibitors such as ketoconazole, itraconazole, voriconazole, posaconazole, telithromycin, clarithromycin, nefazodone and ritonavir. Medicinal products inducing torsades de pointes. QTc Bazett interval >500 milliseconds. Severe hepatic or renal impairment (CrCl <30ml/min). SPECIAL WARNINGS AND PRECAUTIONS FOR USE: The use of MULTAQ[®] is not recommended in stable patients with recent (1-3 months) NYHA class III heart failure or with LVEF <35%. An increase in plasma creatinine has been observed and it is recommended to measure its value 7 days after initiation. Electrolyte imbalance should be corrected before initiation and during therapy. Dronedronone may induce a moderate QTc Bazett prolongation; if it is >500 milliseconds, dronedronone should be stopped. Patients with galactose intolerance should not take this medicine. INTERACTIONS: Dronedronone is a moderate inhibitor of CYP 3A4, a mild inhibitor of CYP 2D6 and a potent inhibitor of P-glycoprotein (P-gp). The digoxin dose should be reduced by 50% and serum levels should be closely monitored. Co-administration of beta-blockers and calcium antagonists with depressant effects on sinus and atrio-ventricular node should be used with caution. Potent CYP 3A4 inducers such as rifampicin, phenobarbital, carbamazepine, phenytoin or St. John's Wort are not recommended. Statins should be used with caution. Lower starting dose and maintenance dose of statins should be considered. PREGNANCY AND LACTATION: It is not recommended during pregnancy and women of childbearing potential should use effective methods of contraception. A decision whether to continue/discontinue breast feeding or to continue/discontinue therapy should be made taking into account the benefit to the child and the benefit to the woman. EFFECT ON ABILITY TO DRIVE AND USE MACHINES: No studies have been performed. UNDESIRABLE EFFECTS: In clinical trials, premature discontinuation occurred in 11.8% of the dronedronone-treated patients and in 7.7% in the placebo-treated group. The most common reasons were gastrointestinal disorders (3.2% of patients versus 1.8% in the placebo group). Very common: Blood creatinine increased, QTc Bazett prolonged. Common: bradycardia, diarrhoea, vomiting, nausea, abdominal pain, dyspepsia, rashes (including generalised, macular, maculo-papular), pruritus, fatigue, asthenia. Uncommon: dysgeusia, erythemas (including erythema and rash erythematous), eczema, photosensitivity reaction, dermatitis allergic, dermatitis. Rare: agranulocytosis. OVERDOSEAGE: There is no specific antidote available; treatment should be supportive. MARKETING AUTHORIZATION HOLDER: Sanofi-Aventis 174, avenue de France, F-75013 Paris. MARKETING AUTHORIZATION NUMBER: EU/1/09/591/001. LEGAL CATEGORY: POM. PACK SIZES: 20 film-coated tablets. FURTHER INFORMATION IS AVAILABLE FROM: Sanofi-Aventis Malta Ltd., Triq Kari K. Prottas, B'Kara, BKR 1114 Tel 21493022/3 or www.multaq-approval.eu/composite.php

References:
1. Singh et al. New England Journal of Medicine 2007;357:987-99.
2. Hohnloser et al. New England Journal of Medicine 2009;360:666-78.
3. MULTAQ[®] Summary of Product Characteristics

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Because health matters

chronic management of AF. It effectively controls ventricular rate both at rest and during exercise with these effects being additive to those of other rate controlling drugs (Dronedronone is not currently approved for rate control in permanent AF).

Dronedronone is a multichannel blocker active at the sodium, potassium and calcium channels which is also endowed with non-competitive antiadrenergic activity.

•Amiodarone

Effective as a rate controlling agent being particularly suited for intravenous administration in the haemodynamically-ill AF sufferer. It should be considered for long term ventricular rate control only if all other measures have failed and in this context the burden of its innumerable extracardiac adverse events must be borne in mind.

Recommended Drugs for Long-term Rhythm Control

The new 2010 guidelines essentially eliminate quinidine from the rhythm controlling armamentarium of drugs and instead propose dronedronone as one of the emerging therapeutic options for achieving and maintaining sinus rhythm.

•Beta-blockers other than Sotalol

Only modestly effective in preventing recurrent AF except in the setting of thyrotoxicosis and exercise-induced, adrenergic, lone AF where they have a specific and valid role. Their use is limited by contraindications in the presence of significant left ventricular hypertrophy, systolic heart failure and pre-existing QT prolongation.

•Flecainide

Safe in the absence of structural heart disease and contraindicated for use in hearts with impaired systolic function and coronary artery disease.

•Propafenone

As for flecainide, propafenone is considered safe in the absence of structural heart disease and contraindicated for use in hearts with impaired systolic function and coronary artery disease.

•Amiodarone

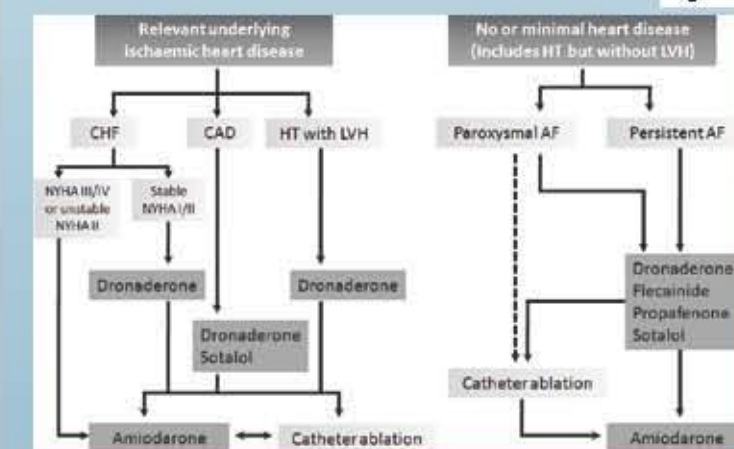
Amiodarone is superior to propafenone and sotalol at preventing recurrent AF and is particularly indicated in symptomatic sufferers where other antiarrhythmic agents have failed to maintain sinus rhythm. It is one of only a few antiarrhythmics which is not contraindicated in the presence of structural heart disease and heart failure. The attendant adverse drug reactions of amiodarone therapy together with its potential interactions with oral VKAs and digoxin beckon watchful vigilance of all patients and their doctors.

•Sotalol

Sotalol has a role in preventing recurrent AF but it's

References

- 1) Camm AJ, Kirchhof P, Lip GY, Schotten U, Savelieva I, Ernst S, et al. Guidelines for the management of atrial fibrillation: The Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). Eur Heart J. 2010 Aug 29. [Epub ahead of print] 2) Kirchhof P, Auricchio A, Bax J, Crijns H, Camm J, Diener HC, et al. Outcome parameters for trials in atrial fibrillation: executive summary. Recommendations from a consensus conference organized by the German Atrial Fibrillation Competence Network (AFNET) and the European Heart Rhythm Association (EHRA). Eur Heart J. 2007;28:2803-2817. 3) Gage BF, Waterman AD, Shannon W, Boechler M, Fitch MW, Radford MJ. Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. JAMA. 2001;285:2864-2870. 4) Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the Euro Heart Survey on atrial fibrillation. Chest. 2010;137:263-272. 5) Pisters R, Lane DA, Nieuwlaat R, de Vos CB, Crijns HJ, Lip GY. A novel user-friendly score (HAS-BLED) to assess one-year risk of major bleeding in atrial fibrillation patients: The Euro Heart Survey. Chest. 2010; March 18 [Epub ahead of print]. 6) AFFIRM Investigators. A comparison of rate control and rhythm control in patients with atrial fibrillation. N Engl J Med. 2002;347:1825-1833. 7) Van Gelder IC, Hagens VE, Bosker HA, Kingma H, Kamp O, Kingma T, et al. A comparison of rate control and rhythm control in patients with recurrent persistent atrial fibrillation. N Engl J Med. 2002;347:1834-1840. 8) Carlsson J, Mikell S, Windeler J, Cuneo A, Haun S, Mikus S, et al. Randomized trial of rate-control versus rhythm control in persistent atrial fibrillation. J Am Coll Cardiol. 2003;41:1690-1696. 9) Opolski G, Torbicki A, Kosior DA, Sulek M, Wozniakowska-Kaplon B, Kolodziej P, et al. Rate control vs. rhythm control in patients with nonvalvular persistent atrial fibrillation: the results of the Polish How to Treat Chronic Atrial Fibrillation (HOT-CAFE) Study. Chest. 2004;125:476-486. 10) Roy D, Talajic M, Nattel S, Wyse DG, Dorian P, Lee KL, et al. Rhythm control versus rate control for atrial fibrillation and heart failure. N Engl J Med. 2008;358:2667-2677. 11) Ogawa S, Yamashita T, Yamazaki T, Aizawa Y, Atarashi H, Inoue H, et al. Optimal treatment strategy for patients with paroxysmal atrial fibrillation: J-RHYTHM Study. Circ J. 2009;73:242-248. 12) Hohnloser SH, Kuck KH, Lilienthal J. Rhythm or rate control in atrial fibrillation—Pharmacological Intervention in Atrial Fibrillation (PIAF): a randomized trial. Lancet. 2000;356:1789-1794. 13) Singh BN, Connolly SJ, Crijns HJ, Roy D, Kowey PR, Capucci A, Radzik D, Alot BM, Hohnloser SH. Dronedronone for maintenance of sinus rhythm in atrial fibrillation or flutter. N Engl J Med. 2007;357:987-999. 14) Le Heuzey J, De Ferrari GM, Radzik D, Saninini M, Zhu J, Davy JM. A short-term, randomized, double-blind, parallel-group study to evaluate the efficacy and safety of dronedronone versus amiodarone in patients with persistent atrial fibrillation: the DIONOSOS study. J Cardiovasc Electrophysiol. 2010;21:597-605. 15) Kober L, Torp-Pedersen C, Malmgren JJ, Gotsche O, Levy S, Crijns H, Amle J, Carlsen J. Increased mortality after dronedronone therapy for severe heart failure. N Engl J Med. 2008;358:2678-2687.



Summary of recommendation for choice of antiarrhythmic drug therapy in AF patients with and without structural heart disease. Adapted from Camm AJ et al.¹

HT=hypertension; AF=atrial fibrillation; CHF=congestive heart failure; CAD=coronary artery disease; LVH=left ventricular hypertrophy; NYHA=New York Heart Association.

proarrhythmic adverse effects become especially taxing in patients with electrolyte abnormalities, particularly hypokalaemia and hypomagnesaemia. Unlike amiodarone it's use is considered imprudent in patients with structural heart disease and systolic heart failure.

•Dronedronone

Admittedly less effective at maintaining sinus rhythm than amiodarone^{13,14} but far less toxic to the thyroid gland, central nervous system, skin and eyes, which equates to better tolerability and a smaller incidence of premature drug discontinuation. It is contraindicated in patients with New York Heart Association (NYHA) class III/IV or more and in unstable heart failure patients but is considered safe in patients with acute coronary syndromes, chronic stable angina, hypertensive heart disease and stable NYHA class I-II heart failure (Figure 3).

Conclusion

Ongoing research into the pathophysiology of AF and innovations in pharmacotherapy have forced a revised set of non-mandatory but advisory recommendations to guide clinicians and cardiologists along the complex labyrinth which is AF management and diagnosis. The purpose of this synopsis was to highlight some of the most relevant changes included in the ESC 2010 guidelines in so far as classification and pharmacotherapy of AF is concerned, while encouraging a more insightful review of the full-text guidance offered by the ESC Committee for Practice Guidelines. For the complete guidelines visit www.escardio.org.

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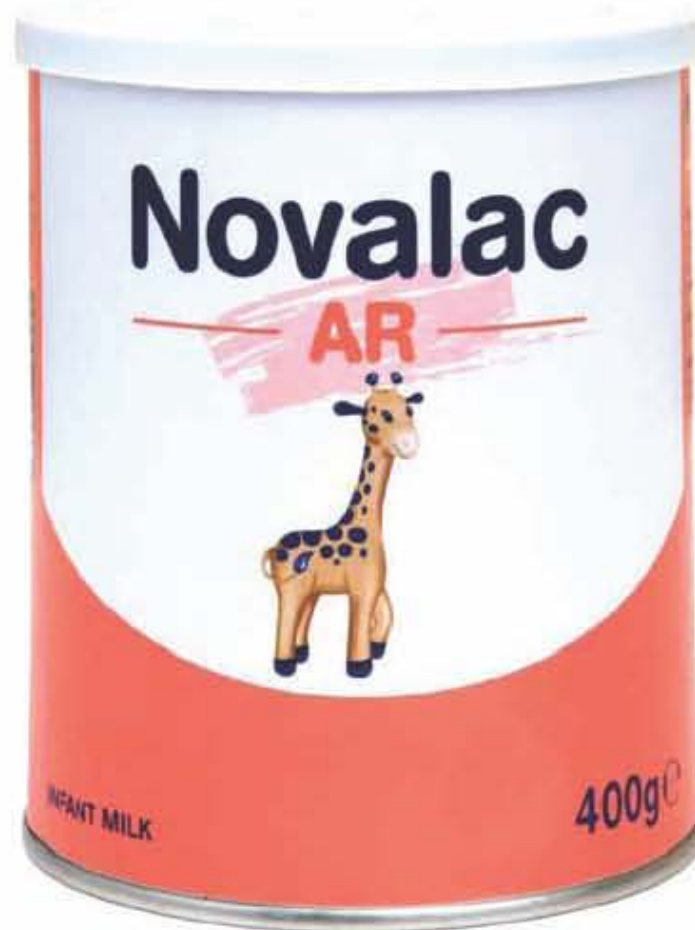
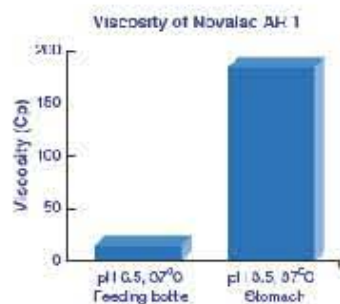
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Focus on

Pediatric Gastroesophageal Reflux Disease

One of the most common complaints referred to primary caregivers in infancy is reflux type emesis in the infant, less frequently and sometimes posing as chest pain and discomfort upon swallowing, reflux can also present in the older child and adolescent. Gastroesophageal reflux disease (GERD) can complicate the management of the child with neurodevelopmental disability wherein a more severe pattern of disease is exacerbated by delayed, sometimes atypical presentation. Moreover, even in otherwise healthy children, there is increasing recognition of non-gastrointestinal presentations of gastroesophageal reflux disease (GERD) that span the gamut from failure to thrive, dental erosion and complicated asthma.

It is important, from the outset, to distinguish physiologic reflux (GER); the passage of gastric contents into the esophagus with or without regurgitation into the mouth, which is a normal process occurring several times a day in, amongst others, healthy infants from Gastroesophageal Reflux Disease (GER); wherein refluxate causes troublesome symptoms (Table 1).

Infancy	Older Child and Adolescent
Recurrent regurgitation with/without vomiting Weight loss or poor weight gain Irritability Ruminative behavior Stridor Cough Hoarseness Apparent life-threatening events & Apnea spells Dystonic neck posturing (Sandifer syndrome) Feeding refusal Recurrent pneumonia	Bitter regurgitation Vomiting Heartburn or chest pain Hematemesis Dysphagia, odynophagia Wheezing Stridor Cough Hoarseness Recurrent pneumonia Anemia Dental erosion

Table 1. Symptoms and signs that may be associated with gastroesophageal reflux disease

GERD is a clinical diagnosis; there is no gold standard investigation, indeed in most uncomplicated cases clinical interview and examination are sufficient. This can be supplemented with an empiric therapeutic trial obviating the need for any further investigations.

There is mounting evidence to support a role of GERD in diverse disease processes including respiratory disease including recurrent pneumonia and atypical asthma, dental erosion and, with less robust evidence, upper airway complaints such as hoarseness, chronic cough, recurrent sinusitis, otitis and the sensation of a lump in the throat (globus). It is also important to bear in mind that GERD is more prevalent in obese children and is associated with greater severity of disease including the development of Barrett's Esophagus and adenocarcinoma in adults.

In cases where a diagnostic workup is needed, for example in children with atypical presentations or who are refractory to standard, or first line management, the choice for investigation falls between upper endoscopy with biopsy – which serves to rule out a gamut of alternative diagnoses based on gastrointestinal pathology (Table 2), and pH or impedance probe. Radiologic modalities such as upper gastrointestinal contrast study (barium meal) and nuclear scintigraphy scan (milk scan) are limited in scope but useful in select clinical scenarios including the need to rule out malrotation and duodenal stenosis (Barium meal – Fig 1), or reflux and aspiration or delayed gastric emptying (Milk scan).

Gastrointestinal obstruction Malrotation with intermittent volvulus Pyloric stenosis Intestinal duplication Hirschsprung disease Antral/duodenal web Foreign body Incarcerated hernia	Infectious Otitis media Metabolic/endocrine Galactosemia Congenital adrenal hyperplasia
Other gastrointestinal disorders Gastroenteritis Peptic ulcer Eosinophilic esophagitis/gastroenteritis Food allergy Inflammatory bowel disease	Renal Obstructive uropathy Cardiac Congestive heart failure Toxic / Medications Iron hypersensitivity A and D
Neurologic Hydrocephalus Migraine Intracranial mass Chiari malformation	Munchausen syndrome by proxy Cyclic vomiting syndrome Autonomic dysfunction

Table 2. Differential diagnosis of vomiting in infants and Children

Continues on page 12



Figure 1. (A) Intestinal malrotation in an 8 year-old with chronic vomiting and heartburn. (B) Achalasia in a 14 year-old girl with chronic vomiting. Previous diagnosis 'psychogenic vomiting'

The management of GERD depends on the consequences of the disease and associated conditions. Longstanding severe GER can lead to scarring and difficulty swallowing as well as transformation of the lower esophageal mucosa into premalignant, intestinal mucosa (Barrett's Esophagus). This latter is rare in children, although the presence of neurodisability and hiatus hernia may be possible risk factors.

Reassurance, education and conservative measures are all that is needed in most cases of infant GERD; lifestyle changes (Table 3) may include a switch to an antireflux formula (AR) although the presence of physiologic GER should not be construed as a justification to stop breastfeeding. First line pharmacologic therapy include the use of ranitidine 2mg/kg/dose three times daily, although locally the liquid formulation (15mg/ml) is only available through the government pharmacy. Although well established for use in infants and children, the emergence of tachyphylaxis as well as the limited acid suppression achievable with Histamine-2 Receptor Antagonists (H2RA) including ranitidine, resulted in now fairly routine use of proton-pump inhibitor agents (PPI) in this age group. Several are licensed for use in children, the usual dose is 1mg/kg / day and the most frequent, usually dose-dependent side effects are headache, diarrhea, constipation and nausea. Although unlicensed

FOR INFANTS	FOR OLDER CHILDREN
Normalize feeding volume and frequency	Avoid large meals
Consider thickened formula	Do not lie down immediately after eating
Positioning	Lose weight, if obese
Consider trial of hypoallergenic formula	Avoid caffeine, chocolate, and spicy foods that provoke symptoms
	Eliminate exposure to cigarette smoke

Table 3. Lifestyle changes for GERD

for use in infants, PPI agents are increasingly used and are generally thought to be safe although, for obvious reasons, the choice is limited to soluble formulations. The routine use of prokinetics in the long term management of GERD in children is not recommended based on the unfavourable risk-benefit relationship.

Surgical options in the management of GERD are, in most clinical scenarios, limited to the last resort. A variety of different techniques for fundoplication purport to recreate or strengthen the physiologic lower esophageal sphincter. Decreased reflux is often achievable but at the risk of several potential long term complications that tend to be more common in younger age at the time of operation and concomitant neurodisability. An alternative surgical option, especially in the latter subgroup of patients includes gastrostomy placement, which facilitates continuous (therefore low volume) feeds, and in rare cases jejunostomy feeds. Endoscopic fundoplication, which is established in adult medicine, is as yet unavailable in children.

Gastroesophageal reflux therefore emerges as a relatively common complaint in the paediatric population. In select scenarios the index of suspicion needs to be heightened and despite tremendous progress in the diagnostic modalities, investigation and treatment needs to be individualized and preferably center around conservative and safe measures.

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Soy Proteins:

metabolic effects and role in the cardiovascular prevention

Several epidemiological studies have proved that elevated plasma levels of total and, in particular, low-density lipoprotein (LDL) cholesterol are associated with an increased risk of coronary and, in general, cardiovascular events. More recently, many controlled studies undertaken with dietary or pharmacological interventions have demonstrated that reduced plasma levels of total and LDL cholesterol (LDL-C) result in a decreased incidence of such events. The risk reduction is strongly related to the magnitude of the decline in LDL-C.

An 1% decrease in plasma levels of total or LDL-C is followed, on average, by a 1% risk-reduction. Moreover, the effect on cardiovascular risk appears to be independent of the methods used to achieve a lower plasma cholesterol level.

Soy-derived protein displayed significant cholesterol-lowering activity in clinical studies that involved patients with different forms of hypercholesterolemia. Some studies reported that soy protein, when partially or fully substituted for dietary animal protein, induced a mean decrease of 22 mg/dl in LDL-C concentrations with a dosage of 20-30 g/day and a decrease of 90 mg/dl with a dosage of 30-50 g/day. The observed reduction was related to the initial plasma cholesterol concentrations, that is it was greater in subjects with established hypercholesterolemia and minor or negligible in those with baseline cholesterolemia below 230 mg/dl.

The most effective cholesterol-lowering soy component is almost certainly protein, whereas isoflavones do not appear to contribute significantly to the effects on lipid metabolism. The cholesterol-lowering effect may be attributable to the ability of soy protein to upregulate the expression of apo-B receptors.

Based on the available scientific evidence, in 1999 the US FDA released a claim that a daily dietary supplementation with four soy-protein servings (6.25 g each) may significantly reduce the risk of cardiovascular disease.

Appropriate assessment of the dietary lipid intake is also important to meet an adequate daily calcium requirement. Milk and dairy products (yogurt, cheese, and ice cream) represent the major source of calcium. This issue is crucial, in particular for women who need to prevent osteoporosis and its complications as well as to prevent coronary heart disease through the control of plasma cholesterol levels. Is therefore advisable to adopt a diet with adequate calcium content while at the same time limiting the total lipid intake. A soy based diet could be recommended.

The use of soy can also positively influence health-related parameters other than the lipid profile, such as diabetes and insulin sensitivity because the shift of calories from carbohydrates to calories from soy is currently adopted as dietary therapy for the metabolic syndrome and type II diabetes, as it reduces plasma triglyceride levels without influencing negatively plasma HDL cholesterol levels.

In overweight and obesity area the consumption of soy proteins could generate effect of satiety and in hypertensive patients the daily intake of 25 g/day could generate a 2-5 mmHg blood pressure lowering.



In conclusion the use of soy can represent an appropriate base for a nutritional strategy aimed to prevent cardiovascular diseases. The effect of such a dietary model on cholesterol levels can be enhanced, whenever necessary, by soy protein full substitution for dietary animal protein.



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References: 1.Mancia G, Laurent S, et al. *Blood Pressure* 2009;18:308-347. 2.Calhoun DA, Lacourcière Y, Chiang YT, Glazer RD. *Hypertension* 2009;54:32-36. 3.Lacourcière Y, Glazer R, Crikleair N, Yen J, Calhoun D. Poster presented at: 19th Scientific Meeting of the ESH; 12-16 June 2009; Milan, Italy. 4.Lacourcière Y, Glazer R, Yen J, Calhoun D. Poster presented at: 19th Scientific Meeting of the ESH; 12-16 June 2009; Milan, Italy.

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Exforge® HCT (amlodipine besylate /valsartan/ hydrochlorothiazide) 10/160/25mg and 10/ 320/ 25mg Film-coated tablets

PRESENTATION: Film-coated tablets containing: 10 mg amlodipine as amlodipine besylate, 160 mg valsartan and 25 mg hydrochlorothiazide or 10 mg amlodipine as amlodipine besylate, 320 mg valsartan and 25 mg hydrochlorothiazide. **INDICATION:** Treatment of essential hypertension as substitution therapy in adult patients whose blood pressure is adequately controlled on the combination of amlodipine, valsartan and hydrochlorothiazide (HCT) taken either as three single-component formulations or as a dual-component and a single-component formulation. **DOSAGE:** One tablet of Exforge HCT 10/160/25 mg or 10/320/25 mg daily. **CONTRAINDICATIONS:** • Known hypersensitivity to the active substances, to other sulfonamides, to dihydropyridine derivatives, or to any of the excipients • Second and third trimesters of pregnancy • Hepatic impairment, biliary cirrhosis or cholestasis • Severe renal impairment (creatinine clearance < 30 mL/min) • Anuria • patients undergoing dialysis • Refractory hypokalaemia • Hyponatraemia • Hypercalcaemia • Symptomatic hyperuricaemia. **WARNINGS/PRECAUTIONS:** • Risk of hypotension in sodium- and/or volume-depleted patients (correction is recommended prior to administration of Exforge HCT). • Caution is advised when administering Exforge HCT to patients with renal impairment or systemic lupus erythematosus. • No data available in patients with unilateral or bilateral renal artery stenosis, stenosis to a solitary kidney or after recent kidney transplantation • Disturbance of serum electrolyte balance (monitoring recommended), glucose tolerance and serum levels of cholesterol, triglycerides and uric acid. • Not recommended in patients below 18 years of age and in patients with primary hyperaldosteronism • Beta-blocker withdrawal should be gradual. • Caution in elderly and in patients with hepatic impairment or biliary obstructive disorders. • Caution in patients with heart failure and coronary artery disease • As with all other vasodilators, special caution in patients suffering from aortic or mitral stenosis, or obstructive hypertrophic cardiomyopathy. • If a photosensitivity reaction occurs during treatment, it is recommended to stop the treatment. • Not recommended during the first trimester of pregnancy. Avoid use in women planning to become pregnant and while breast-feeding. • Caution when driving or using machinery. **INTERACTIONS:** • Monitoring recommended when used concomitantly with lithium. • Caution when used concomitantly with drugs that may increase potassium levels. • Caution if combined with other antihypertensives, curare derivatives, NSAIDs, corticosteroids, ACTH, amphotericin, carbamazepine, Penicillin G, salicylic acid derivatives, digoxin, CYP3A4 inhibitors and inducers, antidiabetic agents, allopurinol, probenecid, sulfinpyrazone, pressor amines, amantadine, diazoxide, cytotoxic drugs, anticholinergic agents, methylidopa, cholestyramine, cholestipol resins, vitamin D, calcium salts, carbamazepine and ciclosporin, alcohol, anaesthetics and sedatives. **ADVERSE REACTIONS:** • Exforge HCT (amlodipine/valsartan/HCT): Common: hypokalaemia, headache, dizziness, hypotension, dyspepsia, poliakuria, oedema, fatigue. Uncommon: anorexia, hypercalcaemia, hyperlipidaemia, hyperuricaemia, hyponatraemia, insomnia/sleep disturbances, abnormal coordination, postural and exertional dizziness, dysgeusia, lethargy, paraesthesia, peripheral neuropathy, neuropathy, somnolence, syncope, visual disturbance, vertigo, tachycardia, orthostatic hypotension, phlebitis, thrombophlebitis, cough, dyspnoea, throat irritation, abdominal discomfort, upper abdominal pain, breath odour, diarrhoea, dry mouth, nausea, vomiting, hyperhidrosis, pruritus, back pain, joint swelling, muscle spasm, muscular weakness, myalgia, pain in extremity, elevation of serum creatinine, acute renal failure, erectile dysfunction, abasia, gait disturbance, asthenia, discomfort, malaise, non cardiac chest pain, increased blood urea nitrogen, increased blood uric acid, decreased serum potassium, weight increase. • Additional adverse reactions with amlodipine monotherapy: Common: palpitations, flushing. Uncommon: mood swings, tremor, tinnitus, rhinitis, change of bowel habit, alopecia, exanthema, purpura, skin discoloration, arthralgia, micturition disorder, nocturia, gynaecomastia, pain, weight decrease. • Additional adverse reactions with HCT monotherapy: Common: increased lipids. Uncommon: hypomagnesaemia, decreased appetite, urticaria. Rare: thrombocytopenia, hyperglycaemia, depression, arrhythmia (including bradycardia, ventricular tachycardia and atrial fibrillation), constipation, intrahepatic cholestasis, jaundice, photosensitivity reaction, renal failure and impairment, glycosuria. **LEGAL CATEGORY:** POM **PACK SIZES:** Packs of 28 film-coated tablets **MARKETING AUTHORISATION HOLDER:** Novartis European Limited, Wimblehurst Road, Horsham, West Sussex, RH12 5AB, United Kingdom. **MARKETING AUTHORISATION NUMBER:** Exforge HCT 10 mg/160 mg/25 mg - EU/1/09/569/038 Exforge HCT 10 mg/320 mg/25 mg - EU/1/09/569/050 Please refer to Summary of Product Characteristics (SmPC) before prescribing. Full prescribing information is available on request from Novartis Pharma Services Inc., Representative Office Malta, P.O. Box 124, Valletta, VLT 1000, Malta. Tel: +356 22983217 2010-MT-01-EXFH-22-Jun-2010

Focus on

Mosquito transmitted viral diseases

An update on Europe and the Mediterranean Basin

By Tanya Melillo

Mosquitoes are insects that have a particular importance in public health as they are vectors of major viral diseases like Dengue, Chikungunya and West Nile fever and can constitute a nuisance to the population.

Dengue and Chikungunya viruses are endemic in tropical countries and are transmitted by infected *Aedes* mosquitoes. During recent years, the incidence of both Dengue and Chikungunya fever has risen worldwide. There is no vaccine available for either of them and prevention relies entirely on mosquito control and personal protection. Besides the international concern over the rising worldwide incidence, there is a specific concern regarding the spread of both diseases within the European Union due to the presence in some of the Member States of the competent vector, *Aedes albopictus*.

Any cases reported from the EU up till the end of September 2010 were related to imported cases from infected travellers returning from endemic countries outside Europe such as

- All South East Asia, except Korea;
- Western Pacific Region and Pacific Islands (like Philippines, Malaysia, Vietnam, Cambodia);
- South America and the Caribbean;
- Sub-Saharan Africa.

The *Aedes albopictus* (Asian Tiger) mosquito has already been introduced into several European countries, including Belgium, Bosnia and Herzegovina, Croatia, France, Greece, the Netherlands, Serbia and Montenegro, Slovenia, Spain, Italy and Switzerland. It is thought to have occurred through the trade of used tyres (the mosquito lays eggs in pools of water in the tyres) and ornamental plants which are transported in water, such as the 'Lucky bamboo'.



The southern part of Europe is most favourable to climate and ecological conditions for the local establishment of *Aedes albopictus* and that is why since its first sighting on our islands in September 2009, over the past summer

months we have seen its presence in a number of towns. The mosquito normally emerges between May and October and it is during this time that mating and proliferation occurs. Mapping of its distribution is being monitored in Malta and Gozo. The general public is also helping the IDCU by providing IDCU with mosquito samples which are being verified by an entomologist. So far the mosquito has been found in Mellieha, Bugibba, Qawra, St. Paul's Bay, Bahar ic-caghaq, Pembroke, Swieqi, Sliema, Mosta, Bunnarad, Attard, Balzan, San Gwann, Kappara, Floriana, Valletta, St. Venera, M'scala and Kalkara.

Outbreaks of Chikungunya have occurred in Europe in the island of La Reunion (South East region of France) in 2006 which resulted in 255,000 cases and 213 deaths over a 10-month period, and in Italy in 2007 which caused 300 cases and 2 deaths over 3 months.

Till the end of September 2010, the Institut de Veille Sanitaire in France reported the first two confirmed cases of locally acquired Chikungunya on the French mainland in two 12 year old girls. This is the first time that a case has been discovered that was not imported.

Since 2005 there have also been reported imported cases of Chikungunya in Germany, UK, Belgium, Czech Republic and Norway.

No Dengue outbreaks have been reported in Europe so far but imported cases have been reported by France, UK, Italy, Spain, Greece and Slovenia. Dengue is being considered as one of the world's major emerging infectious diseases since it has become the most rapid spreading mosquito-borne viral disease in the world with a 30 fold increase in cases over the last 50 years.

In mid-September of this year, the Ministry for Health of France reported a locally acquired case of Dengue fever in Nice. This is the first locally-acquired case of Dengue fever to be reported in mainland Europe since 1928 when outbreaks were reported in Greece.

Another disease, the West Nile fever is transmitted by another mosquito vector, the *Culex pipiens* which is abundant on our island. The primary hosts are bird and horses. Outbreaks of West Nile fever has been recorded in Italy (1998, 2008, 2009) and this year in Hungary, Romania and Greece. Cases have also been reported in Portugal, France, Spain, Austria, Croatia, Czech Republic, Poland, Russia, Morocco, Tunisia and Israel.

West Nile fever is an emerging disease in southern Europe and is endemic in other parts of Europe and the Mediterranean region. The majority of West Nile fever infections (around 80%) are asymptomatic and only 20% of infected persons will develop mild symptoms with less than 1 % developing a severe neurological syndrome of meningitis and/or encephalitis.



Broad protection against rotavirus gastroenteritis (RGE) caused by the 5 most common circulating rotavirus types^{1,2}

RotaTeq 

(Rotavirus Vaccine, Live, Oral, Pentavalent)



RotaTeq is indicated for the active immunisation of infants from the age of 6 weeks for prevention of gastroenteritis due to rotavirus infection.

In clinical trials, efficacy was demonstrated against gastroenteritis due to rotavirus of serotypes G1P1[8], G2P[4], G3P1[8], G4P1[8], and G9P1[8].

Vaccination with RotaTeq may not result in complete protection in all recipients.

The most commonly reported adverse experiences with RotaTeq (frequency >1/10) include pyrexia, diarrhoea and vomiting.

RotaTeq should not be administered to individuals with hypersensitivity to any component of the vaccine.

No safety or efficacy data are available from clinical trials regarding the administration of RotaTeq to immunocompromised patients, those receiving immunosuppressive therapy, individuals infected with HIV, or individuals who have received a blood transfusion or blood products within 42 days of vaccination. Cases of gastroenteritis associated with vaccine virus have been reported post marketing in infants with severe combined immunodeficiency (SCID).

Before administering RotaTeq, please read the full Prescribing Information.

References: 1. Data on file, MSD, Middle East offices. 2. Centers for Disease Control and Prevention (CDC). Rotavirus Surveillance — Worldwide, 2001–2008. *MMWR Morb Mortal Wkly Rep*. 2008;57(46):1255–1257.

Consider the results. Choose RotaTeq.



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ROTATEQ® Rotavirus vaccine (live, oral)
ABRIDGED PRODUCT INFORMATION
Please refer to Summary of Product Characteristics (SPC) before prescribing

PRESENTATION

Oral Solution

2 ml solution in a pre-filled squeezable tube (LDPE), with a twist-off cap (HDPE) in a protective bag, pack size of 1

One 2-ml dose contains:

rotavirus serotype* G1 not less than 2.2 x 10⁶ IU1, 2
rotavirus serotype* G2 not less than 2.8 x 10⁶ IU1, 2
rotavirus serotype* G3 not less than 2.2 x 10⁶ IU1, 2
rotavirus serotype* G4 not less than 2.0 x 10⁶ IU1, 2
rotavirus serotype* P1[8] not less than 2.3 x 10⁶ IU1, 2
* human-bovine rotavirus reassortants (live), produced in Vero cells.

¹ Infectious Units

² As lower confidence limit (p = 0.95)

Excipient:

This product contains sucrose 1080 mg

USES: RotaTeq is indicated for the active immunisation of infants from the age of 6 weeks for prevention of gastroenteritis due to rotavirus infection. In clinical trials, efficacy was demonstrated against gastroenteritis due to rotavirus of serotypes G1P1[8], G2P[4], G3P1[8], G4P1[8], and G9P1[8]. The use of RotaTeq should be in accordance with official recommendations.

DOSAGE AND ADMINISTRATION. Posology:

Three doses of RotaTeq should be administered.

The first dose may be administered from the age of six weeks and no later than the age of 12 weeks. RotaTeq may be given to infants who were born prematurely provided that the period of gestation was at least 25 weeks. These infants should receive the first dose of RotaTeq at least six weeks after birth. There should be intervals of at least 4 weeks between doses. It is preferable that all three doses should be administered before the age of 20-22 weeks. All three doses should be given by the age of 26 weeks. As no data exist regarding the interchangeability of RotaTeq with another rotavirus vaccine, it is recommended that infants who receive RotaTeq for the first immunisation against rotavirus should receive this same vaccine for the subsequent doses. If it is observed or strongly suspected that an incomplete dose has been swallowed (e.g., infant spits or regurgitates the vaccine), a single replacement dose may be given at the same vaccination visit, however, this has not been studied in clinical trials. If the problem recurs, additional replacement doses should not be given.

No further doses are recommended after completion of the 3-dose series. Method of administration: For oral administration only. RotaTeq SHOULD UNDER NO CIRCUMSTANCES BE INJECTED. RotaTeq may be given without regard to food, liquid, or breast milk.

CONTRA-INDICATIONS:

- Hypersensitivity to the active substance or to any of the excipients.
- Hypersensitivity after previous administration of rotavirus vaccines.
- Previous history of intussusception.
- Subjects with congenital malformation of the gastrointestinal tract that could predispose to intussusception.
- Infants who have known or suspected immunodeficiency. Asymptomatic HIV infection is not expected to affect the safety or efficacy of RotaTeq. However, in the absence of sufficient data, administration of RotaTeq to asymptomatic HIV subjects is not recommended.
- Administration of RotaTeq should be postponed in infants suffering from acute severe febrile illness.
- The presence of a minor infection is not a contraindication for immunisation. The admin-

istration of RotaTeq should be postponed in subjects suffering from acute diarrhoea or vomiting.

PRECAUTIONS

No safety or efficacy data are available regarding administration of RotaTeq to immunocompromised infants, infants infected with HIV or infants who have received a blood transfusion or immunoglobulins within 42 days of dosing. In trials, RotaTeq was shed in the stools of 8.9 % of vaccine recipients almost exclusively in the week after dose 1 and in only one vaccine recipient (0.3 %) after dose 3. Peak excretion occurred within 7 days of dosing. It is theoretically possible that transmission of vaccine virus may occur to seronegative contacts. RotaTeq should be administered with caution to individuals with close contacts who are immunodeficient (e.g., individuals with malignancies or who are otherwise immunocompromised or individuals receiving immunosuppressive therapy). Also, those caring for recent vaccinees should observe careful hygiene especially when handling excreta. In a clinical study, RotaTeq was administered to approximately 1,000 infants who were born at a gestational age of 25 to 36 weeks. The first dose was administered from 6 weeks after birth. The safety and efficacy of RotaTeq were comparable between this subset of infants and infants born at term. Safety or efficacy data are not available for infants with active gastrointestinal illnesses (including chronic diarrhoea) or growth retardation. Administration of RotaTeq may be considered with caution in such infants when, in the opinion of the physician, withholding the vaccine entails a greater risk. The level of protection provided by RotaTeq is based on the completion of all 3 doses. As with any vaccine, vaccination with RotaTeq may not result in complete protection in all recipients. RotaTeq does not protect against gastroenteritis due to other pathogens than rotavirus. No clinical data are available on the use of RotaTeq for post-exposure prophylaxis. RotaTeq contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take this vaccine. The potential risk of apnoea and the need for respiratory monitoring for 48-72h should be considered when administering the primary immunisation series to very premature infants (born ≤ 28 weeks of gestation) and particularly for those with a previous history of respiratory immaturity. As the benefit of vaccination is high in this group of infants, vaccination should not be withheld or delayed. Co-administration of RotaTeq with vaccines containing one or more of the following antigens at approximately 2, 4 and 6 months of age demonstrated that the immune responses and the safety profiles of the administered vaccines were unaffected: Diphtheria-tetanus-acellular pertussis vaccine (DTaP), Haemophilus influenzae type b vaccine (Hib), Inactivated poliovirus vaccine (IPV), Hepatitis B vaccine (HBV) and Pneumococcal conjugate vaccine (PCV). Co administration of RotaTeq with DTaP-IPV-HBV-Hib vaccine (Infanrix hexa) at approximately 2, 3, and 4 months of age demonstrated that the immune responses and the safety profiles of the co administered vaccines were unaffected compared to separate administrations. Co administration of RotaTeq with a group C meningococcal conjugate vaccine (MenCC, the vaccine studied was a tetanus toxoid conjugate) at 3 and 5 months of age (and mostly at the same time as DTaP-IPV-Hib vaccine), followed by a third dose of RotaTeq at approximately 6 months of age, demonstrated that the immune responses to RotaTeq and MenCC were unaffected. Co administration resulted in an accept-

able safety profile. Concomitant administration of RotaTeq and oral poliomyelitis vaccine (OPV) did not affect the immune response to the poliovirus antigens. Although concomitant administration of OPV slightly reduced the immune response to rotavirus vaccine, there is currently no evidence that clinical protection against severe rotavirus gastroenteritis would be affected. The immune response to RotaTeq was unaffected when OPV was administered two weeks after RotaTeq. Therefore, RotaTeq can be given concomitantly with monovalent or combination infant vaccines containing one or more of the following antigens: DTaP, Hib, IPV or OPV, HBV, PCV and MenCC.

Pregnancy and lactation: RotaTeq is intended for use in infants only. Thus human data on use during pregnancy or lactation are not available and animal reproduction studies have not been performed. SIDE

EFFECTS: Refer to SPC for complete information on side effects

In a subset of infants from 3 placebo-controlled clinical trials (n=6,130 recipients of RotaTeq and 5,560 placebo recipients), RotaTeq was evaluated for all adverse events within 42 days of vaccination with or without concomitant use of other paediatric vaccines. Overall, 47 % of infants given RotaTeq experienced an adverse reaction compared with 45.8 % of infants given placebo. The most commonly reported adverse reactions that occurred more frequently with vaccine than with placebo were pyrexia (20.9 %), diarrhoea (17.6 %) and vomiting (10.1 %). Adverse reactions more common in the vaccine group are listed below per system organ class and frequency. Based on pooled data from 3 clinical trials in which 6,130 infants received RotaTeq and 5,560 received placebo, the adverse reactions listed occurred with excess incidences in RotaTeq recipients compared to placebo recipients of between 0.2 % and 2.5 %.

Infections and infestations

Common: Upper respiratory tract infection

Uncommon: Nasopharyngitis

Gastrointestinal disorders

Very common: Diarrhoea, Vomiting

Uncommon: Abdominal pain upper

Skin and subcutaneous tissue disorders

Uncommon: Rash

General disorders and administration site conditions

Very common: Pyrexia

Intussusception

The risk of intussusception has been evaluated in a placebo-controlled study in infants. During the combined 42-day periods following each dose, there were 6 cases of intussusception in 34,837 recipients of RotaTeq compared with 5 cases in 34,788 placebo recipients.

Post-marketing reports

The following adverse experiences have been spontaneously reported with RotaTeq: haematochezia, urticaria and apnoea in very premature infants (≤ 28 weeks of gestation).

Marketing Authorisation Number:

EU/1/06/348/001

Marketing Authorisation Holder:

Sanofi Pasteur MSD, SNC 8, rue Jonas Salk, F-69007 LYON, France

RotaTeq is a registered trademark of Merck & Co., Inc., Whitehouse Station, NJ, USA

POM

Date of review of prescribing information: June 2009

There is more to TheSynapse than just



MedClub Card news

Over the past weeks, many Synapse members have been receiving their MedClub membership card. Please call us on 21453973 if you have applied to become a Medclub member but did not receive your membership card yet.

We are delighted to inform the MedClub members that we have secured further offers exclusive for them.

- **Air Malta** is offering MedClub Members 10% discount when using Air Malta scheduled Services (excluding promotional offers). More details will be announced on TheSynapse Portal in the coming weeks.
- **Corinthia Hotels** are offering 20% discount off Corinthia™ Hotels Best Availability Rate on bookings made directly through www.corinthia.com. To benefit from the discount, MedClub Members must simply present their MedClub card on check-in at any Corinthia Hotel and the discount will be immediately applied to their hotel bill.
- **Tuaco Opticians** are offering 10% discount on Optical Frames, lenses, sunglasses as well as sighted sunglasses, and a 5% discount on contact lenses and contact lens solutions. They are also offering an exclusive 15% discount on high quality designer frames including the brands Prada, Dolce & Gabbana, Salvatore Ferragamo as well as Versace.
- **Bridgestone Tyre Center** in Marsa is offering 10% discount.

These add to the offers that The Synapse has already secured from:

- **Vodafone** - unbeatable packages being offered exclusively to MedClub members;
- **The Athenaeum Spa** - 20% when purchasing a 6 month or annual membership;
- **BDL Bookshop** - 15% off online orders with free delivery;

More information on these offers will be announced on The Synapse Portal in the coming weeks. The list of MedClub Benefits is always growing so join as a MedClub member and enjoy these discounts too.

Please visit www.thesynapse.net/medclub to apply for your free membership



Members' Corner

COMPETITION CORNER - ISSUE 4/10

This month's Challenge answers

1. What was the biblical name which featured in the Wine Expectations article's quote?
2. The prize given to the first drawn name of the Update and Win quizz was 2 tickets to the Elton John concert?

The winners are: TO BE changed

1st prize - **Ms. Graziella Gravino** (2 tickets to the Wintermoods concert)

2nd prize - **Dr. Michael Refalo** (1 day membership to the Corinthia Athenaeum Spa, Attard)

3rd prize - **Dr. David Muscat** (1 day membership to the Corinthia Athenaeum Spa, Attard)

TheSynapse team would like to congratulate the winners and thank the sponsors of these competitions.



THIS MONTH'S CHALLENGE

The answers to all questions can be found in issue 3/10. Those who get a correct answer will participate in a draw where the first two drawn names will each win a 1 day membership to the Corinthia Athenaeum Spa, Attard.

1. What was the name of the nurse who came up with the idea of the contraceptive pill?

2. Name one disease transmitted by the Asian Tiger Mosquito Yes / No

Kindly submit the answers by mail by filling the form on this page addressed to The Professional Services Centre, 3 Guzi Cutajar Street, Dingli, DGL 1201 or submit your answers on-line on www.thesynapse.net/quizz. All submissions will participate in a draw. You have up to the 7th November 2010 to submit your answers.

Fill in your details

Name

Address

Email

Mobile

Opportunities

Managing pharmacist Vacancy

Mondays to Thursdays mornings And Friday and Saturday mornings and evenings

Clinic Space available in the morning, Safi Pharmacy

New clinic with all amenities is available in the mornings. Please phone 79060903

Locum Pharmacist Required

Locum Pharmacist required to work two afternoons on a regular basis for St Joseph Pharmacy in Mosta. Any enquiries can be made by phoning 79417593.

Attention Doctors, Consultants and other Medical Specialists

Medical Plaza San Gwann requires the services of locum pharmacists evenings weekdays immediately and Saturdays between 1 and 4 pm as from end December. Kindly contact Ingrid Fenech on 21372195, 21377157 or 99371724.

Attention Doctors, Consultants and other Medical Specialists

Clinic space available in a central locality, adjacent to a Busy Pharmacy in the village core. No rental fee. For more information please call 79861544 or 21820795

Locum Pharmacist Required

Opportunity has arisen for a third general practitioner to work out of an established and busy clinic in the north harbour region. Attending also are a number of specialists and therapists, offering a wide spectrum of services to our clients and enabling an efficient and multidisciplinary approach. Kindly contact me on dwardu@yahoo.com

Current / Upcoming Events

Influenza Vaccine Campaign – log on <http://www.thesynapse.net/articles/viewarticle.asp?artid=12529>

Looking for Melanoma Campaign – log on <http://www.thesynapse.net/articles/viewarticle.asp?artid=12397> or contact Dr Joseph Pace for a free referral on guzeppip@gmail.com OR josephpace@onvol.net. Terms & conditions apply.

Breast Cancer Awareness Campaign – log on <http://www.sahha.gov.mt/pages.aspx?page=318>

Prescribing Humour in Healthcare: and I ain't kiddin! Lectures at Mater Dei Hospital – log on <http://www.thesynapse.net/events/view.asp?eventID=114>

TheSynapse

14th Birthday



In 1996, the plan was clear. It is all proven by a carefully laid out brochure penned way back in preparation for the official launch which happened precisely on October 18th, 1996. The Synapse was in the pipeline, it happened and it's still going strong. Two great friends, Dr Gauden Galea and Dr Wilfred Galea most certainly had foresight when they mapped out what a successful medical professional's network should include.

Fast forward to 2010 and 14 years since its inception, The Synapse can happily tick off a great many of its original targets. Dr Wilfred Galea who has been at the steering wheel since 1998 says, "It is kind of strange to read what we wrote in this brochure in 1996. We certainly had foresight – that of fostering a community and a vision of creating a link between members of professional bodies, academics and corporate businesses. Internet was still in its swaddling clothes back then, but we were perceptive of its potential in facilitating communication."

The concept of providing a constantly updated, inexpensive and professional publication supported by the attention of a bevy of serious visitors and not merely casual passersby took off big time. And today, on the verge of launching a new look and feel to TheSynapse web portal, Wilfred is confident that the future holds even more potential in store.

"We currently supply daily updates on Maltese and international news from the medical world, details on upcoming conferences and fora, new books, locum posts, etc - it is in fact an efficient service designed specifically for busy people. We compliment this with the publication of The Synapse magazine and as always this is all openly and freely available to professionals from the medical field, specifically doctors, pharmacists, dentists and students of these professions."

Dr Galea, a busy family doctor as his main profession, has an effective team of similarly enthusiastic people

working on this project. Whereas in 1996 it was a small, two person team, today, the team is made up of programmers, editors, scientific editors, marketing and administration staff – a fully fledged medical media company with a strong research and development focus and with a pipeline of planned innovations stretching for at least the coming two years. The Synapse today boasts of over 3000 members, 2000 of whom are Maltese. "The audience is actually very international with a wide range of countries passing through. I am constantly impressed by what some people manage to do online – even more so when connecting with people beyond our immediate European confines. People who interact through The Synapse are a boon to the system, helping to bring down barriers which are easily created through a quest for individualism."

And to answer the 'What's in it for users?' question, The Synapse not only supplies a wide range of important information, but also helps promote local and

foreign medical-related events. "Our professionalism has also helped us clinch deals from huge companies for our members – all benefits that can be obtained when members use their MedClub Card"

Dr Galea continues, "We are launching a redesigned version of the portal and the emphasis will be on increased user interaction. Specifically we want to provide information on where members can share educational resources – this is particularly aimed at students from the first year of their undergraduate career to about 95 years post graduate! The aim is to allow members to upload and share useful material between them."

The Synapse - For further details contact editor@thesynapse.net or visit <http://www.thesynapse.net>

A generation of girls and young women is depending on you to vaccinate with SILGARD™



SILGARD—the cervical cancer vaccine that helps prevent HPV^a-related:

Cervical cancer

Genital warts

Vulvar lesions

Vaginal lesions

^aHPV=Human Papillomavirus.

Silgard is a vaccine for the prevention of premalignant genital lesions (cervical, vulvar and vaginal), cervical cancer and external genital warts (condyloma acuminata) causally related to Human Papillomavirus (HPV) types 6, 11, 16 and 18.

The indication is based on the demonstration of efficacy of Silgard in adult females 16 to 26 years of age and on the demonstration of immunogenicity of Silgard in 9- to 15-year old children and adolescents. Protective efficacy has not been evaluated in males.

The use of Silgard should be in accordance with official recommendations.

SILGARD is contraindicated in individuals who are hypersensitive to the active substances or to any of the excipients of the vaccine. Individuals who develop symptoms indicative of hypersensitivity after receiving a dose of SILGARD should not receive further doses of SILGARD.

SILGARD is not recommended for use in pregnant women.

Common adverse reactions that were observed include fever and injection-site erythema, pain, swelling, and pruritus. Syncope, sometimes associated with falling, has occurred after vaccination with SILGARD.

Vaccination with SILGARD may not result in protection in all vaccine recipients.

This vaccine is not intended to be used for treatment of active genital warts; cervical, vulvar, or vaginal cancers; cervical, vulvar, or vaginal intraepithelial neoplasias.

This vaccine will not protect against diseases that are not caused by HPV.

Before administering SILGARD, please consult the full Prescribing Information.

Use of Silgard
 Human Papillomavirus (HPV) Types 6, 11, 16, 18 (Recombinant, adjuvanted).
 ADJUVANT: ALUMINUM PHOSPHATE (ALPHATEC) (see Prescribing Information).
 Refer to Summary of Product Characteristics (SPC) before prescribing.
PREVENTION: Silgard is a vaccine for the prevention of premalignant genital lesions (cervical, vulvar and vaginal), cervical cancer and external genital warts (condyloma acuminata) causally related to Human Papillomavirus (HPV) types 6, 11, 16 and 18. The vaccine is based on the demonstration of efficacy of Silgard in adult females 16 to 26 years of age and on the demonstration of immunogenicity of Silgard in 9- to 15-year old children and adolescents. Protective efficacy has not been evaluated in males. The use of Silgard should be in accordance with official recommendations (see Prescribing Information). The primary vaccination series consists of 3 separate 0.5 mL doses administered according to the following schedule: 0, 1, 2 months. For alternate vaccination schedule, it is necessary that the second dose should be administered at least 1 month after the first dose and the third dose should be administered at least 3 months after the second dose. All three doses should be given using a 1 mL syringe. The vaccine is a suspension and has not been evaluated in immunocompromised individuals. There is no contraindication to the use of Silgard in children before 9 years of age. The vaccine should be administered by intramuscular injection. The preferred site is the deltoid area of the upper arm or the thigh. Silgard may be given to immunocompromised individuals. Further administration may be necessary. The vaccine should be given to individuals who are not immunocompromised. The vaccine is not recommended for use in pregnant women. The vaccine is not recommended for use in individuals who are hypersensitive to the active substances or to any of the excipients of the vaccine. Individuals who develop symptoms indicative of hypersensitivity after receiving a dose of Silgard should not receive further doses of Silgard. Silgard is not recommended for use in pregnant women. Common adverse reactions that were observed include fever and injection-site erythema, pain, swelling, and pruritus. Syncope, sometimes associated with falling, has occurred after vaccination with Silgard. Vaccination with Silgard may not result in protection in all vaccine recipients. This vaccine is not intended to be used for treatment of active genital warts; cervical, vulvar, or vaginal cancers; cervical, vulvar, or vaginal intraepithelial neoplasias. This vaccine will not protect against diseases that are not caused by HPV. Before administering Silgard, please consult the full Prescribing Information.

SILGARD is a trademark of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Whitehouse Station, NJ, U.S.A.



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SILGARD.
[Quadrivalent Human Papillomavirus
(Types 6, 11, 16, 18) Recombinant Vaccine]

11-09 GRD-2008-MVD-1273400-J
 01-2012-GRD-2009-ME-(CY-MQ)-1052-J

Focus on

Bacterial Vaginosis

What is its significance in cervical smear cytology reports?

A frequent bacterial vaginosis (BV) diagnosis, or suggested BV diagnosis, in cervical smear cytology reports is a relatively recent phenomenon, and is probably a source of confusion and concern to both doctors and their patients.

In the past, the same microscopic diagnosis used to be referred to as "clue cells", and I wonder how many doctors understood the clinic significance of this pathological jargon. I have always been totally averse to pathology reports worded in jargon understandable only to pathologists rather than by the recipient of the surgical pathology report, namely, the clinician looking after the patient.

Diagnostic cytology was established and developed by cytologists with no experience of histopathology, and they invented their own nomenclature, often using Greek words, like koilocytosis and dyskaryosis, well before the underlying nature of the pathology was fully understood. Koilocytosis, for example, was coined in the 1950s and regarded as a type of dysplasia, almost 30 years before the causative Human Papilloma Virus (HPV) infection was established. At that stage, the distinction between HPV changes and Cervical Intraepithelial Neoplasia (CIN) was unknown. I personally see no point in using antiquated jargon instead of "HPV" and "CIN" nomenclature which is clearly understood by modern clinicians. The same applies, I feel, to complicated American cervical smear reporting nomenclature, which tries to sound cleverer than others, but actually achieves nothing better than simply using "HPV" and "CIN" diagnostic labels.

But let's get back to BV. This was largely unrecognised by cervical smear reporters until relatively recently. Laboratory staff were also unaware of the connection between this microscopic diagnosis and possible clinical symptoms. As laboratories increasingly diagnosed, or suggested, the presence of BV, patients and some doctors have become concerned, both about the frequency of this diagnosis, and also about its clinical significance.

Of primary importance is reassuring patients that BV is not a sexually-transmitted disease (virgins may acquire it), although it is commoner in the sexually active. It is caused by an imbalance of naturally-occurring bacterial flora, whereby normal lactobacilli are partly or completely replaced by a variety of mainly anaerobic organisms, and vaginal discharge changes from acidic to alkaline.

Bibliography

- Bradshaw CS et al. High recurrence rates of bacterial vaginosis over the course of 12 months after oral metronidazole therapy and factors associated with recurrence. J Infect Dis 2006; 193(11):1478-88.
 Verstraeten H et al. Subclinical iron deficiency is a strong predictor of bacterial vaginosis in early pregnancy. BMC Infect Dis 2005; 5:55.
 Narsel TR et al. The association of psychosocial stress and bacterial vaginosis in a longitudinal cohort. Am J Obst. Gynecol 2006; 194(2):381-6.

BV is the commonest cause of abnormal discharge and up to 30% of women are thought to be affected. The prevalence in pregnant women is said to be even higher. The exact mechanisms of acquiring BV are not fully understood. Having a new sex partner, or multiple sex partners, and douching increase the risk. The mechanisms here might simply be too frequent exposure to alkaline seminal fluid, and the acidity diminishing effect of douching. Similarly, changes in hormonal status during the menstrual cycle, during the peri-menopause and menopause, and those caused by oral or intrauterine contraceptive hormones, would be expected to affect vaginal pH, and might be the triggering mechanism in these situations. In pregnancy, besides hormonal changes in the vaginal epithelium, subclinical iron deficiency anaemia might be another mechanism encouraging BV. Psychological stress has also been claimed to increase the risk.

The commonest symptom of BV is an abnormal homogenous thin whitish-grey vaginal discharge with an unpleasant fishy smell. However, most women report no signs or symptoms, while some do complain of dysuria and/or localised itching, pain and erythema, besides the foul discharge.

The possible complications of BV include increased susceptibility to sexually-transmitted infections (herpes, Chlamydia, gonorrhoea and HIV) and pelvic inflammatory disease with its possible long-term consequences (infertility and ectopic pregnancy), increased risk of infection following hysterectomy or abortion, and increased risk of preterm delivery.

But does cervical smear-reported BV require treatment? BV will sometimes clear up spontaneously, but all women with symptoms of BV should be treated to avoid complications. Male partners are said not to need treatment, but BV may spread between female sex partners.

Treatment is particularly important in pregnant women. A history of premature delivery or low birth weight should elicit an examination for BV. Some recommend treatment for BV in all women undergoing hysterectomy regardless of symptoms. Metronidazole or clindamycin are recommended for treating BV. Both can be used in non-pregnant women but caution should be exercised in pregnant ones. The recommended dosages differ in these two scenarios. BV may recur after treatment, and patients should be advised to take all the medicine prescribed even if the signs and symptoms abate.

The Therapeutic Effects of Dead Sea Mineral-Based Skincare

By Allistair Mallia

Dead Sea mineral-based skincare can be considered a unique part of the 'Sea' cosmetic trend. The sea as a natural source of healing is quite an old concept. In 1750 Richard Russell presented his thesis on the Therapeutic Effect of Seawater at Oxford. And in 1869 the term thalassotherapy, or "bringing together the sea and medicine" was coined by the French physician LaBonardier d'Arachon.

More than 40 different skincare brands based on Dead Sea minerals are sold worldwide. The success of Dead Sea products and the increasing consumer expectations can be attributed to quantifiable consumer satisfaction surveys. These include mineral content, active and natural ingredients, doctor recommendations and their healing capabilities for healthier skin.

A cosmetic product as defined by European Council Directive 76/768/EEC, is "any substance or preparation intended for placing in contact with the various external parts of the human body... with the intention, exclusively or principally of cleaning, perfuming or protecting to keep such parts in good condition, change their appearance or correct body odours." Skincare claims today have moved from the "care" claims originally envisaged by the Directive to "prevention", "protection" and even "healing" claims which are permitted. The 1997 "6th Amendment" however obliges cosmetic producers and marketers to scientifically prove their declared performance claims.¹

The composition of Dead Sea minerals is unique. At a concentration of 32% (w/v) dissolved minerals, the Dead Sea is the richest natural mineral source in the world. The concentration of the divalent cations, magnesium and calcium is very high compared with the monovalent cations, mainly sodium and potassium. In addition, the ionic strength of the solution is very high. Upon

application to skin, a concentration cascade is created with unique absorption kinetics characterized by a steep gradient into the multilayered bio-membrane, that is human skin. The hygroscopic properties of the minerals in turn, enhance intracellular water capacity and add water to the skin tissue from within. This explains the proven positive influence of Dead Sea mineral skincare on the skin's natural moisture content and its beneficial action on eczematous and atopic skin.²

Another common claim of Dead Sea mineral skincare relates to its smoothing effect on skin aged by environmental exposure and senescence. Blinded laser profilometric studies conducted by European dermatologic research institutes, in accordance with the ISO 4287/1, have confirmed that anti-wrinkle gels enriched with Dead Sea ingredient reduce wrinkle depth and skin roughness by more than 40% in female cohorts.³

The unique black hypersaline mud mined from the Dead Sea shores is extensively used in mud packs, masks and topical body and facial treatments in skincare preparations marketed worldwide. The mud has well-documented beneficial properties on, notably, psoriatic and acneic skin. In microbiological studies using conventional bacteriological media, high counts (up to 20,000 colonies per gram) of test microorganisms known to be skin pathogens (*Escherichia coli*, *Staphylococcus aureus*, *Propionibacterium acnes*, *Candida albicans*) rapidly lost their viability when added to plates treated with Dead Sea mud.⁴ This mud also has protective anti-oxidant and anti-inflammatory properties that can antagonize biological the effects of UVB irradiation on skin. It may therefore be able to reduce skin photoaging, and more generally to reduce oxidative stress and inflammation in skin pathologies.⁵

Bibliography

1. http://ec.europa.eu/consumers/sectors/cosmetics/documents/directive/index_en.htm 2. Ma'or Z, Maglassi S, Efron D, Yehuda S. Dead Sea Mineral-Based Cosmetics - Facts and Illusions. *Int J Med Sci*. 1996; 32(suppl 3):28-36. 3. Ma'or Z, Voss W. Skin smoothing effects of Dead Sea minerals: comparative profilometric evaluation of skin surface. *International Journal of Cosmetic Science* 1997; 19(1): 4. Ma'or Z, Henis Y, Alon Y et al. Antimicrobial properties of Dead Sea black mineral mud. *International Journal of Dermatology* 2006; 45(5):504-11. 5. Portugal-Cohen M, Soroka Y, Ma'or Z et al. Protective effects of a cream containing Dead Sea minerals against UVB-induced stress in human skin. *International Journal of Dermatology* 2009; 19(3):781-8.

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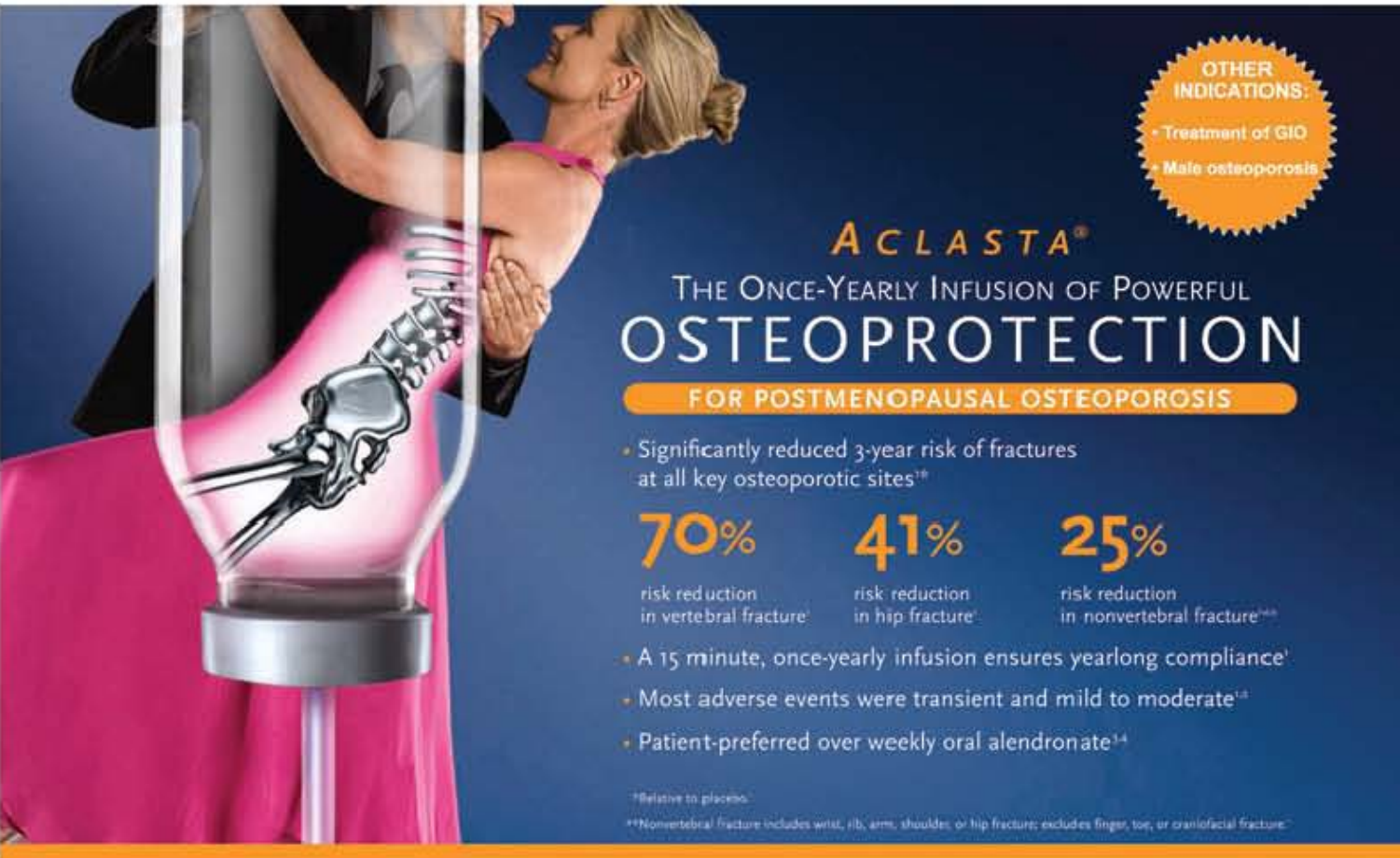
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FOR POSTMENOPAUSAL OSTEOPOROSIS

- Significantly reduced 3-year risk of fractures at all key osteoporotic sites^{1*}

70%	41%	25%
risk reduction in vertebral fracture ²	risk reduction in hip fracture ²	risk reduction in nonvertebral fracture ^{2,3*}

- A 15 minute, once-yearly infusion ensures yearlong compliance⁴
- Most adverse events were transient and mild to moderate^{1,4}
- Patient-preferred over weekly oral alendronate^{1,4}

*Relative to placebo.
**Nonvertebral fracture includes wrist, rib, arm, shoulder, or hip fracture; excludes finger, toe, or craniofacial fracture.

ACLASTA® 5 MG (zoledronic acid) solution for infusion

PRESENTATION: Zoledronic acid, 100 mL solution bottle contains 5 mg zoledronic acid (anhydrous), corresponding to 5.330 mg zoledronic acid monohydrate.

INDICATIONS: Treatment of osteoporosis in post-menopausal women and men at increased risk of fracture, including those with a recent low-trauma hip fracture. Treatment of osteoporosis associated with long-term systemic glucocorticoid therapy in post-menopausal women and in men at increased risk of fracture. Treatment of Paget's disease of the bone.

DOSAGE AND ADMINISTRATION: Osteoporosis: A single intravenous infusion of 5 mg Aclasta administered once a year. In patients with a recent low-trauma hip fracture, it is recommended to give the Aclasta infusion two or more weeks after hip fracture repair. Paget's Disease: A single intravenous infusion of 5 mg Aclasta. Specific re-treatment data are not available for Paget's disease. Aclasta is administered via a vented infusion line and given at a constant infusion rate. The infusion time must not be less than 15 minutes. Adequate calcium and vitamin D are recommended in association with Aclasta administration. In patients with recent low-trauma hip fracture a loading dose of 50,000 IU of Vitamin D is recommended prior to the first Aclasta infusion. No dose adjustment in patients with creatinine clearance ≥ 35 mL/min, or in patients with hepatic impairment, or in elderly patients. The safety and efficacy of Aclasta in children and adolescents below 18 years of age has not been established.

CONTRAINDICATIONS: Hypersensitivity to zoledronic acid or to any of the excipients or to any bisphosphonate; hypocalcaemia; pregnancy; lactation.

PRECAUTIONS AND WARNINGS: Serum creatinine should be measured before each Aclasta dose. Aclasta should not be used in patients with creatinine clearance < 35 mL/min. Transient increase in serum creatinine may be greater in patients with underlying impaired renal function. Monitoring of serum creatinine should be considered in at-risk patients. Patients must be appropriately hydrated prior to administration of Aclasta, especially important for the elderly and for patients receiving diuretic therapy. Use with caution in conjunction with medicinal products that can impact renal function. A single dose of Aclasta should not exceed 5mg and the duration of infusion should be at least 15 minutes. Pre-existing hypocalcaemia and other disturbances of mineral metabolism must be treated by adequate intake of calcium and vitamin D before initiating therapy with Aclasta. It is strongly advised that patients with Paget's disease receive supplemental calcium and vitamin D. Measurement of serum calcium before infusion is recommended for patients with Paget's disease. Severe and occasionally incapacitating bone, joint and/or muscle pain have been infrequently reported with bisphosphonate therapy. A patient being treated with Zometa should not be treated with Aclasta. As a precaution against osteonecrosis of the jaw (ONJ) a dental examination with appropriate preventive dentistry should be considered prior to treatment in patients with concomitant risk factors (e.g. cancer, chemotherapy, corticosteroids, poor oral hygiene). While on treatment, these patients should avoid invasive dental procedures if possible. For patients requiring dental procedures, there are no data available to suggest whether discontinuation of bisphosphonate treatment reduces the risk of osteonecrosis of the jaw. Aclasta is not recommended in women of childbearing potential.

INTERACTIONS: Specific drug-drug interaction studies have not been conducted with zoledronic acid. Caution is recommended when Aclasta is used concomitantly with drugs that can significantly impact renal function, such as aminoglycosides and diuretics that can cause dehydration. In patients with renal impairment, the systemic exposure to concomitant medicinal products that are primarily excreted via the kidney may increase.

ADVERSE REACTIONS: The incidence of adverse reactions (e.g. fever, myalgia, flu-like symptoms, arthralgia and headache) are greatest with the first infusion and decrease markedly with subsequent infusions. The majority of these reactions occur within the first three days and were mild to moderate and resolved within three days of the event onset. The incidence of these adverse reactions can be reduced with the administration of paracetamol or ibuprofen shortly following Aclasta administration. Very common: Fever. Common: Flu-like symptoms, chills, fatigue, pain, asthenia, malaise, arthralgia, myalgia, bone pain, back pain, pain in extremity, vomiting, nausea, headache, dizziness, atrial fibrillation, hypocalcaemia†, ocular hyperaemia, diarrhoea, increased C-reactive protein, infusion site reactions. Uncommon: Hypertension, flushing, palpitations and others. Not known: Scleritis, orbital inflammation, hypotension, renal impairment, osteonecrosis of the jaw, dehydration secondary to post dose symptoms, hypersensitivity reactions.

† Common in Paget's disease only. Please refer to SmPC for a full list of adverse events.

PACK SIZE: Aclasta is supplied in packs containing one 100ml bottle

LEGAL CATEGORY: POM

MARKETING AUTHORISATION NUMBER: EU/1/05/308/001

MARKETING AUTHORISATION HOLDER: Novartis Europharm Limited, Wimblehurst Road, Horsham, West Sussex, RH12 5AB, United Kingdom.

Consult full Summary of Product Characteristics (SmPC) before prescribing. Full prescribing information is available upon request from: Novartis Pharma, P.O. Box 124, Valletta VLT 1000, Malta. Tel +356 22963217. (vsn 2010-MT-001 ACL 18-05-2010)

References: 1. Aclasta SmPC, Novartis Europharm Ltd. 2. Black DM, Delmas PD, Eastell R, et al; for the HORIZON Pivotal Fracture Trial. Once-yearly zoledronic acid for treatment of postmenopausal osteoporosis. *N Engl J Med.* 2007;356:1809-1822. 3. Saag K, Lindsay R, Kriegman A, Beamer E, Zhou W. A single zoledronic acid infusion reduces bone resorption markers more rapidly than weekly oral alendronate in postmenopausal women with low bone mineral density. *Bone.* 2007;40:1238-1243. 4. McClung M, Recker R, Miller P, et al. Intravenous zoledronic acid 5mg in the treatment of postmenopausal women with low bone density previously treated with alendronate. *Bone.* 2007;41:122-128.



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Dermatology

What is on for Health promotion and Disease Prevention for September and October?



World Heart Day

Cardiovascular diseases are the world's largest killers, claiming 17.1 million lives a year. In Malta it is the top cause of mortality counting for 40% of all deaths. Risk factors for heart disease and stroke include raised blood pressure, cholesterol and glucose levels, smoking, inadequate intake of fruit and vegetables, being overweight, obesity, stress and physical inactivity.

26th September 2010 was World Heart Day and the Health Promotion and Disease Prevention Directorate's focus was on prevention of heart disease and early identification of risk factors.

To protect a healthy heart the key messages should be communicated to your patients:

1. Heart attacks and strokes are major – but preventable – killers worldwide.
2. Over 80% of cardiovascular disease deaths take place in low- and middle-income countries and occur almost equally in men and women. Cardiovascular risk of women is particularly high after menopause.
3. Tobacco use, an unhealthy diet, and physical

Breast Cancer awareness

Breast cancer is among the malignancies where good opportunities for both primary and secondary prevention exist. Primary prevention here refers to promotion of healthy lifestyles, especially with regards to a diet that is rich in fruits and vegetables and low in saturated fats, whereas secondary prevention refers to early detection

and treatment. October is pink to remind people of the importance of raising awareness on breast cancer. The

directorate is currently launching a campaign with the collaboration of NGOs on breast cancer awareness. Focus will be made on self-examination at all ages, and referral to health professionals.

inactivity increase the risk of heart attacks and strokes. 4. Cessation of tobacco use reduces the chance of a heart attack or stroke.

5. Engaging in physical activity for at least 30 minutes every day of the week will help prevent heart attacks and strokes.

6. Eating at least five servings of fruit and vegetables a day, and limiting your salt intake to less than one teaspoon a day, also helps to prevent heart attacks and strokes.

7. High blood pressure has no symptoms, but can cause a sudden stroke or heart attack. Have your blood pressure checked regularly.

8. Diabetes increases the risk of heart attacks and stroke. If you have diabetes control your blood pressure and blood sugar to minimize your risk.

9. Being overweight increases the risk of heart attacks and strokes. To maintain an ideal body weight, take regular physical activity and eat a healthy diet.

10. Heart attacks and strokes can strike suddenly and can be fatal if assistance is not sought immediately.

Source: WHO factsheet

Professionals who would like a copy of the material are kindly asked to call on 23266000, email healthpro@gov.mt or visit <http://www.sahha.gov.mt/pages.aspx?page=26>. Alternatively one may also click on <http://www.thesynapse.net/>

Health Promotion Quiz

The Health Promotion and Disease Prevention Directorate is organising free weight management classes in health centres and aerobics in local councils for people who have BMI > _____ to encourage them to lose weight and stay healthy.

The answer can be found in Issue 3/10. The first drawn name will get a 3 month membership for a Parent and Kid at Spinach Fitness Club, Malta's first kids' gym – Melita Training Grounds, Pembroke. The gym may be contacted at www.spinachfitness.com or 21/79383740.

Kindly submit the answers by mail by filling the form on this page addressed to The Professional Services Centre, 3 Guzi Cutajar Street, Dingli, DGL 1201 or submit your answers on-line on www.thesynapse.net/quiz. All submissions will participate in a draw. You have up to the 7th November 2010 to submit your answers

Fill in your details

Name

Address

Email

Mobile



Splitting Of Erectile Dysfunction Pills

Pill splitting is the practice of splitting a pill in half, thus creating two pills, each aimed at being half the dose of the entire pill. This is typically done with a knife, using a pair of scissors, by hand or with a designated pill splitter. The main reason for pill splitting is a financial one. Pharmaco-economically speaking, a drug which is twice as strong as another may not be twice the price, in fact it may indeed be the same price. In order to make costs savings, patients choose to split a high-dose tablet to create two lower dose tablets.

What's the latest data on pill splitting?

In May 2009, Bayer surveyed 500 erectile dysfunction (ED) patients in five European countries (France, UK, Italy, Germany and Spain). The findings shed new light on the prevalence of and reasons for pill splitting¹:

- 50% of those ED patients surveyed admitted to splitting their medication. This rose to 59% amongst high dosage users, which is more than every second patient;
- Of the total number who split their pills, 36% always split them and 40% split them every second time;
- Other reasons cited for pill splitting, over and above cost savings, were the belief that half the dosage is sufficient and that side-effects will be reduced, as well as concerns about too strong / lasting effects;
- Cutting with a knife was identified as the most popular way to split pills.

The implications of pill splitting

There is much debate amongst healthcare professionals and authorities regarding the implications, both positive and negative, of pill splitting. Although the cost-saving benefits are widely accepted, there are concerns about the impact on both patients and healthcare professionals. The US Food and Drug Administration (FDA) and the American Medical Association, for example, advise against pill splitting unless it's specified in the drug's labelling². There are a number of reasons for this:

- Confusion over the correct dose. There have been cases when people have purchased higher strength tablets intending to split them, but then haven't, leading to patients accidentally taking the wrong dose.

Equal distribution of medicine. FDA studies² have shown that the actual dose in each half of a split tablet often is different. So while the two halves may look the same, they don't necessarily contain equal amounts of medicine. For the uniformity of mass of subdivided tablets a requirement has recently been set by the European Pharmacopoeia. Loss of mass upon breaking can be limited to not more than 1%.

- Difficulty splitting. Some tablets are too small to split, may have an unusual shape that makes them hard to split, or may crumble more easily when split. From a healthcare professional's point of view, pill splitting means that they have limited control over the exact dose their patients take.

Reference

1. Market research: 'Pill Splitting Behaviour Among PDE5 users' Conducted by PSYMA in May 2009 2. US Food and Drug Administration: Consumer Updates, July 2009 <http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm171492.htm> 3. Rosenberg MT et al. Improvement in duration of erection following phosphodiesterase type 5 inhibitor therapy with vardenafil in men with erectile dysfunction: the ENDURANCE study. Int J Clin Pract 2009; 63:1

Bayer Cuts Price of its Erectile Dysfunction Drug Levitra®

Levitra® (vardenafil) is available in three different dosages - high (20mg), medium (10mg) and low (5mg) dose

Based on Individual Member State data, the most frequently prescribed dosage is the high one, but the most frequently taken is the medium dosage. This is because of pill splitting. ED treatment is different from many other therapy areas. It is a common, life-changing condition, yet there is no government reimbursement for treatment in most countries.

Because patients have to pay for ED treatment themselves, more than 50% of men with ED have been saving money by buying the high dose tablet and splitting it in half.

Bayer has therefore taken the decision to lower the price of Levitra® dramatically as a responsible course of action to meet men's needs - both therapeutic and economic - to help tackle this important ED treatment issue. Bayer has proactively reduced the price of its medium (10mg) and low (5mg) dose Levitra® (vardenafil HCL) in Malta so each dose is now approximately half the price of the next higher dose.

Now, patients who are currently splitting ED tablets such as Levitra® will have an option that specifically meets their dose requirements at significant savings, and doctors will have better control over the dose they prescribe.

In Malta, Levitra® is being sold at the revised prices with effect from 1st October 2010. The quality and efficacy of

	Previous Price per 4 tablet pack	New Price per 4 tablet pack
Levitra 5mg	EUR 36.19	EUR 12.88
Levitra 10mg	EUR 39.33	EUR 24.02
Levitra 20mg	EUR 44.72	EUR 44.72

Levitra® will not be compromised as a result of this price revision. Bayer Schering Pharma has consistent quality standards, which are checked periodically by local and regional health authorities. On the contrary, the reduced price of Levitra® removes economic hurdles for all ED patients who split pills and offers them greater convenience by removing the hassle to split pills, eliminating the possibility for wastage during splitting and lowering the financial outlay compared with competitor brands.

Levitra® is a proven ED medication which is well tolerated, and with a good safety profile in patients of all ages, with or without underlying medical conditions. It is the only PDE-5 inhibitor that extends duration of erection, as measured by a stopwatch method, up to 3 times over placebo.³ It is now available in pharmacies in Malta and Gozo at a new and more competitive price.



Bayer.
Keeping men
in top form.

Levitra® (vardenafil) Prescribing Information

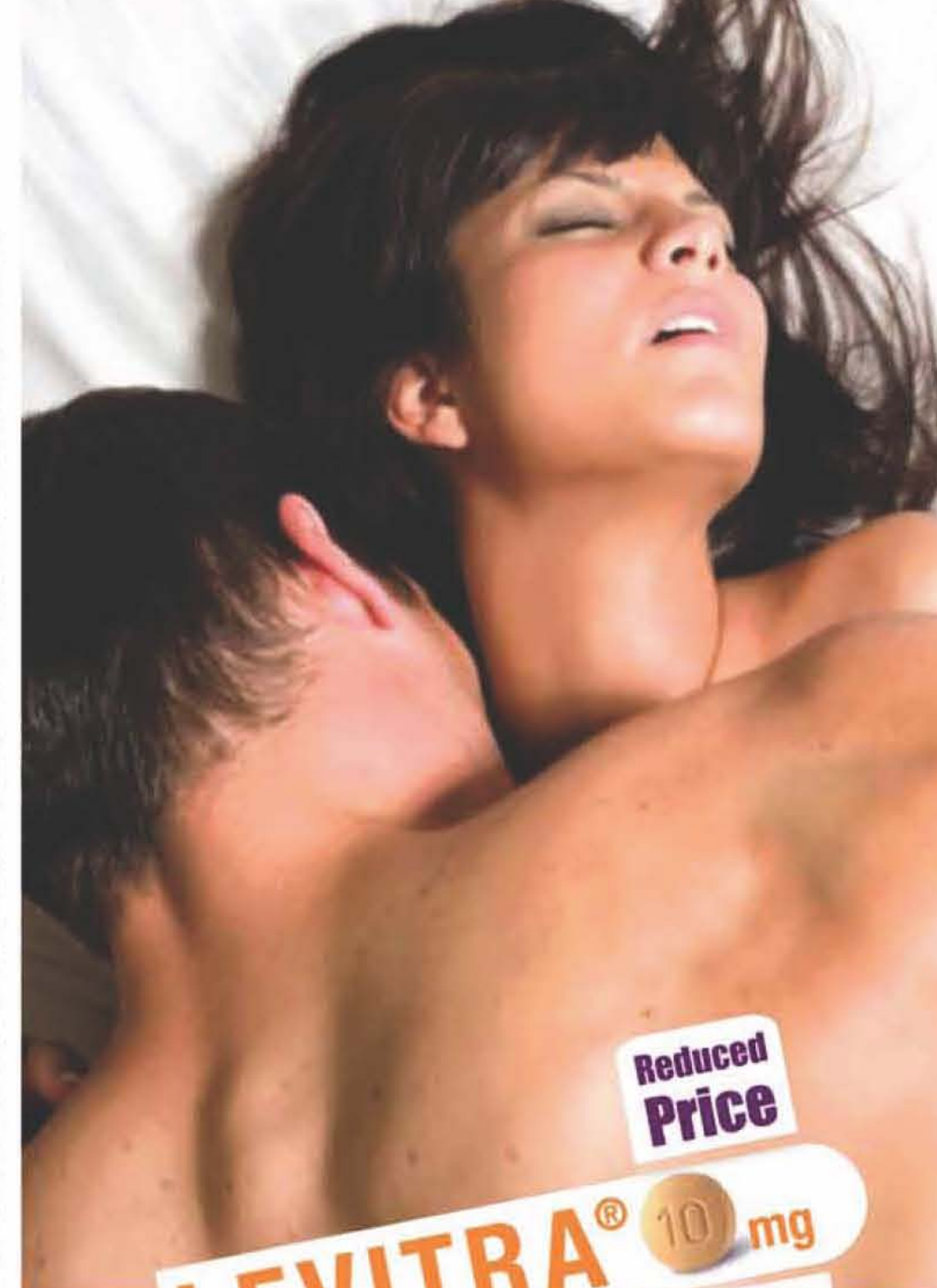
(Refer to full Summary of product Characteristics (SmPC) before prescribing) **Presentation:** Each tablet contains 5mg / 10mg / 20mg vardenafil (as hydrochloride trihydrate). **Indication:** Treatment of erectile dysfunction. To be effective, sexual stimulation is required. Not for use by women. **Posology and method of administration:** Adult men: 10mg approximately 25 to 60 minutes before sexual activity. Based on efficacy and tolerability the dose may be increased to 20mg or decreased to 5mg. The maximum recommended dose is 20mg once per day. Can be taken with or without food, onset of activity may be delayed if taken with a high fat meal. **Elderly men:** no dosage adjustment required, though increase to a maximum 20mg dose should be carefully considered depending on individual tolerability. **Children and adolescents:** not indicated for individuals below 18 years of age. **Mild and moderate hepatic impairment, severe renal impairment:** A starting dose of 5mg should be considered. **With other medicinal products:** in combination with erythromycin or clarithromycin, the dose of Levitra® should not exceed 5mg. **Contra-indications:** Hypersensitivity to vardenafil or to any of the excipients; coadministration with nitrates or nitric oxide donors (such as amyl nitrite) in any form; patients who have loss of vision in one eye because of NAION; men for whom sexual activity is inadvisable (e.g. severe cardiovascular disorders); severe hepatic impairment, end-stage renal disease requiring dialysis; hypotension; recent stroke or myocardial infarction; unstable angina; known hereditary retinal degenerative disorders; concomitant use of potent CYP3A4 inhibitors ketoconazole and itraconazole (oral form) in men older than 75 years; concomitant use of potent HIV protease inhibitors such as ritonavir and indinavir. **Warnings and Precautions:** Medical history and physical examination should be undertaken to diagnose erectile dysfunction and determine potential underlying causes. Consider cardiovascular status, since there is a degree of cardiac risk associated with sexual activity. Vardenafil has vasodilator properties, resulting in mild and transient decreases in blood pressure. Use with caution in patients with anatomical deformation of the penis or conditions which predispose to priapism (such as sickle cell anaemia, multiple myeloma or leukaemia). Combination with other treatments for erectile dysfunction is not recommended. Patients on stable alpha-blocker therapy: initiate vardenafil therapy at a starting dose of 5mg and consider a time separation of dosing. Concomitant use with potent CYP 3A4 inhibitors should be avoided. A dose of 5mg vardenafil must not be exceeded when given concomitantly with erythromycin or clarithromycin. Avoid grapefruit juice. Prolongation of QTc interval - avoid use in patients with relevant risk factors. Advise patients that in the case of sudden visual defect to stop taking Levitra® and consult a physician. Tolerability of the maximum dose of 20mg may be lower in elderly patients (≥ 65 years old). Administration to patients with bleeding disorders or active peptic ulceration only after careful benefit-risk assessment. **Interactions:** Effects on vardenafil: inhibitors of CYP 3A4 may reduce vardenafil clearance. Effects of vardenafil: coadministration with nitrates is contraindicated. Concomitant treatment with alpha-blockers should be initiated only if the patient is stable on alpha-blocker therapy. **Pregnancy and lactation:** not indicated for use in women. **Effects on ability to drive and use machines:** patients should be aware of how they react to Levitra® before driving or operating machinery. **Undesirable Effects:** Very common: flushing, headache. Common: dizziness, nasal congestion, dyspepsia, and nausea. Serious side effects: cf. CWarnings and Precautions - in addition tachycardia, palpitations, angina pectoris, myocardial ischaemia/infarction, seizure, priapism, NAION, visual field defect, laryngeal oedema, intraocular pressure increased, sudden deafness. Serious cardiovascular events, including cerebrovascular haemorrhage, sudden cardiac death, transient ischaemic attack, unstable angina and ventricular arrhythmia reported post marketing in temporal association with another medicinal product in this class. Prescribers should consult the SmPC in relation to other side effects. **Overdose:** an increase in undesirable effects may be observed. **Legal Category:** POM. **Package Quantities and Basic Costs:** 4 x 5mg (EUR 12.88), 4 x 10mg (EUR 24.02), 4 x 20mg (EUR 44.72). **MA Number(s):** EU/1/03/248/001-012. **Further information available from:** Alfred Gera & Sons Ltd, Triq il-Masgar, Gormi, QRM 3217 Malta Telephone: +356 21446205. **Date of revision:** June 2010. Levitra® is a registered trademark of Bayer AG.

References:

- Rosenberg MT et al. Improvement in duration of erection following phosphodiesterase type 5 inhibitor therapy with vardenafil in men with erectile dysfunction: the ENDURANCE study. Int J Clin Pract 2009; 63:1
- Mirre M. et al. Erectile Dysfunction and Dyslipidaemia: International Society of Sexual Medicine 2008
- Montorsi F et al. J Sex Med. 2004; 1: 168-178



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Members' Corner

ILES Grape Expectations

Britanniques

Bordeaux & London

by Albert Cilia-Vincenti

This is the second of a two part series on how the 18th and 19th century British middle classes shaped the wine industry

The wine trade flourished when Britain made peace with France in 1713. Claret was expensive, but rich Londoners (also big spenders on theatres and music produced by fashionable immigrants like Handel) consumed large quantities. Sir Robert Walpole, Britain's first prime minister, is said to have smuggled his favourite French wines in navy ships. The most expensive one he bought was old Burgundy, but that (as now) was only available in tiny quantities, so he relied largely on claret (Margaux and Lafite). In a single year his wine bill amounted to over £1,200 (£100,000 in today's money). British consumers bought the best stuff and paid top prices – they were paying five times as much for their claret as the wine's other main customers, the Dutch, who preferred the cheaper lower-grade stuff. Claret was no longer drunk, or even bought, when young. In 1714, Walpole bought classier bottles of the 1706 vintage. His sophistication was echoed by that of his clerk, who could spell correctly all four top First Growth estates.

Claret was still largely for the very well-off, well into the 19th century. In "Every Man His Own Butler", published in 1839, Cyrus Redding, a wine merchant and author, wrote "claret for a bishop, port for a rector, currant for a curate and gin for the clerk". At that time, for a tradesman, the fine-wine merchant was an unusually respectable figure. Anthony Trollope described one of them, "Mr Prettyman", as "a handsome old gentleman with grey hair, always well-dressed". Indeed, three of his contemporaries survive till this very day – Comey & Barrow in the City of London, Justerini & Brooks and Berry Bros & Rudd in St James's Street.

Claret was beginning to flow down the social hierarchy, and a free-trade treaty between Britain and France in 1860 drastically reduced duty on French wines, encouraging the British middle classes to ape their social superiors. Also that year, the British Chancellor of the Exchequer, William Gladstone, keen to stiffen the nation's moral spine, cut the duty on table wine to 40% of that on the more intoxicating fortified wines such as port and sherry. The year after came the Single Bottle Act, allowing grocers to sell wine by the bottle. A much-despised, enormously popular drink called "grocers' claret" emerged, resulting in sales of cheap Bordeaux wine to rise six-fold to 36 million bottles between 1859 and 1878. The Gilbey family franchised 2,000 grocers licensed to sell wine, largely claret, and became one of the most remarkable commercial dynasties of Victorian England.

As the middle classes turned to claret, the upper classes

"There is simply nothing else that so perfectly encapsulates physical sensation, social well-being and aesthetic exploration at the same time"

abandoned this increasingly common tippie in favour of Hock (German white wine made from Riesling grapes) and Champagne. Because fashion determines price, the records of wine merchants Berry Bros & Rudd reveal that the price, a hundred years ago, of top Hock wines exceeded that of top Bordeaux reds, Margaux and Latour of same vintage ... unbelievable today.

The fortunes of the claret business turned in the late 1870s and 1890s when mildew tainted and ruined the wines. Lafite's reputation, for instance, went downhill when the 1884 vintage turned mouldy after only a couple of years in bottle. At the same time, the phylloxera virus started devastating Bordeaux's vineyards.

Claret recovered in 1960 when the splendid 1959 vintage coincided with the arrival of big American buyers, and its popularity has risen steadily since. London remains at the centre of the fine wine trade, and home of organisations such as the Institute of Masters of Wine, of Decanter and World of Fine Wine magazines, and most of the world's biggest wine auctions. Liv-Ex, the world's first fine wine stock-market, is based in London, and its records show that nine-tenths of the wine trade is still in top ("classed growths") clarets. Newcomers from vineyards in a dozen countries trying to launch their finest wines on the world market come to London first for validation. Yet, though London may still have much knowledge as well as the market, the British, as customers, may be past their best. More than half of fine wine sold globally, by value, is now bought by Asians, most of which are from China and Hong Kong. No wonder therefore that fifteen years ago Berry Bros & Rudd, the three hundred year-old London wine merchant, opened a shop in Hong Kong.

As wealth has shifted from Europe and America to China, First Growth clarets have become one of the status symbols of Asian multimillionaires. Inevitably anything that is scarce and fashionable is bound to become very expensive, and these very top clarets are now out of reach of average wine-lovers' pockets. However, there is no proportionality between price paid and gustatory pleasure offered, and a £1,000 wine will not provide twenty times the aromatic and flavour excitement offered by a £50 one. However whether wine-label romantics like it or not, there is definitely a quality-price ratio for practically anything on earth. The blind-tasting format of our "Il-Qatra" wine club is based on this principle, educating members that when you haven't been influenced by the sight of the bottle labels, you might well prefer a cheaper wine to a more expensive one.



Breast Cancer: Ductal Carcinoma in situ (DCIS)

by Pierre Vassallo

Ductal carcinoma in situ (DCIS) is a breast malignancy that is characterized by the proliferation of malignant ductal epithelial cells without evidence of invasion through the basement membrane. The incidence of DCIS has risen 11-fold between 1981 and 2001 through improved detection rates with screening mammography.

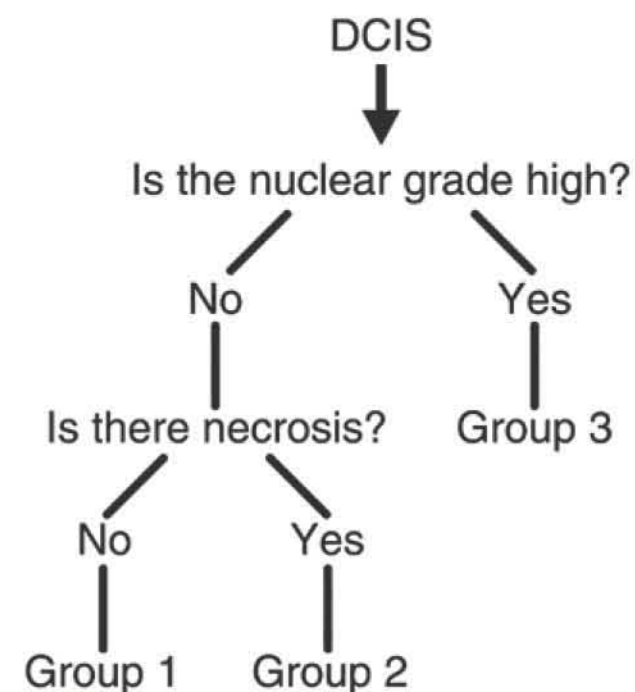
DCIS is not a single entity but a spectrum of disease ranging from low to high grade. DCIS grade is an important prognostic factor with high grade lesions being more likely to recur.

The simplest, most reproducible classification system of DCIS is the Van Nuys system, which identifies three groups of DCIS lesions. In the Van Nuys system, lesions are differentiated first according to nuclear grade (high, intermediate or low grade) and then according to whether necrosis is present or absent. Low-grade lesions contain cells with small nuclei, minimal nuclear pleomorphism, and infrequent mitoses, whereas high-grade lesions have cells with large, pleomorphic nuclei and frequent mitoses. Intermediate-grade lesions contain cells with nuclei that are neither low nor high grade. Figure 1 shows the Van Nuys system for classification of DCIS: First, lesions are classified according to whether they are of a high nuclear grade (group 3) or not. Non-high-grade lesions are further differentiated according to whether necrosis is present (group 2) or absent (group 1).

Mammography is the primary tool for detecting DCIS, but it has limitations. The reported sensitivity of mammography for detection of DCIS is between 87% and 95%. Mammography is more reliable in detecting higher grade lesions, while ultrasound was more useful than mammography for lower grade DCIS.

The most common mammographic finding in DCIS is

Figure 1. Van Nuys Classification



microcalcifications. Microcalcifications tend to correlate with intraductal foci of necrosis. Thus a low-grade lesion without necrosis is less likely to manifest with calcifications than either an intermediate- or a high-grade lesion. Other mammographic findings might include a mass (Figure 2) or architectural distortion (Figure 3) and may be present in any grade lesion. The mass lesion in DCIS may directly correlate with tumor tissue, but may also be the result of periductal fibrosis or elastosis.

The most typical calcifications in DCIS are linear with or without branching (following the ducts) (Figure 4). Fragmentation of the calcifications is also indicative of malignancy, while rounded calcifications if abundant (>5 calcifications within an area 1 cm in diameter) may also suggest DCIS (Figure 5).

Magnetic resonance (MR) imaging has higher sensitivity than mammography for the detection of DCIS and greater accuracy for depicting the extent of disease. However fibrocystic change may be indistinguishable and this leads to a poor specificity and also a limited usefulness of MRI for pre-operative planning. The MR appearance of DCIS depends primarily on the presence and extent of abnormal vascularity (tumor angiogenesis) resulting in the presence of



Figure 2. Mass lesion (arrow) in DCIS Grade 1

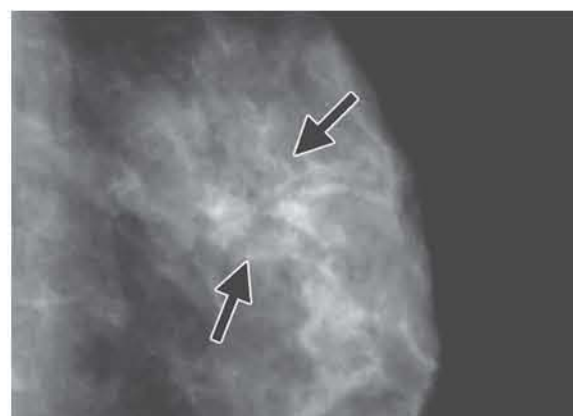


Figure 3. Architectural distortion (arrow) in DCIS Grade 1

abundant and leaky vessels. Therefore contrast-enhanced T1 weighted images are required that are obtained preferably as a 3D acquisition with high spatial resolution in a sequentially repeated fashion in order to observe both the degree and distribution of contrast agent uptake and the temporal the pattern of enhancement.

Non-mass-like (not nodule-shaped) enhancement typically involving a segment of the breast with some dumping is



Figure 4. Linear calcifications in DCIS Grade 3

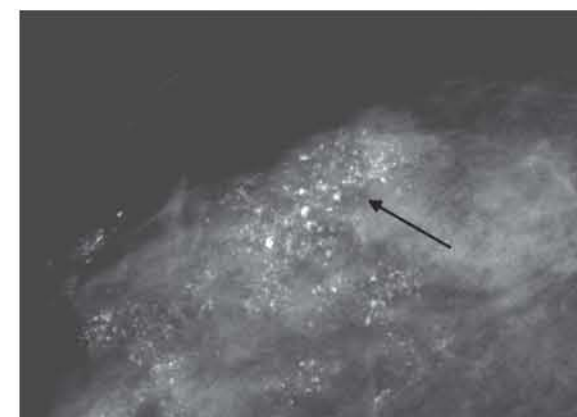


Figure 5. Abundant rounded microcalcification in DCIS Grade 2

suggestive of DCIS (Figure 6). The kinetic pattern of contrast enhancement is more related to histologic grade with low grade lesions showing rapid uptake and loss of contrast material during the later phases (washout), whilst higher grade lesions tend to have slower uptake patterns with a prolonged plateau enhancement (Figure 7). Speed of contrast material uptake is related to vessel abundance, while the degree of prolongation of uptake (length of plateau phase) is a function of vessel permeability (leakiness).

The reported sensitivity of CT for the detection of DCIS ranges from 70% to 88%. In a different study, the detectability of the intraductal component of invasive ductal carcinomas at multidetector CT was compared with that at MR imaging; lesion detectability at multidetector CT was inferior to that at



Figure 6. Segmental enhancement on MRI in DCIS Grade 3

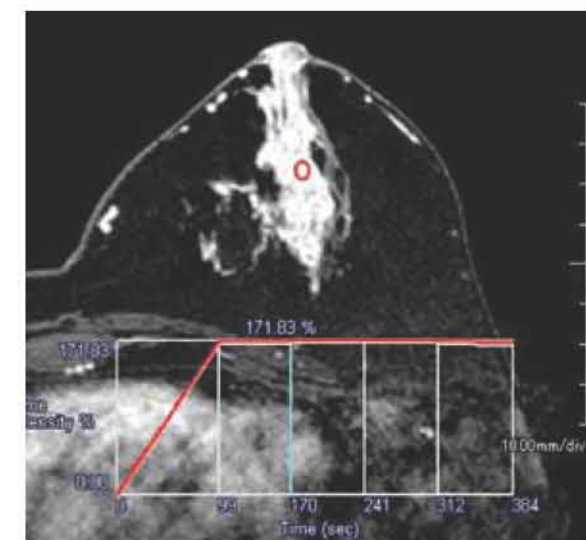


Figure 7. Kinetic analysis of contrast material uptake on MRI in Grade 3 DCIS: graph plotting degree of enhancement vs time shows rapid initial uptake and a prolonged plateau of enhancement

MR imaging. In general, CT has lower sensitivity but higher specificity than MR imaging because the lesion appearance leads to overestimation of fibrocystic changes at MR imaging. Multidetector CT may be used to map lesions for breast-conserving surgery, however presurgical mapping has been shown to be more helpful in invasive ductal cancers than for DCIS.

In summary, the incidence of DCIS has increased dramatically due to increased detection with screening mammography. The definitive correlation of histologic grading of DCIS (Van Nuys Classification) with mammographic findings and the use of MRI particularly in equivocal cases confirms the validity of both investigations, which can therefore strongly contribute to improved patient outcome.



A strategic move

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Donecept is a white, round, film-coated tablet containing 5mg or 10mg of Donepezil hydrochloride. It is used to treat Alzheimer's disease. Donepezil is an anticholinesterase, which means it helps to increase the levels of acetylcholine in the brain. Acetylcholine is a chemical messenger that helps the brain to think and remember. Donepezil helps to slow down the loss of acetylcholine in the brain, which can help to improve memory and thinking. Donecept is available in two strengths: 5mg and 10mg. The 5mg tablets are white and the 10mg tablets are white with a score line. Donecept is taken once a day, with or without food. It is important to take Donecept exactly as you are told to, and not to stop taking it without talking to your doctor. Donecept may cause some side effects, such as nausea, vomiting, and diarrhoea. If you experience any of these side effects, you should talk to your doctor. Donecept is a prescription medicine and should only be used under the supervision of a doctor. For more information about Donecept, please see the patient information leaflet that comes with your tablets. If you have any questions about Donecept, please ask your doctor or pharmacist.

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Healing & Disease Reversal

by Albert Cilia-Vincenti

This series explores Dean Ornish's 30-year research experience into healing & disease reversal by dietary and lifestyle changes. He is a Californian University Professor of Medicine in San Francisco.

The good news, according to Dean Ornish, is that it's not difficult to eat and live in a healthy way. These articles, summarising his programme, amount to a scientifically proven field guide to help distinguish fact from fiction, hype from hope.

Ornish says he never intended becoming a veteran of diet wars. He has been forced into debating the late Dr Atkins at scientific meetings of the American Heart Association, the American College of Cardiology, and the American Dietetic Association, where he usually found himself described as the "low fat" doctor and Dr Atkins the "low carb" doctor. He insists that was not accurate, because he has always advocated that an optimal diet is low in total fat, very low in "bad fats" (saturated fat, hydrogenated fats, trans-fatty acids), high in "good carbs" (fruits, vegetables, whole grains, legumes and soy products), low in "bad carbs" (sugar, white flour), and that has enough of the "good fats" (omega-3 fatty acids) and high-quality proteins.

We need practical, clear, scientifically based information and not controversies between experts. Many people feel more bewildered than ever when they hear seemingly contradictory advice about different diets, and in fact a convergence of recommendations is evolving. Some significant differences remain, but a greater consensus is emerging among nutrition experts.

The first rule in Ornish's programme is to consume some omega-3 fatty acids every day. Omega-3 fatty acids are found in cold-water fatty fish (salmon, mackerel, herring, trout, sardines, albacore tuna), as well as canola (rapeseed), soy-bean, flaxseed and walnut oils. (In contrast, olive oil does not contain much omega-3 fatty acids). They are also present in smaller concentrations in dark green leafy vegetables such as kale and collard greens.

Omega-3 fatty acids reduce blood triglycerides, lower blood pressure, and decrease inflammation (hence reducing symptoms of arthritis, dermatitis and other inflammatory diseases as well as autoimmune diseases such as lupus). They reduce inflammation in blood vessels walls and prevent blood clots, thus decreasing the risk of heart attack and stroke. They also help prevent irregular heartbeats such as atrial fibrillation, another potential cause of stroke. Studies have in fact shown a potential reduction of risk of sudden cardiac death by 40-90% by stabilising the heart rhythm; the American Heart Association recommends at least two servings of cold-water fatty fish per week^{1,2}

References

1. Birch EE et al. A randomized controlled trial of early dietary supply of long-chain polyunsaturated fatty acids and mental development in term infants. *Dev Med Child Neurol* 2000; 42 (3):174-81.
2. Hibbeln JR et al. Maternal seafood consumption in pregnancy and neurodevelopmental outcomes in childhood (ALSPAC study). *Lancet* 2007; 369 (9561):578-85.
3. Leaf A. Prevention of sudden cardiac death by n-3 polyunsaturated fatty acids. *Fundamen Clin Pharmacol* 2006; 20(5):625-38.
4. Tavazzi L et al. Effect of n-3 polyunsaturated fatty acids in patients with chronic heart failure (the GISSI-HF trial): a randomised, double-blind, placebo-controlled trial. *Lancet* 2008; 372(9645):1223-30.

Other benefits are claimed for omega-3 fatty acids. They are important components of all our cell membranes, including neurons and, when given to pregnant and lactating women, they increase IQ and reduce incidence of allergy in the offspring, and also reduce the risk of maternal postpartum depression³. They also decrease the risk of dementia, improve immunity and reduce the risk of prostate, breast and colon cancer.

In non-breast-fed babies, omega-3 fatty acids-enriched feeding formulas have been shown to increase intelligence test scores by up to seven points. A study published in *The Lancet* stated that children of mothers who consumed more than 340 grams per week of omega-3 fatty acids-rich seafood had higher IQs, better behaviour, fewer problems with their peers, less hyperactivity, fewer emotional disorders and better communications skills than those mothers who consumed less or no seafood⁴.

Ornish says he's been taking fish oil capsules (3g daily) for many years and advises practically everyone to do the same. It is advisable to take a high quality fish oil (not cod liver oil) which has been purified of all possible fish pollutants, such as mercury, dioxin and PCBs. This gives all the benefits of omega-3 fatty acids without the extra fat, calories and pollutants that come with eating fish.

Are omega-3 fatty acids universally beneficial? There are conflicting reports about their usefulness in heart failure, some claiming benefit and others a dangerously negative effect, so caution would need to be exercised in this serious situation. For most people, omega-3 fatty acids are highly beneficial.

Can you consume too many good fats? One of the few remaining differences in the consensus of what constitutes an optimal diet has to do with how much "good fat" to include in your diet. Is olive oil the healthiest fat? In a word, no – it's a better fat but not the best one. The Harvard School of Public Health, and some authors of popular books, have promoted the idea that it doesn't matter how much fat you consume as long as it's "good fats", such as olive oil. While good fats are better than bad fats, the total amount of fat in your diet also plays an important role. Oils are 100 per cent fat, and because fat has more than twice the calories per gram compared to those of protein and carbohydrates, it's very easy to consume a lot of extra calories if you have a lot of fat. So remember ... dipping bread in olive oil and pouring it on salads does increase substantially your caloric consumption!

With Chemistry in her character



post at the relatively young age of 30 is significant. Starting from a first post at the Extemporaneous and Chemotherapy Section in St Luke's Hospital, she was thrown in at the deep end. "My work was in compounding specialised medication for very special patients, mostly paediatrics. For me, at such a young age, being given the responsibility of preparing medicine for children in a situation where their health was so precarious..... well, let's say it was an extremely sobering experience. It made me fully aware of the great responsibility shouldered by a pharmacist. It's not simply about picking bottles off a shelf."

Her next experience was in the Out-Patients and In-Patients Department when she went into Formulary Management, taking care to keep a balance in stocks of medication, dealing with shortages and the general running of the biggest pharmacy on the Islands. Alison speaks somewhat fondly of this experience because she knows fully well that if one learns to manage such a fluid pharmacy, one can manage any pharmacy. Then came the migration to Mater Dei Hospital.

"The migration was another big task which landed on my lap and which taught me a great deal. Admittedly, I am always seeking new ways of enlarging my expertise where pharmacy and pharmaceutical supplies are involved. I got the opportunity of training in Disaster Preparedness which helped me in learning to work in collaboration with the Emergency Department. It wasn't and isn't something I do for the money because in most instances it is something done on a voluntary basis. I volunteered at the huge public events such as Isle of MTV and was also involved in the 2005 CHOGM. It is the kind of work which allows me as a pharmacist to

work in collaboration with doctors, advising on the best medication to take 'on the field' so to say."

Today, she admits she misses that direct contact with doctors, with medics, with staff on the ward rounds and with patients. Her role as Principal Pharmacist is mostly administrative but she keeps tabs on the hands-on



the present state of the profession, Alison points out, "Some pharmacists appear to be deeply rooted in the traditional approach, mainly to the distributive practice model. To ensure a high-quality advanced practice, pharmacists need to come in line and identify more with modern practices, such as pharmaceutical care and drug information."

She also tackles the hot issue of pharmacist prescribing. "In other countries this practice has been going on for years. Pharmacists possess a wealth of knowledge on medicine so I believe that collaboration between doctors and pharmacists will work in favour of the patient whom both professions have at heart – priority is our patients!"

As a sideline, Alison speaks of her passion for travelling which helps her unwind and put aside real life issues associated to illnesses. It can become overwhelming to say the least, and whilst reading and watching films remain her two strongest favourite pastimes, she admits she prefers to read or watch fiction rather than true-life stories. "I have to deal with enough drama as it is. When I unwind, it has to be really and truly to try and get a good laugh every so often. There is more to life than just playing chemist."

part of the profession by doing regular locum hours in community pharmacies. Alison amazes me further when she flippantly mentions that since her graduation, and in her free time, she has also managed to cram in a course in Nutrition and Dietetics which she completed successfully and also got a Masters in Pharmacy. And she is actually in her first year of studies for a PhD in Pharmacy, delving into the research of a very specific topic – Pharmaceutical Case Models in Heart Failure. Her work at the DPPM is pretty intense and involves responsibilities linked to all Government and Health Centre pharmacies. The DPPM is responsible for the Medicines Entitlement Unit; the inclusion of new drugs on the government formulary; ongoing formulary maintenance; the Pricing Unit; the management of exceptional and urgent treatment cases and the participation within EU international foras. Being also involved in the Pharmacy Council as one of the elected members, Alison is serious about raising awareness on the general needs and obligations of pharmacists. She looks forward to work with the other council members to ensure that pharmacists in Malta continue to perform to the highest standards to protect and promote public wellbeing, thus, keeping a well-regulated dynamic profession.

"From my experience in teaching pharmacy students at the University of Malta, I find that the numbers of new recruits in our profession is increasing every year. There are more female than male pharmacists, so we face the usual employment issues that can greatly hamper manpower – you know, pharmacists get pregnant too! Having said that, females still outnumber male pharmacists." Asked about what she thinks of



When Alison Anastasi started studying to become a pharmacist, little did she know she'd become one through and through. Seven years down the line, she is today Principal Pharmacist at the Directorate of Pharmaceutical Policy and Monitoring (DPPM) at St Luke's Hospital, and has been in this post for the past year. We meet at her office in a building which is surprisingly neat and well-organised.... But then what would one expect of a place housing professional pharmacists intent on monitoring the profession? Alison is herself very disciplined in what she does and the simple fact that she holds such an important

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1. The ADVANCE Collaborative Group. *N Engl J Med.* 2008;358:2560-2572. 2. The GUIDE Study. *Eur J Clin Invest.* 2004;34:535-542. 3. The STENO 2 Group Study. *N Engl J Med.* 2008;358:580-591. 4. The CONTROL Study. *Diabetologia.* 2009;52:2288-2298. 5. Khalangot M, Tronko M, Kravchenko V et al. *Diabetes Res Clin Pract.* 2009;20(6):611-615. 6. Diamicron MR 60 mg. *Product Monograph.* 7. Drouin P and the Diamicron MR Study Group. *J Diabetes Complications.* 2000;14:185-191. 8. Sawada F, Inoguchi T, Tsubouchi H, et al. *Metabolism.* 2008;57(8):1038-1045. 9. Del Guerra S, D'Aleo V, Lupi R, et al. *Diabetes Metab.* 2009;35(4):293-298. 10. Katakami N, Yamasaki Y, Hayashi-Okano R, et al. *Diabetologia.* 2004;47:1906-1913.

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