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THESYNAPSE

THE MEDICAL PROFESSIONALS' NETWORK

- Constipation factors leading to admission at Gozo General Hospital
- Attitudes and Knowledge of Parents on Vaccination
- Novel Dental Implant Coating Materials
- Meeting Alfie Palmier

Volume 14 Issue 04 ISSN number 2313-8084

NEW

Augmentin® ES

600 mg/42.9 mg/5 ml

Amoxicillin/Clavulanate Potassium

Powder for oral suspension

- ✓ Provides extended antibacterial coverage to include the most penicillin-resistant strains.[1]
- ✓ Recommended by leading Guidelines as first line treatment in AOM.[2,3]
- ✓ Most common adverse effects are diarrhoea, nausea, vomiting and mucocutaneous candidiasis.[4]
- ✓ Indicated for children <40 kg and older than 3 months; dosed at 90/6.4 mg/kg/day in 2 divided doses.[4]

Spreading infectious energy!

Mini Abridged Prescribing Information: *Please refer to full Summary of Product Characteristics (SPC) before prescribing.* **TRADE NAME:** Augmentin ES. **ACTIVE INGREDIENTS:** Amoxicillin (as trihydrate) and potassium clavulanate. **PRESENTATION:** 600 mg/42.9 mg/5 ml powder for oral suspension. Supplied in 100 ml glass bottle with a dosing spoon. **INDICATION**: treatment of acute otitis media and community acquired pneumonia infections in children aged at least 3 months and less than 40 kg body weight, caused or thought likely to be caused by penicillin-resistant *Streptococcus pneumoniae*. **POSOLOGY & ADMINISTRATION:** Oral use. Recommended dose is 90/6.4 mg/kg/day in two divided doses. To minimise potential gastrointestinal intolerance, administer at the start of a meal. **CONTRAINDICATIONS:** Hypersensitivity (and past history of) to the active substances, to any penicillins or to any of the excipients. **SPECIAL WARNINGS & PRECAUTIONS:** Before initiating therapy careful enquiry of previous hypersensitivity reactions to beta-lactams. Where an infection is proven to be due to an amoxicillin susceptible organism, a switch to an amoxicillin-only preparation should be considered. Convulsions may occur in patients receiving high doses or who have impaired renal function. Concomitant use of allopurinol increase likelihood of allergic skin reactions. Prolonged use may occasionally result in overgrowth of non-susceptible organisms. Contains aspartame (E951), a source of phenylalanine. The suspension also contains maltodextrin (glucose). **INTERACTIONS:** Penicillins may reduce the excretion of methotrexate causing a potential increase in toxicity. Concomitant use of probenecid is not recommended. If co-administration with oral anticoagulants is necessary, the prothrombin time or international normalised ratio should be carefully monitored with the addition or withdrawal of amoxicillin. Moreover, adjustments in the dose of oral anticoagulants may be necessary. Clinical monitoring should be performed during the combination with mycophenolate mofetil and shortly after antibiotic treatment. **PREGNANCY & LACTATION:** Use should be avoided unless considered essential by the physician. **UNDESIRABLE EFFECTS:** Very common (≥1/10): diarrhoea. Common (≥1/100, <1/10): mucocutaneous candidosis, nausea, abdominal pain. *Refer to SPC's for full list of undesirable effects*. **AUTHORISATION NUMBER:** AA 1051/00101. **MARKETING AUTHORISATION HOLDER:** GlaxoSmithKline Bulgaria EOOD. **LEGAL CATEGORY:** POM. **DATE OF PREPARATION:** July 2014. **In order to ensure that this product information reflects the most up-to-date clinical and post-marketing surveillance data, please always refer to the latest Summary of Product Characteristics (SPC) which is available from GlaxoSmithKline (Malta) Ltd (Tel: +356 21238131).** ***REPORTING ADVERSE EVENTS (AEs):*** **If you become aware of any AEs, medication errors and/or use during pregnancy in association with GSK products, please report the event promptly to:** GSK (Malta) Limited, 1, De la Cruz Avenue, Qormi QRM 2458, Malta (Tel: +356 21238131). **Alternatively, any suspected AEs and medication errors can also be reported via the national Adverse Drug Reactions (ADRs) reporting system:** Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and posted to the Malta Medicines Authority, Post-licensing Directorate, 203, Level 3, Rue D'Argens, Gżira GŻR 1368, MALTA, or sent by email to postlicensing.medicinesauthority@gov.mt.

References:

1. Anthony R. White *et al*. Augmentin® amoxicillin/clavulanate) in the treatment of community-acquired respiratory tract infection: a review of the continuing development of an innovative antimicrobial agent Journal of Antimicrobial Chemotherapy (2004) 53, Suppl. S1, i3–i20.
2. Gilbert DN, *et al*. Sanford guide to Antimicrobial Therapy v.3.11 – last updated March 11, 2014. Sperryville; Antimicrobial Therapy, Inc. 2014.
3. Lieberthal AS *et al*. The Diagnosis and Management of Acute Otitis Media. Pediatrics. 2013; 131; e964 Epub 2013 Feb 25.
4. Augmentin ES Summary of Product Characteristics, Nov 2013.

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OXFORD UNIVERSITY: LICENCE TO SHOOT BUBBLES

We have experienced various podcasts and read various articles on targeted drug delivery mechanisms, including the use of liposomes, micelles and dendrimers, biodegradable particles as well as nanotechnology. Nonetheless, one of the more recent revelations is the use of microbubbles to increase the bioavailability and in parallel, decrease the adverse effects of treatment. This technology is being spearheaded by a biomedical engineer, Prof. Eleanor Stride hailing from Oxford University. Basically, the bubbles currently being investigated are similar to the soap bubbles generated by the bubbleblowers which we find in the hands of children at our summer feasts.

This technology revolves around the use of ultrasound. A gas (such as fluorocarbon) and the active ingredient which we are interested in are bubbled into a liquid which contains the coating material (such as phospholipids). The mixture is then agitated by using ultrasound in order to generate a foam. 1-4µm microbubbles are then extracted from this foam. In essence, each microbubble consists of a phospholipid layer surrounding a fluorocarbon core, with the active ingredient situated either within the phospholipid layer or attached to it.

The bubbles produce a strong echo on ultrasound, so following parenteral administration, ultrasound is used to track the bubble inside the body. The drug stays in the bubble until it is released - also by ultrasound - onto the site of action. The mechanism of release is simple. Since the bubbles are filled with a gas, when they are exposed to ultrasound, they expand and contract. Thus, if the ultrasound power in gradually increased, the bubbles will eventually rupture, releasing the active ingredient. **By varying the ultrasound power, the amount of drug released can also be controlled.** Interestingly, some bubbles can be loaded with magnetic nanoparticles so they can be moved to the target site with an external magnetic field. Obviously this technology poses various challenges, the most important of which is microbubble uniformity since this will determine the accuracy of the dosing.

This technology also appears to simultaneously make cells more permeable, thus increasing the bioavailability of the active ingredient. This effect is not completely understood, however it seems to result from a combined effect of ultrasound and the aforementioned mode of delivery. Till now, this technology has been successfully studied in mouse models. The next step is clinical trials.

Now, close your eyes ... and imagine the application of this technology in myocardial infarction ... or oncology ... or ...

Cover: Spinola Palace in St Julians was completed in 1688 by Chev. Fra Paolo Rafael Spinola. In Sept 1860 it was leased by the military from the church authorities for £20 a year. Spinola Palace Hospital was named Forrest Military Hospital. It was intended as a sanatorium and a reception centre for the sick from Pembroke barracks.

Photo credit: Parliamentary Assembly of the Mediterranean

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OUR COLLABORATORS

GMMS GERMAN-MALTESE MEDICAL SOCIETY

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MPSA

MADS

The magazine is distributed free of charge to all Maltese doctors, pharmacists & dentists, as well as students of the aforementioned professions, with a print run of 3500 copies.

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A maintenance bronchodilator treatment for patients with COPD who are breathless

ANORO™ ELLIPTA™

umeclidinium/vilanterol

breathe...

Anoro® Ellipta® (umeclidinium bromide/vilanterol) Abridged Prescribing Information

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 on SPC how to report adverse reactions.

Kindly consult the full Summary of Product Characteristics (SmPC) before prescribing

Trade Name: Anoro® Ellipta® **Active Ingredients:** 55 micrograms umeclidinium bromide and 22 micrograms vilanterol (as trifenatate). **Pharmaceutical Form:** 55 micrograms/22 micrograms inhalation powder, pre-dispensed. **Indications:** Maintenance bronchodilator treatment to relieve symptoms in adult patients with Chronic Obstructive Pulmonary Disease (COPD). **Dosage and administration:** Inhalation only. One inhalation once daily of Anoro® Ellipta® at the same time of the day. **Contraindications:** Hypersensitivity to the active substances or to any of the excipients (lactose monohydrate and magnesium stearate). **Precautions:** Anoro® Ellipta® should not be used in patients with asthma. Treatment with Anoro® Ellipta® should be discontinued immediately in the event of paradoxical bronchospasm and alternative therapy initiated if necessary. Cardiovascular effects may be seen after the administration of muscarinic receptor antagonists and sympathomimetics therefore Anoro® Ellipta® should be used with caution in patients with severe cardiovascular disease. Anoro® Ellipta® should be used with caution in patients with urinary retention, narrow angle glaucoma, convulsive disorders, thyrotoxicosis, hypokalaemia, hyperglycaemia and severe hepatic impairment. No dosage adjustment is required in the elderly, in renal impairment or mild to moderate hepatic impairment. **Acute symptoms:** Anoro® Ellipta® is not indicated for acute episodes of bronchospasm. Warn patients to seek medical advice if use of short-acting inhaled bronchodilator increases. A re-evaluation of the patient and of the COPD treatment regimen should be undertaken. **Interactions with other medicinal products:** Interaction studies have only been performed in adults. Avoid beta- adrenergic blockers since this may weaken or antagonize the effect of $beta_2$-adrenergic agonists. Caution is advised when co-administering with strong CYP3A4 inhibitors (e.g. ketoconazole, clarithromycin, itraconazole, ritonavir, telithromycin). Anoro® Ellipta® should not be used in conjunction with other long-acting muscarinic antagonists, long-acting $beta_2$-adrenergic agonists or medicinal products containing either of these agents. Caution is advised with concomitant use with methylxanthine derivatives, steroids or non-potassium-sparing diuretics as it may potentiate possible hypokalaemic effect of $beta_2$-adrenergic agonists. **Fertility, pregnancy, and breast-feeding:** No available data. Balance risks against benefits. **Side effects:** Common: Urinary tract infection, sinusitis, nasopharyngitis, pharyngitis, upper respiratory tract infection, headache, cough, oropharyngeal pain, constipation and dry mouth. Uncommon: Atrial fibrillation, supraventricular tachycardia, rhythm idioventricular, tachycardia, supraventricular extrasystoles and rash. **Legal category:** POM. **Presentation:** Anoro® Ellipta®. 1 inhaler x 30 doses. Anoro® Ellipta® 55/22mcg. **Marketing authorisation (MA) nos:** 55/22mcg 1x30 doses [EU/1/14/898/002]; **MA holder:** Glaxo Group Ltd, 980 Great West Road, Brentford, Middlesex, TW8 9GS, UK. **Last date of revision:** October 2014. Anoro® and Ellipta® are registered trademarks of the GlaxoSmithKline group of companies. All rights reserved. Anoro® Ellipta® was developed in collaboration with Theravance, Inc.

In order to ensure that this product information reflects the most up-to-date clinical and post-marketing surveillance data, please always refer to the latest Summary of Product Characteristics (SPC) which is available from GlaxoSmithKline (Malta) Ltd (Tel: +356 21238131)

REPORTING ADVERSE EVENTS (AEs):

Malta & Gibraltar: **If you become aware of any AEs, medication errors and/or use during pregnancy in association with GSK products, please report the event promptly to:** GSK (Malta) Limited, 1, De la Cruz Avenue, Qormi QRM 2458, Malta (Tel: +356 21238131)

Malta: **alternatively, any suspected AEs and medication errors can also be reported via the national Adverse Drug Reactions (ADRs) reporting system:**

Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and posted to the Malta Medicines Authority, Post-licensing Directorate, 203, Level 3, Rue D'Argens, Gżira GŻR 1368, MALTA, or sent by email to postlicensing.medicinesauthority@gov.mt

Gibraltar: **alternatively, any suspected AEs and medication errors can also be reported via the UK regulatory authority (MHRA):** https://yellowcard.mhra.gov.uk/

ANORO ELLIPTA was developed in collaboration with Theravance

Theravance

MLT_GIB/UCV/0004/15 Date of preparation: March 2014

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ISSUE GUIDE

TheSynapse

astellas

Prescribing Information Presentation: Betmiga™ prolonged release tablets containing 25 mgor 50 mg mirabegron. **Indication:** Symptomatic treatment of urgency, increased micturition frequency and/or urgency incontinence as may occur in adult patients with overactive bladder (OAB) syndrome. **Dosage:** Adults (including the elderly): Recommended dose: 50 mg once daily. Children and adolescents: Should not be used. **Contraindications:** Hypersensitivity to active substance or any of the excipients. **Warnings and Precautions:** Should not be used in patients with end stage renal disease, severe hepatic impairment and severe uncontrolled hypertension. Not recommended in patients with severe renal impairment and moderate hepatic impairment concomitantly receiving strong CYP3A inhibitors. Dose adjustment to 25 mg is recommended in patients with moderate renal and mild hepatic impairment receiving strong CYP3A inhibitor concomitantly. Caution in patients with a known history of QT prolongation or in patients taking medicines known to prolong the QT interval. Not recommended during pregnancy and in women of childbearing potential not using contraception. Not recommended during breastfeeding. **Interactions:** Clinically relevant drug interactions between Betmiga™ and medicinal products that inhibit, induce or are a substrate for one of the CYP isozymes or transporters are not expected, except for inhibitory effect on the metabolism of CYP2D6 substrates. Betmiga™ is a moderate and time-dependant inhibitor of CYP2D6 and weak inhibitor of CYP3A. No dose adjustment needed when administered with CYP2D6 inhibitors or CYP2D6 poor metabolisers. Caution if co-administered with medicines with a narrow therapeutic index and significantly metabolised by CYP2D6. When initiating in combination with digoxin the lowest dose for digoxin should be prescribed and serum digoxin should be monitored. **Adverse Effects:** Urinary tract infection, tachycardia, palpitation, atrial fibrillation, blood pressure increase, leukocytoclastic vasculitis. Prescribers should consult the Summary of Product Characteristics in relation to other side effects. **Pack and Prices:** Country specific. **Legal Category:** POM. Product Licence Number: Betmiga™ 25 mg EU/1/12/809/003; Betmiga™ 50 mg EU/1/12/809/010. **Date of Preparation:** November 2012 **Further information available from:** Astellas Pharma Europe B.V. P.O. Box 344, 2300 AH Leiden, The Netherlands. Betmiga™ is a Registered Trademark. For full prescribing information please refer to the Summary of Product Characteristics. 20140312-UR-BTMA-08

Adverse events should be reported. Report adverse events to E.J. Busuttil Ltd. Tel: +356 21 44 7184

CATRIONA ZAMMIT, CHRISTINE VELLA
& RACHEL ABELA

AUDIT OF THE AETIOLOGICAL FACTORS OF CONSTIPATION LEADING TO ADMISSION AT GOZO GENERAL HOSPITAL

ABSTRACT

Constipation accounted for 2.31% of admissions at Gozo General Hospital in 2012. This audit was primarily designed to identify populations affected and causative aetiological factors. A secondary aim was to determine practices that required modification with a view to improve community management of the condition and thus possibly reduce unnecessary admissions.

INTRODUCTION

Constipation constituted 2.31% of admissions at Gozo General Hospital (GGH) in 2012 accounting for 148 days (0.65%) of total adult bed occupancy. This study looked at the causes of constipation in these patients and examined how these admissions could be minimized by being diagnosed and managed better in the community setting.

As described by Addison et. al,[1] in a similar study carried out by a group at Harvard University, polypharmacy and inappropriate use of laxatives were a significant contributing factor predisposing to increasing constipation admissions. Another study by Hertzberg[2] showed that many community-based patients were poorly controlled even though they were receiving laxatives regularly. This was also shown to increase burden on NHS resources.

A better approach at handling constipation in the community setting will decrease the amount of hospital admissions which can be very distressing both to patients and their relatives and carers. Moreover, patients would benefit from not undergoing any inconvenient procedures such as enemas and not being exposed to the hospital environment which in itself predisposes the patient to a higher rate of infections.

METHODOLOGY

Patients admitted to GGH with constipation between 1st January 2012 and 31st December 2012 were identified from the GGH Hospital Activity Data. Patient files for the relevant admission were reviewed. Previous case notes were also reviewed for any relevant data. In total, 58 admissions for 57 patients were reviewed (one patient was admitted twice). Those deceased were excluded.

The following data were reviewed:

1. Age and sex of the patient
2. Structural and functional colonic and intestinal conditions possibly contributing to constipation including:
   - Past abdominal surgery
   - Irritable bowel syndrome
   - Anal fissures
3. Lifestyle factors:
   - Dietary habits - inadequate fibre intake, overuse of caffeine or alcohol, intake of large amounts of dairy products
   - Dehydration / Poor water intake
   - Immobility issues – being bed-bound, having arthritis, using wheelchairs
   - Stress
4. Medical Conditions:
   - Hypercalcaemia
   - Hyperparathyroidism
   - Hypokalaemia
   - Hypothyroidism
   - Diabetes mellitus
   - Neurologic Disorders - stroke, Hirschsprung disease, Parkinson's disease, multiple sclerosis, spinal cord lesion, head injury, cerebrovascular accidents, Chagas disease, familial dysautonomia
   - Connective tissue disorders - scleroderma, amyloidosis, mixed connective-tissue disease
   - Psychological issues - depression, anxiety, somatisation and eating disorders

5. Medications
   - Antidepressants
   - Anticholinergics
   - Opioids
   - Calcium channel blockers
   - Diuretics
   - Psychotropic drugs (excluding antidepressants)
   - Cholestyramine and stimulant laxatives (long-term use) & stool softeners
   - Other medications including metals e.g. iron supplements, NSAIDs, sympathomimetics e.g. pseudoephedrine, antacids, oral contraceptives, thalidomide, calcium supplements.

In order to investigate any faecal loading, the patients' electronic records were reviewed to analyse the investigations carried out on admission, including ultrasounds, abdominal X Rays (AXR), CT scans and contrast studies.

RESULTS

As seen in figure 1, the 41- 60 age group was the most susceptible to constipation, with the medical factors being the commonest cause, followed by medications.

Relevant findings from table 1 include a high prevalence of immobility and a low prevalence of a poor fibre diet and fluid intake. This highlights that such information is not sought during primary assessment or admission, making it difficult to give advice on discharge.

As shown in table 2 the low incidence of hypercalcaemia and the absence of hyperparathyroidism may be attributed to the fact that the calcium levels were not tested during admission. Only 6 out of 58 admissions (10.34%) were already on treatment for constipation.

As can be seen in figure 2, in total there were 19 patients who were admitted with colonic factors (one of whom was admitted twice), out of which only 4 had no other medical/ pharmaceutical contributing factors. Of the latter, only one had lifestyle factors (in this case stress) which possibly contributes to constipation. 15 out of these 19 patients had past abdominal surgery. 8 patients had past appendicectomies.

Figure 1. Prevalence of constipation in different age groups according to different risk factors

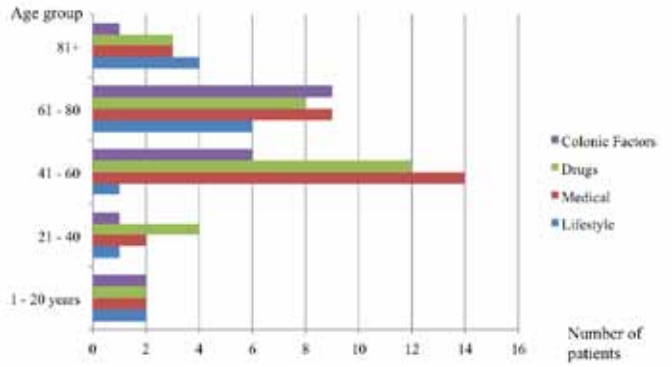

Figure 2. The number of admissions (20 in total) in our sample having structural and functional colonic factors in combination with medical conditions and medications which contribute to constipation

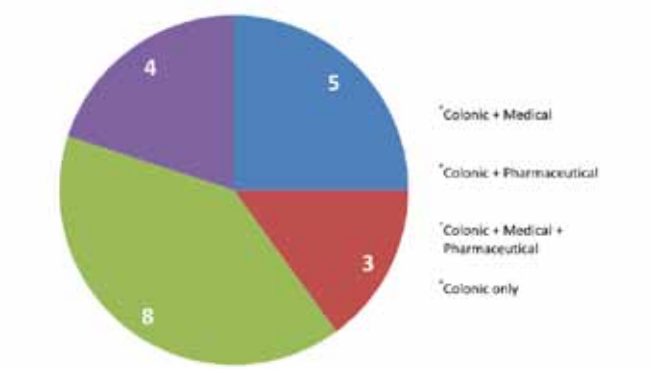

Table 1. The number and percentage of admissions with different lifestyle factors. the number and percentage of admissions with colonic factors, with and without concurrent medical and pharmaceutical contributing factors being present

Colonic Factors	Number and % of total admissions (58)	
Colonic only	4	6.90%
Colonic + Medical	5	8.62%
Colonic + Pharmaceutical	3	5.17%
Colonic + Medical + Pharmaceutical	8	13.79%

Lifestyle Factors	Number and % of total admissions (58)	
Lack of fibre	0	0%
Lack of fluid	1	1.72%
Immobility	12	20.69%
Stress	2	3.45%

GALVUS and EUCREAS
COMPREHENSIVE POWER TO ADVANCE TYPE 2 DIABETES TREATMENT

GALVUS is a DPP-4 inhibitor that improves glycemic control through powerful islet enhancement[1]

EUCREAS is the combination of a DPP-4 inhibitor, GALVUS, and metformin[2]

Galvus®
PRESENTATION: Each tablet contains 50 mg of vildagliptin. **INDICATIONS:** For the treatment of type 2 diabetes mellitus in adults. As monotherapy in patients inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to contraindications or intolerance. As dual oral therapy in combination with metformin in patients with insufficient glycaemic control despite maximal tolerated dose of monotherapy with metformin; a sulphonylurea in patients with insufficient glycaemic control despite maximal tolerated dose of a sulphonylurea and for whom metformin is inappropriate due to contraindications or intolerance; a thiazolidinedione in patients with insufficient glycaemic control and for whom the use of a thiazolidinedione is appropriate. As triple oral therapy in combination with a sulphonylurea and metformin when diet and exercise plus dual therapy with these medicinal products do not provide adequate glycaemic control. Vildagliptin is also indicated for use in combination with insulin (with or without metformin) when diet and exercise plus a stable dose of insulin do not provide adequate glycaemic control. **DOSAGE:** When used as monotherapy or in combination with metformin and a sulphonylurea or in combination with insulin (with or without metformin), the recommended daily dose of vildagliptin is 100mg, administered as one dose of 50 mg in the morning and one dose of 50 mg in the evening. When used in combination with a sulphonylurea, a lower dose of the sulphonylurea may be considered to reduce the risk of hypoglycaemia. Galvus can be administered with or without a meal. Doses greater than 100 mg are not recommended. Galvus is not recommended for use in children and adolescents (< 18 years). The safety and efficacy of Galvus in children and adolescents (< 18 years) have not been established. No data are available. The recommended dose for patients with moderate renal impairment is 50mg once daily. If a dose of Galvus is missed, it should be taken as soon as the patient remembers. A double dose should not be taken on the same day. No dose adjustments are necessary in elderly patients ≥ 65 years. The safety and efficacy of Vildagliptin as triple oral therapy in combination with metformin and a thiazolidinedione have not been established. **CONTRAINDICATIONS:** Hypersensitivity to the active substance or to any of the excipients. **WARNINGS / PRECAUTIONS:** Galvus should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. There is limited experience in patients with CSRD on haemodialysis. Therefore Galvus should be used with caution in these patients. Galvus is not recommended in patients with hepatic impairment, including patients with pre-treatment ALT or AST >3x the ULN. Liver function tests should be performed prior to treatment initiation, at three month intervals during the first year and periodically thereafter. Should an increase in AST or ALT of 3xULN or greater persist, withdrawal of Galvus therapy is recommended. Patients who develop jaundice or other signs suggestive of liver dysfunction should discontinue Galvus. Clinical experience in patients with NYHA functional class III treated with Vildagliptin is still limited and results are inconclusive. Routine monitoring of diabetic patients for skin disorders such as blistering or ulceration is recommended. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine. Galvus should not be administered during pregnancy or breast-feeding since no studies on the effect on human fertility have been conducted for Galvus. Should be used with caution in patients with renal impairment. Sulphonylureas are known to cause hypoglycaemia. Patients receiving Vildagliptin in combination with a sulphonylurea may be at risk for hypoglycaemia. Therefore, a lower dose of sulphonylurea may be considered to reduce the risk of hypoglycaemia. Use of Vildagliptin has been associated with a risk of developing acute pancreatitis. If pancreatitis is suspected, Vildagliptin should be discontinued. If acute pancreatitis is confirmed, Vildagliptin should not be restarted. Caution should be exercised in patients with a history of acute pancreatitis. **INTERACTIONS:** Vildagliptin has a low potential for drug interactions. Its clinically relevant interactions with other antidiabetics (glyburide, pioglitazone, metformin, amlodipine, digoxin, ramipril, simvastatin, virazidon or warfarin) were observed after co-administration with Vildagliptin. As with other oral antidiabetic medicines, the hypoglycaemic effect of Vildagliptin may be reduced by certain active substances, including thiazides, corticosteroids, thyroid-products and sympathomimetics. **ADVERSE REACTIONS:** Rare cases (>1/10,000 to <1/1,000): angioedema, abnormal liver function tests, hepatic dysfunction (including hepatitis). Monotherapy: Common (>1/100 to <1/10): dizziness. Uncommon (>1/1,000 to <1/100): headache, constipation, asthenia, hypoglycaemia, oedema peripheral. Very rare (<1/10,000): URTI, nasopharyngitis. Combination with metformin: Common: tremor, headache, dizziness, nausea, hyperglycaemia, hyperhidrosis, asthenia. Uncommon: fatigue. Combination with sulphonylurea: Common: tremor, headache, dizziness, asthenia, hypoglycaemia. Uncommon: constipation. Very rare: nasopharyngitis. Combination with Thiazolidinedione: Common: weight measure, oedema peripheral. Uncommon: headache, asthenia, hypoglycaemia. Combination with insulin: Common: decreased blood glucose, headache, chills, nausea, gastro-oesophageal reflux disease. Uncommon: Diarrhoea, flatulence. Frequency not known: urticaria, pancreatitis, hepatitis and abnormal liver function tests (reversible upon discontinuation of the medicinal product), bullous or exfoliative skin lesions. Combination with metformin and a sulphonylurea: Common: hypoglycaemia, dizziness, tremor, hyperhidrosis, asthenia. **LEGAL CATEGORY:** POM **PACK SIZES:** 7, 28 tablets. **MARKETING AUTHORISATION HOLDER:** Novartis Europharm Limited, Frimley Business Park, Camberley GU16 7SR United Kingdom. **MARKETING AUTHORISATION NUMBERS:** EU/1/07/414/001, 003. **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 4, Marsa, MRS 1000, Malta. Tel +356 21222872. 2015-MT-GAL-19-JUN-2015

Eucreas®
PRESENTATION: Each 50 mg/850 mg film-coated tablet contains 50 mg of vildagliptin and 850 mg metformin hydrochloride. Each 50 mg/1000 mg film-coated tablet contains 50 mg of vildagliptin and 1000 mg metformin hydrochloride. **INDICATIONS:** Eucreas is indicated as the treatment of type 2 diabetes mellitus patients. Indicated in the treatment of adult patients who are unable to achieve sufficient glycaemic control at their maximally tolerated dose of oral metformin alone or who are already treated with the combination of vildagliptin and metformin as separate tablets. Eucreas is indicated in combination with a sulphonylurea (i.e. triple combination therapy) as an adjunct to diet and exercise in adult patients inadequately controlled with metformin and a sulphonylurea. Eucreas is indicated in triple combination therapy with insulin as an adjunct to diet and exercise to improve glycaemic control in adult patients when insulin at a stable dose and metformin alone do not provide adequate glycaemic control. **DOSAGE:** The dose of antihyperglycaemic therapy with Eucreas should be individualised on the basis of the patient's current regimen, effectiveness and tolerability while not exceeding the maximum recommended daily dose of 100 mg vildagliptin. Eucreas may be initiated at either the 50 mg/850 mg or 50 mg/1000 mg tablet strength twice daily, one tablet in the morning and the other in the evening. For patients inadequately controlled at their maximal tolerated dose of metformin monotherapy. The starting dose of Eucreas should provide vildagliptin as 50 mg twice daily (100 mg total daily dose) plus the dose of metformin already being taken. For patients switching from co-administration of vildagliptin and metformin as separate tablets, Eucreas should be initiated at the dose of vildagliptin and metformin already being taken. For patients inadequately controlled on dual combination with metformin and a sulphonylurea. The doses of Eucreas should provide vildagliptin as 50 mg twice daily (100 mg total daily dose) and a dose of metformin similar to the dose already being taken. When Eucreas is used in combination with a sulphonylurea, a lower dose of the sulphonylurea may be considered to reduce the risk of hypoglycaemia. For patients inadequately controlled on dual combination therapy with insulin and the maximal tolerated dose of metformin. The dose of Eucreas should provide vildagliptin dosed as 50 mg twice daily (100 mg total daily dose) and a dose of metformin similar to the dose already being taken. Eucreas should be taken with or just after food to reduce gastrointestinal symptoms associated with metformin. Patients > 65 taking Eucreas should have their renal function monitored regularly. Eucreas is not recommended for use in patients less than 18 years old. For use in renal or hepatic impairment, see contraindications and precautions below or refer to the SmPC for more information. The safety and efficacy of vildagliptin and metformin as triple oral therapy in combination with a thiazolidinedione have not been established. **CONTRAINDICATIONS:** Hypersensitivity to vildagliptin or metformin hydrochloride or to any of the excipients. Diabetic precoma or diabetic pre-coma. Renal failure or renal dysfunction (defined as creatinine clearance < 60 ml/min). Acute conditions with the potential to alter renal function e.g. dehydration, severe infection, shock or intravascular administration of iodinated contrast agents. Acute or chronic disease which may cause tissue hypoxia e.g. cardiac or respiratory failure, recent myocardial infarction, shock, hepatic impairment, acute alcohol intoxication, alcoholism, lactation. **WARNINGS / PRECAUTIONS:** Eucreas is not a substitute for insulin in insulin-requiring patients and should not be used in patients with type 1 diabetes. Due to the risk of lactic acidosis, renal function should be monitored at least once yearly in patients with normal renal function and at least two to four times/year in patients with serum creatinine at the upper limit of normal and in elderly patients. Eucreas is not recommended in patients with hepatic impairment, including patients with pre-treatment ALT or AST >3x the ULN. LFTs should be performed prior to treatment initiation, at three month intervals during the first year and periodically thereafter. Should an increase in AST or ALT of 3x ULN or greater persist, withdrawal of Eucreas therapy is recommended. Patients who develop jaundice or other signs suggestive of liver dysfunction should discontinue Eucreas. Routine monitoring of diabetic patients for skin disorders such as blistering or ulceration is recommended. As Eucreas contains metformin, treatment should be discontinued 48 hours before elective surgery with general anaesthesia and not usually resumed earlier than 48 hours afterwards. The IV administration of iodinated contrast agents can lead to renal failure. Therefore due to metformin active ingredient, Eucreas should be discontinued prior to or at the time of the test and not restarted until 48 hours afterwards and only after renal function has been re-evaluated and found to be normal. Eucreas should not be administered during pregnancy or lactation. Sulphonylureas are known to cause hypoglycaemia. Patients receiving vildagliptin in combination with a sulphonylurea may be at risk for hypoglycaemia. Therefore, a lower dose of sulphonylurea may be considered to reduce the risk of hypoglycaemia. The use of vildagliptin has been associated with a risk of developing acute pancreatitis. If pancreatitis is suspected, vildagliptin should be discontinued. If acute pancreatitis is confirmed, vildagliptin should not be restarted. Caution should be exercised in patients with a history of acute pancreatitis. **INTERACTIONS:** Vildagliptin has a low potential for drug interactions. No clinically relevant interactions with other antidiabetics (glyburide, pioglitazone, metformin, amlodipine, digoxin, ramipril, simvastatin, valsartan or warfarin were observed after co-administration with vildagliptin. Interactions with metformin hydrochloride that are not recommended: alcohol, iodinated contrast agents, danazol, chlorpromazine, beta2-agonists and diuretics. The dose of antihyperglycaemic medicinal products may need to be adjusted in combination with ACE inhibitors. **ADVERSE REACTIONS:** Rare cases (>1/10,000 to <1/1,000) angioedema, hepatic dysfunction (including hepatitis) have been reported with vildagliptin. Vildagliptin Monotherapy: Common (>1/100 to <1/10): dizziness. Uncommon (>1/1,000 to <1/100): headache, constipation, asthenia, hypoglycaemia, oedema peripheral. Very rare (<1/10,000): URTI, nasopharyngitis. Metformin monotherapy: Very common (>1/10): Nausea, vomiting, diarrhoea, abdominal pain and loss of appetite. Common: metallic taste. Combination vildagliptin with metformin: Common: tremor, headache, dizziness, nausea, hyperglycaemia. Uncommon: fatigue. Combination with metformin and sulphonylurea: Common: hypoglycaemia, dizziness, tremor, hyperhidrosis, asthenia. Uncommon: decreased blood glucose, headache, chills, nausea, gastro-oesophageal reflux disease, diarrhoea, flatulence. Rare cases: refer to the SmPC. **LEGAL CATEGORY:** POM **PACK SIZES:** 30, 60 film-coated tablets. **MARKETING AUTHORISATION HOLDER:** Novartis Europharm Limited, Frimley Business Park, Camberley GU16 7SR, United Kingdom. **MARKETING AUTHORISATION NUMBER:** EU/1/07/402/003-005, EU/1/07/402/008-020. Please refer to Summary of Product Characteristics (SmPC) before prescribing. Full prescribing information is available upon request from Novartis Pharma Services Inc. Representative Office Malta, P.O. Box 4, Marsa, MRS 1000, Malta. Tel +356 21222872. 2015-MT-EUC-17-JUN-2015

GAL Ad1 09/15 MT

NOVARTIS PHARMACEUTICALS

1. Novartis Europharm Ltd. Galvus®. Summary of Product Characteristics.
2. Novartis Europharm Ltd. Eucreas®. Summary of Product Characteristics.

Galvus vildagliptin

Eucreas vildagliptin/metformin

Figure 3. Number of medicines being reported to be taken by patients which contributed to constipation

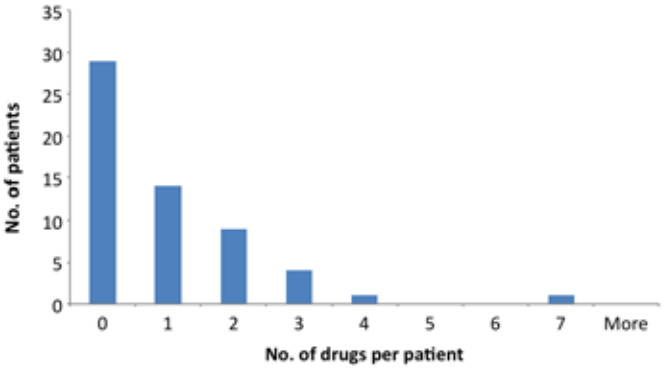

Figure 4. Venn diagram relating the number of admissions with individual or combinations of medical disorders, lifestyle factors & pharmaceutical factors contributing to constipation

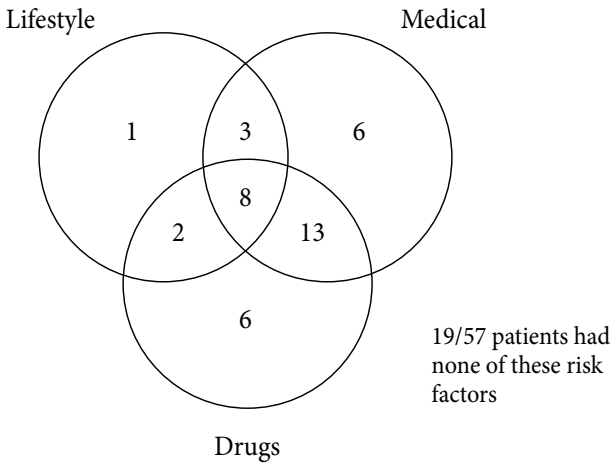

Table 2. Incidence of different classes of drugs and medical disorders contributing to constipation

Class of Drugs	Number and % of total admissions (58)	
Antidepressants	10	17.24%
Anticholinergics	2	3.45%
Opioids	2	3.45%
Calcium Channel blockers	3	5.17%
Diuretics	1	1.72%
Psychotropic	12	20.69%
Others	6	10.34%

Medical Disorders	Number and % of total admissions (58)	
Hypercalcaemia	2	3.45%
Hyperparathyroidism	0	0%
Hypokalaemia	0	0%
Hypothyroidism	3	5.17%
Diabetes Mellitus	10	17.24%
Neurological disorders	10	17.24%
Psychological disorders	11	18.97%
Connective Tissue Disease	2	3.45%

As seen in figure 3, of those patients who were not taking any medications (29 patients):

- 16 had no risk factors (55.17%) – of which 10 were ≤ 25 years old
- 3 had only colonic factors (10.34%)
- 3 had only medical factors (10.34%)
- 3 had both medical and colonic factors (10.34%)
- 1 had both medical and lifestyle factors (3.45%)
- 2 had colonic, lifestyle and medical factors (6.90%)

Figure 4 is a Venn diagram representing the number of patients having one or more overlapping contributing lifestyle, medical or pharmaceutical factors. The most important observation from this Venn diagram is that it shows that the majority of patients admitted with constipation were already under medical care.

CONCLUSION

The GGH study showed that the predominant age group of those admitted because of constipation was between 41 and 60 years, followed closely by those between 61 and 80 years. In addition to this, the commonest factors contributing to constipation were noted to be medical conditions and regular medications. This shows that the patients who constituted the highest risk are those who are being treated by professionals, thus suggesting that management of constipation should be improved. A high incidence of past appendicectomies in admissions for constipation was also an interesting finding in

our study, however, no related literature could be found, and so, it was concluded that this is an incidental finding since it is a common surgical procedure.

During the data collection it was noted that sometimes history-taking, discharge advice and investigations were not thorough enough. Frequently, dietary habits and the mobility status were not noted in detail except in cases where it was obvious that the patients were bed-bound. Few were the cases in which dietary habits were recorded in files. The latter is especially important in elderly patients who may live alone and do not cook for themselves, and also for those patients with neurological deficits such as stroke and cerebral palsy who have special diets and difficulty in feeding.

All these issues need to be addressed and managed better. If the management is improved, the rate of admissions for constipation can be decreased. In view of this, following the study, a check-list was devised which was targeted at documentation and consideration of all factors discussed. A meeting with GPs in Gozo was also held where the data arising from the study was presented and the check-list explained. The importance of correctly filling this check list for patients was discussed with a view to help decrease the amount of admissions to hospital. The check-list may be accessed on **www.thesynapse.eu**

ACKNOWLEDGEMENTS

We would like to thank the staff of Gozo General Hospital, especially Mr Salvu Azzopardi and the staff of the records office for their help.

REFERENCES CAN BE ACCESSED ON THESYNAPSE.NET

THIS MONTH IN *medical history*

257 YEARS AGO 6 Sep 1758 – Birth of Dr Cosme Argerich, Argentine physician, founder of the Medicine School of Buenos Aires.

243 YEARS AGO 26 Sep 1772 – New Jersey passes bill requiring a licence to practice medicine.

4 YEARS AGO 16 Sep 2011 – President Obama announced that NIH will collaborate with the FDA and the Defense Advanced Research Projects Agency to develop a chip to screen for safe and effective drugs more efficiently than current methods, and before they are tested in clinical trials.

THESYNAPSE augurs medical, dental and pharmacy students success in the forthcoming academic year

NEW

Augmentin® SR

1000 mg/62,5 mg

Amoxicillin/Clavulanic Acid

Prolonged release tablets

- ✓ Unique bilayer tablet with immediate and sustained release delivery of amoxicillin provides superior efficacy against resistant pathogens[1,2]
- ✓ Recommended by leading Guidelines in the treatment of Community Acquired Pneumonia[3,4]
- ✓ Most common adverse effects are diarrhoea, nausea, vomiting and mucocutaneous candidiasis[5]
- ✓ Indicated for use in adults & adolescents aged ≥16 years; 2 tablets BD for 7-10 days[5]

Spreading infectious liveliness!

Mini Abridged Prescribing Information: *Please refer to full Summary of Product Characteristics (SPC) before prescribing.* **TRADE NAME:** Augmentin SR. **ACTIVE INGREDIENTS:** Amoxicillin (as trihydrate) and potassium clavulanate. **PRESENTATION:** 1000 mg/62.5 mg prolonged-release tablets. Supplied in 28 tablet packs. **INDICATION**: Treatment of community acquired pneumonia in adults and adolescents aged at least 16 years, caused or thought likely to be caused by penicillin-resistant *Streptococcus pneumoniae.* **POSOLOGY & ADMINISTRATION:** Oral use. Recommended dose of two tablets twice daily for seven to ten days. To minimise potential gastrointestinal intolerance, administer at the start of a meal. **CONTRAINDICATIONS:** Hypersensitivity (and past history of) to the active substances, to any penicillins or to any of the excipients. **SPECIAL WARNINGS & PRECAUTIONS:** Before initiating therapy careful enquiry of previous hypersensitivity reactions to beta-lactams. Where an infection is proven to be due to an amoxicillin susceptible organism, a switch to an amoxicillin-only preparation should be considered. Convulsions may occur in patients receiving high doses or who have impaired renal function. Concomitant use of allopurinol increase likelihood of allergic skin reactions. Prolonged use may occasionally result in overgrowth of non-susceptible organisms. Contains 29.3 mg (1.3 mmol) of sodium per tablet. *Refer to SPC's for full list of precautions.* **INTERACTIONS:** Penicillins may reduce the excretion of methotrexate causing a potential increase in toxicity. Concomitant use of probenecid is not recommended. If co-administration with oral anticoagulants is necessary, the prothrombin time or international normalised ratio should be carefully monitored with the addition or withdrawal of amoxicillin. Moreover, adjustments in the dose of oral anticoagulants may be necessary. Clinical monitoring should be performed during the combination with mycophenolate mofetil and shortly after antibiotic treatment. **PREGNANCY & LACTATION:** Use should be avoided unless considered essential by the physician. **UNDESIRABLE EFFECTS:** Very common (≥1/10): diarrhoea. Common (≥1/100, <1/10): mucocutaneous candidosis, nausea, abdominal pain. *Refer to SPC's for full list of undesirable effects*. **AUTHORISATION NUMBER:** AA 1051/00102. **MARKETING AUTHORISATION HOLDER:** GlaxoSmithKline Bulgaria EOOD. **LEGAL CATEGORY:** POM. **DATE OF PREPARATION:** July 2014. **In order to ensure that this product information reflects the most up-to-date clinical and post-marketing surveillance data, please always refer to the latest Summary of Product Characteristics (SPC) which is available from GlaxoSmithKline (Malta) Ltd (Tel: +356 21238131).** ***REPORTING ADVERSE EVENTS (AEs):*** **If you become aware of any AEs, medication errors and/or use during pregnancy in association with GSK products, please report the event promptly to:** GSK (Malta) Limited, 1, De la Cruz Avenue, Qormi QRM 2458, Malta (Tel: +356 21238131). **Alternatively, any suspected AEs and medication errors can also be reported via the national Adverse Drug Reactions (ADRs) reporting system:** Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and posted to the Malta Medicines Authority, Post-licensing Directorate, 203, Level 3, Rue D'Argens, Gżira GŻR 1368, MALTA, or sent by email to postlicensing.medicinesauthority@gov.mt.

References:

1. Benninger MS. Amoxicillin/clavulanate potassium extended release tablets: a new antimicrobial for the treatment of acute bacterial sinusitis and community-acquired pneumonia. Expert Opin Pharmacother. 2003 Oct; 4(10): 1839-46.
2. Anthony R. White *et al.* Augmentin® (amoxicillin/clavulanate) in the treatment of community-acquired respiratory tract infection: a review of the continuing development of an innovative antimicrobial agent Journal of Antimicrobial Chemotherapy (2004) 53, Suppl. S1, i3–i20.
3. Gilbert DN, *et al.* Sanford guide to Antimicrobial Therapy v.3.11–last updated March 11, 2014. Sperryville; Antimicrobial Therapy, Inc. 2014 .
4. Mandell LA, Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis. 2007 Mar 1; 44 Suppl 2: S27-72.
5. Augmentin SR SPC, November 2013.

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ATTITUDES AND KNOWLEDGE OF PARENTS ON VACCINATION

ABSTRACT

Despite vaccinations being a breakthrough in preventive care, parents' decisions on vaccination programmes may be difficult. This study investigated parents' attitudes and knowledge on vaccines and vaccine-preventable illnesses. This was done with a view to identify discrepancies between the perceived and actual knowledge on vaccination schedules as well as to determine the main reasons for missing vaccinations. Following a review of the needs and concerns of parents, an information resource which best meets those needs was compiled.

INTRODUCTION

Vaccinations are a vital element in preventive healthcare programmes since they reduce the associated morbidity and mortality of illnesses.[1] Vaccinations have brought a decrease in the burden of infectious disease and are considered as the greatest success of public health in the last century.[2] Apart from protecting vaccinated individuals, successful vaccination programmes benefit society in general as the incidence of disease in the unvaccinated population is indirectly reduced.[2]

In Malta, vaccination against diphtheria, tetanus and polio is obligatory for all children and the rubella vaccine is obligatory for females. In addition, parents have to decide which other vaccines to give to their children. This involves an important but challenging decision. Unfortunately, even though the benefits of vaccination are undeniable, vaccines are sometimes considered as 'victims of their own success'. The reason for this is that their success in preventing certain illnesses has resulted in generations of parents who never experienced the vaccine preventable illnesses. This gives the perception that vaccination is futile and more attention is thus given to the perceived risks of vaccines rather than to the diseases they prevent.[3] For this reason a need was felt to assess the knowledge, perception and attitudes of Maltese parents on vaccines and vaccine-preventable illnesses, as well as the factors which affect parents' decisions to this regard.

METHODOLOGY

Data was collected by means of a validated questionnaire which was compiled by 270 parents in different settings. Stratified random sampling was used to identify representative settings - community pharmacies, clinics and other places with a high parent attendance.

The questionnaire consisted of three sections. The first section consisted of questions on the decision-making process, sources of information used by parents and parents' perception of the need for more information. The second section collected information on the children's vaccination status and reasons why specific vaccinations were not given while the third section looked at parents opinions on vaccinations not offered for free by the NHS and on the parents' willingness to pay for these vaccinations.

RESULTS

The questionnaire was compiled by 270 participants. Most respondents were between 30 and 45 years of age (71.3%), 12.3% of parents were over 45 years while 16.4% were younger than 30 years. The average age of the parents' children was 7.7 years.

SOURCES OF INFORMATION

81.2% of parents stated that they search for information when deciding on their childrens' vaccination programmes. The three main sources of information chosen by parents were the paediatrician (35.2%), the family doctor (20.9%) and the internet (19.8%). Unfortunately the pharmacist is the source of information parents refer to the least (3%).

PARENTS' PERCEIVED AND ACTUAL KNOWLEDGE AND FAMILIARITY WITH VACCINATION SCHEDULES

When asked to rate how familiar they feel with recommended vaccination schedules and vaccine-preventable illnesses, almost 90% claimed that they feel very familiar, familiar or moderately familiar. Only 10% of the 259 parents who answered this question stated that they feel slightly or not familiar with the recommended vaccination schedules. However, when in another section parents were presented with a list of vaccine preventable illnesses and asked to rate their knowledge about the illnesses, their perceived susceptibility for an unvaccinated individual and the risk of the illness having permanent consequences, the questions had a high non-response rate as well as well as a big number of parents who expressed their lack of knowledge and familiarity. This may suggest that parents feel more familiar than they actually are and that they are making less informed decisions than perceived.

Table 1. Reasons for not giving a vaccination

Reason for not vaccinating	No. of participants
I do not feel my child is at risk of being infected with such a disease	80
The disease is not serious enough so as to justify vaccination	10
I am not aware that this vaccine exists	145
The vaccine is too expensive	15
I am concerned about safety and side-effects of this vaccine	86
I heard the vaccine can have harmful effects	30
I do not believe in vaccines	12
I forgot	5
I want to give my children the least possible number of vaccines	19
I feel that there are too many vaccinations required	16
I feel that vaccines other than those given for free by the government are not necessary	20

DECISIONS NOT TO VACCINATE

Parents were presented with a list of non-obligatory vaccinations and asked to mark whether they have either have given or plan to give the particular vaccine to their children or did not give and do not plan to give it. Parents were further asked to select reasons why they chose not to give the particular vaccines. From the given options, the option that parents did not know that the vaccine exists was by far the most selected one. As shown in Table 1, this reason was selected by 145 parents, far more than the second most cited reason, i.e. safety and side effects of vaccines.

ATTITUDES TOWARDS VACCINATIONS NOT PROVIDED FOR FREE

When asked to rank their agreement with the statement 'I am willing to consult my trusted healthcare professional and pay for the recommended vaccines', 92% of responding parents claimed that they agree or strongly agree with the statement. Furthermore, when presented with the statement, 'I will wait until it is free' only 6% of responding parents answered that they agree or strongly agree with the statement.

DEVELOPMENT OF TILQIM.INFO

The findings of the research were used to develop **tilqim.info**, a website aimed to provide parents with necessary information to support them in making an informed decision. The website content was validated by a seven-member validation panel including professionals qualified and experienced in the subject as well as people who are not in the medical field. This ensured that all content is correct, concise and also understandable to the target audience. The website includes information on vaccine-preventable illnesses including risks and sequelae. It also illustrates the vaccination schedule including vaccines offered through the NHS as well as vaccines available in the private market. Other sections in the website contain information on the project and its findings as well as useful contacts. **Tilqim.info** was launched in July 2015 and has been very well received by healthcare professionals and parents alike.

DISCUSSION

The study found that the lack of awareness of the availability of vaccines, and lack of knowledge about preventable illnesses are principal reasons for missed vaccinations. However, encouragingly, the findings show that parents are interested and willing to obtain more information by discussing with their trusted healthcare professionals.

Being one of the most accessible healthcare professionals, the pharmacist is in the ideal position to build a relationship of trust and support parents in the process of making informed decisions. Unfortunately, the study identified the pharmacist as the healthcare professional parents refer to the least. This should motivate pharmacists to seek ways of increasing their role in this sector. Apart from being open to discussion with parents, it is recommended that pharmacists participate in initiatives such as education campaigns. Furthermore, pharmacists may promote robust information resources which are specifically targeted to parents with a view to disseminate evidence-based information and decrease the number of vaccinations missed simply due to lack of awareness. **Tilqim.info** is the ideal tool to optimise the role of pharmacists and healthcare professionals in this field.

REFERENCES CAN BE ACCESSED ON THESYNAPSE.NET

LEVOXA

Levofloxacin 500mg tablets
Fluoroquinolone
Available in 5 and 7 tablet packs

For further information please refer to the full summary of product characteristics or to our website: www.actavis.com.mt

Actavis

ACT no. 12/2013 - JPA39022

COPD

Relvar Ellipta is for symptomatic treatment of patients with a FEV_1 <70% predicted normal (post-bronchodilator) and an exacerbation history[1]

For many patients like Joe with a history of exacerbations, COPD already takes up too much space in their life, yet they fear losing even more. So, when they need maintenance therapy, choose new Relvar Ellipta:

- The first ICS/LABA combination to deliver continuous 24-hour efficacy[2]
- In a practical, once-daily dose[1]
- Delivered in an easy to use device that patients prefer to their current inhaler[3,4*]

RELVAR™ ELLIPTA™

(fluticasone furoate and vilanterol inhalation powder)

Practical efficacy

Relvar Ellipta (fluticasone furoate/vilanterol) Abridged Prescribing Information

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 on SPC how to report adverse reactions.

Please refer to the full Summary of Product Characteristics before prescribing

Trade Name: RELVAR ELLIPTA. **Active Ingredients:** 92 micrograms or 184 micrograms of fluticasone furoate and 22 micrograms of vilanterol (as trifenatate). **Pharmaceutical Form:** 92 micrograms/22 micrograms or 184 micrograms/22 micrograms inhalation powder, pre-dispensed. **Indications:** *The 92 micrograms/22 micrograms dose:* for the regular treatment of asthma in adults and adolescents aged 12 years and older where use of a combination medicinal product (long-acting $beta_2$-agonist and inhaled corticosteroid) is appropriate; and for the symptomatic treatment of adults with COPD with a FEV_1 <70% predicted normal (post-bronchodilator) with an exacerbation history despite regular bronchodilator therapy. *The 184 micrograms/22 micrograms dose:* for the regular treatment of asthma in adults and adolescents aged 12 years and older where use of a combination medicinal product (long-acting $beta_2$-agonist and inhaled corticosteroid) is appropriate. **Dosage and Method of Administration:** *For Athsma:* One inhalation of Relvar Ellipta 92/22 micrograms or 184/22 micrograms once daily. Patients usually experience an improvement in lung function within 15 minutes of inhaling Relvar Ellipta. However, the patient should be informed that regular daily usage is necessary to maintain control of asthma symptoms and that use should be continued even when asymptomatic. If symptoms arise in the period between doses, an inhaled, short-acting $beta_2$-agonist should be taken for immediate relief. A starting dose of Relvar Ellipta 92/22 micrograms should be considered for adults and adolescents 12 years and over who require a low to mid dose of inhaled corticosteroid in combination with a long-acting $beta_2$-agonist. If patients are inadequately controlled on Relvar Ellipta 92/22 micrograms, the dose can be increased to 184/22 micrograms, which may provide additional improvement in asthma control. *For COPD:* One inhalation of Relvar Ellipta 92/22 micrograms once daily. Relvar Ellipta 184/22 micrograms is not indicated for patients with COPD. Relvar Ellipta is for inhalation use only. It should be administered at the same time of the day, each day. **Contraindications:** *Hypersensitivity* to the active ingredient or excipients. **Precautions for Use:** Fluticasone furoate/vilanterol should not be used to treat acute asthma symptoms, for which a short-acting bronchodilator is required. Caution in severe cardiovascular disease, moderate-to-severe hepatic impairment, pulmonary tuberculosis or in patients with chronic or untreated infections, history of diabetes mellitus and for paradoxical bronchospasm and pneumonia in patients with COPD. **Drug Interactions:** Beta-blockers, CYP3A4 inhibitors, P-glycoprotein inhibitors and sympathomimetic medicinal products (refer to the full Summary of Product Characteristics for list of drugs). **Fertility, Pregnancy and Lactation:** ***Pregnancy:*** No adequate data available. ***Lactation:*** insufficient information available. ***Fertility:*** There is no data in humans. Animal studies indicate no effect on fertility. **Effect on Ability to Drive or Use Machines:** No or negligible influence. **Undesirable Effects:** Very common side effects include headache and nasopharyngitis (refer to the full Summary of Product Characteristics for complete list of undesirable effects). **Overdose:** There is no specific antidote. Treatment of overdose should consist of general supportive measures. **Local Presentations:** Relvar Ellipta 92 micrograms/22 micrograms inhalation powder, pre-dispensed and Relvar Ellipta 184 micrograms/22 micrograms inhalation powder, pre-dispensed. **Legal Category:** POM. **Marketing Authorisation Holder:** Glaxo Group Limited, 980 Great West Road, Brentford, Middlesex TW8 9GS, United Kingdom **Marketing Authorisation Numbers:** EU/1/13/886/001-6 **DATE OF PREPARATION:** December 2013

In order to ensure that this product information reflects the most up-to-date clinical and post-marketing surveillance data, please always refer to the latest Summary of Product Characteristics (SPC) which is available from GlaxoSmithKline (Malta) Ltd (Tel: +356 21238131).

REPORTING ADVERSE EVENTS (AEs):

Malta & Gibraltar: **If you become aware of any AEs, medication errors and/or use during pregnancy in association with GSK products, please report the event promptly to:** GSK (Malta) Limited, 1, De la Cruz Avenue, Qormi QRM 2458, Malta (Tel: +356 21238131)

Malta: **alternatively, any suspected AEs and medication errors can also be reported via the national Adverse Drug Reactions (ADRs) reporting system:** Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and posted to the Malta Medicines Authority, Post-licensing Directorate, 203, Level 3, Rue D'Argens, Gżira GŻR 1368, MALTA, or sent by email to postlicensing.medicinesauthority@gov.mt

Gibraltar: **alternatively, any suspected AEs and medication errors can also be reported via the UK regulatory authority (MHRA):** https://yellowcard.mhra.gov.uk/

References: 1. Relvar Ellipta Summary of Product Characteristics. GlaxoSmithKline; 2013. **2.** Boscia JA *et al.* Effect of Once-Daily Fluticasone Furoate/Vilanterol on 24-Hour Pulmonary Function in Patients With Chronic Obstructive Pulmonary Disease: A Randomized, Three-Way, Incomplete Block, Crossover Study. *Clin Ther.* 2012; **8**: 1655-66. **3.** Riley JH *et al.* Delivery of umeclidinium/vilanterol using a new twin strip device (ELLIPTA™) to COPD patients. 2013 (in press). **4.** Woepse M *et al.* Qualitative assessment of a two-strip dry powder inhaler (ELLIPTA™) for COPD and asthma. *EAACI.* 2013.

MLT_GIB/RESP/0007/14 Date of preparation: January 2014

Theravance | gsk

MALTA ASSOCIATION OF DENTAL STUDENTS

LAURA CUSCHIERI

The Malta Association of Dental Students (MADS) is a non-profit student organisation aimed to represent dental students, promote oral health knowledge and awareness, as well as enriching community dentistry competence amongst dentistry students. This is achieved during several events organized and set up by its members. Events include the World Oral Health Day, Smoke-free Smile for Life and the US Embassy Health Festival.

One of the MADS aims is to embed certain values, when it comes to oral health, to the younger generation, and educate them with the most entertaining and interactive ways possible. This is achieved during several school visits in which games and other activities related to dentistry are set up with a view to aid the comprehension of the concept of oral health and hygiene. Prevention is better than cure, hence MADS strives to create a bridge between health care professionals and the public, along the idea of a well maintained healthy lifestyle. In fact, MADS had collaborated with MMSA during several health awareness events for that particular collective aim. This includes the World Diabetes Day and MMSA Health Fest which were a huge success. Another important annual event is Science and the City, in which MADS sets up a stand with several interesting and appealing demonstrations and games.

MADS doesn't focus only on local knowledge, as it is an active member of EDSA (European Dental Student Association) and IADS (International Association for Dental Students). Annually, members of the organization attend a conference in which Malta and MADS are promoted along with the organisation's work. MADS also started organizing an educational summer camp, which was held for the first time in September 2014. Students from several European universities attended the weeklong event and provided good feedback, so much so that MADS is collaborating once again with EDSA to set up the Malta EDSA Summer Camp 2015 this September. MADS continues to strengthen its collaboration with other local student organisations to help promote its message amongst a wider spectrum of people.

SKINCARE
NOT JUST FOR THE SUMMER MONTHS

TRICIA MICALLEF

As summer comes to an end, many seem to decreasingly exercise proper skin care as they think there is no longer the risk for developing melanomas. It is of utmost importance that head-to-toe examinations in order to look for any suspicious lesions are practiced throughout the year. Although the UV index may decrease, the symptoms of damage may appear at a later stage. Special care should be taken if the person is fair, has many freckles and spends a lot of time in the sun. If caught early enough, melanomas can be effectively treated.

Melanomas are the most dangerous form of skin cancer, which develop when unrepaired DNA damage to skin cells triggers mutations. This damage is often caused by exposure to UV radiation from the sun and tanning beds. These tumours originate in the pigment-producing melanocytes in the basal layer of the epidermis.

When carrying out these self-checks one must be familiar with the ABCDEs of melanoma.

A - Asymmetry: If one draws a line through the middle of the sun spot, the two sides should be equal.

B - Borders of an early melanoma tend to be uneven.

C - Colour: Having a variety of colours and shades of brown, tan and black are a warning sign. A melanoma may also become red, white or blue.

D - Diameter: Melanomas are usually larger than 6mm in diameter, however, they may be smaller when first detected.

E - Evolving: Any change in size, shape, colour, elevation or any other trait or any new symptom such as bleeding, itching or crusting should prompt the patient to immediately seek professional help.

59% of children wake at night due to their asthma[1]

Seretide® Evohaler®
50 mcg from 4 years[3]

Poppy is **50%** less likely to wake at night when using Seretide compared to baseline[2]

Seretide® Diskus®
100 mcg from 4 years[4]

Help Poppy by prescribing Seretide

Seretide is the only ICS/LABA proven to achieve guideline-defined asthma control in children[2]

Safety Information

Very common side effects: Headache and nasopharyngitis.
Common side effects: Candidiasis of mouth and throat, pneumonia, bronchitis, hypokalaemia and hoarseness/dysphonia
Special warnings and precautions for use: Systemic effects may occur with any inhaled corticosteroid, particularly at high doses prescribed for long periods. These effects are much less likely to occur than with oral corticosteroids.
It is important that patients are reviewed regularly and the dose of inhaled corticosteroid is reduced to the lowest dose at which effective control of asthma is maintained. Monitor height of children on prolonged inhaled steroid therapy.

Seretide™ (salmeterol xinafoate and fluticasone propionate)
Kindly refer to full Summary of Product Characteristics (SPC) before prescribing.
Abridged prescribing information. Presentations: For Malta and Gibraltar: *Seretide Diskus* – Each dose provides 50 microgram salmeterol xinafoate and 100 microgram, 250 microgram or 500 microgram respectively of fluticasone propionate. *Seretide 50 Evohaler* - Each dose provides 25 microgram salmeterol xinafoate and 50 microgram of fluticasone propionate. For Gibraltar only: *Seretide 125, 250 Evohaler:* Each dose provides 25 microgram salmeterol xinafoate and 125 microgram or 250 microgram of fluticasone propionate. **Therapeutic Indications:** For Malta and Gibraltar: *Seretide Diskus and Evohaler:* is indicated in the regular treatment of asthma where use of a combination (long-acting beta-2-agonist and inhaled corticosteroid) is appropriate. *Seretide Diskus* is indicated for the symptomatic treatment of patients with COPD with a FEV_1<60% predicted normal (pre-bronchodilator) and a history of repeated exacerbations, who have significant symptoms despite regular bronchodilator therapy. *Seretide 50 Evohaler* is used in patients not adequately controlled with inhaled corticosteroids and 'as needed' inhaled short acting beta-2-agonist or patients already adequately controlled on both inhaled corticosteroid and long-acting beta-2-agonist. For Gibraltar only: *Seretide 125, 250 Evohaler:* is indicated in the regular treatment of asthma where use of a combination (long-acting beta-2-agonist and inhaled corticosteroid) is appropriate. Used in patients not adequately controlled with inhaled corticosteroids and 'as needed' inhaled short acting beta-2-agonist or patients already adequately controlled on both inhaled corticosteroid and long-acting beta-2-agonist. **Dosage and administration:** Seretide is for inhalation use only. ***Seretide Diskus:*** Asthma – Adults and adolescents 12 years and over: one puff twice daily of Seretide 100 or Seretide 250 or Seretide 500 (each containing 50 mcg of salmeterol xinafoate and 100 mcg, 250 mcg or 500 mcg respectively of fluticasone propionate). Patients should be given the strength of Seretide containing the appropriate, lowest fluticasone propionate dosage for the severity of their disease. A short term trial of Seretide may be considered as initial maintenance therapy in adults or adolescents with moderate persistent asthma (defined as patients with daily symptoms, daily rescue use and moderate to severe airflow limitation) for whom rapid control of asthma is essential. In these cases, the recommended initial dose is one inhalation of 50 micrograms salmeterol and 100 micrograms fluticasone propionate twice daily. Once control of asthma is attained treatment should be reviewed and consideration given as to whether patients should be stepped down to an inhaled corticosteroid alone. Regular review of patients as treatment is stepped down is important. Seretide is not intended for the initial management of mild asthma. Seretide 50/100 micrograms strength is not appropriate in adults and children with severe asthma. Children 4-11 years: Seretide 100 Diskus (50 mcg salmeterol and 100 mcg fluticasone propionate) – one puff twice daily. ***Seretide Diskus:*** COPD: Seretide 500 Diskus (50 mcg of salmeterol xinafoate and 500 mcg fluticasone propionate) – one puff twice daily. ***Seretide 50 Evohaler:*** Adults and children 4 years and older: Two inhalations twice daily. For Gibraltar only: ***Seretide 125, 250 Evohaler:*** Adults and adolescents 12 years and older: Two inhalations twice daily. **Contra-indications:** Hypersensitivity. **Warnings and Precautions:** Seretide should not be used to treat acute asthma symptoms for which a fast- and short-acting bronchodilator is required. Patients should not be initiated on Seretide during an exacerbation, or if they have significantly worsening or acutely deteriorating asthma. Serious asthma-related events and exacerbations can occur during Seretide therapy; sudden and progressive deterioration in control or increased use of bronchodilator therapy warrants urgent medical assessment especially in patients of African-American origin (SMART). As with all inhaled medication containing corticosteroids, Seretide should be administered with caution in patients with pulmonary tuberculosis, severe cardiovascular disorders, including heart rhythm abnormalities, diabetes mellitus, untreated hypokalaemia/patients predisposed to hypokalaemia or thyrotoxicosis. In case of paradoxical bronchospasm discontinue Seretide, assess patient and give alternative therapy if necessary. Systemic effects may occur with any inhaled corticosteroid, particularly at high doses prescribed for long periods, but are less likely than with oral steroids. It is important, therefore, that the patient is reviewed regularly and the dose of inhaled corticosteroid is reduced to the lowest dose at which effective control of asthma is maintained. Prolonged treatment of patients with high doses of inhaled corticosteroids may result in adrenal suppression and acute adrenal crises. Rarely, a range of psychological or behavioural effects such as psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children) may develop on prolonged use. Monitor height of children on prolonged inhaled steroid therapy. Transfer from oral steroids: Special care needed. Monitor adrenal function. Consider appropriate steroid therapy during periods of stress or elective surgery. Ritonavir can greatly increase the concentration of fluticasone propionate in plasma, therefore avoid concomitant use. There is also an increased risk of systemic side effects with other potent CYP3A inhibitors. There was an increased reporting of lower respiratory tract infections (particularly pneumonia and bronchitis) in the TORCH study in patients with COPD receiving Seretide compared with placebo; older patients, patients with a lower body mass index (<25kg/m^2) and patients with very severe disease (FEV_1<30% predicted) were at greatest risk of developing pneumonia regardless of treatment. Concomitant use of systemic ketoconazole significantly increases systemic exposure to salmeterol. This may lead to an increase in the incidence of systemic effects (e.g. prolongation in the QTc interval and palpitations). Concomitant treatment with ketoconazole or other potent CYP3A4 inhibitors should therefore be avoided unless the benefits outweigh the potentially increased risk of systemic side effects of salmeterol treatment. **Drug Interactions:** Avoid beta-blockers. Concomitant use with other beta-adrenergic containing drugs can have a potentially additive effect. Potent CYP3A4 inhibitors: Co-administration of ketoconazole (400 mg orally once daily) and salmeterol (50 mcg inhaled twice daily) resulted in a significant increase in plasma salmeterol exposure which may lead to an increase in the incidence of other systemic effects of salmeterol treatment (e.g. prolongation of QTc interval and palpitations) compared with salmeterol or ketoconazole treatment alone. The concomitant administration of ketoconazole should be avoided, unless the benefits outweigh the potentially increased risk of systemic side effects of salmeterol treatment. There is likely to be a similar risk of interaction with other potent CYP3A4 inhibitors (e.g. itraconazole, telithromycin, ritonavir). **Pregnancy and Lactation:** Experience limited. Balance risks against benefits. **Undesirable effects:** *Very Common/Common* - candidiasis of mouth and throat, pneumonia, bronchitis, hypokalaemia, headache, hoarseness/dysphonia, throat irritation (uncommon with Seretide 50 Evohaler), nasopharyngitis, sinusitis, contusions, traumatic fractures, arthralgia and myalgia, muscle cramps (uncommon with Seretide 50 Evohaler). See SPC for information on all adverse events. **Overdose:** *due to Salmeterol:* tremor, headache, tachycardia; *due to Fluticasone propionate:* temporary adrenal suppression.
MA Holder (Malta): GlaxoSmithKline (Ireland) Ltd. Trading as: Allen & Hanburys Ltd. **MA Numbers (Malta):** *Seretide Diskus:* MA 192/00901-3; *Seretide 50 Evohaler:* AA 192/00904. **Legal category**: POM. Not all pack sizes may be marketed. Date of revision of text: August 2013.

In order to ensure that this product information reflects the most up-to-date clinical and post-marketing surveillance data, please always refer to the latest Summary of Product Characteristics which is available from GlaxoSmithKline (Malta) Ltd (Tel: +356 21238131)

REPORTING ADVERSE EVENTS (AEs):
If you become aware of any AEs, medication errors and/or use during pregnancy in association with GSK products, please report the event promptly to: GSK (Malta) Limited, 1, De la Cruz Avenue, Qormi QRM 2458, Malta (Tel: +356 21238131) or e-mail: mt.info@gsk.com
Malta: any suspected AEs and medication errors can also be reported via the national Adverse Drug Reactions (ADRs) reporting system:
Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and posted to the Malta Medicines Authority, Post-licensing Directorate, 203, Level 3, Rue D'Argens, Gżira GŻR 1368, MALTA, or sent by email to postlicensing.medicinesauthority@gov.mt
Gibraltar: any suspected AEs and medication errors can also be reported via the UK regulatory authority (MHRA): https://yellowcard.mhra.gov.uk/

References
1. Wildhaber, J *et al. Pediatr. Pulmonol* 2012; 47:346–357.
2. DeBlic J *et al. Pediatr Allergy Immunol* 2009: 20:763–771
3. Seretide Evohaler (fluticasone propionate/salmeterol xinafoate) Summary of Product Characteristics, Allen & Hanburys Ltd. October 2014.
4. Seretide Accuhaler (fluticasone propionate/salmeterol xinafoate) Summary of Product Characteristics, Allen & Hanburys Ltd. October 2014.

Date of Preparation: **January 2015** ZINC CODE: **MLT_GIB/SFC/0002/15**

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salmeterol/fluticasone propionate

A SUMMER WEEKEND BREAK IN CHEMICAL PATHOLOGY

DR MICHELLE MUSCAT
MD MRCS(Ed) MSc

Chemical pathology is a somewhat lesser known medical sub-specialty. It is also known as clinical biochemistry or clinical chemistry. It comprises an array of laboratory investigations that range from simple routine tests such as renal, liver and lipid profiles to cardiac markers, endocrine investigations, therapeutic drug monitoring and many other tests within the clinical chemistry repertoire. These investigations are central to clinical pathways.

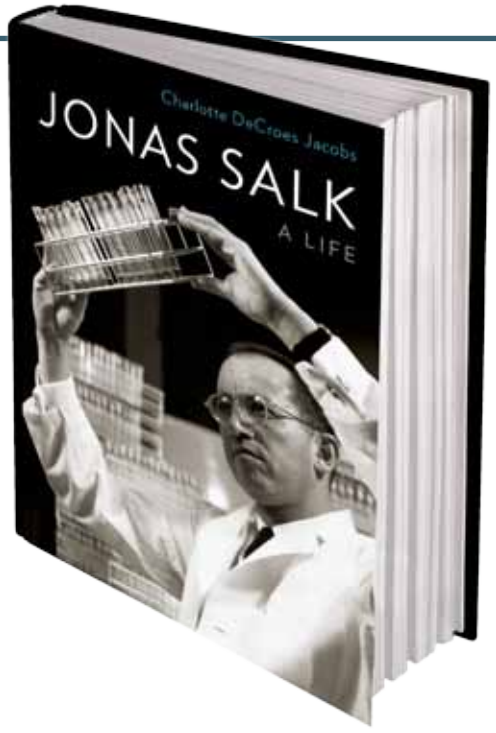
Chemical pathology also shows great promise in the research arena. There are numerous emerging new biomarkers that are finding their way into clinical use, for example, heart-type fatty acid binding protein (hFABP) which is a recent cardiac biomarker, carbohydrate-deficient transferrin (CDT) for alcohol abuse, and many more.

Chemical Pathology is currently included in the University of Malta medical course third year undergraduate pathology module. Medical and scientific advances in the field of chemical pathology impinge directly on other medical specialties, since biochemical tests are pivotal in the diagnosis and management of numerous medical conditions.

Notwithstanding the fact that the use of clinical chemistry tests is virtually ubiquitous in clinical practice, it is still somewhat one of the lesser known disciplines or 'Cinderella specialties' of the medical profession.

An upcoming event, scheduled for 26 and 27 September 2015 at the Plaza Hotel Sliema will be aimed primarily at students who will be completing their pathology module this upcoming academic year. A more engaging, innovative, non-traditional format and unique approach will be used to help promote understanding and stimulate the interest of younger generations of medical students. For details on how to make a reservation please contact **sylvana@aghl.com.mt**

EDITOR'S PICK FOR BOOKWORMS



When a waiting world learned on April 12, 1955, that Jonas Salk had successfully created a vaccine to prevent poliomyelitis, he became a hero overnight. Born in a New York tenement, humble in manner, Salk had all the makings of a twentieth-century icon - a knight in a white coat. And yet the one group whose adulation he craved - the scientific community - remained ominously silent. "The worst tragedy that could have befallen me was my success," Salk later said. "I knew right away that I was through-cast out." In the first complete biography of Jonas Salk, Charlotte DeCroes Jacobs unravels Salk's story to reveal an unconventional scientist and a misunderstood and vulnerable man. Asked why he did not get a Nobel prize, Salk replied: "Everybody thinks I got it. So that's fine." And yet Salk remained, in the eyes of the public, an adored hero.

Salk's story has never been fully told; until now, his role in preventing polio has overshadowed his part in co-developing the first influenza vaccine, his effort to meld the sciences and humanities in the magnificent Salk Institute, and his pioneering work on AIDS...

JONAS SALK: A LIFE

Charlotte DeCroes Jacobs
Oxford University Press; 559 pages; $25.13
Published in May 2015

Source: **www.amazon.com**

NOVEL DENTAL IMPLANT COATING MATERIALS

MARIA XUEREB
& JOSETTE CAMILLERI

ABSTRACT

An implant coating must be biocompatible, not compromise the long term function and success of the prosthesis and must be strong enough to withstand and transfer all loads without delamination. In this study, six different tricalcium silicate cements were investigated in the mixed and sintered form while hydroxyapatite was used as a control. The properties of each material were studied carefully to propose an innovative coating material and coating process. The hypothesis is that there is no difference between the prototype mixed and sintered cements. It is also hypothesised that there will be no difference between the prototype cements and the control hydroxyapatite.

INTRODUCTION

A dental implant is a fixture inserted in the jaw bone so as to support a dental prosthesis including a crown, bridge or denture. The purpose is to replace a missing tooth or a number of teeth. The implant actually consists of an abutment holding the fixed prosthesis. Several materials have been proposed as abutment materials including metals such as titanium and its oxides, ceramics, polymers and carbon compounds.

Tricalcium silicate cements have been described as secondary generation cements. They are derived from the first generation tricalcium silicates. The latter are the core materials from which the second generation cements are derived following certain chemical and elemental changes. Tricalcium silicates are actually based on Portland cement, a cement used in construction and buildings, which was introduced to dentistry in the mineral trioxide aggregate material. Unfortunately, Portland cement has impurities like arsenic, lead and chromium which can be leached out and can cause toxicity in the body. It also contains an aluminium phase which has been linked to Alzheimer's and Parkinson's disease.[1] On the other hand, pure tricalcium silicate cement does not contain any of these impurities as it is not produced in a kiln like Portland cement, but is produced by a sol-gel method.[1]

Over the years, dental implant systems have become the most sought after way to replace a missing tooth or teeth. A dental implant can be simplistically described as the replacement for the root of a missing tooth. The latter then serves as an attachment to replace the missing tooth. When an implant is inserted into the bone, a series of bone modelling and remodelling processes, known as osseointegration, are required for the prosthesis to be accepted by the human body and allow healing and integration of the prosthesis. Osseointegration has actually been described as the direct structural and functional connection between the human bone and the prosthesis.[2] The most commonly used dental implants are composed of titanium or titanium alloys due to their high biocompatibility, minimal toxicity, high strength and high resistance to corrosion especially since they have to be in contact with tissue fluids in the body on insertion.[3,4] The success of such implants has been quoted to be over 95%.[3] Still, over the years, different implant coating materials have been proposed so as to improve the osseointegrative potential of implants while giving a biocompatible and non-toxic prosthesis. Even though hydroxyapatite is the most widely used implant coating material, in the literature several cases of delamination and failure of such a coating where the implant coating detaches from the actual implant have been reported.[3]

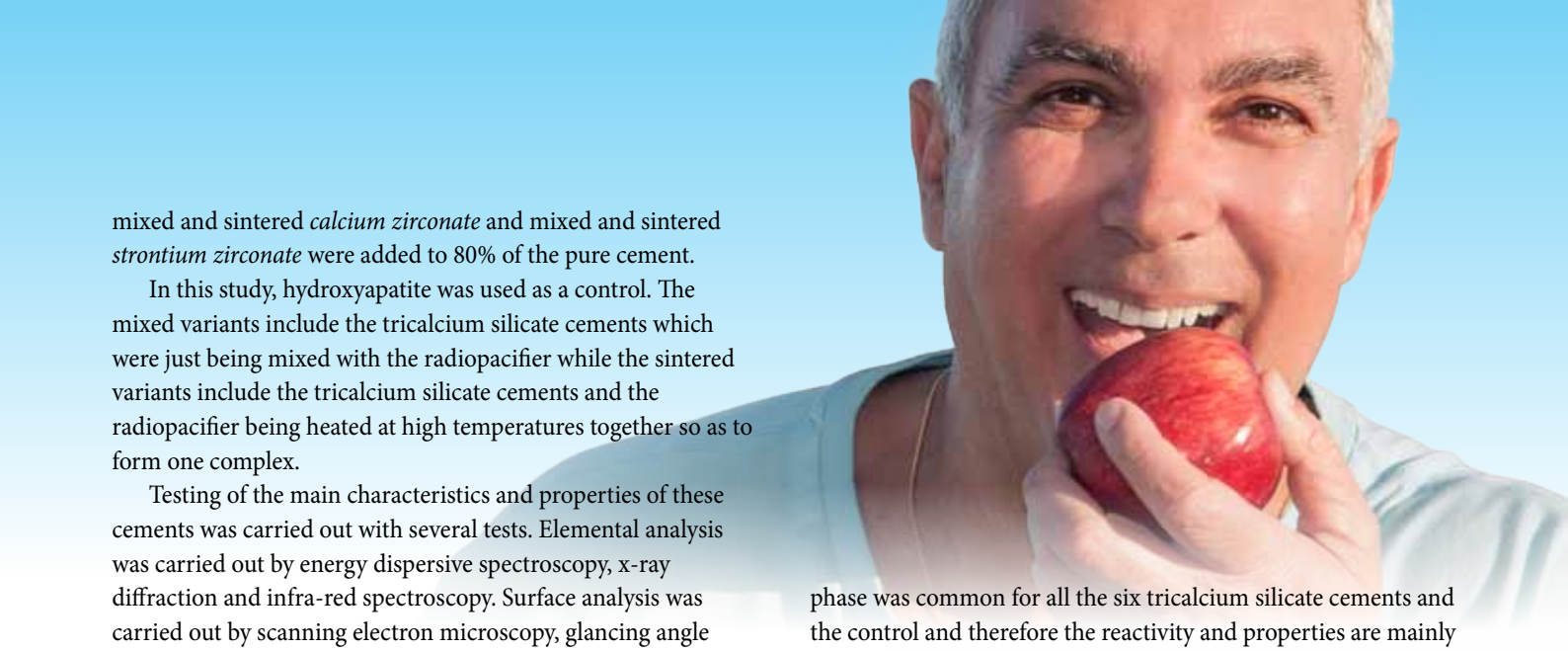
The aim of this research was to investigate innovative materials that can be used as implant coatings so as to provide a good biocompatible prosthesis while providing a more cost-effective prosthesis when compared to the conventional implants found on the market. One type of coating method, known as magnetron sputtering, was also investigated and used so as to coat titanium stubs to mimic the actual coating process.

A group of secondary generation cements, known as tricalcium silicate cements, were used in this study. These materials were chosen for this study as they have the unique ability of producing calcium hydroxide which then forms hydroxyapatite on being hydrated or upon contact with tissue fluids in the body/physiologic solution in the lab. This characteristic means that they have bioactivity. Several studies have been carried out on these cements in different fields in dentistry.[5-7]

The main advantage of using the pure tricalcium silicate cement in this study instead of the Portland cement, is to have a pure cement, free from any contaminants and thus being non-toxic.

METHODOLOGY

All tricalcium silicates have the disadvantage of not being radiopaque and therefore they cannot be distinguished on X-rays. This is quite a disadvantage since one must monitor the prosthesis radiographically to see if there are any signs of failure or peri-implantitis. For this reason, materials known as radiopacifiers are added so that the prosthesis can be viewed and monitored on X-rays. Due to this, a 20% amount of radiopacifiers, including mixed and sintered *barium zirconate*,



mixed and sintered *calcium zirconate* and mixed and sintered *strontium zirconate* were added to 80% of the pure cement.

In this study, hydroxyapatite was used as a control. The mixed variants include the tricalcium silicate cements which were just being mixed with the radiopacifier while the sintered variants include the tricalcium silicate cements and the radiopacifier being heated at high temperatures together so as to form one complex.

Testing of the main characteristics and properties of these cements was carried out with several tests. Elemental analysis was carried out by energy dispersive spectroscopy, x-ray diffraction and infra-red spectroscopy. Surface analysis was carried out by scanning electron microscopy, glancing angle x-ray diffraction, calorimetry, pH assessment, assessment of radiopacity, compressive strength and leachate analysis. The properties of each of the materials on hydration and on contact with physiologic solution were tested for 28 days in an incubator at 37°C.

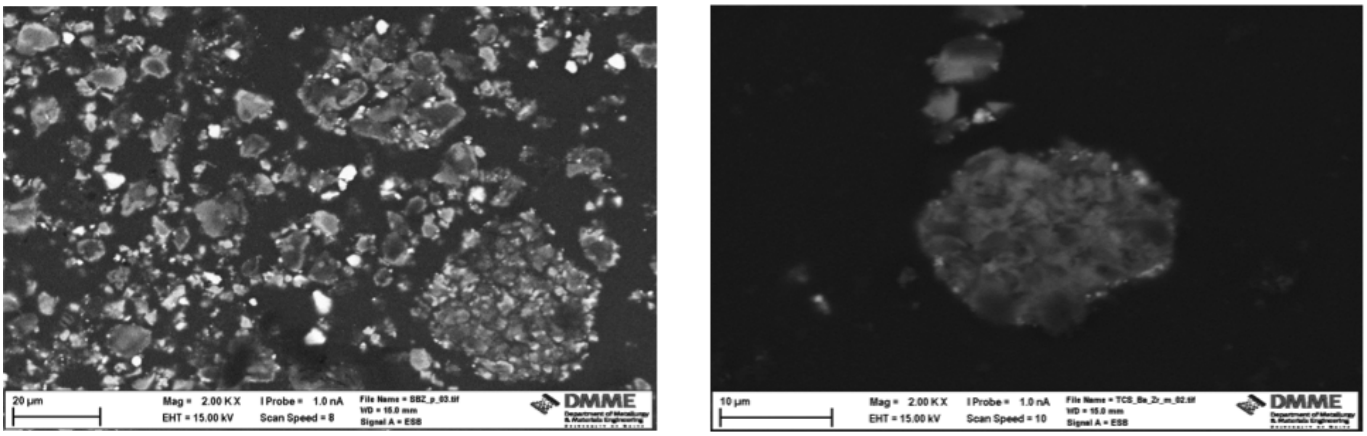
After the cement characterization, titanium stubs were coated with these cements by magnetron sputtering and the coating obtained was investigated by microscopy and x-ray diffraction analysis so as to mimic the implant coating scenario. This coating method involves high power impulses to deposit materials over a surface.

RESULTS

All the six cements and the control portrayed different properties and characteristics for each test performed. The aim of using a sintered cement, and not just a mixed cement was to obtain a more homogenous material as each cement particle is theoretically bonded to a radiopacifier molecule, whereas with a mixture one can get clumps of radiopacifier in certain areas, with other areas lacking radiopacity as can be seen in figure 1, depending on the mixing process.

This principle was mainly observed with the scanning electron microscopy. On contact with physiologic solution, all the cements portrayed the typical formation of hydroxyapatite at the surface of the material (figure 2). The tricalcium silicate phase was common for all the six tricalcium silicate cements and the control and therefore the reactivity and properties are mainly due to the radiopacifier phases in the cements. From the results obtained from the different tests one may conclude that the radiopacifiers are inert as they do not cause any chemical change in the cement phase present in the sample. Testing the powdered unreacted cements apart from the set cements, after being mixed with water or physiologic solution, allows good characterization of the materials while also allowing the investigators to see what happens upon contact with water and also identify any products formed during the setting reaction. X-ray diffraction can give compound composition identification and thus it can identify crystalline phases contained in the sample to be tested. From all the tests carried out it could be noticed that the sintered cements gave inferior properties when compared to their mixed counterparts especially when considering the strength and reactivity of the materials. On being hydrated, there was a very limited reactivity for the sintered cements while the mixed cements exhibited a mild exothermic reaction thus showing material dissolution (figure 3). Still, even though the sintered cements gave inferior properties to the mixed counterparts, all the sintered cements exhibited better characteristics over the hydroxyapatite which is being commonly used as an implant coating material. This shows that hydroxyapatite is not such an ideal implant coating material. Unfortunately the sintered barium and strontium variants showed high leaching values of the strontium and barium when compared to the calcium

Figure 1. Scanning electron micrographs in back scatter mode of powders showing the more homogenous composition of the sintered forms (left image) when compared to the mixed forms (right image)



variant. This is not an ideal scenario as the metals barium and strontium are leached out in solution and can lead to high toxic amounts. Only zirconium was stable during the leaching analysis when compared to the other radiopacifier components.

Closed-field unbalanced magnetron sputtering was used to co-deposit titanium with an interlayer of zirconia on the titanium stub (figure 4). Even though the coating deposited did not give high peaks of deposited material on the spectra, still, some of the cement was deposited on the surface of the titanium stub thus showing that this type of coating method can actually give some positive results. By applying different sputtering conditions, dental implants can actually be coated with novel cement types.

DISCUSSION

All materials gave different properties for each and every test performed. The main problem with the sintered barium and strontium zirconate variants was the high leaching of both barium and strontium in solution. The least problematic cement was the calcium variant. The calcium present can be used as both a radiopacifier while also being a non-toxic element that may contribute in the hydration and bioactivity process, in this case producing hydroxyapatite. Unfortunately *barium zirconate*, *calcium zirconate* and *strontium zirconate* did not exhibit ideal physical properties, including the compressive strength. Still, these properties could be improved by adding certain materials to the cements to improve their properties, such as inert materials to increase their flexural strength. Magnetron sputtering is also a novel type of coating technique. Even though the coating deposited did not give high peaks on the spectra, still, some of the cement was deposited on the surface of the titanium stub. Different sputtering conditions to coat the titanium stubs can be further investigated together with other novel coating techniques.

CONCLUSION

All these results show that the study of cements is an ongoing process with each test highlighting particular properties of the material. One may thus conclude that tricalcium silicate cements can be a promising coating material apart from their use in other dental fields including root canal treatments, if a good radiopacifier is added to the material to improve their properties and physical characteristics.

Figure 2. Scanning electron micrograph showing the calcium phosphate hydroxyapatite precursor forming at the surface of the hydrated cements

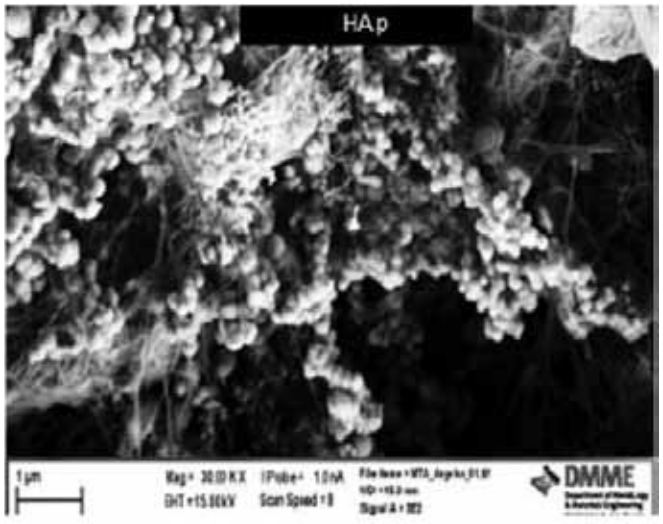


Figure 3. Calorimetry results showing the heat flux obtained on hydration of the materials tested with Hank's balanced salt solution (HBSS) which is a physiologic solution

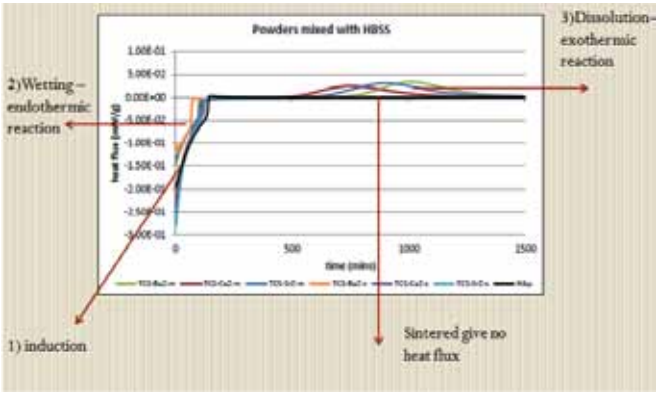
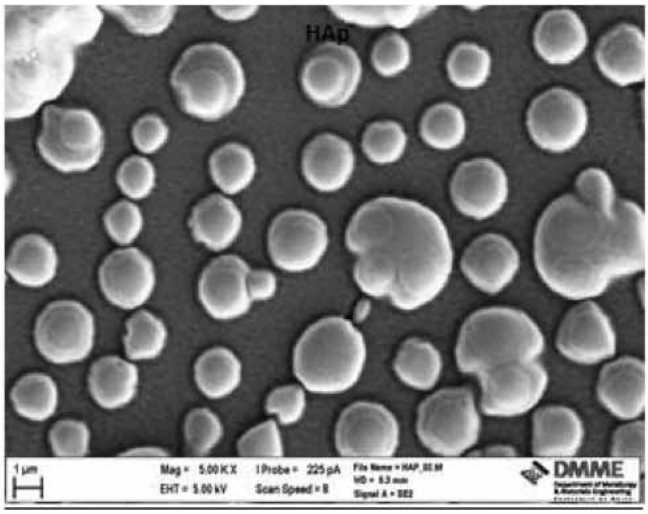


Figure 4. Scanning electron micrograph depicting the sputtered cement (in this case hydroxyapatite) over the titanium surface



ACKNOWLEDGEMENTS

The Directorate for Lifelong Learning, Ministry of Education and Employment for offering the STEPS (Strategic Educational Pathways Scholarship Scheme) throughout the Master's Program. The University of Malta Department of Dental Surgery, Department of Building and Civil Engineering, Department of Metallurgy and Materials Engineering and Chemistry Department for all their help with the testing. All the staff in Ecoles de Mines University, Douai, France, for the opportunity to do some of the testing for one month at their institution.

REFERENCES CAN BE ACCESSED ON THESYNAPSE.NET

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SMOKING AND LUNG CANCER MORTALITY IN MALTA

KATHLEEN ENGLAND
& DOROTHY GAUCI

ABSTRACT

In the European region tobacco is responsible for 16% of all deaths in adults and 12% of all deaths in the Maltese population. While locally, fewer adult females smoke when compared to males, there is an increasing trend of smoking amongst females whilst in males we are seeing a decline. Also, while mortality rates in males from lung cancer in Malta are much higher than in females, a downward trend is being observed in males, whilst in females mortality rates are showing a slowly rising trend.

INTRODUCTION

Tobacco use or exposure to tobacco smoking has a negative impact on health across the life-course from infancy to old age. The World Health Organisation (WHO) estimates that the global yearly death toll as a result of tobacco use is currently 6 million. Of these, more than 5 million are the result of direct tobacco use while more than 600,000 are the result of non-smokers being exposed to second-hand smoke.[1]

The regions with the highest proportion of deaths attributable to tobacco are the American and the European regions where tobacco has been used for a longest period of time. According to the WHO Global Report, 25% of adult male deaths and 7% of adult female deaths are attributable to tobacco in the European Region.[2]

Smoking is a primary cause of preventable illness and premature deaths, being strongly associated with lung cancer, respiratory diseases and heart diseases as well as numerous other cancers.

For both males and females, lung cancer is the disease with the largest fraction caused by smoking. Overall 92% of all lung cancer deaths among males and 71% of all lung cancer deaths among females in industrialised countries are attributable to smoking.[3]

SMOKING BEHAVIOUR IN THE MALTESE POPULATION

According to the European Health Interview Survey carried out by the Directorate of Health Information and Research in 2008, in persons between the ages of 25-64, 28% of males and 19% of females smoke daily in Malta. In comparison to this, the MONICA project (Multinational monitoring of trends and determinants in Cardiovascular Disease) which was carried out in 1984 reported rates of 47% in males and 14% in females.[4] The percentage of smokers categorised by age group and gender are as per figures 1 and 2. These reported proportions are showing that smoking amongst males in the 1980s was very high but has fallen considerably over the past two decades. In contrast, smoking amongst females has always been considerably lower than in males, however we observe an increase from 1984 to 2008.

Figure 1. % of regular (daily) male smokers in 1984 compared to 2008 by age group

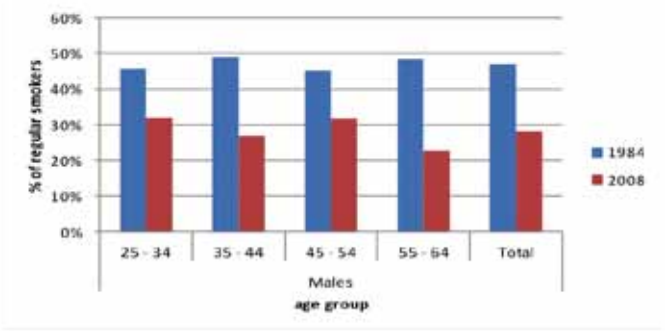
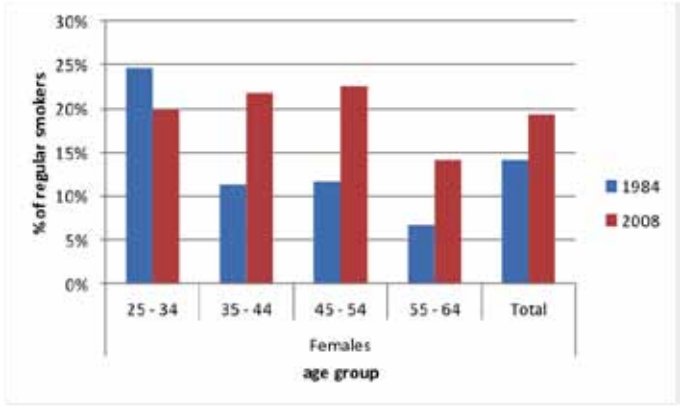


Figure 2. % of regular (daily) female smokers in 1984 compared to 2008 by age group

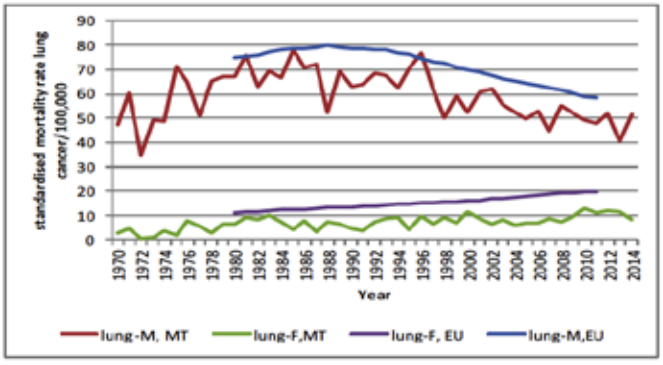


In adolescents, the European School Survey Project on Alcohol and Drugs study (ESPAD) carried out by SEDQA in 2011, reported that 23% of boys and 20% of girls aged 15-16 years smoked during the 30 days prior to the conduct of the survey. However, there is a falling trend in reported smoking in adolescents since its first report in 1995.[5,6]

LUNG CANCER MORTALITY IN MALTA

The different patterns of lung cancer deaths rates in men and women reflect past smoking behaviour. According to the National Mortality Registry within the Directorate of Health Information and Research,[7] during 2014 there were 142 deaths in males and 28 deaths in females in Malta from lung cancer, representing 9% of all male deaths and 2% of female deaths. It is the commonest cause of cancer death among both genders combined and among male cancer deaths. As seen in figure 3, mortality rates in males from lung cancer in Malta have been showing decreasing trends from the 1980s, following a similar pattern to the EU average. Mortality rates for females in Malta are much lower than in males and also lower than the EU average, however no similar decline in mortality as observed in males is being seen. On the contrary, there is a slow rising trend in mortality from lung cancer in females in Malta similar to what is seen in the EU. These trends are reflecting the smoking habits being observed in Malta.

Figure 3. Trends in standardised mortality rate from lung cancer in Malta compared to the EU for males and females 7,8



INTERNATIONAL COMPARISON

In the age groups 20-64 years the EU-25 average (excluding Malta, Cyprus and Croatia) report that 37% of men and 26.9% of women are current smokers. In Malta smoking prevalence for current smokers aged 20-64 was reported at 33.4% for males and 21.5% for females. These reported figures for Malta were the 8th and 7th lowest current smoking prevalence in males and females respectively, among the EU member states.[9] Also according to the ESPAD study conducted in 2011 among adolescents (15-16 year olds), comparison of reported cigarette use during the 30 days prior to the study, ranks Malta as 5th lowest in boys and 2nd lowest in girls.[6]

Similarly, lung cancer mortality rate comparisons between all EU member states report Malta as having the 7th and 3rd lowest lung cancer mortality rates in males and females respectively.[8]

CONCLUSIONS

To address the global burden of tobacco, the World Health Assembly in 2003 unanimously adopted the WHO Framework Convention on Tobacco Control. It is a legally binding treaty which binds parties to develop and implement a series of evidence-based tobacco control measures.[2] Malta was the second EU Member State after Ireland to prohibit smoking in public places. Locally much has been done to raise awareness regarding the negative consequences of tobacco smoking and smoking cessation initiatives are ongoing. However tobacco smoking is still posing a major burden on Maltese society and much more remains to be done.

The adverse repercussions of tobacco use and exposure extend well beyond the health risks to individuals. For families, communities and government, tobacco use and exposure to second hand smoke represent a significant social and economic handicap, but also importantly constitute a major risk factor in a looming epidemic of non-communicable diseases that threatens to undo many of the global health gains achieved with difficulty over the past 50 years.[2]

REFERENCES CAN BE ACCESSED ON THESYNAPSE.NET

"FOR YEARS MANY PHARMACISTS FELT THAT THEIR NEEDS WERE BEING IGNORED"

ALFIE PALMIER IS THE PRESIDENT OF *MOVIMENT VUĊI GĦALL-ISPIŻJARA*. HE SPEAKS TO THE SYNAPSE ABOUT HIS VISION FOR THE MOVEMENT AND ITS CONTRIBUTION TO THE PHARMACISTS' PROFESSION

TS: Why did you choose pharmacy as profession?

The obsession of mixing things together started in my parent's kitchen when I was a child and it has gone on ever since. My intrigue with science started upon my discovery of the chemistry set at the age of seven. I was so persistent on convincing my father to buy me one that I resolved to doing an impromptu dance performance on the kitchen table; surprisingly it worked! Throughout my schooling, sciences were an obvious choice, however, opting to read for a degree in pharmacy was not! Other courses seemed more appealing at the time, nevertheless, I ended up enrolling in pharmacy – with reservations. During the first semester I was still unsure of whether I made the right choice but by the end of the first year all doubts had faded away. I was part of a group of classmates who throughout the years became close friends and eventually respected colleagues.

TS: You are currently the president of the *Moviment Vuċi għall-Ispiżjara*. When was this 'moviment' conceived? What are its aims and objectives?

In my career as a pharmacist, I have so far touched upon three different sectors, namely community pharmacy, regulatory work and medical representation. All three sectors entail interaction with a variety of people from all walks of life, including other pharmacists; and this is what allowed me to excel on the job. In my opinion the deciding factor in securing my appointment as president of *Moviment Vuċi għall-Ispiżjara* is my approachability. I have always been a sociable creature and I have been told that I am easy to talk to. I trust that my vision of unity is shared by many fellow pharmacists. For years many pharmacists felt that their needs were being ignored. Furthermore, many issues were being dealt with behind closed doors which, although done in good faith, limited room for dialogue.

The idea of *Moviment Vuċi għall-Ispiżjara* was conceived at a wedding during a casual chat between pharmacists on issues affecting the pharmacy profession. The strongest sentiment shared was the need for a radical change! The talk didn't stop there, as we started discussing with other pharmacists on the matter and found a common element that resonated – the fear to take a stand single-handedly. The new-born movement, set up in 2014, seemed to be the ideal platform where people felt secure enough to speak their mind without fear of retribution.

TS: The Chamber of Pharmacy has made contributions towards, example, the Medicines Act, the Healthcare Act, and most notably, the inception and running of the POYC. Nonetheless, last year, your association presented a petition signed by hundreds of pharmacists to call an election to elect new members of the Chamber board. Why did you feel that their board members had to change?

For six years running, the Chamber had no annual general meeting with no change in Chair. I appreciate that the Chamber is made up of volunteers with busy schedules, howbeit, in a profession such as ours, which has far-reaching effects on the public in general, there are pressing issues that must be attended to promptly. The time for change had come! The baton had to be passed on to the younger generation of pharmacists experienced in different aspects of the profession to be part of the moulding process that would bring about effective and tangible change.

TS: Following the election, on 19th December 2014, a new Executive Council was elected. Notwithstanding your shortcomings such as lack of funding, no website, etc, your association lobbied its ideas intensively through social media. Despite this, only one of your eight candidates was elected, i.e. Marisabelle Bonnici. Were you expecting such a result?

I must stress the fact that this movement is not a union nor a legal entity. We garnered enough interest and trust to open a separate union but we believe that we stand stronger together. I got 123 votes of 278 which is a fair amount for a novice. People were fired up enough to contribute strongly to the Chamber

2009 - Awarded the Order of Merit by the Hospitaller Order of St Lazarus of Jerusalem. In the photo he is appearing alongside his mother, Amanda

On the set of *13 Hours - The Secret Soldiers of Benghazi.* Actor with David Costabile

and although only one of our team was elected, I am pleased to see that the Chamber understands the need for inclusion. We were instrumental in increasing the number of new and young members on the Chamber by arousing interest in its activities. The Chamber is a legacy, it is our house and it has done a great deal of good. We simply wanted to re-ignite vocation towards the profession and through our manifesto (which is still on-line & which is based on people's feedback).

TS: Has your association found support from other champions, worth mentioning, in the pharmacy field?

It might be surprising to know that we funded ourselves from our own pockets. Our work is based on the support which we receive from the pharmacists who believe in having a voice without any bias.

TS: How can one become a member of *Moviment Vuċi għall-Ispiżjara?* Are there any membership fees?

There is no membership fee and it is open to all pharmacists.

TS: Returning to yourself, in the past, you had singing stings. Are you still active in this field or now, you have other hobbies

My grandfather was a tenor in the UK who kicked off his career at the age of 10 on the BBC and performed alongside great British entertainers such as Shirley Bassey and Bernie Clifton. For many years I was merely a passionate shower singer but during my time at Junior College my chemistry teacher suggested that I should sing in public. I did eventually form part of the band *The Elements* and began singing at soirees. Music has always helped me cope with stress and my skills now include piano playing and strings. I also enjoy acting and was one of the Maltese actors in the film *13 Hours: The Secret Soldiers of Benghazi* directed by Michael Bay and due for release in January 2016.

TS: Describe yourself in three adjectives.

Hardworking, humble, and optimistic.

I READ THE SYNAPSE BECAUSE...

I respect it as a professional journal written for all local practitioners which showcases the innovative work conducted by Maltese Healthcare professionals. The journal features interesting studies, however, I feel that it should include more contributions by local pharmacists.

The First Once-Daily Dual Bronchodilator[1]

THE FIRST ONCE-DAILY DUAL BRONCHODILATOR
ULTIBRO® BREEZHALER®

Once-daily ULTIBRO BREEZHALER is indicated as maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD).[1]

Ultibro Breezhaler inhalation powder, hard capsules

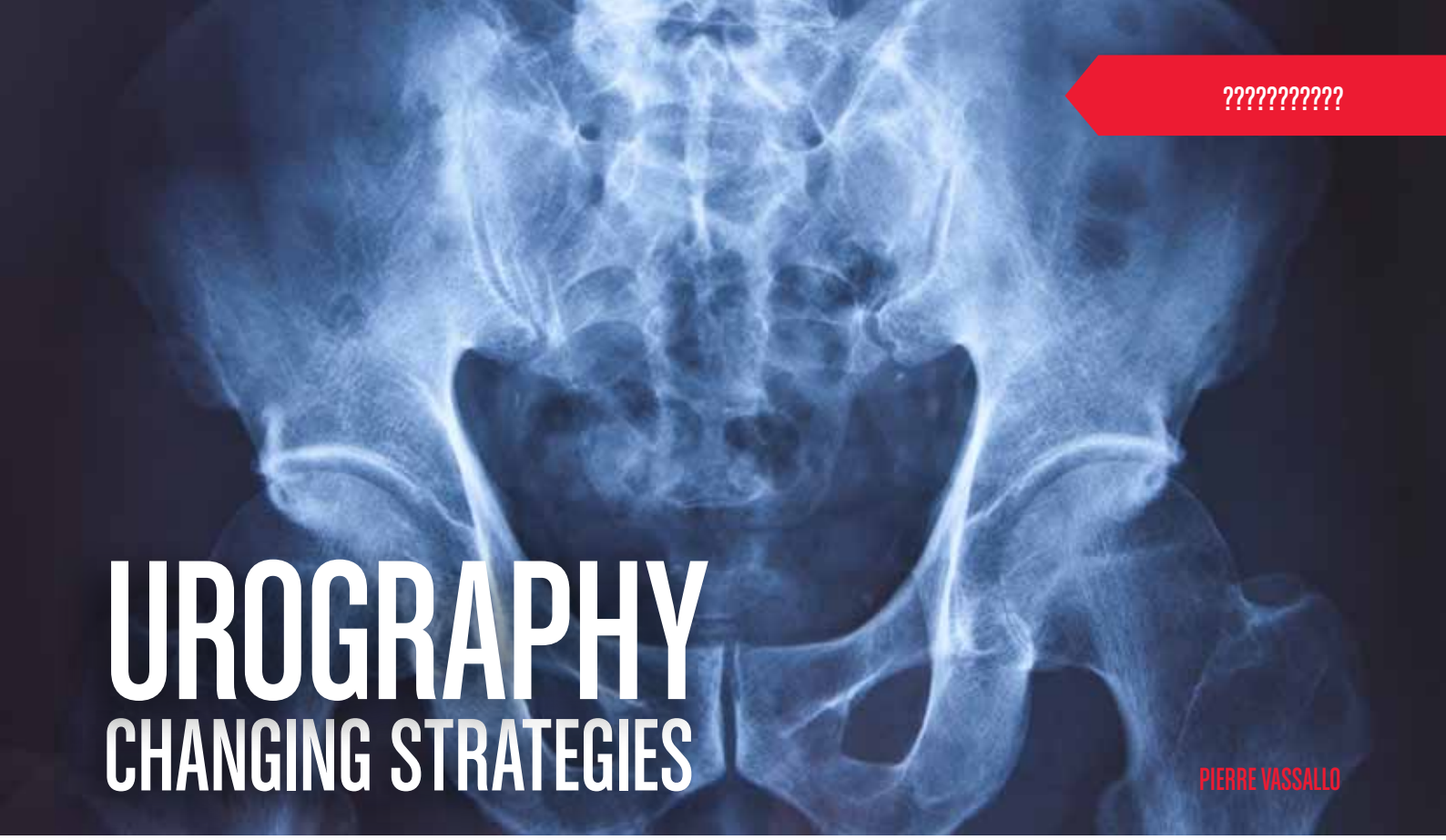
▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. Refer to section 4.8 of the SmPC for how to report adverse reactions. **PRESENTATION:** Each capsule contains 143 µg of indacaterol maleate equivalent to 110 µg of indacaterol and 63 µg of glycopyrronium bromide equivalent to 50 µg of glycopyrronium. Each delivered dose (the dose that leaves the mouthpiece of the inhaler) contains 110 µg of indacaterol maleate equivalent to 85 µg of indacaterol and 54 µg of glycopyrronium bromide equivalent to 43 µg of glycopyrronium. **INDICATIONS:** Ultibro Breezhaler is indicated as a maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD). **DOSAGE AND ADMINISTRATION:** The recommended dose is the inhalation of the content of one capsule once daily using the Ultibro Breezhaler inhaler. Ultibro Breezhaler is recommended to be administered at the same time of the day each day. If a dose is missed, it should be taken as soon as possible on the same day. Patients should be instructed not to take more than one dose in a day. Ultibro Breezhaler can be used at the recommended dose in elderly patients (75 years of age and older). Ultibro Breezhaler can be used at the recommended dose in patients with mild to moderate renal impairment. In patients with severe renal impairment or end-stage renal disease requiring dialysis it should be used only if the expected benefit outweighs the potential risk. Ultibro Breezhaler can be used at the recommended dose in patients with mild and moderate hepatic impairment. There are no data available for the use of Ultibro Breezhaler in patients with severe hepatic impairment, therefore caution should be observed in these patients. There is no relevant use of Ultibro Breezhaler in the paediatric population (under 18 years) in the indication COPD. The safety and efficacy of Ultibro Breezhaler in children have not been established. No data are available. Method of administration: For inhalation use only. The capsules must not be swallowed. The capsules must be administered only using the Ultibro Breezhaler inhaler. Patients should be instructed on how to administer the product correctly. Patients who do not experience improvement in breathing should be asked if they are swallowing the medicine rather than inhaling it. **CONTRAINDICATIONS:** Hypersensitivity to the active substance or to any of the other excipients. **WARNINGS/PRECAUTIONS:** Ultibro Breezhaler should not be administered concomitantly with medicinal products containing other long acting beta adrenergic agonists or long acting muscarinic antagonists, the pharmacotherapeutic groups to which the components of Ultibro Breezhaler belong. Asthma: Ultibro Breezhaler should not be used for the treatment of asthma due to the absence of data in this indication. Long acting beta2 adrenergic agonists may increase the risk of asthma related serious adverse events, including asthma related deaths, when used for the treatment of asthma. Not for acute use: Ultibro Breezhaler is not indicated for the treatment of acute episodes of bronchospasm. Hypersensitivity related to indacaterol or glycopyrronium. Immediate hypersensitivity reactions have been reported after administration of indacaterol, one of the components of Ultibro Breezhaler. If signs suggesting allergic reactions (in particular, difficulties in breathing or swallowing, swelling of tongue, lips and face, urticaria, skin rash) occur, treatment should be discontinued immediately and alternative therapy instituted. ***Paradoxical bronchospasm:*** In clinical studies with Ultibro Breezhaler, paradoxical bronchospasm was not observed. However, paradoxical bronchospasm has been observed with other inhalation therapy and can be life threatening. If this occurs, treatment should be discontinued immediately and alternative therapy instituted. *Narrow-angle glaucoma:* No data are available in patients with narrow angle glaucoma, therefore Ultibro Breezhaler should be used with caution in these patients. Patients should be informed about the signs and symptoms of acute narrow angle glaucoma and should be informed to stop using Ultibro Breezhaler should any of these signs or symptoms develop. *Urinary retention:* No data are available in patients with urinary retention, therefore Ultibro Breezhaler should be used with caution in these patients. Patients with severe renal impairment: These patients should be monitored closely for potential adverse reactions. ***Cardiovascular effects:*** Ultibro Breezhaler should be used with caution in patients with cardiovascular disorders (coronary artery disease, acute myocardial infarction, cardiac arrhythmias, hypertension). ***Hypokalaemia:*** Beta2 adrenergic agonists may produce significant hypokalaemia in some patients, which has the potential to produce adverse cardiovascular effects. The decrease in serum potassium is usually transient, not requiring supplementation. In patients with severe COPD, hypokalaemia may be potentiated by hypoxia and concomitant treatment, which may increase the susceptibility to cardiac arrhythmias. Clinically relevant effects of hypokalaemia have not been observed in clinical studies of Ultibro Breezhaler at the recommended therapeutic dose. ***Hyperglycaemia*** Inhalation of high doses of beta2 adrenergic agonists may produce increases in plasma glucose. Upon initiation of treatment with Ultibro Breezhaler plasma glucose should be monitored more closely in diabetic patients. Ultibro Breezhaler should be used with caution in patients with convulsive disorders or thyrotoxicosis, and in patients who are unusually responsive to beta2 adrenergic agonists. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose galactose malabsorption should not take this medicine. ***Pregnancy and Lactation:*** There are no data from the use of Ultibro Breezhaler in pregnant women available. Indacaterol may inhibit labour due to a relaxant effect on uterine smooth muscle. Therefore, Ultibro Breezhaler should only be used during pregnancy if the expected benefit to the patient justifies the potential risk to the foetus. It is not known whether indacaterol, glycopyrronium and their metabolites are excreted in human milk. The use of Ultibro Breezhaler by breast feeding women should only be considered if the expected benefit to the woman is greater than any possible risk to the infant. **INTERACTIONS:** Information on the potential for interactions is based on the potential for each of its two components. Beta adrenergic blockers may weaken or antagonise the effect of beta2 adrenergic agonists. Therefore Ultibro Breezhaler should not be given together with beta-adrenergic blockers (including eye drops) unless there are compelling reasons for their use. Where required, cardioselective beta adrenergic blockers should be preferred, although they should be administered with caution. The co administration of Ultibro Breezhaler with other anticholinergic containing medicinal products has not been studied and is therefore not recommended. Concomitant administration of other sympathomimetic agents (alone or as part of combination therapy) may potentiate the adverse events of indacaterol. 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. Inhibition of the key contributors of indacaterol clearance, CYP3A4 and P glycoprotein (P gp), raises the systemic exposure of indacaterol up to two fold. The magnitude of exposure increases due to interactions does not raise any safety concerns given the safety experience of treatment with indacaterol in clinical studies of up to one year at doses up to twice the maximum recommended indacaterol dose. **ADVERSE REACTIONS:** The presentation of the safety profile is based on the experience with Ultibro Breezhaler and the individual components. Ultibro Breezhaler showed similar adverse reactions to the individual components. As it contains indacaterol and glycopyrronium, the type and severity of adverse reactions associated with each of these components may be expected in the combination. The most common adverse reactions with Ultibro Breezhaler are: Upper respiratory tract infections. Common: Pyrexia, chest pain, musculoskeletal pain, dyspepsia, dental Caries, gastroenteritis, cough, oropharyngeal pain including throat irritation, dizziness, headache, nasopharyngitis, urinary tract infections, sinusitis, rhinitis, chest Pain, oropharyngeal pain including throat irritation. Uncommon: Fatigué, peripheral oedema, muscle spasm, myalgia, pain extremity, bladder obstruction and urinary retention, dry mouth, pruritis, rash, glaucoma, myalgia, musculoskeletal pain, pruritis/rash, paradoxical bronchospasm, epistaxis, tachycardia, palpitations, hypersensitivity, diabetes mellitus and hyperglycaemia, insomnia. Please refer to SmPC for a full list of adverse events for Ultibro Breezhaler. **LEGAL CATEGORY:** POM **PACK SIZES:** Single pack containing 6x1 or 30x1 hard capsules, together with one inhaler. **MARKETING AUTHORISATION HOLDER:** Novartis Europharm Limited, Frimley Business Park Camberley GU16 7SR, United Kingdom **MARKETING AUTHORISATION NUMBERS:** EU/1/13/862/001 - EU/1/13/862/003 **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 4, Marsa, MRS 1000 Malta. Tel: +35621222872 2015-MT-ULT-26-JAN-2015

1. Novartis Europharm Ltd. Ultibro Breezhaler Summary of Product Characteristics.

ONCE DAILY
ultibro®
breezhaler®
indacaterol maleate/glycopyrronium bromide
inhalation powder

NOVARTIS
PHARMACEUTICALS

ULT Ad1 08/15 MT



UROGRAPHY
CHANGING STRATEGIES

PIERRE VASSALLO

Urography is defined as the imaging of the urinary tract, so essentially any form of imaging done for the urinary system falls under this heading. There are two main reasons for imaging the urinary tract: renal colic and haematuria (particularly painless haematuria).

The first imaging studies to directly target the urinary tract were plain X-rays, which could detect the presence of a stone along the urinary tract and possibly just identify the renal outline. However, <80% of stones are visible on plain X-rays even with today's digital technology, whilst a renal mass would need to be at the edge of the kidney and be large enough to deform the renal outline in order to be detected on plain X-rays. The presence of gas and stool in the colon often obscures the urinary tract on plain X-rays severely limiting its value.

X-ray based intravenous urography (IVU) was later developed (Figure 1), which for several decades was the primary imaging modality for the urinary tract. This technique was first described in 1923, when Rowntree and co-workers injected 10% sodium iodide intravenously and noted that it enhanced the renal parenchyma. Sodium iodide is excreted through the urinary tract and this was visible on X-ray imaging. This was later combined with conventional tomography in an attempt to visualise the renal parenchyma in more detail and to detect small filling defects in the collecting system. However, even with the inclusion of conventional tomograms, IVU was virtually useless for imaging renal masses <3cm in diameter. In addition IVU requires relatively good renal function as it depends on renal excretion of intravenously injected contrast material to depict the urinary tract. Also, since IVU fails to provide any information to help characterise a renal mass, one must resort to cross-section imaging modalities such as ultrasound (US), computed tomography (CT) or magnetic resonance imaging (MRI) to help reach a diagnosis.

US is an excellent tool for evaluating the urinary system and improving technologies have come to provide detailed morphological depiction of kidneys and bladder (Figure 2). However, due to their retroperitoneal location, the ureters are not visible on ultrasound. Until recently, US did not provide any information on renal function, but with the recent introduction of contrast-enhanced US, this is likely to change. Notwithstanding the fact that US is an excellent first imaging modality when investigating painless haematuria, in case of painful haematuria or suspicion of renal colic, a CT urogram is more appropriate as the first imaging exam.

CT urography is the cross-sectional equivalent of the X-ray IVU, but has the major advantage of having a much higher soft tissue resolution and has no interference from gas and stool within the bowel. CT detects urinary tract stones with much greater accuracy that any other technique, including MRI, with detection rates reaching 100% even for stones as small as 1mm in diameter (Figure 3). The only known exceptions are stones related to treatment with antiretroviral agents used in the treatment of AIDS; these medications have a tendency to crystallize within the urinary tract and are non-radiopaque making them invisible on CT. The presence of such stones may be diagnosed through knowledge of the clinical history and indirectly through the presence of obstruction caused by the stone. No intravenous contrast material is required to detect stones on CT urography, which is particularly advantageous in those patients with impaired renal function.

Intravenous contrast injection is required in cases of painless haematuria and in those individuals with either abnormal findings on the non-contrast scan or where there is clinical suspicion of a renal mass. The contrast-enhanced

CT urogram shows the exact size of the renal mass (Figure 4), whether there is extension of the lesion through Gerota's fascia or there is the presence or otherwise of hilar and intravascular extension (Figure 5). All these criteria help characterise the lesion, but more importantly assist with surgical planning. This information is required to decide whether either a partial or a total nephrectomy should be performed. Other important information that is visualised by CT urography is the presence of a synchronous lesion in the opposite kidney, as well as lymph node or distant (e.g. liver, lung or bone) metastasis. Delayed imaging after intravenous contrast material injection results in filling of the collecting systems and ureter as well as the bladder. Small urothelial tumors are best seen in these delayed scans (Figure 6).

MR urography is a more recent imaging modality that has potential benefits but also has its limitations. MR urography is insensitive to calculi. Examinations times are longer, spatial image resolution is lower that CT or IVU, it is more susceptible to motion artefacts and it is more expensive that other urographic modalities. However, it utilises no ionising radiation and is therefore more suitable for the paediatric population and during pregnancy. Tissue contrast resolution is also higher in MR urography than in CT urography or US, making it more useful in patients with impaired renal function in whom intravenous contrast material administration is not indicated. The MR urography protocol is divided into two parts: (a) the static fluid imaging part, in which heavily T2 (water)-weighted images are obtained to depict the collecting system, ureters and bladder in both 2D and 3D modes, and (b) the dynamic contrast enhanced imaging part, which uses T1 (fat)-weighted images and intravenous contrast material injection similar to the early phases of an IVU but depicts cross-sectional anatomy and can therefore more accurately display pathology.

Static-fluid MR urography obtains images of the free fluid within the ureters and if serial images are obtained and played in a cine loop, temporary ureteric narrowing due to peristalsis can be distinguished from fixed stenosis that may be caused by inflammatory disease or a neoplasm. Static-fluid MR urography is best suited to imaging dilated collecting systems and ureters as occurs in the presence of obstruction (Figure 7). It is particularly useful to evaluate paediatric patients with congenital causes of urinary tract obstruction and in ureteric obstruction occurring during pregnancy.

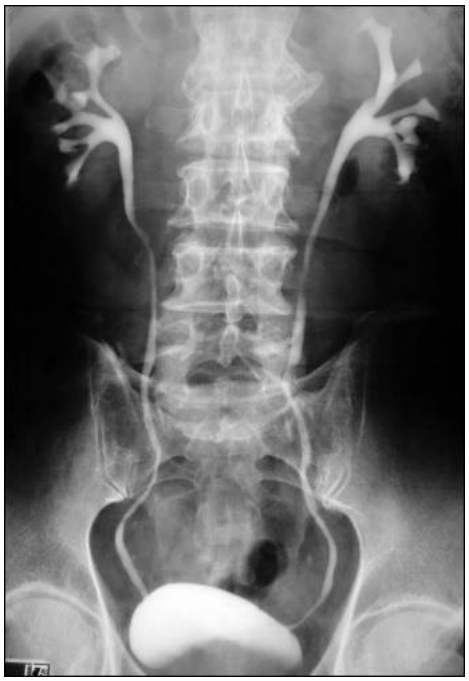


Figure 1. IVU depicting normal collecting systems, ureters and a bladder: the darker region noted within the bladder is the result of the prostatic impression

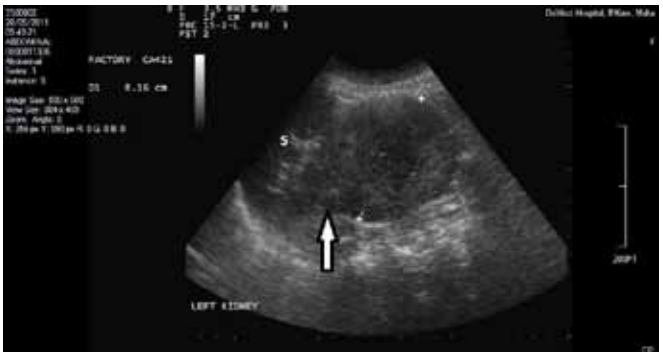


Figure 2. US scan of a left kidney showing an 8.2cm mass (between cross-hairs) occupying almost all of the said kidney with a normal upper renal pole (arrow) and the spleen (S) located to the left in the image

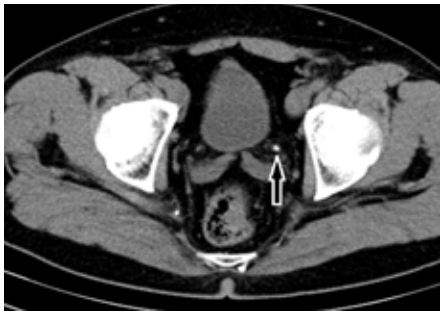


Figure 3. A 3mm stone located in the distal left ureter (arrow) is seen on non-contrast enhanced CT urogram

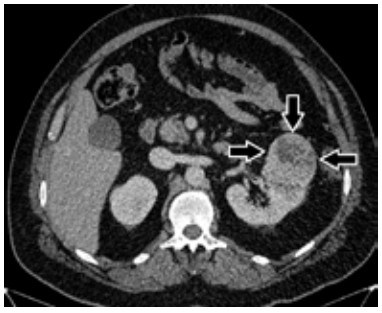


Figure 4. Incidental left renal mass noted during an abdominal ultrasound in a patient undergoing a routine medical check-up. CT shows size, location and margins of the left renal mass (arrows) along with the absence of renal hilar and vascular infiltration

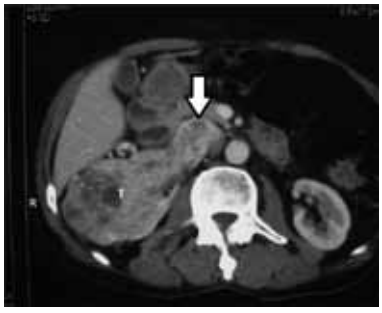


Figure 5. Post-IV contrast CT scan shows right kidney completely replaced by tumor (T) and extension of tumor into the inferior vena cava (arrow)

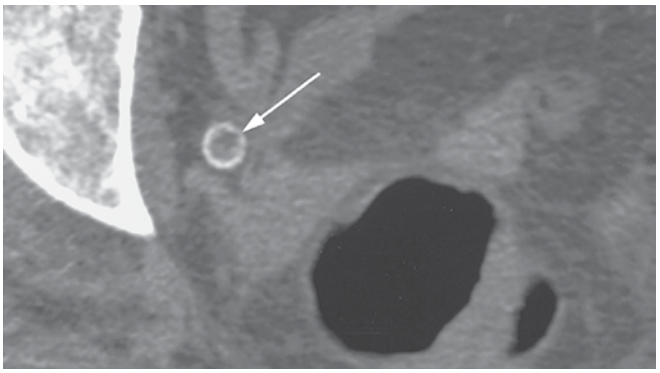


Figure 6. Filling defect in the distal right ureter surrounded by a rim of contrast material (arrow). The absence of calcification with the filling defect raised the suspicion of an urothelial tumor. This was confirmed to be a transitional cell carcinoma by retrograde ureteroscopy

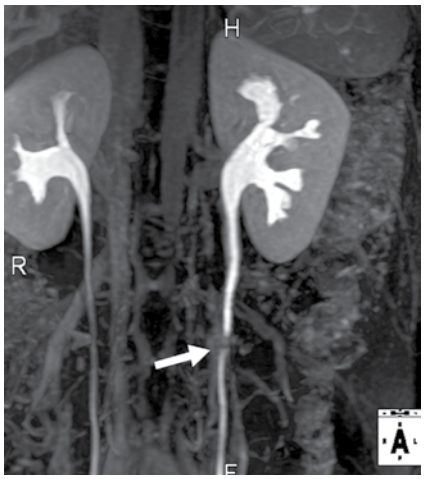


Figure 8. MR dynamic urogram showing partial obstruction of the left ureter by a stone (arrow). Note that the stone gives no signal and hence appears as a filling defect

Dynamic MR urography involves a process similar to that of dynamic CT urography and IVU. IV injected contrast material is excreted through the kidneys and is concentrated in the collecting systems and ureters. The problem with MR contrast material is that in high concentration it results in signal loss (susceptibility effects) and can actually obscure a lesion in the collecting system. To counter this phenomenon, various protocols have advocated use of smaller doses of IV contrast material, parallel use of diuretics and different levels of intravenous hydration prior to the exam. The image quality and accuracy of dynamic MR urography using these enhancements is now close to that of CT urography, but the technique is more time consuming (Figure 8).

Urography has seen significant development over the decades since its first use almost 100 years ago. The diagnostic accuracy with which we can evaluate urologic symptoms has been key to our detailed planning of treatment particularly with stone disease and urologic tumors. Selection of the best imaging algorithm will lead to rapid and accurate diagnosis and will improve the outcome of treatment.

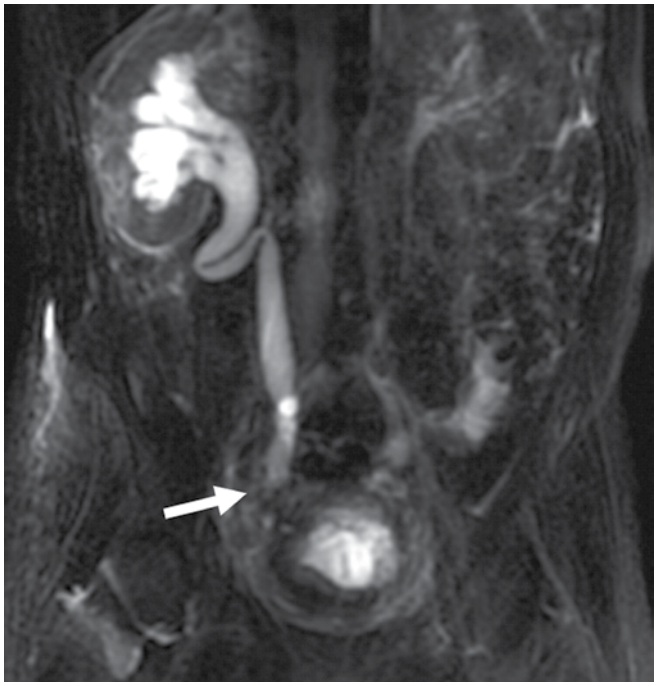


Figure 7. MR static urogram showing a dilated right renal collecting system and ureter extending down to the level of the pelvic brim (arrow). The obstruction at this level was due to an enlarged lymph node containing metastasis from a prostate cancer

HEARD IN THE Grapevine

SURGERY

Last July, the first bionic retinal eye implant to treat dry age-related macular degeneration has been performed at the Manchester Royal Eye Hospital. The Argus II implant, manufactured by the US firm Second Sight, receives visual information from a camera mounted on glasses worn by the patient. Images are converted into electrical pulses and transmitted wirelessly to electrodes attached to the retina which in turn sends the information to the brain.

TECHNOLOGY

Last July, the FDA approved the first 3D printed tablet, Spritam. It has been developed by Aprecia Pharmaceuticals. 3D printing allows layers of medication to be packaged more tightly in precise dosages. In addition, it is claimed to be more bioavailable. Spritam will be launched in the first quarter of 2016.

Relvar Ellipta is for patients (≥12 years) in need of asthma maintenance therapy[1]

Asthma

Because I simply don't have space for asthma

For patients like Maria, every day is full on, so even small reminders of asthma can have an impact. So, when they're uncontrolled on ICS alone, choose new Relvar Ellipta:

- The first ICS/LABA combination to deliver continuous 24-hour efficacy[2]
- In a practical, once-daily dose[1]
- Delivered in an easy to use device that patients prefer to their current inhaler[3,4*]

RELVAR™ ELLIPTA™

(fluticasone furoate and vilanterol inhalation powder)

Practical efficacy

Relvar Ellipta (fluticasone furoate/vilanterol) Abridged Prescribing Information

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 on SPC how to report adverse reactions.

Please refer to the full Summary of Product Characteristics before prescribing

Trade Name: RELVAR ELLIPTA. **Active Ingredients:** 92 micrograms or 184 micrograms of fluticasone furoate and 22 micrograms of vilanterol (as trifenatate). **Pharmaceutical Form:** 92 micrograms/22 micrograms or 184 micrograms/22 micrograms inhalation powder, pre-dispensed. **Indications:** *The 92 micrograms/22 micrograms dose:* for the regular treatment of asthma in adults and adolescents aged 12 years and older where use of a combination medicinal product (long-acting beta$_2$-agonist and inhaled corticosteroid) is appropriate; and for the symptomatic treatment of adults with COPD with a FEV_1<70% predicted normal (post-bronchodilator) with an exacerbation history despite regular bronchodilator therapy. *The 184 micrograms/22 micrograms dose:* for the regular treatment of asthma in adults and adolescents aged 12 years and older where use of a combination medicinal product (long-acting beta$_2$-agonist and inhaled corticosteroid) is appropriate. **Dosage and Method of Administration:** *For Athsma:* One inhalation of Relvar Ellipta 92/22 micrograms or 184/22 micrograms once daily. Patients usually experience an improvement in lung function within 15 minutes of inhaling Relvar Ellipta. However, the patient should be informed that regular daily usage is necessary to maintain control of asthma symptoms and that use should be continued even when asymptomatic. If symptoms arise in the period between doses, an inhaled, short-acting beta$_2$-agonist should be taken for immediate relief. A starting dose of Relvar Ellipta 92/22 micrograms should be considered for adults and adolescents 12 years and over who require a low to mid dose of inhaled corticosteroid in combination with a long-acting beta$_2$-agonist. If patients are inadequately controlled on Relvar Ellipta 92/22 micrograms, the dose can be increased to 184/22 micrograms, which may provide additional improvement in asthma control. *For COPD:* One inhalation of Relvar Ellipta 92/22 micrograms once daily. Relvar Ellipta 184/22 micrograms is not indicated for patients with COPD. Relvar Ellipta is for inhalation use only. It should be administered at the same time of the day, each day. **Contraindications:** *Hypersensitivity* to the active ingredient or excipients. **Precautions for Use:** Fluticasone furoate/vilanterol should not be used to treat acute asthma symptoms, for which a short-acting bronchodilator is required. Caution in severe cardiovascular disease, moderate-to-severe hepatic impairment, pulmonary tuberculosis or in patients with chronic or untreated infections, history of diabetes mellitus and for paradoxical bronchospasm and pneumonia in patients with COPD. **Drug Interactions:** Beta-blockers, CYP3A4 inhibitors, P-glycoprotein inhibitors and sympathomimetic medicinal products (refer to the full Summary of Product Characteristics for list of drugs). **Fertility, Pregnancy and Lactation:** ***Pregnancy:*** No adequate data available. ***Lactation:*** insufficient information available. ***Fertility:*** There is no data in humans. Animal studies indicate no effect on fertility. **Effect on Ability to Drive or Use Machines:** No or negligible influence. **Undesirable Effects:** Very common side effects include headache and nasopharyngitis (refer to the full Summary of Product Characteristics for complete list of undesirable effects). **Overdose:** There is no specific antidote. Treatment of overdose should consist of general supportive measures. **Local Presentations:** Relvar Ellipta 92 micrograms/22 micrograms inhalation powder, pre-dispensed and Relvar Ellipta 184 micrograms/22 micrograms inhalation powder, pre-dispensed. **Legal Category:** POM. **Marketing Authorisation Holder:** Glaxo Group Limited, 980 Great West Road, Brentford, Middlesex TW8 9GS, United Kingdom **Marketing Authorisation Numbers:** EU/1/13/886/001-6 **DATE OF PREPARATION:** December 2013.

In order to ensure that this product information reflects the most up-to-date clinical and post-marketing surveillance data, please always refer to the latest Summary of Product Characteristics (SPC) which is available from GlaxoSmithKline (Malta) Ltd (Tel: +356 21238131).

REPORTING ADVERSE EVENTS (AEs):

Malta & Gibraltar: **If you become aware of any AEs, medication errors and/or use during pregnancy in association with GSK products, please report the event promptly to:** GSK (Malta) Limited, 1, De la Cruz Avenue, Qormi QRM 2458, Malta (Tel: +356 21238131).

Malta: **alternatively, any suspected AEs and medication errors can also be reported via the national Adverse Drug Reactions (ADRs) reporting system:**

Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and posted to the Malta Medicines Authority, Post-licensing Directorate, 203, Level 3, Rue D'Argens, Gżira GŻR 1368, MALTA, or sent by email to postlicensing.medicinesauthority@gov.mt

Gibraltar: **alternatively, any suspected AEs and medication errors can also be reported via the UK regulatory authority (MHRA):** https://yellowcard.mhra.gov.uk/

*Patients' current or previous maintenance inhalers: HandiHaler/ DISKUS/ MDI/ HFA (COPD); DISKUS/ MDI/ HFA (asthma).[4]

References: 1. Relvar Ellipta Summary of Product Characteristics. GlaxoSmithKline; 2013. **2.** Bleecker ER *et al.* Fluticasone furoate/vilanterol 100/25mcg compared with fluticasone furoate 100mcg in asthma: a randomized trial. *JACI In Practice* 2013 (in press). **3.** Svedstater H *et al.* Ease of use of a two-strip dry powder inhaler (DPI) to deliver fluticasone furoate/vilanterol (FF/VI) and FF alone in asthma. *ERS.* 2013. **4.** Woepse M *et al.* Qualitative assessment of a two-strip dry powder inhaler (ELLIPTA™) for COPD and asthma. *EAACI.* 2013.

MLT_GIB/RESP/0006/14 Date of preparation: January 2014

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