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THESYNAPSE

THE MEDICAL PROFESSIONALS' NETWORK

- Monitoring of Winter Deaths
- Moviment Vuċi Għall-Ispiżjara
- Diabetes type 2 prevalence in Malta
- ADPKD
- Meeting Dr Pierre Vassallo

Volume 14 Issue 02 ISSN number 2313-8084

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

C STANDS FOR CANCER... COLLEAGUES... COMPASSION

Very unfortunately last month I was informed that three doctors have been diagnosed with cancer.

What are your first thoughts when you hear that someone you do not know has fallen seriously ill, example cancer? And when you do *know* that person, be it family or a colleague, does this change your feelings?

Everyone agrees that any illness is taxing on both the physical and mental wellbeing of the patient and the immediate family alike; let alone a serious one. Following the diagnosis, the patient faces most important considerations, ranging from treatment decisions to life-style changes. Such considerations always take a more bleak perspective when one has dependents, including elderly parents or young children.

In reality, little imagination is needed to put yourself in the shoes of a colleague who has just been struck by illness. Simply imagine that you wake up tomorrow and realise that you cannot open your clinic because the day before you have been diagnosed with a debilitating condition which warrants urgent treatment, locally or abroad. What are your thoughts? The previous day you were juggling treatment options for your patients, chores and trying to squeeze some quality time with your partner, whilst earning a decent solid income and … today …

In such a situation, apart from physical and financial woes, we seem to anchor ourselves to the question '*Why me?*', rather than '*Why not me?*' and this causes us to experience extensive psychological distress … do you imagine yourself asking whether you will actually die, whether you need to make/change your will, where the money needed to drag oneself forward will come from? Would you question whether you will now lose your patients? Would you have any regrets, maybe about skipping that endoscopy some months ago because you have been docked at your clinic? And would it really have mattered if you had closed your clinic for a single evening to do those tests which you so strongly advocate to your patients? I will not delve into the various barriers which doctors experience when accessing health care, including embarrassment and time; these have been aptly described by Kay et al.[1] However, what is most important, the authors have highlighted the importance of overcoming these system barriers by the profession *as a whole.*

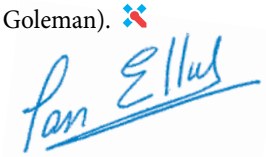
In view of this, three years ago, the 1984 medical graduates got together and set up a bank account whereby colleagues from the same graduation year were invited to contribute to help a seriously ill colleague. That proved to be a crucial helpline and the person is now back on his feet.

Although limited, the principal lesson learnt from the organisation of this campaign can be summed up in the words of the late Mattie Stepanek ... *"Unity is strength ... when there is teamwork and collaboration, wonderful things can be achieved."*

The same group of doctors met recently to discuss what can be done when *any* doctor is affected by the same misfortune. Obviously, if the experience has to be extended to the whole medical profession, a much wider group of colleagues is required.

So, is it time to establish a permanent medical solidarity mechanism? If you are interested or would like to discuss issues/experiences please get in touch with the group on medicalsolidarity@thesynapse.net. Thank you.

True compassion means not only feeling another's pain … but also being moved to help relieve it (Daniel Goleman).



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1. Kay M, Mitchell G, Clavarino A, Doust J. Doctors as patients: a systematic review of doctors' health access and the barriers they experience. Br J Gen Pract. 2008;58(552):501-8.

Cover: Pharmacy at Santo Spirito Hospital. This is the oldest pharmacy in Malta dating back to the late 16th century and is found in Rabat.
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Editor-in-Chief: Dr Wilfred Galea
Managing Editor: Dr Ian C Ellul
Sales & circulation Director: Carmen Cachia

Email: mpl@thesynapse.net
Telephone: +356 21453973/4

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OUR COLLABORATORS

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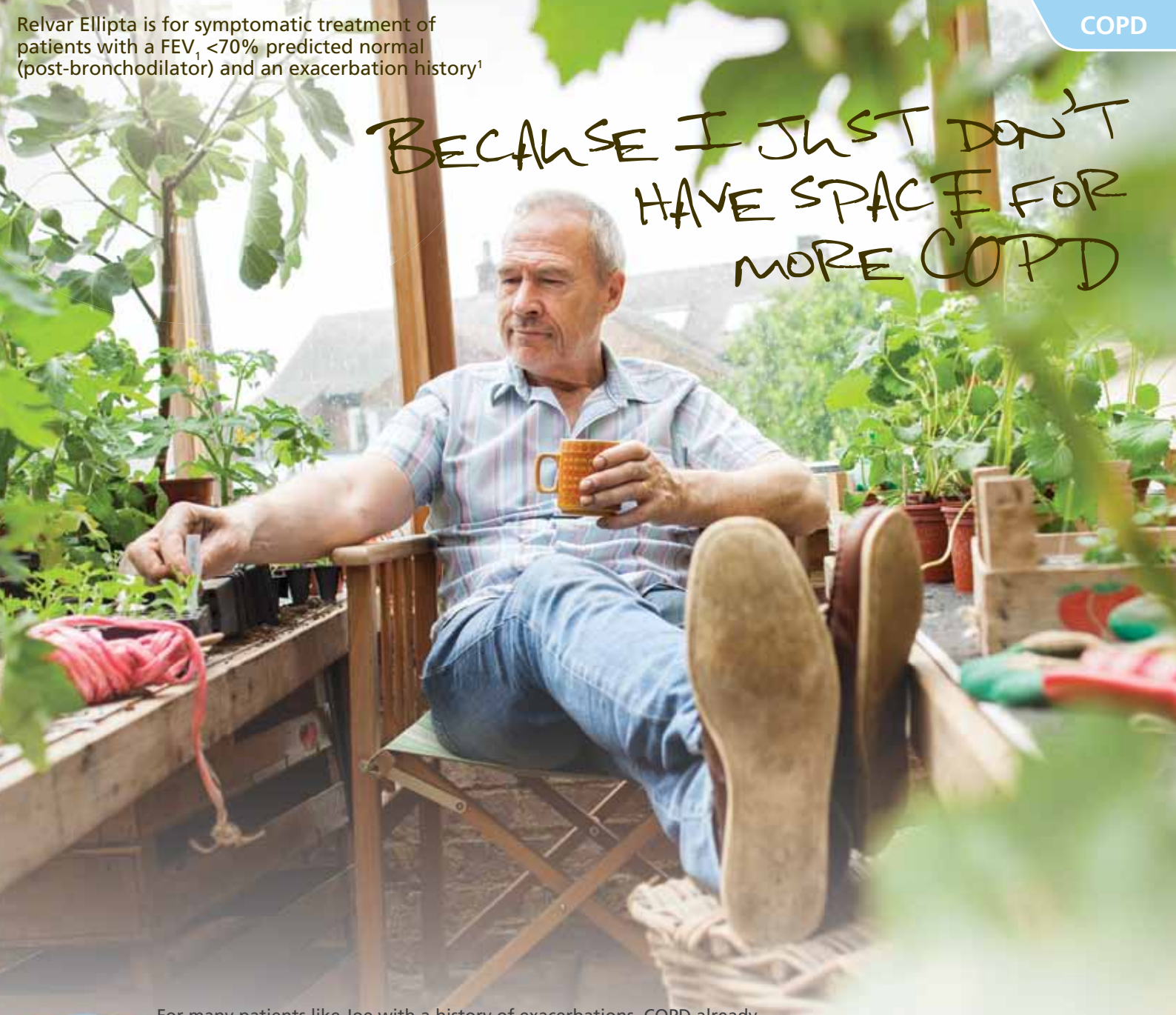
MMSA

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

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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.

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AUTHORS

Alfie Palmier OLJ BPharm(Hons)
is a Managing Pharmacist practicing in community healthcare, has consultative roles in Regulatory Affairs and works as a Responsible Person. He is the current president of the Association - Moviment Vuċi Għall-Ispiżjara- representing pharmacists' rights.

Dr James Vassallo MD MRCS
graduated in 2011 and obtained the MRCS in 2013. He is currently a BST2 in the department of ophthalmology at MDH. The co-author of the article is Dr Suzanne Pirotta.

Dr Kathleen England MD MSc
is a consultant public health specialist within the Directorate of Health Information and Research. Her main areas of work and interest are health statistics and epidemiological research in health. The co-author of the article is Dr Neville Calleja.

Dr Sarah Cuschieri MD PG Dip. Diabetes (Cardiff) OLJ
is a medical doctor, assistant lecturer and researcher with the Department of Anatomy, UOM. She has just finished an MSc in diabetes with the University of Cardiff and is currently reading for a PhD studies with UOM on the prevalence and determinants of diabetes in Malta. The co-author of the article is Dr Julian Mamo.

Dr Pierre Vassallo MD PhD FACA Arzt für Radiologie
specialised in radiology at the Institute of Clinical Radiology at the University of Muenster, Germany and the Memorial Sloan-Kettering Cancer Center, New York, US. He is currently Consultant Radiologist and Managing Director at DaVinci Hospital, Malta.

Professor Albert Cilia-Vincenti MD FRCPath
is a private consultant pathologist in Malta, a scientific delegate to the European Medicines Agency (London), and Chairman of the Academy of Nutritional Medicine (London). He is a former pathology services director to the British and Maltese health services, and a former teacher of London and Malta Universities. He trained at London's Royal Marsden, Royal Free, St George's, Charing Cross and The Middlesex hospitals.

Dr Stephanie Attard MD MRCP (Edin)
is a Higher Specialist Trainee in Nephrology and General Medicine. She graduated from the UOM in 2009 and obtained her MRCP from the Royal College of Physicians of Edinburgh in 2012.

ISSUE GUIDE

TheSynapse

MONITORING OF WINTER DEATHS

KATHLEEN ENGLAND
NEVILLE CALLEJA

ABSTRACT

Active monitoring of weekly deaths at a European level will assist member states by providing rapid assessment of the impact of threats in order to further guide policy development and risk management. In January 2015 an excess all-cause mortality has been reported in some European Countries.

INTRODUCTION

The influence of seasonality on mortality is well documented, and mortality among residents of the Maltese Islands typically sees increasing number of deaths during the winter (December-March) when compared to the rest of the year.[1] This is pronounced in the elderly population. This is commonly attributed to the cold weather as well as increased circulation of respiratory viruses.

According to the European Monitoring of excess mortality for Public Health Action[2] (Euro MOMO) excess all-cause mortality (represents all deaths irrespective of the cause of death) has been observed among the elderly since the beginning of the year in nine of 15 reporting countries. An excess number of deaths among the elderly was observed in Portugal, England, Scotland, Wales, France, Netherlands, Belgium, Spain and Switzerland.

The latest official statistics on deaths in England and Wales reported that in the last two weeks of December 2014 there was a significant excess mortality mainly in the elderly (65+), coinciding with circulating influenza and cold snaps.[3] A significant excess mortality was also seen in the last three weeks of January 2015.[4]

According to Flu News Europe,[5] which reports from the WHO Global Influenza Surveillance and Response System, Influenza A(H1N1)pdm09, A(H3N2) and type B viruses continued to circulate in the European Region, with A(H3N2) predominating. Most of the A(H3N2) viruses characterized so far show antigenic differences from the virus included in the 2014–2015 northern hemisphere influenza vaccine. A reduction in the effectiveness of the A(H3N2) component of the vaccine was therefore expected, which in turn may have contributed to the excess mortality reported among elderly people in some European countries. However the vaccine is still expected to provide some cross-protection against A(H3N2) viruses, which may reduce the likelihood of severe outcomes such as hospitalization or death, in some cases. The A(H1N1)pdm09 and B components of the vaccine are likely to be effective.

The circulation of respiratory syncytial virus (RSV) has decreased across the Region, following peak activity during the first two weeks of 2015.[5]

Table 1: Deaths per week from week 51 (December 2014) to week 4 (January 2015) compared to the average of the last 3 winter seasons, in all age groups. Source: National Mortality Registry, Directorate of Health Information and Research

Weekly and average daily deaths per week in all age groups							
Dec 2014/ Jan 2015	No of deaths per week	Average daily no. of deaths in residents	Lower and Upper CI per week	Average of: Dec13/Jan14, Dec12/Jan13, Dec11/Jan12;	No of deaths per week	Average daily no of deaths in residents	Lower and Upper CI per week
Week 51	76	10.86	(10.0;11.70)	Week 51	75	10.71	(10.36;11.07)
Week 52	83	11.86	(10.06;13.66)	Week 52	76	10.81	(10.22;11.40)
Week 1	84	12.00	(11.03;12.97)	Week 1	80	11.38	(10.93;11.83)
Week 2	94	13.43	(12.85;14.00)	Week 2	76	10.90	(10.11;11.70)
Week 3	93	13.29	(12.19;14.39)	Week 3	84	12.00	(11.61;12.39)
Week 4	72	10.29	(9.74;10.83)	Week 4	82	11.76	(11.01;12.51)
Overall	**502**	**11.95**	**(10.90;13.01)**	**Overall**	**473**	**11.26**	**(10.23;12.29)**

THE SITUATION IN MALTA

What is the situation in Malta? Are more deaths being reported in the general population or in the more vulnerable groups, such as those aged 65 years and over?

The National Mortality Registry within the Directorate of Health Information and Research collects death certificates of all deaths occurring within the Maltese Islands. In order to study whether a situation similar to the above is occurring in Malta, deaths during the last two weeks of 2014 (week 51, 52) as well as first four weeks in 2015 (week 1-4) were compared to the average number of deaths during the same weeks over the past three years. The average number of daily deaths during the whole six weeks for the last 3 years were compared to the daily number of deaths during the present season. More detailed analysis included comparing the average number of daily deaths on a weekly basis as well as analysing deaths in persons aged 65 years and over. Only residents of the Maltese Islands were included in the analysis.

RESULTS

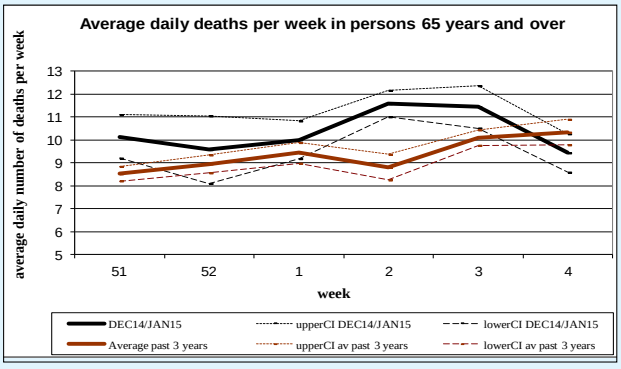
As seen in table 1 the overall number of deaths for all age groups during the six week period was greater during Dec 2014/Jan 2015 then the past 3 year average. Although the average number of daily deaths during Dec 2014/Jan 2015 (11.95, CI 10.90;13.01) was greater than the past 3 year average (11.26, CI 10.23;12.29), there was no significant difference between the two periods as confidence intervals overlap.

Interestingly, when looking at deaths during each week separately, overall there are more deaths per week during the present winter season, in all weeks except the last week of January 2015, with significantly more deaths during the second and third weeks of January (highlighted in table 1). During the last week of January there were significantly less deaths when compared to the past average 3 year period.

DEATHS IN PERSONS OVER 65 YEARS OF AGE

A more detailed analysis was undertaken to compare weekly deaths in persons 65 years and over (figure 1). During week 51, as well as weeks 2 and 3 there was a significant increase in the average number of daily deaths compared to the past 3 year average. The opposite was true for week 4. Overall the current average number of daily deaths in persons 65 years and over was 10.36 (CI 9.42;11.30) and this was marginally but significantly higher than the past 3 year average, in which the average number of daily deaths was 9.36 (CI 8.40;10.31).

Figure 1: Average number of daily deaths per week during December 2014 and January 2015 compared to the average of the last 3 winter seasons in persons aged 65 years and over. Source: National Mortality Register, Directorate of Health Information and Research



DISCUSSION

Excess all-cause mortality cannot with certainty be attributed to specific causes, but may be associated with circulating influenza, extreme cold or increase in acute respiratory illness. Malta, similar to another 21 countries - predominantly in western, northern and central Europe and the Russian Federation - reported medium-intensity, i.e. usual-level, influenza activity this year.[5] In Malta this is based on a sentinel surveillance system in which a group of physicians report the weekly number of patients seen with influenza-like illness (ILI) to the Infectious Disease Prevention and Control Unit.[6]

Further analysis of this mortality data is warranted in order to verify whether these deaths represent 'excess deaths' or are a result of harvesting or short- term forward shift in mortality, in debilitated, older persons.

While in Malta attention and health warnings are given for hot weather, due to the mildness of our winters, fewer precautions are taken.[1] In view of this fact, health care professionals are encouraged to continue to engage and advise their patients regarding precautions to take in order to reduce the risks associated with developing chest infections (e.g. good hygiene and stopping smoking). Furthermore, one should stress the importance of keeping warm. It is important to continue encouraging vulnerable groups especially the elderly and those with chronic diseases to take the influenza vaccine. It is well documented that even if there is a mismatch in the vaccine and circulating virus during the influenza season there is a degree of cross protection and this plays a part in reducing to some degree the likelihood of severe outcomes like hospitalisation and death.[7]

The Euro MOMO[8] provides a standardised approach developed and utilised by a European network of national surveillance centres, which reports expected number of deaths and observed number of deaths by week of death corrected for reporting delay. Malta has recently indicated its interest in forming part of the Euro MOMO network. Its activities improve the member states capacity for generic preparedness and response by providing data that support crisis management and evaluate impact of public health interventions. It increases in particular the capacity to deal with pandemic influenza and tackle European health threats by providing real-time data on deaths related to pandemic influenza, newly emerging infections, bioterrorism and other threats such as heat waves and cold snaps. The data may serve as an early warning of impending catastrophes and will provide rapid assessment of the impact of threats to further guide policy development and risk management.

REFERENCES CAN BE ACCESSED ON THESYNAPSE.NET

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500mg
film-coated tablets

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Actavis

ALFIE PALMIER

MOVIMENT VUĊI GĦALL-ISPIŻJARA

We are living in an unprecedented era of economic, demographic and technological change, which present both challenges and opportunities for the pharmacy profession. There are many visions for pharmacy in circulation, and many new models of practice have been discussed over time. However, as yet there has been little to bring these together in a coherent narrative for the profession's future role on the Maltese Islands.

Undoubtedly, the year 2014 will be forever etched in the history of our profession as the year of change; the year that saw the synchronised efforts of a team of motivated and passionate individuals. The vision of unity involving progressive liberal and innovative thinking was established. Led by its think-tank, representing all sectors of our diverse profession, the *Moviment Vuċi għall-Ispiżjara* was born.

Pharmacy is a broad profession spanning from manufacturing and quality assurance to the clinical role pharmacists fill within our primary health sector, and the dispensing of medication to patients. We all form part of a strong chain made of the individual, yet indispensable links, without which the whole system fails.

Stronger links are formed through continual communication and dialogue that yield active and fruitful creative discussions with the end result being an improvement in the performance of the sector one practices in. If each link is stronger, that makes us all stronger. This can be further achieved through continual professional development, where all professionals practicing in the field are kept regularly informed with current information, and challenged on the knowledge they possess already. We are seeing this happen in various European states, where continued professional development is becoming mandatory by law. This does not only profit the profession, but it also creates enhanced quality healthcare for the patients that we treat.

Although there are numerous differences of style and emphasis amongst the various specialities within our profession, we all share the same convictions; that democracy means active participation by all pharmacists in social, moral and ethical decisions that will affect their profession and their patients.

The involvement of engaged pharmacists, according to this perspective, involves two essential elements:

1. *Respect for diversity*, meaning that each individual should be recognised for his or her own abilities, interests, ideas, needs, and professional identity, and the
2. *Development of critical, socially engaged awareness*, which enables individuals to understand and participate effectively in the affairs of their profession in a collaborative effort to achieve a common goal.

Both elements are being practiced by educators in various other fields including academia, and while in extreme forms they have sometimes been separated, we see them as being necessarily related to each other.

We need to be more active in the moulding of our future. This is the principle that fuses the *Moviment Vuċi għall-Ispiżjara* together. Over the past months we have actively listened to hundreds of our esteemed colleagues who share the same love and passion we have for the future of our profession. Over the past few weeks we have experienced an influx of people willingly participating in this process in record numbers.

So, where do we go from here? The *Moviment Vuċi għall-Ispiżjara* has already set milestones through the creation of a pathway built by the pharmacists it represents. At a pristine stage of its creation it has already secured a representation on a leading professional council. The *Moviment Vuċi għall-Ispiżjara* pledges to bring up effective proposals and ideas and participate to the best of its abilities to ensure that the will of the pharmacists we have met and listened to, will be adhered to, in an unbiased and independent manner.

Participation is a key factor. The movement belongs to the people it represents and hence involvement by all pharmacists in all areas of practice will lead to a stronger union. Understandably, this is not easy, but definitely not impossible. It is a challenge that can be overcome; we need to make an effort to pull our weight and leave our mark in our history ... our footprint in the success that we will all share together ... our legacy. Let us be inspired by each other and never fear one another.

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

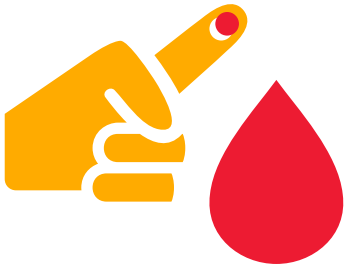
▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. Refer to section 4.8 of the SmPC for how to report adverse reactions. **PRESENTATION:** Each capsule 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: Fatigue, 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-25-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 04/15 MT



SARAH CUSCHIERI
JULIAN MAMO

DIABETES TYPE 2 PREVALENCE IN MALTA
AN UPDATE AND MORE

ABSTRACT

Diabetes Mellitus Type 2 is a global burden. The University of Malta is currently undertaking a cross-sectional survey to update the prevalence of diabetes as well as conduct the first representative prevalence of obesity, hypertension, physical activity, smoking, alcohol and nutrition in Malta. Links and co-relations between these factors and genetics would be established. These are of public health importance.

Diabetes Mellitus type 2 (T2DM) is a disease of increasingly pandemic proportions. T2DM affected 56 million Europeans in 2013 with an estimated economic burden for the year of 56.3 million Euro.[1] Malta and its population is not exempt - in fact, back in 1981 the World Health Organization (WHO) had declared that Malta had a very high T2DM prevalence, comparable to that of the Pima Indians.[2]

Both environmental and genetic factors play a part in insulin secretion and sensitivity, and thus, to the development and control of the disease. The shift to a more sedentary lifestyle and the dietary changes from a more Mediterranean diet to a Westernized diet may result in insulin resistance and an increase in body weight, predisposing the population to develop T2DM.[3]

Two cross-sectional studies were conducted in Malta in 1964 and 1981 in order to establish the prevalence of T2DM among the population in Malta and as a basis for public health plans and services.

In 1981, using a nationally representative sample, the adult prevalence of T2DM was reported as 7.7% (1.8% newly diagnosed and 5.9% previously diagnosed).[2] By 2010, a pilot study - part of the European Health Examination Study - took a relatively small sample (n = 221) and found that 9.8% suffered from T2DM.[4] Assuming a 95% degree of confidence, a sample size of 221 observations from a very large number of observations results in a maximum margin of error of 6.59% This leaves some questions on its accuracy and hence these results must therefore be considered with caution.

During the past 33 years, there have not been any other nationally representative epidemiological studies to update the prevalence of T2DM in Malta. The time is right to update the situation on the prevalence of diabetes type 2 and to use a more reliable estimate for planning services and making health plans for the disease. A prevalence study is an opportunity to look at the Maltese population's changing determinants and associated (changing) risk factors as well to provide the evidence-based infrastructure on which to base preventive strategies.

The University of Malta, with the help of the Ministry of Health and the private sector, is to undertake a health and wellbeing survey on a stratified, randomized and weighted representative population sample of 4000 adults living in Malta and Gozo. This will measure the associated anthropometric and biochemical markers, as well as the genetic factors linked with impaired glucose regulation and diabetes type 2.

"SAHHTEK" - The University of Malta Health and Wellbeing Study fieldwork – started in November 2014 and will continue for a duration of 2 years. Invitation letters are being send out one town after the other, as the study moves from one locality peripheral center (berġa) / health center to another. The chosen participants are being offered a free health check consisting of blood pressure, weight, height, hip and waist circumference measurements as well as blood testing for fasting blood glucose and lipid profile. A separate blood sample will be taken for genetic testing. Each participant would also take part in a short health-related interview. Data protection approval was granted from the Information and Data Protection Commissioner. The University of Malta Research Ethics committee approval was also obtained.

The study will establish the prevalence of T2DM in Malta including subgroups such as previously diagnosed diabetic type 2, newly diagnosed diabetes and pre-diabetes (impaired glucose tolerance and impaired fasting glucose). It will also establish the prevalence of hypertension and obesity while quantifying national rates for an improper dietary intake and for a lack of physical activity. It will also establish national smoking habits and alcohol consumption.

By means of subsequent nested case-control studies, links and correlations would be established between T2DM and different associated factors including obesity and genetics. This will lead to the development of risk scores to be utilized by both general medical practitioners and the general public in Malta in order to help determine the risks of developing pre-diabetes and diabetes. Ultimately, it will establish the financial and physical costs in relation to subjects living with diabetes and the added costs for those having the disease but who are not aware of it.

FURTHER INFORMATION MAY BE ACCESSED ON WWW.SAHHTEK.COM

REFERENCES CAN BE ACCESSED ON THESYNAPSE.NET

BLEPHARITIS

JAMES VASSALLO
SUZANNE PIROTTA

Blepharitis is a very common and under-appreciated eyelid margin condition which causes non-specific ocular irritation, significant patient distress. Chronic blepharitis is often difficult to manage. The true prevalence of blepharitis is difficult to estimate; figures cited in the literature range from 12%-79% due to the different ways how blepharitis may manifest itself and ill-defined diagnostic criteria.[1]

Blepharitis can be classified in several ways – the anatomical classification is probably more useful clinically (Figure 1). The disease is usually bilateral and can be divided into anterior and posterior blepharitis.[2]

The pathophysiology of blepharitis is multifactorial and bacteria play a central role.[3] The most common organisms cultured from blepharitic lids are *Streptococcus epidermidis* (96%), *Proprionibacterium acnes* (93%), *Corynebacterium* sp. (77%) and, *Staphylococcus aureus* (49%). Anterior blepharitis is mostly bacterial, either due to direct infection, toxin-mediated reactions, or due to a hypersensitivity reaction to bacterial antigens. Posterior blepharitis is associated with underlying structural and functional changes of the meibomian glands, hence the term meibomian gland dysfunction (MGD). The mechanism of posterior blepharitis may also be due to the presence of bacteria, specifically via the production of lipases which alter the components of the meibum. This process may ultimately lead to glandular obstruction and formation of internal hordeola and chalazia. Lack of normal lipid secretion from the meibomian glands leads to many of the symptoms reported by patients. *Demodex* mites are an overlooked cause of anterior and posterior blepharitis and should always be considered in recalcitrant cases, lash abnormalities and cylindrical dandruff, and recurrent chalazia.[4] Other aetiological factors include seborrhoeic dermatitis (associated with *Demodex folliculorum* infestation), ocular acne rosacea, and isotretinoin.[2,5]

Patients often complain of non-specific irritation, burning or foreign body sensation, itching, watery and red eyes, crusting, mild discharge and a fluctuating blurring of vision. Symptoms tend to be worse in the morning and their severity does not always correlate with the severity of the underlying blepharitis.[4] The manifestations of the disease may be asymmetrical but features of a unilateral blepharitis should always prompt the examining doctor to consider other pathologies which may mimic this condition, primarily, sebaceous gland carcinoma.[5] Other differential diagnoses include lid infections, hypersensitivity reactions, and discoid lupus. Some normal age-related changes, such as mild telangiectasia, may be erroneously attributed to blepharitis.[2]

External examination of the lid in blepharitis shows thickening, scaling, swelling, redness and eyelash abnormalities.[5] Under the higher magnification of the slit lamp other features of anterior blepharitis include lid telangiectasia, greasy matted lashes, collarettes around the bases and sleeves along the shafts of the lashes (Figure 2). In posterior blepharitis, there is pouting of meibomian gland orifices from which thickened lipid secretions may be expressed together with a frothy tear film (Figure 3).[4]

Figure 1: Cross-section of the eyelid showing position of the meibomian glands. Source: AAO ONE Network

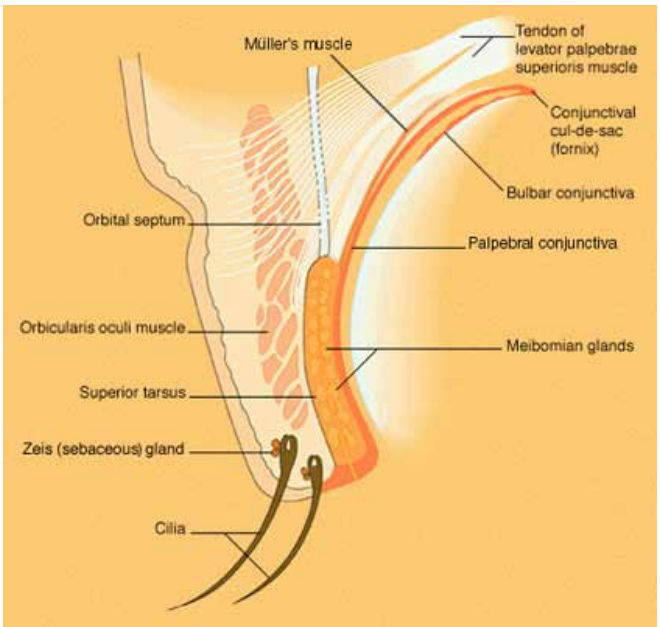


Figure 2: Anterior blepharitis with collarettes. Source: eyerounds.org

Severe chronic blepharitis may lead to several lid and corneal complications (Table 1). Intraocular procedures such as cataract surgery in a patient with blepharitis are associated with a higher risk of infectious endophthalmitis.[6]

This is a challenging condition to manage and one must start by educating the patient about the disease itself as the patient needs to have an active role in the treatment. Investing time in education early on will help improve compliance, achieve realistic expectations, and maximize outcomes. Combination treatment tailored for the individual patient with a trial and error approach is often needed.[7]

Management of this problem includes both non-pharmacological and pharmacological options. The former focuses on eyelid hygiene and mechanical methods to decrease bacterial load and improve meibomian gland function thus decreasing inflammation and restoring the natural tear film. Mechanical methods include lid scrubs, warm compresses and lid massage. There are commercially available products dedicated for this purpose, or else the patient may use simple items such as diluted baby shampoo, cotton wool, and warm face towels. Since most patients with blepharitis have dry eyes, lubricating drops should be prescribed and there are formulations specifically designed for MGD.

Topical antibiotic ointment, with or without a steroid, applied to the lid margin may be needed. The treatment regimen is individualised according to disease severity and patient response. Steroid use should be minimised and topical cyclosporine is an alternative (not available locally). Long- term antibiotic treatment may lead to antimicrobial resistance and therefore the antibiotics used should be changed regularly.

For patients not responding to treatment, especially those with MGD, oral tetracyclines or macrolides may help. The

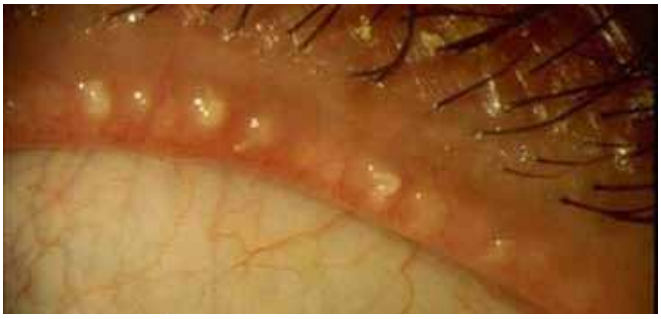


Figure 3. Pouting Meibomian gland orifices. Source: www.dryeyezone.com

Table 1: Lid and corneal complications associated with severe chronic blepharitis

Lid	Cornea
Recurrent chalazia	Dry eyes
Scarring	Recurrent erosions
Punctal misdirection	Bacterial keratitis
Trichiasis (inward misdirected lashes)	Marginal keratitis
Madarosis (lash loss)	Contact lens intolerance
Poliosis (whitening of lashes)	Scarring
	Perforation (rare)

diagnosis of *Demodex* infestation should be considered in such cases and treatment of this includes metronidazole gel (locally available preparations are licensed for cutaneous use and contact with the eyes should be avoided), tea tree oil preparations, and oral ivermectin.

Significant symptomatic improvement generally takes several weeks unless it is due to acute infection, in which case it may resolve with appropriate antibiotic therapy.[8] It is of utmost importance that the patient and caring doctor realize that blepharitis is generally a chronic condition which has to be controlled long-term and is not curable. This understanding can help minimize patient and doctor dissatisfaction that is often associated with the management of the condition.

It is important to keep blepharitis in mind when assessing children with chronic red eyes, irritation and recurrent chalazia in order to prevent corneal complications, which in children may be amblyogenic. Treatment is mostly the same as for adults, with erythromycin being used instead of tetracyclines when an oral antibiotic is needed.[9]

As with other chronic conditions, blepharitis is associated with anxiety and depression and so decreases the health-related quality of life. In patients who are failing to improve, presenting repeatedly, or not complying with treatment, an underlying psychological issue must be considered.[10]

REFERENCES CAN BE ACCESSED ON THESYNAPSE.NET

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

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

Theravance | gsk

JEAN CLAUDE SCICLUNA

A STUDENT'S EXPERIENCE

MMSA
Malta Medical Students' Association
L-Ghaqda tal-Istudenti tal-Mediċina ta'Malta
www.mmsa.org.mt

The life of a medical student is rarely one to be presented with much fanfare. Studying to be done, books to be read, lectures to attend, cadavers to inspect, breakfasts to be skipped, coffee to be drunk and good night sleep to be forgotten altogether. Given such an abstract by my peers last summer, I questioned the validity of their claims ... surely not true, right? Well, yes they are actually.

However, this is but one aspect of a medical student's habitat. What is rarely mentioned and frequently overlooked is the vast array of experiences one's life is coloured with on admission to this course. A large degree of this contributes to the "hidden curriculum" of the MD course. Notably, the personal development we undergo, as a result of our relationships with our faculty but mostly with each other. An aspect which I personally had not been exposed to before was the advent of peer teaching, where certain skills, both clinical and otherwise, are taught by a fellow student. Finding this wonderfully helpful, I cannot overstress the importance of learning and teaching in this way, since a fellow student has only recently been exposed to the relevant information himself/herself, so will be in a better position to understand the problems the newer students face in their own learning. Needless to say, this system still benefits from the wealth of experience given by our lecturers and professors.

And how can one mention peer teaching and student initiative without the letters MMSA cropping up? The local medical students association is pivotal to improving our medical education, indeed having one of its standing committees, SCOME (Standing Committee of Medical Education) dedicated to this purpose. Despite initially not knowing at all what MMSA was about, let alone having any interest to participate, I was immediately drawn to it after starting to take part in the myriad of events it organises in diverse areas, ranging from sexual health, to human rights and peace and public health. From my experience, I can safely say that what the medical student learns from these events, which are always forward to a good cause, is not only additional, but pivotal in the holistic education towards becoming doctors. Finally, it is these events which we will remember in the years to come.

THIS MONTH IN *medical history*

153 YEARS AGO

20 April 1862 – Louis Pasteur and his colleague Claude Bernard conducted an experiment based on a theory Pasteur developed where the belief was that foods (most commonly liquids) heated to the proper temperature and for the correct amount of time could destroy harmful bacteria without overly compromising the benefits of the food. The experiment led to what is now called pasteurization.

139 YEARS AGO

22 April 1876 - Birth of Robert Bárány Born (he also died during this month – 8 April 1936). He received the the Nobel Prize in Physiology or Medicine 1914 for his work on the physiology and pathology of the vestibular apparatus.

51 YEARS AGO

24 April 1964 - Death of Gerhard Johannes Paul Domagk who was a German pathologist and bacteriologist. He is credited with the discovery of Sulfonamidochrysoidinee, the first commercially available antibiotic for which he received the 1939 Nobel Prize in Physiology or Medicine.

TOP WEB READS
THESYNAPSE.NET

1

FOOD EMULSIFIERS PROMOTES COLITIS, OBESITY AND METABOLIC SYNDROME

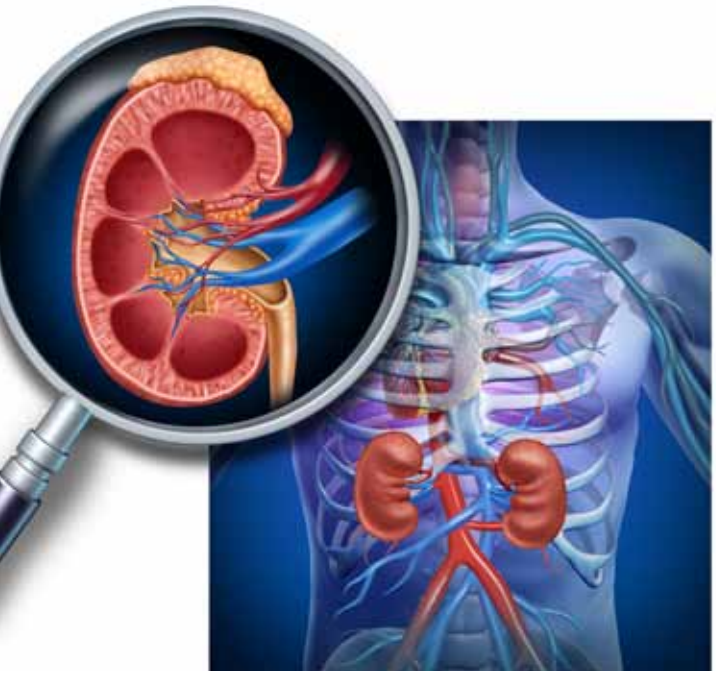
2

CLARITHROMYCIN AS AN ANTI-CANCER AGENT

3

DOCTORS, PATIENTS AND THE SOCIAL MEDIA

STEPHANIE ATTARD



AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE

ABSTRACT

Polycystic kidney disease (PKD) is the commonest life-threatening genetic disease, affecting 12.5 million people worldwide. It is found in all races and occurs equally in men and women. PKD is characterized by the growth of numerous fluid-filled cysts that can profoundly enlarge while replacing much of the normal renal structure, resulting in reduced kidney function and subsequently to renal failure.[1]

TWO MAJOR INHERITED FORMS OF PKD:

The adult type of PKD has an autosomal dominant type of inheritance (aka ADPKD) and accounts for approximately 90% of all PKD cases. Symptoms usually develop between the ages of 30 and 40, but they can begin earlier, even in childhood.

The less common childhood form of PKD is characterised by an autosomal recessive pattern of inheritance (aka ARPKD). Symptoms of ARPKD begin in the earliest months of life, even in the womb.[2]

AUTOSOMAL DOMINANT PKD

ADPKD is a multi-systemic and progressive disorder characterized by cyst formation and enlargement in the kidney and other organs. Up to 50% of patients with ADPKD require renal replacement therapy by 60 years of age.

A number of conditions are well-recognised as being associated with ADPKD:

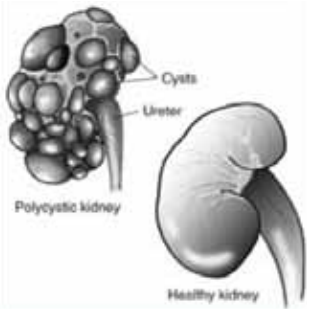
- cerebral berry aneurysms
  - found in 6% of patients with ADPKD without a family history of aneurysms
  - found in up to 16% of patients with ADPKD with a family history
- intracranial dolichoectasia: 2-3% of ADPKD cases
- hypertension: up to 80% of ADPKD cases
- diverticular disease
- valvular heart disease eg. bicuspid aortic valve or mitral valve prolapse (up to 25% of ADPKD cases)
- aortic dissection
- cysts in other organs including: liver, spleen, pancreas, ovaries, seminal vesicles and prostate.

SYMPTOMS

Clinical presentation is variable and includes:

- dull flank pain of variable severity and time course
- abdominal / flank masses
- haematuria or recurrent urinary tract infections
- hypertension which usually develops at the same time as renal failure
- renal functional impairment to renal failure.

Other symptomatology can arise when above-mentioned complications arise.[3]



PKD IS CHARACTERIZED BY THE GROWTH OF NUMEROUS FLUID-FILLED CYSTS THAT CAN PROFOUNDLY ENLARGE WHILE REPLACING MUCH OF THE NORMAL RENAL STRUCTURE

DIAGNOSIS

1. Imaging studies most commonly with ultrasonography; CT or MRI scans are also widely used.
2. Genetic testing is used to detect mutations in one of two genes: PKD1 or PKD2.[4]

PKD1 is located on chromosome 16p and is responsible for 85% of cases. It is associated with earlier presentation and is more likely to progress to ESRD.

PKD2 is located on chromosome 4q, is responsible for 15% of cases of ADPKD and is typically less severe.

A third rare type of ADPKD (termed ADPKD 3) has been described, however the gene has yet to be identified.[5]

OTHER INVESTIGATIONS INCLUDE:

- Standardized blood pressure screening as per American Heart Association recommendations.
- Measurement of blood lipid concentrations because hyperlipidemia is a correctable risk factor for progressive renal disease.
- Urine studies to detect the presence of microalbuminuria/ proteinuria, which in the presence of severe renal cystic disease, indicates an increased likelihood of disease progression and mandates strict control of the blood pressure.
- Echocardiography to diagnose valvular heart disease.
- Echocardiography or cardiac MRI to screen patients at high risk because of a family history of thoracic aortic dissections.
- Head MRI or CT angiography to screen patients for intra-cerebral aneurysms.[4]

DIAGNOSTIC CRITERIA

For patients from families with ADPKD of unknown genotype, the following is sufficient for making the diagnosis:

1. in individuals between 15 and 39 years of age, the presence of ≥3 unilateral/bilateral kidney cysts;
2. in individuals between 40 and 59 years of age, ≥2 cysts in each kidney;
3. in individuals ≥60 years of age, ≥ 4 cysts in each kidney;
4. at least 2 cysts in each kidney by age 30 in a patient with a family history of ADPKD can confirm the diagnosis. If there is any question about the diagnosis, a family history of ADPKD and cysts found in other organs make the diagnosis more likely.[6]

MANAGEMENT

Current therapy is directed towards reducing morbidity and mortality from the renal and extra-renal complications.

Hypertension The antihypertensive agent(s) of choice have not been clearly established. Because of the role of the renin-angiotensin system in the pathogenesis of hypertension in ADPKD, ACE inhibitors and angiotensin II receptor antagonists may be superior to other agents in individuals with preserved renal function.[7]

Flank pain After excluding causes of flank pain that may require intervention, such as infection, stone, or tumor, an initial conservative approach to pain management is best:

- Nonopioid agents are preferred and care should be taken to avoid long-term administration of nephrotoxic agents such as analgesic and nonsteroidal anti-inflammatory drug combination.
- Tricyclic antidepressants.
- Narcotic analgesics should be reserved for the management of acute episodes.
- Splanchnic nerve blockade with local anesthetics/steroids.

When conservative measures fail, therapy can be directed toward cyst decompression with cyst aspiration and sclerosis. In individuals with many cysts contributing to pain, surgical interventions can be considered including:

- Laparoscopic or surgical cyst fenestration through lumbotomy or flank incision,

- Renal denervation
- In those who have reached ESRD - nephrectomy.[8]

Cyst hemorrhage and gross hematuria - usually self-limiting and respond well to conservative management with bed rest, analgesics, and adequate hydration to prevent development of obstructing clots.

Rarely, episodes of bleeding are severe with extensive subcapsular or retroperitoneal hematoma, significant drop in hematocrit, and hemodynamic instability. In such cases, individuals require hospitalization, transfusion, and investigation by CT or angiography. In cases of unusually severe or persistent hemorrhage, segmental arterial embolization can be successful. If not, surgery may be required to control bleeding.[8]

Nephrolithiasis - The treatment of nephrolithiasis in individuals with ADPKD is the same as that for individuals without ADPKD:

- High fluid intake and potassium citrate are the treatment of choice in uric acid lithiasis, hypocitraturic calcium oxalate nephrolithiasis, and distal acidification defects.
- Urine alkalinization (to maintain a pH of 6-6.5), and administration of allopurinol.
- Extracorporeal shock-wave lithotripsy and percutaneous nephrostolithotomy.[4]

Cyst infection - often difficult to treat and has a high treatment failure rate despite prolonged therapy with an antibiotic to which the organism is susceptible. Treatment failure results from the inability of certain antibiotics to penetrate the cyst epithelium successfully and achieve therapeutic concentrations within the cyst. Therapeutic agents of choice include trimethoprim-sulfamethoxazole and fluoroquinolones. Clindamycin, vancomycin, and metronidazole are also able to penetrate cysts well. Chloramphenicol has shown therapeutic efficacy in otherwise refractory disease.[9]

Malignancy - The diagnosis of renal cell carcinoma in a PKD patient requires a high index of suspicion. MRI with gadolinium enhancement is particularly helpful to detect atypical solid or cystic masses, tumor thrombi, and regional lymphadenopathy.

The diagnosis of transitional cell carcinoma in a polycystic kidney is equally challenging and usually requires retrograde pyelography or ureteroscopy.

End-stage renal disease - Therapeutic interventions aimed at slowing the progression of ESRD in ADPKD include control of hypertension and hyperlipidemia, dietary protein restriction, control of acidosis, and prevention of hyperphosphatemia.

Actuarial data indicate that individuals with ADPKD do better on dialysis than individuals with ESRD from other causes. Females appear to do better than males. The reason for this improved outcome is unclear but may relate to better-maintained haemoglobin levels through higher endogenous erythropoietin production.[10]

SURVEILLANCE

Intracranial aneurysms - Widespread screening is neither cost-effective nor indicated because most intracranial aneurysms found by screening asymptomatic individuals are small, have a low risk of rupture, and require no treatment.

Indications for screening in 20- to 50-year-olds with a good life expectancy include a family history of intracranial aneurysms or subarachnoid hemorrhage, previous rupture of an aneurysm, preparation for elective surgery with potential hemodynamic instability, high-risk occupations such as airplane pilots, and significant anxiety on the part of the individual despite adequate risk information.

Magnetic resonance angiography is the diagnostic imaging modality of choice for presymptomatic screening. Schrier et al recommended rescreening after an interval of ten years because one of 76 individuals with an initial negative study had a new intracranial aneurysm after a mean follow-up of 9.8 years.[11,12]

Aortic dissection - Until more information becomes available, it is reasonable to screen first-degree adult relatives of individuals with thoracic aortic dissection using either echocardiography or MRI. If aortic root dilatation is found, yearly follow-up and strict blood pressure control with beta blockers should be recommended.

AGENTS/CIRCUMSTANCES TO AVOID

- Long-term administration of nephrotoxic agents such as analgesic and NSAID combinations.
- Caffeine because it interferes with the breakdown of cAMP and hence may promote renal cyst growth.
- Use of estrogens in individuals with severe polycystic liver disease.
- Smoking.

ONGOING RESEARCH

Several promising candidate drugs have been suggested including:

- Tolvaptan, a vasopressin type 2 receptor antagonist - a 5-year multicentre trial which was concluded in 2012 showed that Tolvaptan, as compared with placebo, slowed the increase in total kidney volume and the decline in kidney function over a 3-year period in patients with ADPKD. However, it was associated with a higher discontinuation rate, owing to adverse events.[13]
- Octreotide, a somatostatin analogue, has been shown to inhibit kidney growth in a small double-blind, placebo-controlled study done in 2010.[14] A phase 3 clinical trial investigating the efficacy of Octreotide in slowing or even halting the kidney enlargement and renal function decline in ADPKD patients with moderate/severe renal failure, is underway (ALADIN 2 study).
- Calcineurin inhibitors - initial studies had shown that treating adults with ADPKD and early chronic kidney disease with sirolimus did not halt polycystic kidney growth.[15] On the other hand, when compared with placebo over a 2-year study period, everolimus slowed the increase in total kidney volume of patients with ADPKD but did not slow the progression of renal impairment.[16] Further clinical trials on the efficacy and long-term safety of sirolimus and everolimus are underway.

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 in combination with thiazolidinediones, 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/severe 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 ESRD 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. No clinically relevant interactions with other antidiabetics (glyburide, pioglitazone, metformin), amlodipine, digoxin, ramipril, simvastatin, valsartan 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, arthralgia, hypoglycaemia, oedema peripheral. Very rare (<1/10,000): URTI, nasopharyngitis. Combination with metformin: Common: tremor, headache, dizziness, nausea, hypoglycaemia, hyperhidrosis, asthenia. Uncommon: fatigue. Combination with sulphonylurea: Common: tremor, headache, dizziness, asthenia, hypoglycaemia. Uncommon: constipation. Very rare: nasopharyngitis. Combination with Thiazolidinedione: Common: weight increase, 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, 002. **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. 2014-MT- GAL-10-DEC-2014

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 in 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 taken 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 coadministration 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 dose 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 ketoacidosis 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. LFT's 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 reinstituted 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 include alcohol, cationic active substances e.g. cimetidine and intravascular administration of iodinated contrast media. Combinations requiring caution include metformin hydrochloride with medicines tending to produce hyperglycaemic activity e.g. glucocorticoids, beta 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, arthralgia, 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, hypoglycaemia. Uncommon: fatigue. Combination with Metformin and sulphonylurea: Common: hypoglycaemia, dizziness, tremor, hyperhidrosis, asthenia, decreased blood glucose, headache, chills, nausea, gastro-oesophageal reflux disease, diarrhoea, flatulence. For a full list of Advarse reactions, please refer to the SmPC. **LEGAL CATEGORY:**POM **PACK SIZES:** 30, 60 film-coated tablets **MARKETING AUTHORISATION HOLDER:** Novartis Europharm Limited. Wimblehurst Road, Horsham, West Sussex, RH12 5AB, United Kingdom. **MARKETING AUTHORISATION NUMBER:** EU/1/07/425/060-063; EU/1/07/425/068-069. **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. 2014-MT-EUC-09-JUN-2014

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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

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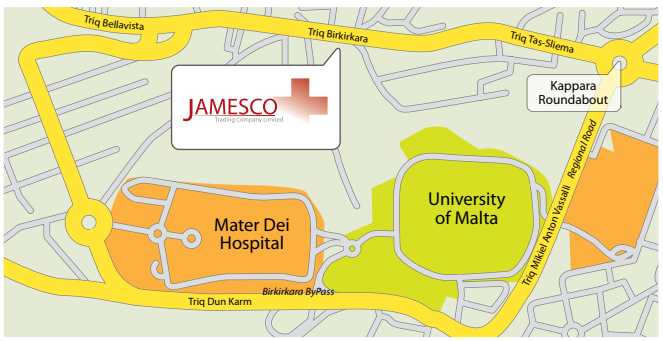

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San Ġwann SGN 4190
Tel: 2131 4333
info@jamescotrading.com

THE CHOLESTEROL CONTROVERSY – PART I

ALBERT CILIA-VINCENTI

The relationship between saturated fats and cholesterol in foods, and blood cholesterol levels and cardiac pathology, is the most serious current controversy in nutritional science. It is not only confusing doctors but also undermining the credibility of medical science among the general public.

Generations of doctors that since the 1950s had been led to believe that too much dietary saturated fats and cholesterol was linked to increased risk of atherosclerotic cardiovascular disease, are now expected to accept claims that this was all a fable based on bad science. This must be one of the most serious U-turns in medical science. How could this have happened?

As Richard Smith, former editor of the *British Medical Journal,* said recently about this controversy, "over 40 years I've come to recognise what I might have known from the beginning, that science is a human activity with the error, self-deception, grandiosity, bias, self-interest, cruelty, fraud and theft that is inherent in all human activities (together with some saintliness), but these new revelations shook me".

Ancel Keys, a Minnesota University biologist, launched his "diet-heart hypothesis" at a meeting in 1952 at the peak of the US's heart disease epidemic, by showing a close correlation between heart disease deaths and the dietary fat content in men from Japan, Italy, England and Wales, Australia, Canada and the US.[1] Keys studied few men and had no accurate method for diet assessment and, with the Japanese and Italians, he studied them during food shortages soon after the war. Other researchers studying 22 countries found little correlation between cardiac mortality and fat consumption, and suggested that there might be other causes, including tobacco and sugar consumption.[2]

Following severe criticism of Keys' hypothesis at a WHO meeting in 1955, he designed the Seven Countries Study, published in 1970, showing a strong correlation between saturated fat and cardiac deaths.[3] Keys did not select counties like France, Germany and Switzerland (where the correlation wasn't so neat), and in Crete and Corfu he studied only 9 men. Although the study had 12,770 participants, diet was evaluated in only 3.9%, and some of the Greek studies were during Lent when no animal products were eaten. A follow-up of Keys' study (1984) showed that variation in saturated fat consumption could not explain variation in cardiac mortality.[4] An analysis of the Seven Countries Study's data (1999) showed a higher correlation of cardiac deaths with sugar products and pastries than with animal products.[5] John Yudkin, a London physiology professor, had proposed in the late 1950s that sugar might be more important than fat in cardiac pathology,[6] but Keys dismissed his hypothesis as utter nonsense. Other scientists critical of Keys' hypothesis were steadily silenced, not least through difficulty getting funding to challenge Keys.

A series of interventional studies tried to test the fat hypothesis, but they were small, short term, and suffered from the problem of changing more than one variable at once. A *Lancet* editorial (1974) said that little could be concluded from them.[7] The American Heart Association (1961) recommended the substitution of saturated fat with polyunsaturated fats (corn or soybean oil).[8] Through the political process, the fat hypothesis massively changed the US and subsequently, international diet.

The Women's Health Initiative was the saturated fat hypothesis' greatest test, enrolling 49,000 premenopausal women in a randomised trial lasting 10 years.[9] The low fat arm reduced total fat consumption from 37% to 29% of energy intake and saturated fat from 12.4% to 9.5%. There was no reduction in cardiac disease or stroke, and no more weight loss than controls. A 2010 review concluded that there was no evidence that a high fat diet causes heart disease.[10] A 2012 Cochrane review of 24 comparisons with 65,508 participants found no benefit from total fat reduction and no effect on cardiovascular or total mortality.[11]

With the fat hypothesis falling apart, Walter Willet, Harvard epidemiology professor, together with colleagues in Italy and Greece, started promoting the "Mediterranean" diet. The science behind it was weak, as a Cochrane review found.[12]

A 2015 study followed 2,412 angiogram-documented coronary artery disease patients for an average of 4.8 years, noting angina development or myocardial infarction in 292 (12%). They looked at saturated fat consumption, dividing them into four groups, group one with the lowest intake and group four with the highest. The high saturated fat patients had 15% less complications than the low-fat group but was not statistically significant. However, the authors could conclude, "there was no association between dietary saturated fats and incident coronary events or mortality in patients with established coronary artery disease".[13]

REFERENCES CAN BE ACCESSED ON THESYNAPSE.NET

MARIKA AZZOPARDI

BETWEEN LEONARDO AND LONG, LONG WALKS

I meet Dr Pierre Vassallo in his office at the *Da Vinci Hospital* in Birkirkara. I start the interview by quizzing this distinguished radiologist, artist and successful entrepreneur [these are all facets of the same man] on the reasons which motivated him to choose radiology as profession.

"Back in my days at university there was not really much of a choice as to what one could go for. I studied medicine, but my main interest was technology. When I discovered radiology, I realised that it neatly combined both areas and I was pretty much hooked. The fact that during my fourth year at university (this was in 1982) the first CT scanner started being used at St Luke's Hospital only served to motivate me further in my decision to specialize in radiology. Before the use of diagnostic apparatus such as scanners, ultrasound and the like, it was common practice for a surgeon to carry out lapartomies to find out what was wrong. Radiology changed all this."

In this regard *Da Vinci Hospital* has an avant-garde set-up including a fully equipped radiology department, laboratory and pharmacy plus an operating theatre supported by state-of-the-art equipment. In fact, the hospital which was officially opened in the year 2000 started out as a radiology unit (with the name of *Medical Imaging Centre)* which slowly but steadily expanded into a centre incorporating various outpatient clinics as well as inpatient beds.

"We have certainly not yet reached all our goals. We started out with one house and then purchased the adjacent premises.

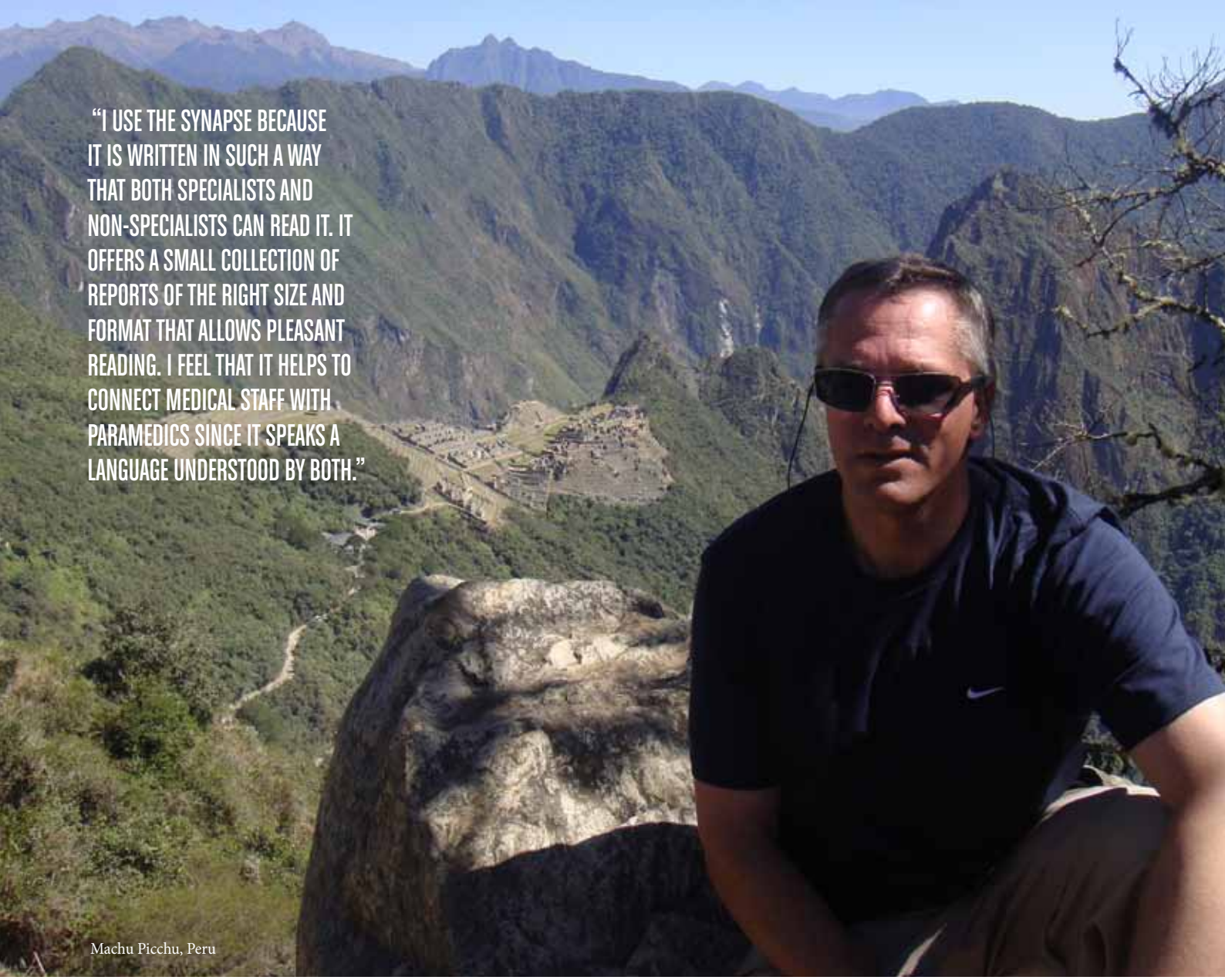
Mount Kilimanjaro

Eventually we also managed to secure an adjacent parking area. Our next big project promises further physical expansion, that will see an increase of 30 beds. This is possible since we have recently acquired a plot of land close by in order to further expand our ground floor premises; in parallel we are also in the process of adding a new floor on top of *Da Vinci Hospital*."

The hospital is pretty busy all year round. Attracting patients from all over the island, it is most popular for the treatment of injuries and sports injuries, as well as for its cancer care in the diagnostic, treatment and monitoring stages. The hospital also shoulders various projects in collaboration with the State Health Department, as well as admitting foreign patients from Eastern Europe and North Africa.

"We have a fully integrated hospital information system which allows our doctors to share all patient data within the hospital; our infrastructure also features direct electronic sharing of image-based data with Mater Dei Hospital. We are also working on a system which will allow our patients to access their personal health records with a view to make them accessible to other professionals elsewhere, as required by individual care regimens."

The artist in Dr Vassallo must have strongly influenced his choice of name for his hospital. Dr Vassallo admits that he admires Leonardo da Vinci, not only as an artist, but also as a scientist, a thinker, and the ingenuous creator of machinery. This multi-talented renaissance man has been highly inspirational to the point that the hospital also supports art and artists by exhibiting paintings and works of arts in its foyer. "I used to love painting in the past, but now I don't really have time for that now. I painted a lot of landscapes in oils and the great outdoors is still a great



Machu Picchu, Peru

inspiration for me. Incidentally, I play the guitar and keyboards; I used to play on a regular basis with my colleagues and friends."

Even as we speak, I am well aware that I am taking precious time out of the doctor's daily walking routine. Walking between 7 to 15 kilometers on a daily basis is something which he strives to maintain. On a free day his rambling escapades can even stretch to 5 hours. This love of open spaces led him to take on a climbing expedition to Mount Kilimanjaro where he reached the peak on August 8 2013. This experience, which he shared with his partner and right-hand at the hospital, Kathleen Schembri, had the purpose of raising funds for the construction of a hospital for disabled children in Ethiopia. "We raised a total of €16,000 during the nine months ahead of the expedition itself. We covered the trip from our own pockets, spending nine days in Africa. The first seven days were dedicated to acclimatization and the last two days involved the final climb to the peak of the fifth highest mountain in the world. The philanthropic event was highly successful and a great satisfaction to all those who participated."


Tranquil moment, painting by Pierre Vassallo

Symbicort® Turbohaler®

(budesonide/formoterol)

Easy to use[1]

Patients do not need to hold their breath after inhalation

High lung deposition (25-40% of delivered dose)[2]

Peak Inspiratory Flow from around 30 L/min[3]

Symbicort® Turbohaler® – For Asthma and severe COPD

Consult SmPC for full information

Symbicort Turbohaler

ABRIDGED PRESCRIBING INFORMATION
Refer to Summary of Product Characteristics (SmPC) before prescribing

Symbicort® Turbohaler® 100 micrograms/6 micrograms/inhalation, inhalation powder
Symbicort® Turbohaler® 200 micrograms/6 micrograms/inhalation, inhalation powder
(budesonide/formoterol fumarate dihydrate)

Indication Asthma: Treatment of asthma where the use of a combination (inhaled corticosteroid and long acting β2 adrenoceptor agonist) is appropriate. Symbicort Turbohaler 100/6 is not appropriate for patients with severe asthma. **COPD *(Symbicort 200/6 only)*:** Symptomatic treatment of patients (with severe COPD (FEV1 <50% predicted normal) and a history of repeated exacerbations, who have significant symptoms despite regular therapy with long-acting bronchodilators.
Presentation Inhalation powder. ***Symbicort Turbohaler 100/6*** Each metered dose contains 100 mcg budesonide/inhalation and 6 mcg formoterol fumarate dihydrate/inhalation. ***Symbicort Turbohaler 200/6*** Each metered dose contains 200 mcg budesonide/inhalation and 6 mcg formoterol fumarate dihydrate/inhalation. Refer to the SmPC for information on the method of administration.
Dosage and Administration Asthma Not intended for the initial management of asthma. Dose should be individualised. If a patient requires dosages outside recommended regimen, appropriate doses using individual inhalers should be prescribed. When long-term symptoms are controlled, titrate to the lowest effective dose, which could include a once daily dosage. **Symbicort maintenance therapy – regular maintenance treatment with a separate rescue medication:** ***Adults* (≥18 years, *including elderly*):** 1-2 inhalations twice daily (maximum 4 inhalations twice daily). ***Adolescents (12-17 years):*** 1-2 inhalations twice daily. ***Children 6-11 years (Symbicort 100/6 only):*** 2 inhalations twice daily. ***Children under 6 years:*** Not recommended.
Symbicort maintenance and reliever therapy – regular maintenance treatment and as needed in response to symptoms: consider for patients with (i) inadequate asthma control and in frequent need of reliever medication (ii) previous asthma exacerbations requiring medical intervention. ***Adults (including elderly):*** 1 inhalation twice daily or as 2 inhalations once daily. 2 inhalations twice daily may be appropriate for some patients (200/6 strength only). Patients should take 1 additional inhalation as needed in response to symptoms. If symptoms persist after a few minutes, an additional inhalation should be taken. Not more than 6 inhalations should be taken on any single occasion. A total daily dose of more than 8 inhalations is not normally needed; however, up to 12 inhalations a day could be used for a limited period. Patients using more than 8 inhalations daily should be strongly recommended to seek medical advice and should be reassessed; their maintenance therapy should be reconsidered. Patients should be advised to always have Symbicort for reliever use. ***Children and adolescents under 18 years of age:*** not recommended. ***COPD (Symbicort 200/6 only): Adults (≥ 18 years):*** 2 inhalations twice daily.
Contraindications Hypersensitivity to active substances or excipient.
Warnings and Precautions If treatment is ineffective, or exceeds the highest recommended dose therapy should be reassessed. Sudden and progressive deterioration in control requires urgent medical assessment. Treatment should not be stopped abruptly. Patients should have their appropriate rescue medication available at all times i.e. either Symbicort or a separate reliever. If needed before exercise a separate reliever should be used. Therapy should not be initiated during an exacerbation. Serious asthma-related adverse events and exacerbations may occur. If asthma symptoms remain uncontrolled or worsen patients should continue treatment but seek medical advice. If paradoxical bronchospasm occurs Symbicort should be discontinued. It responds to a rapid-acting inhaled bronchodilator and should be treated straightaway. Systemic effects may occur, particularly at high doses prescribed for long periods e.g. Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, cataract, glaucoma and more rarely a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children). Height of children should be monitored. Potential effects on bone should be considered especially in patients on high doses for prolonged periods that have co-existing risk factors for osteoporosis. Prolonged treatment with high doses of inhaled corticosteroids, particularly higher than recommended doses, may also result in clinically significant adrenal suppression. Additional systemic corticosteroid cover should be considered during periods of stress e.g. severe infections or elective surgery. Transfer from oral steroid therapy to Symbicort may result in the appearance of allergic or arthritic symptoms which will need treatment, in rare cases, tiredness, headache, nausea and vomiting can occur due to insufficient glucocorticosteroid effect and temporary increase in the dose of oral glucocorticosteroids may be necessary. To minimise risk of oropharyngeal candida infection patients should rinse mouth with water. Observe caution in patients with thyrotoxicosis, phaeochromocytoma, diabetes mellitus, untreated hypokalaemia, or severe cardiovascular disorders. Re-evaluate need for Symbicort in patients with active or quiescent pulmonary tuberculosis, fungal and viral infections in the airways. Hypokalaemia may occur at high doses. Particular caution recommended in unstable or acute-severe asthma. Monitor serum potassium levels. In diabetic patients consider additional blood glucose monitoring. The small amounts of milk proteins present may cause allergic reactions.
Drug Interactions Concomitant treatment with potent CYP3A4 inhibitors should be avoided. If this is not possible the time interval between administration should be as long as possible. Symbicort maintenance and reliever therapy is not recommended in these patients. Not recommended with beta adrenergic blockers (including eye drops) unless compelling reasons. Concomitant administration with quinidine, disopyramide, procainamide, phenothiazines, antihistamines (terfenadine) and TCAs can prolong the QTc-interval and increase the risk of ventricular arrhythmias. L-Dopa, L-thyroxine, oxytocin and alcohol can impair cardiac tolerance. Concomitant administration with MAOIs, including agents with similar properties such as furazolidone and procarbazine, may precipitate hypertension. Elevated risk of arrhythmias in patients receiving anaesthesia with halogenated hydrocarbons. Hypokalaemia may increase the disposition towards arrhythmias in patients taking digitalis glycosides
Fertility, Pregnancy and Lactation No data available on the potential effect on fertility. During pregnancy, use only when the benefits outweigh the potential risks. Budesonide is excreted in breast milk, however at therapeutic doses no effects on the child are anticipated.
Undesirable effects Common: headache, palpitations, tremor, Candida infections in the oropharynx, coughing, mild irritation in the throat, hoarseness. Uncommon: tachycardia, muscle cramps, nausea, dizziness, bruises, aggression, psychomotor hyperactivity, anxiety, sleep disorders. Rare: hypokalaemia, cardiac arrhythmias including atrial fibrillation, supraventricular tachycardia and extrasystoles, bronchospasm and immediate and delayed hypersensitivity reactions including exanthema, urticaria, pruritus, dermatitis, angioedema and anaphylactic reaction. Very Rare: depression, behavioural changes (predominantly in children), angina pectoris, prolongation of QTc-interval, hyperglycaemia, taste disturbance, Cushing's syndrome, adrenal suppression, growth retardation, decrease in bone mineral density, cataract, glaucoma and variations in blood pressure. As with other inhalation therapy, paradoxical bronchospasm may occur in very rare cases.
Package Quantities Each Symbicort Turbohaler contains 120 inhalations. **Legal Status** POM. **Marketing Authorisation Numbers** MA 046/00001-2. **Marketing Authorisation Holder (MAH)** AstraZeneca AB, Gartunavagen, S-151 85 Sodertalje, Sweden. **Further product information available on request from** Associated Drug Company Limited, Triq l-Esportaturi, Mriehel, Birkirkara BKR 3000, Malta. Tel: (+356) 2277 8115.
Abridged Prescribing Information prepared 12/14.
Symbicort and Turbohaler are trademarks of the AstraZeneca group of companies.

AstraZeneca
Respiratory

Reference: 1. Adelphi Respiratory Disease Specific Programme 2009. 2. Olof Selroos et al. *Treat Respir Med* 2008; 5 (5): 305-315. 3. Engel et al. Br J Clin Pharmacol 1992; 33(4): 438-44.

US-GUIDED TREATMENT OF CALCIFIC ROTATOR CUFF TENDONOPATHY

PIERRE VASSALLO

Calcium hydroxyapatite crystal deposits in the rotator cuff are a common source of shoulder pain. Calcified tendinitis can lead to chronic disability and may interfere with daily living activities. Traditionally, the initial conservative therapeutic approach consists of oral nonsteroidal anti-inflammatory drugs, physical rehabilitation to prevent loss of joint mobility and local steroid injections. When conservative treatment fails, open surgical or arthroscopic excision of calcium deposits can be performed.

Removal of the calcium deposits from the tendon significantly accelerates healing of the tendonopathy, however, the open surgical and even arthroscopic techniques are prone to prolonged post-operative disability and complications such as reflex sympathetic muscle dystrophy. Image-guided interventions to remove calcium deposits in the rotator cuff have been used as far back as 30 years ago. However, these procedures were mainly done under X-ray fluoroscopic guidance and utilized two large-bore needles, one to inject normal saline and the other to fragment the calcification and aspirate the fluid containing the calcium fragments. Use of these needles generally resulted in significant damage to the tendon.

More recently, ultrasound (US) (figure 1) has been utilized to guide the intervention; this allows better visualization of smaller deposits, while avoiding radiation exposure to the patient and the performer. In addition, a single small-bore needle technique is being used to minimize the extent of trauma to tendon. Combining US-guidance with the use of a small-bore single needle reduces collateral damage.

The procedure requires a full initial US assessment of the rotator cuff to establish calcification size, location, and number as well as the presence of local tendon swelling, rotator cuff tears, cortical irregularities of the greater tuberosity and the presence of fluid in the subacromio-subdeltoid bursa. This information should be documented prior to the intervention. Calcification of the rotator cuff is depicted as a hyperechoic focus with or without acoustic shadowing, or occasionally, only by a faint shadow (figure 2).

For calcifications in the supraspinatus and infraspinatus tendons, the procedure is best performed with the patient in the seated position preferably on a swivel chair. For calcifications in the subscapularis tendon, the supine position is used.

The procedure is performed by using sterile technique and surgical gloves. A skin mark is placed on the skin for localization of the calcified deposit. Then the skin is cleaned and antiseptically draped. The transducer head is also antiseptically cleaned. Local anesthesia (1% lidocaine hydrochloride) is administered in the subdeltoid bursa adjacent to the tendon. After identifying and localizing the calcified deposit at US, the calcification is punctured under constant US monitoring using a 22 to 25-gauge needle. A horizontal course and an antero-posterior direction of the needle are favored because of easier US localization of the needle and calcification; in addition, having the syringe in the horizontal position results in sedimentation of any aspirated calcium fragments to the dependent portion of the syringe, while keeping the syringe nozzle free, minimizing the risk of blockage.

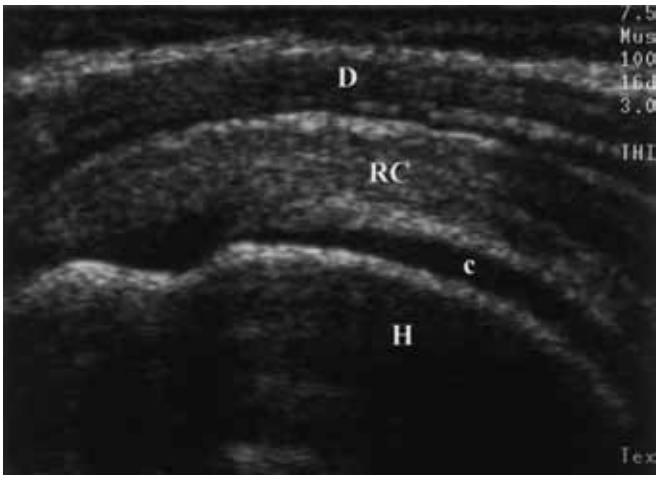


Figure 1: Longitudinal US scans of a normal rotator cuff (RC) of right shoulder. C = cartilage of the humeral head, D = deltoid muscle, H = humeral head.

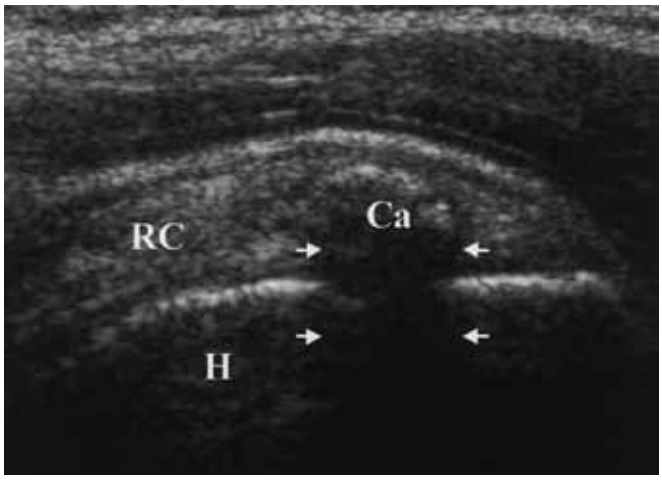


Figure 2: Longitudinal US scans of a calcium (Ca) deposit in the supraspinatus tendon of the left shoulder (rotator cuff: RC) with hyperechoic superior contour and posterior acoustic shadow (solid arrows). H = humeral head.

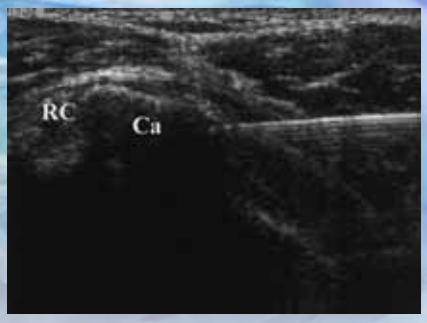


Figure 3: Transverse scans of US-guided percutaneous needle aspiration in the left shoulder. RC = rotator cuff. Scan shows the needle as it enters the calcification (Ca). The distal part of the needle is not visible because of the posterior acoustic shadow generated by the calcium.

Figure 4: Syringe after rotator cuff calcification lavage with lidocaine. White calcified material (*) has accumulated at the bottom.

Once positioned in the center of a calcification, the tip of the needle is gently rotated followed by an attempt to aspirate the fragmented calcified material by using a 5–10mL syringe filled with lidocaine 1% (figure 3). Occasionally, fragmentation of the calcified deposit is performed better by initially injecting lidocaine into the calcification followed by aspiration. The success of aspiration varies depending on the calcification consistency at the time of the procedure. When the calcification is very hard and no material can be extracted, grinding of the calcified deposit is performed by using gentle rotation of the needle tip; this has the added advantage of accelerating any spontaneous resorption. When the calcification has a paste-like consistency, a lavage manoeuver is possible by using the lidocaine-containing syringe without any attached tubing. Successive propulsion and aspiration with the syringe plunger is performed to retrieve the calcified material, with constant US monitoring of the needle position.

The extracted calcium is readily identified in the syringe as a white cloud-like substance mixing with the lidocaine that would then deposit in the dependent portion of the syringe (figure 4); this is why retaining the syringe in a horizontal position prevents the risk of injecting calcium back into the rotator cuff and also prevents nozzle and needle blockage.

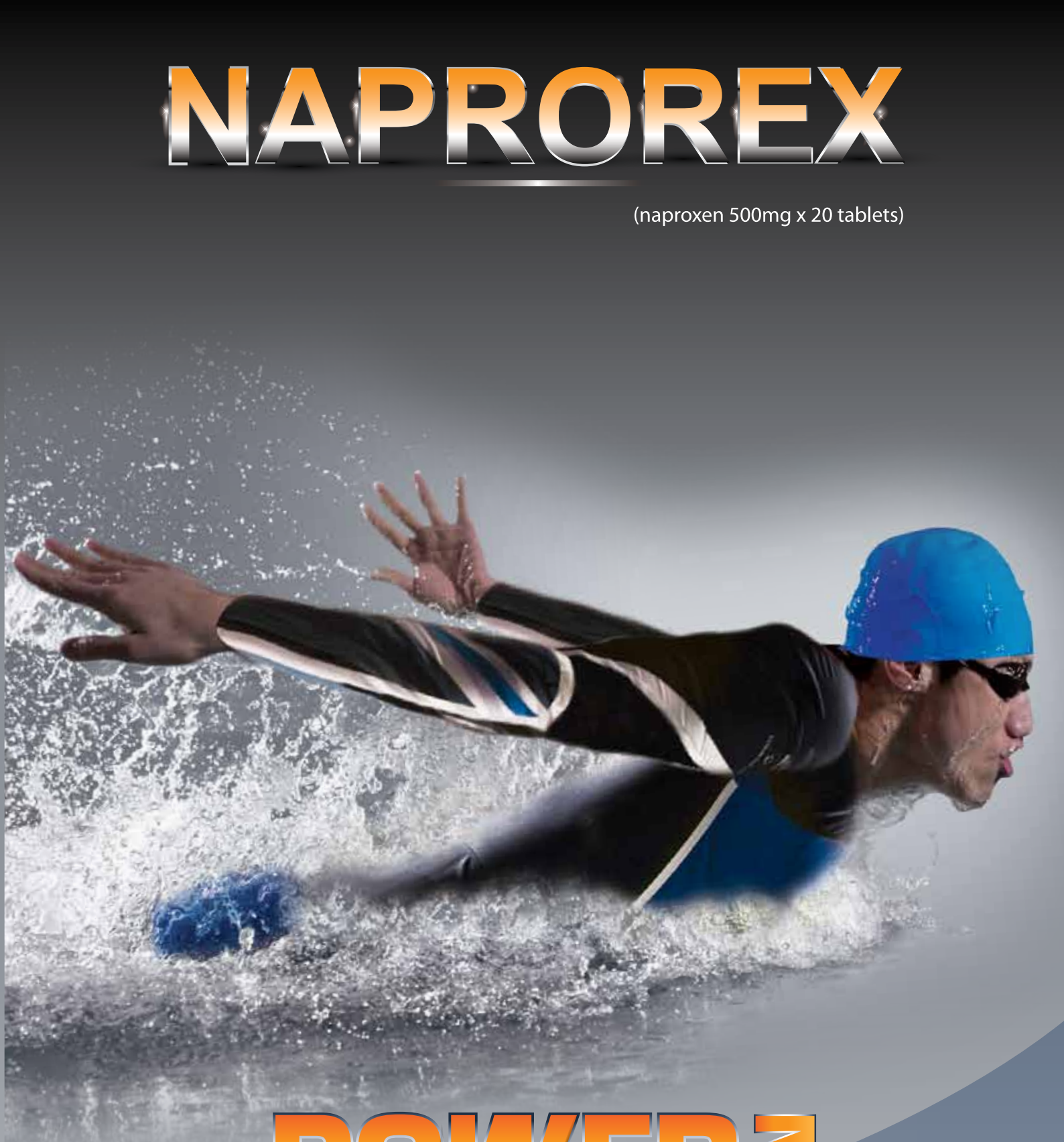
Following this maneuver, the needle tip is retrieved slightly and 40mg Depo-Medrone® (methylprednisolone acetate) combined with 1–2mL of bupivacaine 0.5% or with 1–2mL of lidocaine 1% are injected at the surface of the calcified tendon in the subacromial-subdeltoid bursa. Patients are thereafter discharged with a prescription for oral nonsteroidal anti-inflammatory agents for the eventuality of exacerbation of pain in the shoulder during the day following the procedure. Complications following the above procedure are virtually non-existent.

Patients should be re-evaluated after an 8-10 week period. At this stage, correlation with the pre-therapeutic US findings is crucial in order to assess the impact of the intervention. Aspiration of calcium deposits from the rotator cuff is not always completely successful. The amount of calcium that is removed is proportional to the extent of clinical improvement seen on follow-up evaluation. Partial evacuation of calcium deposits however, results in a decrease in pressure within the inflammatory area in the tendon, which accelerates healing. Depending on different study groups, this technique has a success rate of 60-75% with a significant reduction in morbidity as compared to an open surgical or arthroscopic procedure.

ERRATA CORRIGE. The contribution *Spinal Fractures in Malta Over One Year*, published in the last issue, Issue 1/14, has been erroneously attributed to both Drs Glenn Abela and Paul Calleja. The sole author was in fact Dr Glenn Abela. The error is regretted.

NAPROREX

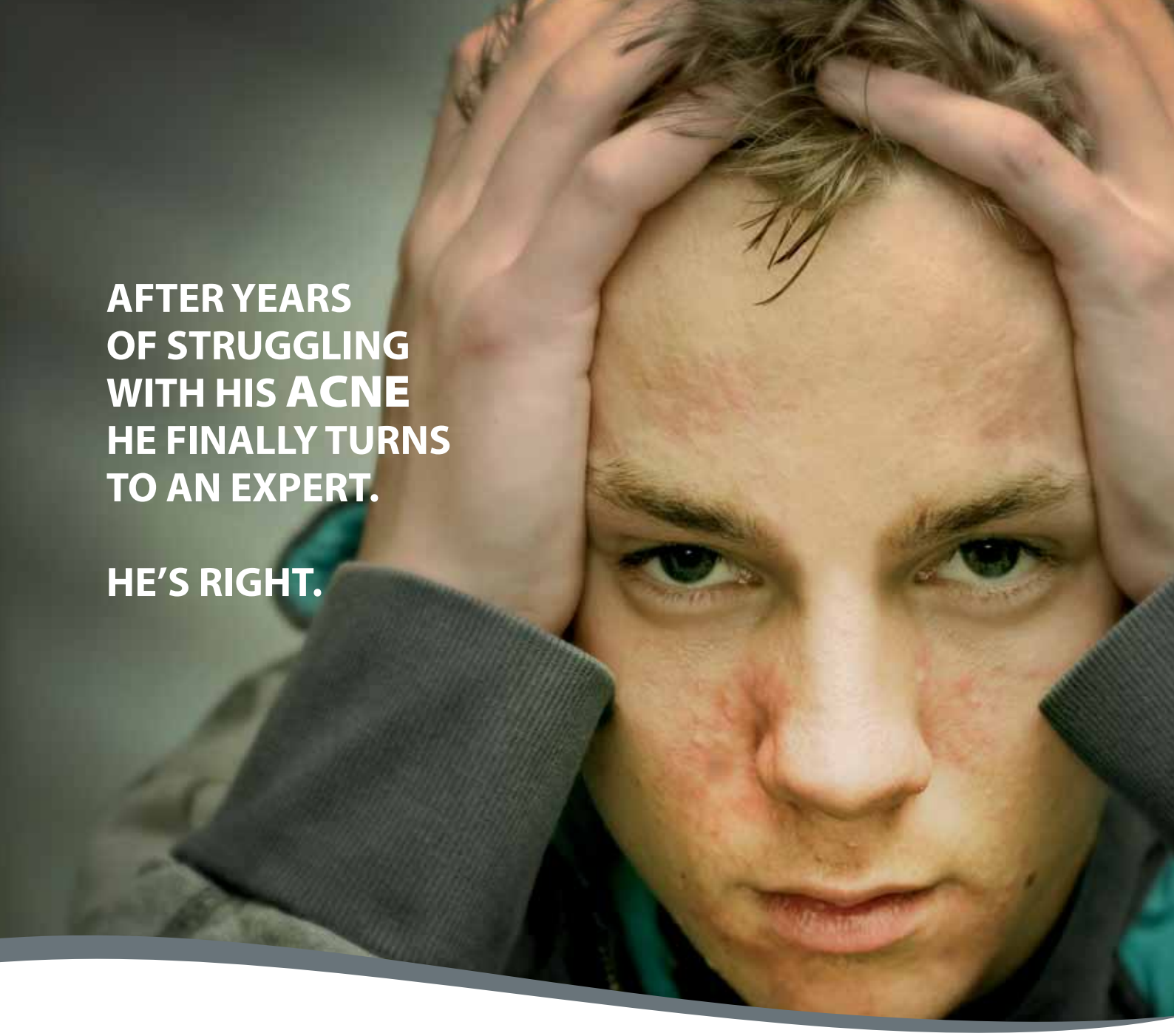
(naproxen 500mg x 20 tablets)



POWER OVER PAIN

For further information please refer to
the full summary of product characteristics or to our website: **www.delorbispharma.eu**

DELORBIS



Zineryt® supports you in restoring his confidence

Unique dual mode of action

- Visible results within 2 weeks[1]
- Effectively treats different types of acne vulgaris[2]
- Treatment effects maintained for up to 12 weeks[3]

Easy to apply

- A simple, dap-on applicator applies Zineryt® directly to the affected area
- Clean and hygienic
- No bleaching or staining

The image represents an average patient experience, and does not show an actual patient.

References: 1 Terpstra IJ, Acne treatment with 4% erythromycin and 1.2% zinc acetate Cardiff 1988; 255-259. **2** Stainforth J et al. Dermatol Treat 1993 4: 119-122. **3** Schachner L et al. J Am Acad Dermatol 1990; 22(3): 489-495.

Prescribing information: Zineryt® Abbreviated Prescribing Information for 30 ml:
Presentation: After constitution, Zineryt® contains 40 mg/ml erythromycin and 12 mg/ml zinc acetate, as an erythromycin-zinc complex. **Uses:** Topical treatment of acne vulgaris. **Dosage and administration:** For children, adults and the elderly: Apply twice daily over the whole of the affected area for a period of 10 to 12 weeks. **Contra-indications:** Contra-indicated inpatients hypersensitive to erythromycin, macrolide antibiotics, zinc, di-isopropyl sebacate or ethanol. **Other warnings and precautions:** Cross-resistance may occur with macrolide antibiotics, with lincomycin, or clindamycin. Contact with the eyes and mucous membranes of the nose and mouth should be avoided. **Use in pregnancy and lactation:** Not-contra-indicated. **Side-effects:** Occasionally a burning sensation or slight redness of the skin due to the alcohol base of Zineryt®; this is transient and of minor clinical significance. **Overdosage:** Not expected in normal use. In idiosyncratic hypersensitivity wash well with soap and water. Zineryt® is a Registered Trademark. Please refer to the full Summary of Product Characteristics before prescribing.

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2012-ZNT-003