THESYNAPSE

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THE MEDICAL PROFESSIONALS' NETWORK

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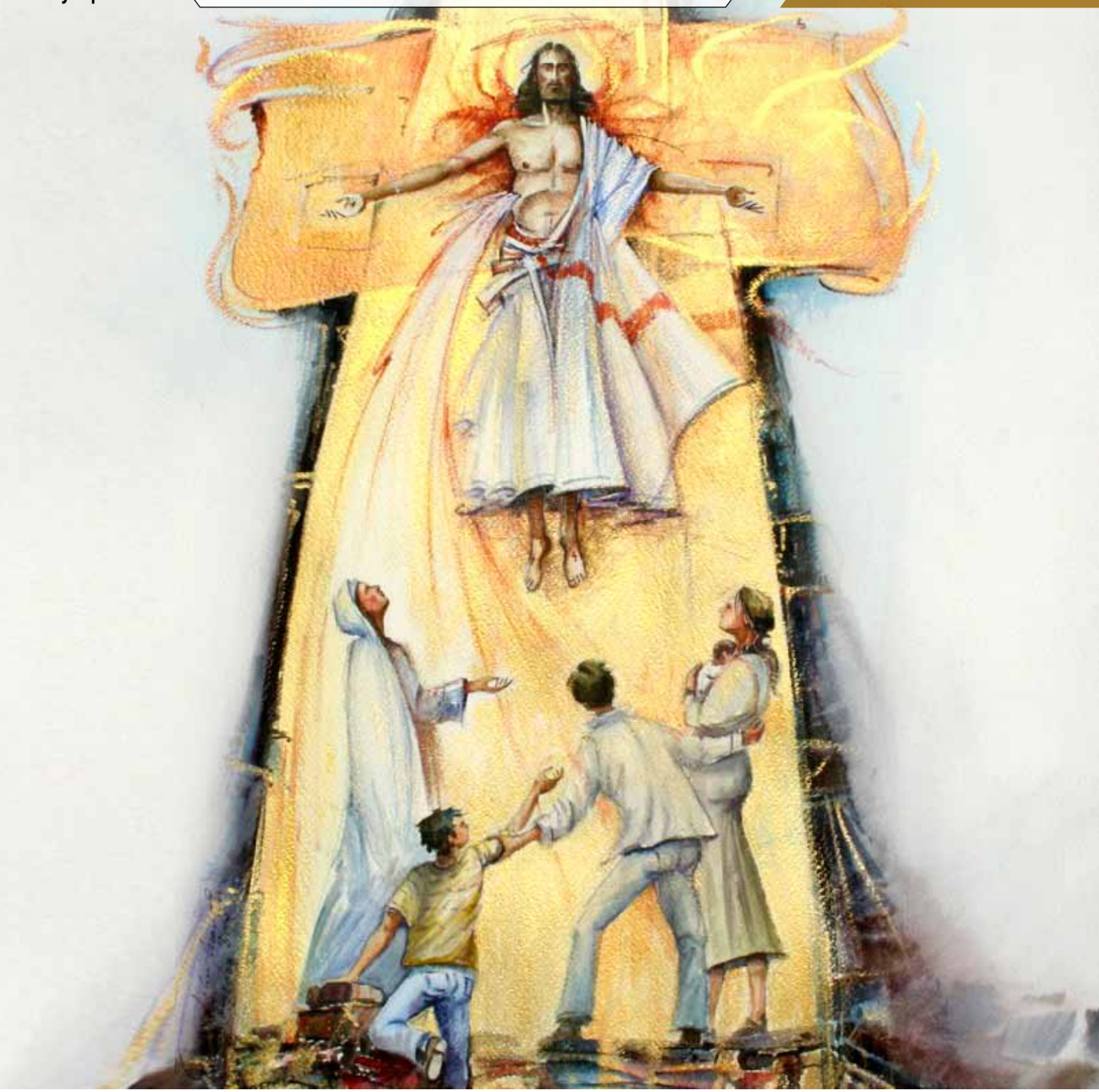

GALVUS and EUCREAS

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® (vildagliptin) tablets

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 intolerances; 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 thiazolidinedione, in combination withmetformin and sulphoxylurea 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. **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, flatulenceFrequency not known: urticaria, pancreatitis, hepatitis and abnormal liver function tests (reversible upon discontinuation of the medicinal product), bullous or exfoliative skin lesions **LEGAL CATEGORY:** POM **PACK SIZES:** 7, 28 tablets **MARKETING AUTHORISATION HOLDER:** Novartis Europharm Limited, Wimblehurst Road, Horsham, West Sussex, RH12 5AB, United Kingdom **MARKETING AUTHORISATION NUMBERS:** UI/0074/414/001, 003. **Please refer to Summary of Product Characteristics (SmPC) before prescribing.** Full prescribing information is available on request from Novartis Pharma Services Inc, Representative Office Malta, P.O. Box 4, Marsa, MRS 1000, Malta. Tel +356 22983217 / +356 21222872. 2013-MT- GAL-07-AUG-2013

Eucreas® (vildagliptin/metformin hydrochloride) film-coated tablets

PRESENTATION: Each 50 mg/500 mg film-coated tablet contains 50 mg of vildagliptin and 500 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 twice daily, one tablet in the morning and the other in the evening. For patients inadequately controlled at their maximal tolerated dose of metformin monotherapy: The starting dose of Eucreas should provide vildagliptin as 50 mg twice daily (100 mg total daily dose) plus the dose of metformin already being taken. For patients switching from co-administration of vildagliptin and metformin as separate tablets: Eucreas should be initiated at the dose of vildagliptin and metformin already being taken. For patients inadequately controlled on dual combination with metformin and a sulphonylurea: The 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 could be reanlysed 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. **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 or 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. Combination with insulin: Decreased blood glucose, headache, chills, nausea, gastro-oesophageal reflux disease, diarrhoea, flatulence. For a full list of Adverse 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/1/07/425/002–003, EU/1/07/425/008–009. 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 22983217 / +356 21222872. 2013-MT-EUC-01-JUL-2013

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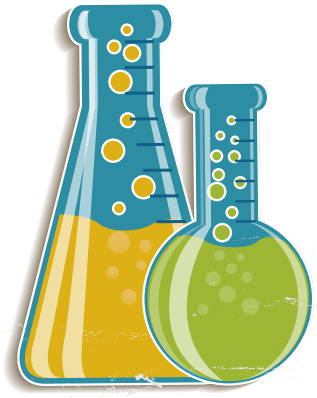
NOVARTIS PHARMACEUTICALS

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

Galvus vildagliptin

Eucreas vildagliptin/metformin



CHASING PANDORA

When it comes to the armamentarium of medicines available locally, recently we have made great advances, mainly heralded by innovator pharmaceutical companies. These are represented locally by PRIMA (*Pharmaceutical Research-based Industry Maltese Association),* which was established in 2006. On the other side of the coin, one must also not underestimate the essential contribution of generic companies. Of the most reputable generic companies operating locally is Actavis which manufactures a phletoria of products.

Innovative products logically include combination medicines. Although we are mainly accustomed to seeing combinations of active ingredients to treat acute conditions, the advent of combination products to treat chronic conditions is quite recent. These include **Eucreas**® (Novartis) which contains vildagliptin and metformin, the **Coveram**® range (Servier) which contains perindopril and amlodipine and **Symbicort**® **Turbohaler**® (AstraZeneca) which contains budesonide and formoterol. Interestingly, the latter has also received the Good design award (Japan, 2010). However, we are now also seeing triple combination products, i.e. **Exforge HCT**® (Novartis), which contains amlodipine, valsartan and hydrochlorothiazide in a single tablet. Advantages obviously include increased compliance by patients.

A different albeit equally innovative formulation is **Diamicron MR**® **60mg** (Servier), containing gliclazide. When I had a fuller head of hair, I was taught that modified release formulations could not be divided. Well, this product is an exception since its product literature specifically states that the tablets can be broken into two *equal* halves. Another recently launched range of products, marketed under the brand name **Tricef**® (Bial), containing cefixime, offering a once daily posology; obviously this increases patient compliance, especially in children.

Other newer generation products worth mentioning include **Xarelto**® tablets (Bayer), containing rivaroxaban, which are the first orally available active direct factor Xa inhibitor; **Onbrez**® **Breezhaler**® (Novartis), containing indacaterol, which is the only ultra-long-acting beta-adrenoceptor agonist; **Exelon**® patches (Novartis), containing rivastigmine for the treatment of mild to moderately severe dementia; and **Resolor**® (Shire), containing prucalopride, which is a selective, high affinity serotonin receptor agonist indicated for chronic constipation in women.

At times, an already existing product can be improved simply by reformulating it. Taking **Panadol**® **Advance** (GSK) as an example, this product contains Optizorb® technology which allows the tablets to disintegrate in the stomach up to five times faster than standard paracetamol tablets.

Obviously, increasing the availability of the medicines for a population of 400,000 has also been made possible following an adaptation of our registration system. In fact in 2005, the previous administration implemented the provisions of article 126(a) of Directive 2001/83/EC. A medicinal product which has been introduced in this manner is **Solupred**® tablets (Sanofi Aventis) which offer a fast-dissolving oral prednisone formulation. This has filled up a lacuna in our healthcare system which is created each time rectal prednisolone is out of stock. Another unique formulation which has been marketed via an article 126(a) authorisation with a view to increase compliance, is **Forcid**® tablets (Astellas), containing co-amoxiclav, which offer the versatility of either swallowing the tablet whole or dissolving it in water prior to intake.

Cover:
When I am lifted up
by John Martin Borg

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ISSUE GUIDE

TheSynapse

DRY EYES- A COMMONLY MISSED EYE CONDITION

MARIO VELLA

Tears are an important component in providing moisture and lubrication for the eyes, thereby maintaining vision and comfort. The tear film itself is made up of three components:

1. The outermost **oily layer** is produced by the meibomian glands which line the edge of the **eyelids** and produce lubrication. These smooth the tear surface and slow evaporation of the middle watery layer. If these glands don't produce enough oil, the watery layer evaporates too quickly, causing dry eyes. Dry eyes are common in people whose meibomian glands are clogged. Meibomian dysfunction is more common in people with inflammation along the edge of their eyelids (blepharitis), rosacea and other skin disorders.
2. The **watery portion** of the tear film is produced by the lacrimal gland. This gland lies just below the eyebrow under the superior outer orbital rim and it produces moisture. This watery layer cleanses the eyes and washes away foreign particles or irritants. If the eye produces inadequate amounts of water, the oil and mucous layers can touch and cause a stringy discharge.
3. The **mucous layer** comes from microscopic goblet cells in the **conjunctiva** and these contribute to the even spreading of the tear film.If the eyes do not produce enough mucus to cover the eyes, dry spots can form on the cornea.

With each blink the tear film is spread evenly across the surface of the cornea. The blinking motion of the eyelids forces the tears through the medial puncta into the upper and lower canaliculus, which empty into the lacrimal sac. The lacrimal sac drains into the nasolacrimal duct which connects to the nasal passage.

Dry eyes (keratoconjunctivitis sicca) result when there is either decreased production of tears or by poor tear quality which in turn lead to more rapid evaporation. The presenting symptoms in evaporative dry eyes are burning and foreign body sensation, sensitivity to light, and eye fatigue. The signs are redness, blurred vision, often worsening at the end of the day or after focusing for a prolonged period of time and excessive tearing. Patients find it difficult to understand how excessive tearing is a result of dry eyes. Tears produced which are of poor quality tend to dry off quickly and there is also an uneven spread of the tears leading to dry patches on the cornea. This leads to a vicious cycle and overproduction of tears.

Factors which make it more likely for a patient to develop dry eyes are:

- Age older than 50 years. It is a known fact that as we grow older the production of tears diminishes.
- Post-menopausal women. This may be due in part to hormonal changes.
- Medical conditions associated with decreased production of tears, like diabetes, rheumatoid arthritis, lupus, scleroderma, Sjogren's syndrome, thyroid disorders and vitamin A deficiency.
- Tear gland damage. Damage to the tear glands from inflammation or radiation can hamper tear production.
- Corrective laser eye surgery. Refractive eye surgery may cause decreased tear production and dry eyes. Symptoms of dry eyes related to these procedures are usually temporary.
- Eyelid problems. If there is an eyelid problem that makes it difficult to blink, tears may not be spread across the eye adequately or tears may evaporate too quickly, causing dry eyes. Eyelid problems can include an out-turning of the lids (ectropion) or an in-turning of the lids (entropion).

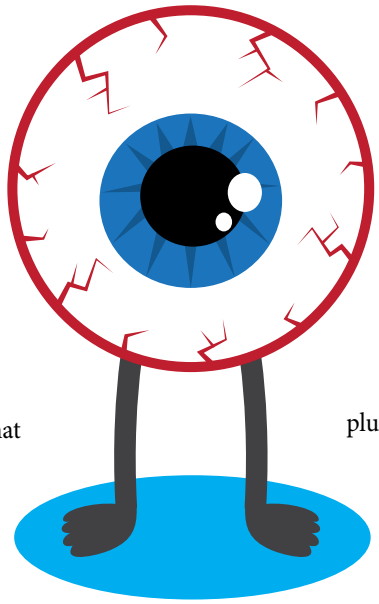
Medications that can cause dry eyes include:

- Some drugs used to treat high blood pressure, example, propranolol, prazosin and atenolol
- Antihistamines and decongestants, example, cetirizine and loratadine

- Hormone replacement therapy
- Certain antidepressants example, amitriptyline, promethazine and thioridazine
- Isotretinoin-type drugs for treatment of acne

Other causes of dry eyes include:

- Wind
- Dry air
- Tasks that require enough concentration that you blink less often, such as working at a computer, driving or reading. In all these actions the blink rate is less, as patients tend to "stare" more concentrating on the task at hand.



The consequences of dry eyes may result in a decreased quality of life as everyday tasks become difficult especially in the severely affected. The tears also protect the surface of the eye and the integrity of the corneal epithelium and any problems with this may lead to an increased risk of eye infection. Dry eyes may lead to chronic inflammation and in severe cases may even lead to corneal surface scarring and problems with vision.

DRY EYES MAY LEAD TO CHRONIC INFLAMMATION AND IN SEVERE CASES MAY EVEN LEAD TO CORNEAL SURFACE SCARRING AND PROBLEMS WITH VISION

Like any other ophthalmic condition, taking a good history including a drug history is important in reaching a diagnosis. The production of tears may be assessed by the Schirmer. In this test, blotting strips of paper are placed under the lower eyelids of each eye. After five minutes the doctor measures the amount of strip which has been moistened with the tears. A much simpler and more widely used test is the tear break-up time (TBUT). Here one needs to instill sodium fluorescein solution in the eye, then the patient is asked not to blink and the doctor counts the seconds until dry patches appear on the cornea meaning that the fluorescein film starts to break up without blinking. Normally this takes about 15 seconds in normal individuals; any result under 10 seconds is a strong indicator of dry eyes.

The main treatment of dry eyes is the administration of lubricating drops, and when started these should be continued for a minimum period of four weeks. Simple lubricating drops are usually recommended; it is advisable to avoid lubricating drops which contain vasoconstrictors as when the latter are stopped there tends to be a rebound phenomenon with recurrence of the red eye. The role of the lubricating drops are to increase the tear film stability; the idea is to restore the natural homeostasis of the ocular surface and tear film and to improve the patient's ocular comfort and quality of life. There is a wide range of products available and it is up to the doctor or the ophthalmologist to choose one that is best for the patient. Lubricating drops are safe to use long-term and can come with or without preservatives. In some cases where the patient is producing normal tears but the quantity is not enough, blocking the lacrimal duct is sometimes used. The lacrimal ducts may be blocked temporarily with collagen plugs which dissolve over a few weeks or more permanently with silicone plugs or cauthery, although the latter is rarely indicated. The puncta of the lower eyelid are blocked first as these drain over 70% of the tears into the nasal cavity.

It is important to remember that dry eyes are a very common problem that can affect anywhere between 5 to 35% of the population. Lubricating drops are still considered to be the main treatment as they provide a safe and effective way of treatment and provide symptomatic relief to patients.

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Seebri Breezhaler 44 micrograms inhalation powder, hard capsules

This medicinal product is subject to additional monitoring to 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 63 micrograms of glycopyrronium bromide equivalent to 50 micrograms of glycopyrronium. The delivered dose (the dose that leaves the mouthpiece of the inhaler) is equivalent to 44 micrograms of glycopyrronium.

INDICATIONS:
Indicated as a maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD).

DOSAGE:
The recommended dose is the inhalation of the content of one capsule once daily. Seebri Breezhaler is recommended to be administered, at the same time of the day each day. If a dose is missed, the next dose should be taken as soon as possible. Patients should be instructed not to take more than one dose in a day.

CONTRAINDICATIONS:
Hypersensitivity to the active substance or to any of the excipients.

WARNINGS/PRECAUTIONS: Seebri Breezhaler is not indicated for the initial treatment of acute episodes of bronchospasm. Paradoxical bronchospasm has been observed with other inhalation therapy and can be life threatening. If this occurs, Seebri-Breezhaler should be discontinued immediately and alternative therapy instituted. Caution in patients with narrow angle glaucoma or urinary retention. Patients should be informed about the signs and symptoms of acute narrow angle glaucoma and-should be informed to stop using Seebri Breezhaler and to contact their doctor imme diately should any of these signs or symptoms develop. In patients with severe renal impairment including those with end stage renal disease requiring dialysis, Seebri Breezhaler should be used only if the expected benefit outweighs the potential risk. Seebri Breezhaler should be used with caution in patients with a history of cardiovascular disease. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine. There are no data from the use of Seebri Breezhaler in pregnant women. Glycopyrronium should only be used during pregnancy if the expected benefit to the patient justifies the potential risk to the foetus. The use of glycopyrronium by breast feeding women should only be considered if the expected benefit to the woman is greater than any possible risk to the infant. Glycopyrronium has no or negligible influence on the ability to drive and use machines.

INTERACTIONS: The co administration of Seebri Breezhaler with other anticholinergic containing medicinal products has not been studied and is therefore not recommended. No clinically relevant drug interaction is expected when glycopyrronium is co administered with cimetidine or other inhibitors of organic cation transport.

ADVERSE REACTIONS: Common (≥1/100 to <1/10): Nasopharyngitis, insomnia, headache, dry mouth, gastroenteritis, urinary tract infection. Uncommon (≥1/1,000 to <1/100): Rhinitis, cystitis, hyperglycaemia, hypoaesthesia, atrial fibrillation, palpitations, sinus congestion, productive cough, throat irritation, epistaxis, dyspepsia, dental caries, rash, pain in extremity, musculoskeletal chest pain, dysuria, urinary retention, fatigue, asthenia

LEGAL CATEGORY: POM

PACK SIZES: Single pack containing 30x1 hard capsules, together with one inhaler.

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

MARKETING AUHORISATION NUMBER:
Seebri Breezhaler 44 micrograms inhalation powder, hard capsules - EU/1/12/788/001-006

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 22983217/21222872

2014-MT-SBR-3-MAR-2014

For information on Seebri Breezhaler dose expression, please refer to full prescribing information.

References: 1. Partridge MR, Karlsson N, Small IR. Patient insight into the impact of chronic obstructive pulmonary disease in the morning: an internet survey [published correction appears in Curr Med Res Opin. 2012;28(8):1405]. Curr Med Res Opin. 2009;25(8):2043-2048. 2. Barnett M. Chronic obstructive pulmonary disease: a phenomenological study of patients' experiences. J Clin Nurs. 2005;14(7):806-812. 3. Kessler R, Partridge MR, Miravitlles M, et al. Symptom variability in patients with severe COPD: a pan-European cross-sectional study. Eur Respir J. 2011;37(2):264-272. 4. Novartis Europharm Ltd. Seebri® Breezhaler® Summary of Product Characteristics.

Please see SPC for full prescribing information.

NOVARTIS

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Once Daily
seebri®
breezhaler®
glycopyrronium bromide inhalation powder

THE IMPORTANCE OF PROPER SUPPLEMENTATION WITH CALCIUM AND VITAMIN D IN THE PREVENTION OF FRACTURES

ERIKA CARACHI
ANDREW BORG

ABSTRACT

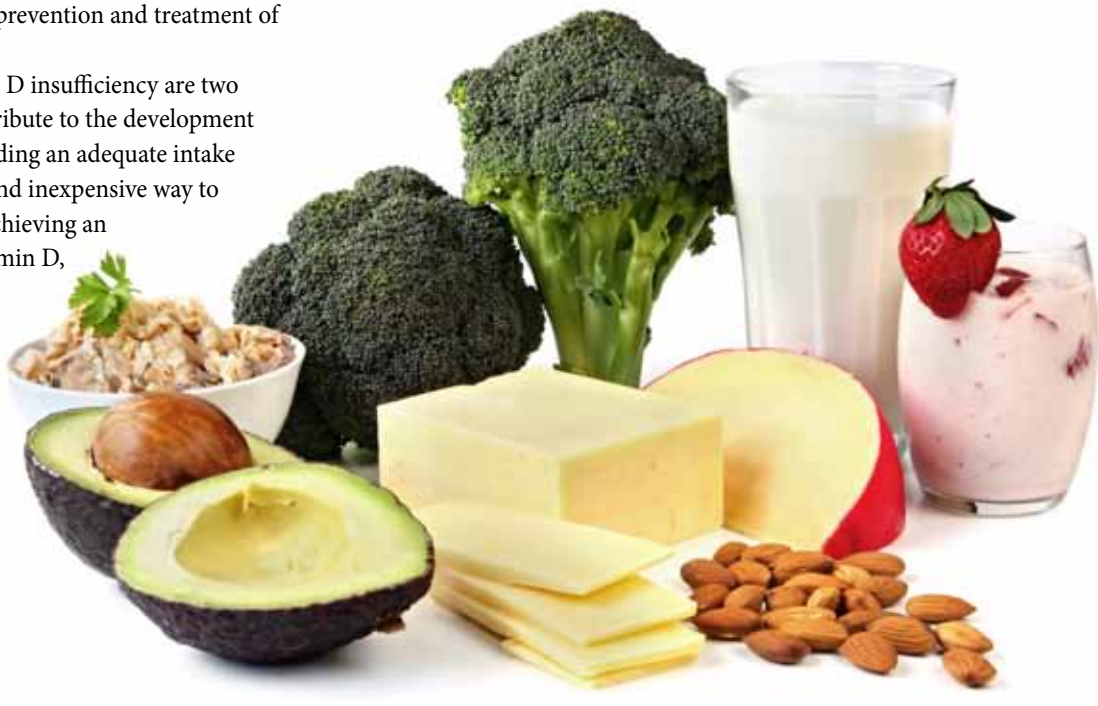
Osteoporosis is the commonest bone disorder affecting humans and it can lead to fractures in critical areas such as the proximal femur. These fractures can have a significant impact on the morbidity and mortality of the patient. Calcium and vitamin D have an important role in the prevention and treatment of osteoporosis. Identifying and correcting a low calcium intake and vitamin D insufficiency is an essential step in the management of osteoporosis. Failure to do so can seriously compromise fracture risk reduction.

Osteoporosis is a silent disease until it is complicated by fractures which often occur with minimal trauma[1]. These fractures affect critical areas such as the vertebrae and proximal femur so they can pose a serious threat to the health of the patient, as well as a significant financial burden to the health sector. Osteoporosis is the commonest bone disorder in humans and it is characterized by low bone mass, deterioration of bone tissue and disruption of bone architecture. Calcium and vitamin D play a crucial role in the prevention and treatment of osteoporosis.

Low calcium intake and vitamin D insufficiency are two important lifestyle factors that contribute to the development of osteoporosis and fractures. Providing an adequate intake of calcium and vitamin D is a safe and inexpensive way to help reduce fracture risk[1]. In fact, achieving an adequate intake of calcium and vitamin D, together with life-long participation in weight-bearing exercise, tobacco cessation, identification and treatment of alcoholism and other risk factors for fractures, such as impaired vision, are considered universal recommendations that should be given to the general population.

ROLE OF CALCIUM

Lifelong adequate calcium intake is vital to reach the peak bone mass and thereafter maintain bone health[1]. In order to maintain adequate calcium levels there has to be a balance of intake, absorption and excretion. Key operators in achieving this balance are the parathyroid glands which upon detecting low levels of ionized calcium, secrete parathyroid hormone (PTH). PTH works by increasing intestinal and tubular reabsorption of calcium, as well as promoting renal production of calcitriol ($[1,25\text{-}(OH)_2D]$ and bone resorption. 99% of the calcium body stores are situated within the skeleton where it provides mechanical strength. Bone acts as a mineral reservoir so when the exogenous supply is insufficient bone tissue will inevitably be resorbed from the skeleton to maintain serum calcium at a constant level. Obligatory losses of calcium that occur in urine, digestive tract, skin and nails need to be accounted for.



Idéos

Calcium/Vitamin D_3 500mg/400IU

An innovative idea of osteoporosis

Calcium & Vitamin D supplementation*

2 tablets per day

Chewable tablets
Lemon flavour

Convenient for patients with:
- **Diabetes**
- **High blood pressure**

Can be associated with specific treatments of osteoporosis

For further information and safety data please refer to the SPC.

IDEOS®, chewable tablets. **COMPOSITION*:** Elemental calcium 500 mg (corresponding to 1250 mg of calcium carbonate), cholecalciferol (Vitamin D3) 400 IU (corresponding to 4 mg of cholecalciferol concentrate, powder form). **PHARMACEUTICAL FORM :** Chewable tablets. **THERAPEUTIC INDICATIONS*:** Vitamin D and calcium deficiency correction in the elderly. Vitamin D and calcium supplementation, as an adjunct to specific therapy for osteoporosis, in deficient patients or in patients with a high risk of vitamin D and calcium deficiency. **POSOLOGY AND METHOD OF ADMINISTRATION :** Oral use. For adults only. Suck or chew the tablets. One tablet twice a day. **CONTRAINDICATIONS :** Hypersensitivity to one of the constituents. Hypercalcaemia, hypercalciuria, calcium lithiasis. In patients where prolonged immobilisation is accompanied by hypercalcaemia and/or hypercalciuria, vitamin D and calcium treatment should only be resumed when the patient becomes mobile. **SPECIAL WARNINGS AND PRECAUTIONS FOR USE :** In case of long term treatment, the urinary calcium excretion must be monitored and treatment must be reduced or temporarily suspended if urinary calcium excretion exceeds 7.5 mmol/24 h, i.e. 300 mg/24 h. In case of simultaneous treatment with digitalis glycosides, diphosphonates, sodium fluoride, thiazide diuretics, tetracyclines, see "Interactions". Take into account the dose of vitamin D per tablet (400 IU) in case of simultaneous treatment with another vitamin D preparation. Administration of supplementary vitamin D or calcium should be done under medical surveillance with monitoring of calcaemia and calciuria. The product should be prescribed carefully to patients suffering from sarcoidosis because of the potential increase of vitamin D metabolism into its active form. For these patients calcaemia and calciuria should be monitored. In case of renal insufficiency, adapt the dosage according to creatinine clearance . **INTERACTION WITH OTHER MEDICAMENTS AND OTHER FORMS OF INTERACTION*:** Digitalis glycosides, thiazide diuretics, oral tetracyclines, - diphosphonates, sodium fluoride, high doses of vitamin D, phenytoin, barbiturics, glucocorticoids. **PREGNANCY*:** Ideos can be used during pregnancy and lactation. However, the daily dose should not exceed 1500 mg of calcium and 600 IU of vitamin D3. During pregnancy, overdose of cholecalciferol and vitamin D should be avoided. **LACTATION:** Vitamin D and its metabolites enter the breast milk. **UNDESIRABLE EFFECTS :** Hypercalciuria and exceptionally hypercalcaemia, in case of long term treatment in high dosage: constipation, flatulence, epigastric pains, diarrhoea. **OVERDOSE*. PHARMACOLOGICAL PROPERTIES* :** VITAMIN D-CALCIUM SUPPLEMENT (Drug acting on calcium balance - Alimentary tract and metabolism). **PHARMACEUTICAL FORMS AND PRESENTATIONS:** Box of 60 tablets in tube of 15 tablets. MA number: MA093/00201 **MARKETING AUTHORISATION HOLDER:** LABORATOIRE INNOTECH INTERNATIONAL 22 Avenue Aristide Briand 94110 ARCUEIL-FRANCE. **TEXT REVISION DATE:** 14 April 2010. ***For complete information, please refer to the therapeutic references.**

A balanced diet consisting of low-fat dairy products, vegetables and fruit can provide sufficient calcium and a number of other essential nutrients required for our health. The average dietary calcium intake is 600-700mg per day in adults aged over 50. This should be increased as a first line approach with the addition of calcium supplements when dietary calcium intake does not suffice. The US National Osteoporosis Foundation (NOF) and US Institute of Medicine (IOM) recommend a daily calcium intake of 1000mg/day in men aged 50-70 years, whilst in men aged 71 years or older and in women aged 51 years or older a daily intake of 1200mg/day is recommended[2]. Higher levels of intake have not been proven to confer an additional benefit but may on the other hand increase the risk of kidney stones, stroke and cardiovascular disease.

ROLE OF VITAMIN D

Vitamin D is essential for calcium absorption and to maintain bone health. The active metabolite 1,25-dihydroxyvitamin D regulates calcium absorption in the bowel, mediates mineralization of osteoid tissue within bone and has an important role in muscle function[3]. Thus vitamin D status is crucial in maintaining the integrity of the system which regulates calcium balance. The main source of vitamin D is cutaneous production after ultraviolet radiation. Regular exposure of hands, arms and face without the use of sunblock for 10 minutes between April-October two or three times a week will produce sufficient vitamin D to supply the annual nutritional requirements[4]. Dietary sources such as vitamin-D fortified milk, cereals, saltwater fish and liver can compensate for lack of sunlight exposure.

Vitamin D deficiency can be classified as mild (serum 25(OH) D 25-50nmol/L), moderate (serum 25(OH)D 12.5- 25nmol/L) and severe (serum 25(OH)D < 12.5nmol/L)[5]. The NOF recommends a daily intake of 800-1000 international units (IU) vitamin D in adults aged 50 and over. On the other hand, the IOM recommends an intake of 600IU until the age of 70 which increases to 800IU per day for those aged over 70[1]. There is a high prevalence of vitamin D deficiency in osteoporosis, especially those with hip fractures[6]. Identifying and correcting vitamin D deficiency is important in the management of patients with osteoporosis who are at risk, and it is also part of the universal recommendations. Individuals who are at risk include patients suffering from gastro-intestinal disorders, chronic kidney disease and chronic illnesses. Lack of sun exposure, obesity and dark skin are other common risk factors for vitamin D deficiency. In these patients serum 25(OH) D levels should be checked at baseline and sufficient replacement and maintenance therapy should be administered with the aim to achieve a target vitamin D level of approximately 75nmol/L. A significant proportion of patients will need more than 800-1000IU per day to correct the deficiency. The safe upper limit for vitamin D intake in the general population was increased to 4000IU per day in 2010[2].

Vitamin D deficiency can be treated with 50,000IU D_2 or D_3 per week or a daily dose of 6000IU for the duration of 8-12 weeks followed by a daily dose of 1500-2000IU. These doses may be higher in patients who are obese, on drugs that alter metabolism of vitamin D or suffer from malabsorption. Vitamin D supplementation is equally important to calcium supplementation in patients with osteoporosis and failure to do so can impede improvement of bone mineral density.

There is strong evidence to suggest that combined calcium and vitamin D supplementation can provide significant reduction in the risk of hip and non-vertebral fractures. They should always be prescribed in adequate doses in patients receiving osteoporosis treatment to achieve an optimal increase in bone mineral density and a reduction of fracture risk, together with regular weight-bearing exercise and smoking cessation.

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3. Francis RM. Prevention and treatment of osteoporosis: calcium and vitamin D. In: Compston JE, ed. *Osteoporosis. New perspectives on causes, prevention and treatment.* London, Royal College of Physicians of London, 1996: 123-34.
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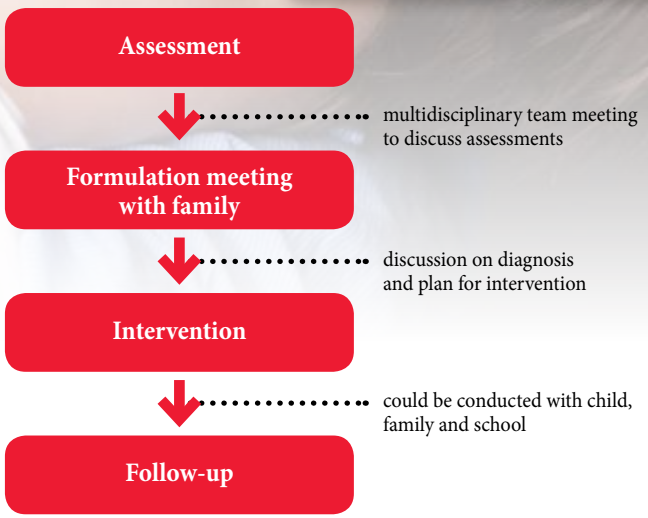
NEW: ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) & AUTISM SPECTRUM DISORDER (ASD) SERVICES

SAINT JAMES HOSPITAL has set up two clinics focused on children that introduce new assessment and diagnosis procedures to the Maltese Islands. One is an ADHD service and the other is an ASD service. Both are led by a multidisciplinary team. These services have been set up according to the gold standards set out by the National Institute for Clinical Excellence (NICE) in the UK. Saint James Hospital's multidisciplinary team comprises two psychiatrists, a clinical neuropsychologist/ psychologist, a speech and language therapist, an occupational therapist and a community mental health nurse (care co-ordinator).

There is no single, simple, definite test for ADHD and ASD. The diagnosis requires a specialist assessment that revolves aroundrecognising patterns of behaviour, observing the child and obtaining reports of their behaviour at home and at school.

The following diagram illustrates the pathway of care at Saint James Hospital. This isindividualised to meet every child's needs.



SOME MEMBERS OF THE MULTIDISCIPLINARY TEAM

Dr Nigel Camilleri
is a Child Psychiatrist. He studied medicine and surgery at the UOM where he graduated in 2003. In 2006 he started his psychiatry training at Mount Carmel Hospital, Malta. In 2008 he moved to the UK and trained in the Northern Deanery. He is a Tier 4 Consultant in Child and Adolescent Psychiatry in the Tees Esk and Wear Valleys NHS Foundation Trust. He currently works at the Newbury adolescent in-patient unit and Westwood Low Secure Forensic Unit. Previous to this he worked as a locum consultant from September 2013 to March 2014 at the Child and Family Department in Durham. He is also an Associate Clinical Researcher at Newcastle University, currently working with Paediatric Bipolar Disorder Team on research projects in this field.

Ms Ramona Vella Vidal
is a Paediatric Occupational Therapist and has been working in this field for the past 20 years. She started her career working at St. Luke's Hospital and then joined the team at the Child Development and Assessment Unit (CDAU) since its inception in the early 90s. In her final years at CDAU, she led the team of Occupational Therapists as a Principal OT. Throughout this time she has always sought to further her studies through seminars and courses held locally and abroad especially in the area of Sensory integration. During the last two years she has been working in the private sector as a freelance Occupational Therapist giving lectures and seminars to OT students, parents and other allied professions.

Ms Veronica Montanaro
is a Speech and Language Pathologist who practices as a Clinical Specialist in Alternative and Augmentative Communication. MsMontanarospecialised in Language and Communication Impairment in Children at the University of Sheffield. She also addresses seminars for parents and children who benefit from Alternative and Augmentative Communication, carries out training for professionals interested in the area and offers consultancy in language development in young children. She is also a visiting assistant lecturer at the UOM.

Dr Kristina Vella
is a Clinical Neuropsychologist. She studied Psychology at the UOM where she graduated in 2002. She completed an MSc in Rehabilitation Psychology and a PhD in Paediatric Neuropsychology at the University of Nottingham. She is currently at the final stages of completing her Doctorate in Clinical Psychology also at the University of Nottingham. During her 10 years in the UK, Kristina worked in various inpatient and outpatient paediatric settings. Her work focused on child mental health, including acquired and organic developmental difficulties. Since September 2013, she has been working as the resident psychologist at Saint James Hospital, Malta. She is also a resident lecturer in Neuropsychology at the University of Nottingham.

THE RIGHTS OF PERSONS WITH MENTAL DISORDER

MIRIAM CAMILLERI
JOHN M CACHIA

We refer to the paper by Dr Anthony Zahra and Dr Nigel Camilleri entitled "An Overview of the New Mental Health Act for the Maltese Islands" published in the *The Synapse Magazine,* Volume 13 Issue 01, and submit our comments, remarks and clarifications from a patient rights' perspective.

THE DEFINITION OF "MENTAL DISORDER"

The authors suggest that a specific reference to either the World Health Organisation International Classification of Diseases or the American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders could provide more definite guidance to users of the Mental Health Act. However if legislation is too prescriptive or prefers one international classification over another, then it may diminish clinical autonomy and as a result hamper rather than guide the service provider. As a result this may negatively impact the beneficiary of the service.

FORMULATION OF THE MULTIDISCIPLINARY CARE PLAN IN PATIENTS ADMITTED VOLUNTARILY TO A MENTAL HEALTH LICENSED FACILITY

Patient management should start as early as possible and service providers should take up the proposed recommendations by the authors that "an initial care plan should be written up in the first 48 hours of the patients' admission into hospital". The health care facility is already obliged to draw up its own operational procedures and patient care management protocols in terms of care to be provided from the point of admission onwards. Legislation allows a reasonably long period of time to ensure that at the latest, the multidisciplinary care plan should be fully finalised and operational within a week of admission to voluntary care. Service providers should aspire to bettering this deadline for the benefit of patients and in accordance with best professional practice.

DETENTION OF UP TO 4 HOURS BY NURSE IN CHARGE OF A VOLUNTARY PATIENT TO ALLOW MEDICAL REVIEW IF IT IS PERCEIVED THAT THERE ARE GROUNDS FOR INVOLUNTARY ADMISSION

Since this subarticle is already in force, concerns should be immediately addressed by the mental health facility's management structure and documented in clear operational guidelines and/or patient care management protocols as required by the Mental Health Act itself. The Act places the onus on the clinical director responsible to ensure that healthcare staff comply with such patient care management protocols.

INVOLUNTARY ADMISSION FOR OBSERVATION

The authors outline the procedure used in the UK and such an approach would indeed be welcome as a truly multidisciplinary proactive planned approach to care and treatment in Malta. The role taken by the approved mental welfare officer (AMPH) in the UK in the patient admission process is not applicable to old or new local mental health legislation. The mental welfare officer in the local legislation takes the place of the "responsible carer" and will only be involved in those admissions wherein such responsible carer is not willing to sign the application or is untraceable. The new legislation allows the mental welfare officer to dissent from medical opinion, documenting reasons on the application form, without hampering the admission process. Given that all applications for involuntary admission for observation will be forwarded by the Clinical Director to the Commissioner within 48 hours of the admission, such divergence of opinion will be noted and looked into, thus providing adequate checks and balances between the medical and the social viewpoints on involuntary admissions.

EMERGENCY ADMISSION FOR OBSERVATION

This is the most frequently used route of involuntary admission in Malta. We support the recommendation that there should be more widespread efforts for joint planned admission with the examination of the specialist psychiatrist provided within 72 hours of the first examination and prior to the actual admission. It is not in patients' best interests to exclude the possibility for emergency admissions based on one medical recommendation only. As a safeguard for the patient, the new law requires that the second medical assessment by a psychiatry specialist be carried out within 24 hours of admission.

THE ROLE OF THE RESPONSIBLE CARER IN AN APPLICATION FOR INVOLUNTARY ADMISSION FOR OBSERVATION

We understand the concerns raised by the authors with respect to the responsible carer. Article 4 states that the responsible carer shall be a person "who maintains a close personal relationship with the patient and manifests concern for his welfare". This article also provides a clear process by which a responsible carer can be identified in the event that a patient lacks mental capacity or otherwise fails to appoint a responsible carer in writing. The responsible specialist can request a change in responsible carer through the Commissioner in circumstances such as those mentioned by the authors.

If at application for involuntary admission for observation stage, the patient has not made a previously expressed choice of responsible carer in writing, Article 4 should be followed to identify the responsible carer. Given that there is a medical recommendation for admission, the application can be filled by a mental welfare officer if the responsible carer does not agree with the need for an involuntary admission or if the responsible carer is absent or cannot be identified at this stage.

INVOLUNTARY ADMISSION FOR OBSERVATION – CAN TREATMENT BE PROVIDED?

Whilst the legal text may not be sufficiently clear in this regard, it is our opinion that the period of involuntary admission for observation with a maximum duration of 10 days should be an active period of observation accompanied by full treatment as required. The clinical assessment performed by the specialist within 24 hours of admission is a legal requirement and should hopefully be followed by subsequent regular assessments which should guide clinical management on a case by case approach, as happens in other non-psychiatric clinical specialties. We fully agree with the authors' recommendation for regular clinical audit.

MENTAL CAPACITY

The new mental health act covers mental capacity stemming from a mental disorder. Hence only a specialist in psychiatry will be able to certify a person suffering from a mental disorder as having mental capacity or lack thereof. However we agree with the authors that local legislation may need to move forward to a wider view of capacity. Our office has launched this debate in a highly successful and well attended seminar held on 22nd February of this year. The contributors to this debate included the President of Malta, the Speaker of the House of Representatives, the Minister for Health, the EU Commissioner for Health, the current Maltese Judge in the European Court of Human Rights, and a panel of experts from the legal, ethical, geriatric, notarial and psychiatric fields. The debate included seminal ideas about the possibility of moving towards stand-alone capacity legislation, introduction of advance directives and other legislative action. We agree that all doctors and indeed all healthcare professionals should receive adequate training in capacity assessment. We need to expand upon the notion that capacity can be assessed only in relation to a specific decision and that capacity can fluctuate over time and therefore may require repeated assessments. This means providing patients with enough time and assistance to understand the information given to them, reflect on it, and communicate their decision to the clinical team. We need to relearn to discover patience in dealing with patients.

PRACTICAL IMPLICATIONS

The authors refer to changes in the "period of time for which an emergency order will remain valid". We would like to clarify this statement. Under current legislation, a patient may be admitted involuntarily to a psychiatric hospital for up to 72 hours on the strength of a single signature. In the new legislation which is coming into force, an involuntary emergency/urgent admission for observation on the strength of one signature will perforce necessitate specialist assessment within 24 hours. Furthermore a specialist assessment within 24 hours of admission will also be a requirement in involuntary admission for observation even when 2 assessments and signatures have been carried out prior to admission. This change in legislation is linked to patients' rights and does not in any manner impinge on professional capabilities and performance. A person detained involuntarily is being deprived of freedom and hence a safeguard to the patient, his/her responsible carer and the service delivery team is contained in the legislative requirement for a specialist assessment within 24 hours of admission. Hence an admission for observation whether urgent conditions or not provides the service provider with a holding capacity of not more than 10 days. In those 10 days decisions need to be taken. There are four possible outcomes: (1) patient is discharged home, (2) patient is placed on a compulsory/involuntary community treatment order, (3) patient requires further inpatient treatment and care but his/her admission can be changed into a voluntary type of admission, and (4) patient requires further involuntary inpatient treatment and care. In all of these instances, a multidisciplinary care plan should be formulated. In the first and third options, there is no obligation for involving the Commissioner for Mental Health. In the second and fourth option there is a formal process which is set in motion which requires the service providers and the Office of the Commissioner to work together for the benefit of the patient.

The Office of the Commissioner has to date provided around 25 sessions to healthcare professionals working within the mental health services, primary health, the social welfare sector, and probation services, in both Malta and Gozo. We have also provided an in-house document of "Explanatory notes to healthcare professionals". The Office has also disseminated a number of leaflets pertaining to the salient features of the Mental Health Act and the functions of our Office. We remain open to further specific requests which may be sent on **mentalhealthcommissioner.mfh@gov.mt**

CELEBRATING A NEW AND PROMISING COLLABORATION!

THERESIA DALLI,
GABRIEL ELLUL, MELANIE GRIMA
MMSA - THESYNAPSE LIAISON TEAM

In a world where communication takes precedent over almost everything else, it is almost no surprise that TheSynapse has grown so much in the past years! By serving as a link for the medical community, both local and foreign, it has expanded to meet the needs of an ever-changing group of dynamic professionals, all working together for a single purpose: the patient.

Looking at it from this perspective, it is of no surprise that the Malta Medical Students' Association and TheSynapse have finally teamed up to keep on strengthening this network of medical contacts.

With this in mind, we look back to the past weeks with satisfaction. We believe that we have managed to establish a very good rapport with Dr Wilfred Galea, TheSynapse managing director, and his team, who so keenly introduced us to their ever-growing project. We are very grateful for the opportunities they are offering us medical students: we can now contribute to this online resource platform with our own articles or by using the site's infrastructure to interact with other medical professionals.

Starting off with the launch of TheSynapse mobile app, an event which attracted local media and which highlighted our newly-founded relationship, the MMSA has grown to accomodate this new and welcome partnership. More and more medical students are registering to make use of TheSynapse's services. And more and more students are offering to submit their articles for the whole world to see, even though most of these literary works are still in the pipeline.

This brief message is an invitation to all those students who want to help themselves succeed in their career. Become members of TheSynapse community! Thanks to TheSynapse, MMSA members are being offered the chance to grow academically in a different and original way. By joining the multitude of registered students who have now become TheSynapse members, you are laying the foundation to a medical career based on community spirit and on the altruistic sharing of knowledge, for the good of the patient.

PHARMACY SYMPOSIUM WEEK 2014

MPSA

This annual event held at Aula Magna, organized by the Department of Pharmacy is one which is looked forward to by many students. This is where students showcase their projects along with their colleagues via posters and discussions. A brief summary of all the hard work done throughout the year by the students with their respective tutor was presented. The various topics presented included point of care testing, pharmacotherapy, pharmaceutical care, pharmacy administration, industrial pharmacy, clinical analysis, medicinal chemistry and drug design. The symposium is also an opportunity for all students to mingle and catch up with their colleagues. Elections for the new MPSA executive 2014-2015 are also held.

During the opening ceremony a number of distinguished guests were invited, which included Honourable Ministers of Health and Education and the respective shadow ministers. The common principle which was brought up in their speeches was the importance of preparing the student for the industrial sector in the pharmaceutical profession which should be linked with enhancing entrepreneurship capabilities.

By the end of the week, all the students had presented their work. A small videoclip was also presented, a tradition which has been upheld for a number of years ... heartbreaking for the final year students, and an inspiration to the younger ones.

Finally, the whole week of academia was concluded with the annual MPSA Gala Dinner. For this event, all the students participating in the symposium as well as the staff of the department, are invited to wine and dine together. This glamorous event was held at Monte Kristo Estates which was successful with a good turnout.

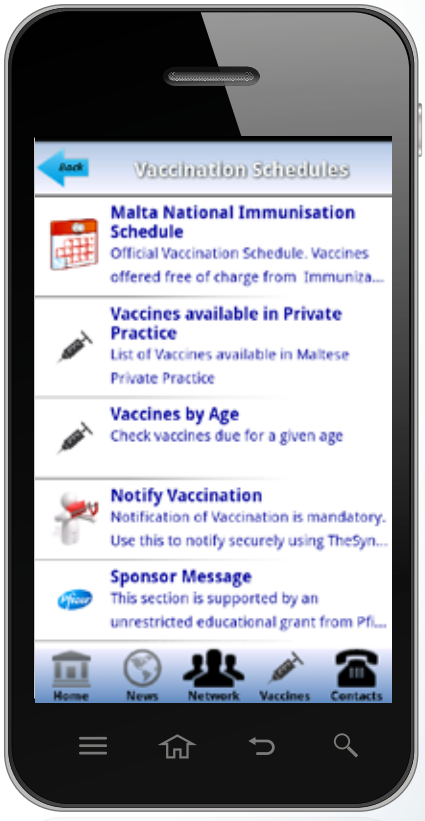
THESYNAPSE

Complete Vaccine Resource

NOW AVAILABLE AT YOUR FINGERTIPS

A few months ago TheSynapse celebrated it's seventeenth year since launch. TheSynapse has had several important milestones through the years and has always kept abreast with the developments in technology. The launch of TheSynapse app in October 2013 was such an important milestone.

Get 'TheSynapse' app on your iphone or andriod device TODAY



- ✔ Users of TheSynapse app can keep touch with the latest news from the medical world as well as local news of interest and announcements for medical professionals.
- ✔ In April 2014, TheSynapse app continued to expand with the addition of a comprehensive vaccine information resource for medical professionals. The aim of this resource is to deliver all the information regarding vaccinations that one may need, when it is needed, directly on the personal mobile phone.
- ✔ The app has a number of sections which include the latest Malta National Immunisation schedule, the list and respective schedules of all vaccines available in private practice as well as a quick reference list of all vaccines from birth to one year, to those in the second year of life, as well as vaccines from the age of two years to adolescence.
- ✔ For each vaccine listed one can access a page with relevant vaccine information. This enables the user to have the relevant information that is needed in hand whenever and wherever one needs. One can also access the relevant official abridged or detailed SPC regarding each vaccine.

Once a vaccine has been given, the app gives the facility for the doctor to perform the statutory vaccination notification through the app. This is done through a secure internet connection. The only requirements are that the phone is connected to the internet and that the doctor logs on using TheSynapse registered email address and TheSynapse Direct Personal Identification Code (PIC Code). Once the vaccination is notified, the doctor will have an acknowledgement with a unique reference ID to the particular vaccination.

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ANDROID APP ON Google play

www.thesynapse.net

Pfizer

The vaccination section of TheSynapse app is supported by an unrestricted grant by ***Pfizer***

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- The first ICS/LABA combination to deliver continuous 24-hour efficacy[2]
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(fluticasone furoate and vilanterol inhalation powder)

Practical efficacy

Relvar Ellipta (fluticasone furoate/vilanterol) Abridged Prescribing Information

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

Please refer to the full Summary of Product Characteristics before prescribing

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

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

REPORTING ADVERSE EVENTS (AEs):

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

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

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

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

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

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

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

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PATIENT CENTRICITY

THE PATIENT AMBASSADOR PROGRAM AT GRÜNENTHAL

We, at Grünenthal, want to place the patient at the centre of our way of thinking and behavior.

Our daily work, as well as all strategic measures and decisions, are always guided by this vision. This means we set patient priorities and health as our first corporate goal to ensure we have a better understanding of the patient's needs so that we can develop our business accordingly.

For us, to be patient-centric means: understanding and integrating the patients' perspective and their unmet needs in our day-to-day activities and decision making. Identifying patients' needs helps us to reflect how we, as a pharmaceutical company, can improve their situation with our daily work. This not only implies better treatment by e.g. providing better formulations, packaging and labeling, but also offering easy access to information on pain management.

In 2011 we decided to set up a patient ambassador program allowing us to stay in close contact with chronic pain patients. A patient ambassador at Grünenthal is either someone living with chronic pain or someone caring for a pain patient. In addition, these patient ambassadors share our objective: we all want to improve and change the lives of those suffering from chronic pain.

Through the patient ambassador program these patients or their carers have shared their stories with us and through them we have gained an in-depth insight into their lives and learned a lot about the challenges chronic pain patients are facing in their day-to-day life, their dreams and wishes.

The direct contact and integration of the ambassadors in our field of business also enable us to ask them for their open feedback and consultancy on various topics. In the past, several colleagues and departments took the opportunity to invite ambassadors to workshops or discussion rounds to ask for their input on e.g. formulations, packaging, how they rate different side-effects, and feedback on educational material for patients. Additionally they have access to our internal social network. This means that every employee has the possibility of starting discussions with the patient ambassadors and vice versa. This ensures that there is a continuous dialogue between employees and patient ambassadors which is one reason why the ambassadors are really integrated in the Grünenthal culture.

Sometimes, they also participate in external events organized in co-operation with health insurances, patient organizations, physicians and physiotherapists to raise awareness for a multimodal pain therapy approach among the general public. On these occasions the ambassadors share their experience and encourage other patient living with chronic pain not to give up and to work actively with their healthcare teams to find a treatment plan that works for them.

The Grünenthal Group is an independent, family-owned, international research-based pharmaceutical company headquartered in Aachen, Germany.

Building on its unique position in pain treatment, its objective is to become the most patient-centric company in the field of pain and thus to be a leader in therapy innovation. Grünenthal is one of the last remaining five research-oriented pharmaceutical companies with headquarters in Germany which sustainably invests in research and development.

ERRATA CORRIGE - VOLUME 13 ISSUE 01

THE ARTICLE SUBMITTED BY MMSA, ENTITLED 'POLYCYSTIC OVARY SYNDROME' SHOULD HAVE INCLUDED THE FOLLOWING AUTHORS:

SARA CRAUS, WHO IS A 4TH YEAR MEDICAL STUDENT & PROFESSOR JOSANNE VASSALLO.

REVIEW ARTICLE

RATES OF POST-TONSILLECTOMY BLEEDING IN MALTA

A TEN YEAR STUDY

STEPHAN FENECH
HERMANN K. BORG XUEREB
STEFAN MALAGUTI

ABSTRACT

Patients presenting with post-tonsillectomy haemorrhage are frequently readmitted to hospital, usually for observation, but surgical intervention may sometimes be necessary. A 10 year retrospective analysis of 3553 patients who underwent tonsillectomy with or without adenoidectomy at the Mater Dei hospital was carried out. Clinical notes were used to determine the post-tonsillectomy haemorrhage rate and its relationship to the use of antibiotics.

INTRODUCTION

Post-tonsillectomy haemorrhage is a well known and relatively common, potentially life-threatening complication. It is the single most important factor to be discussed with patients in the process of obtaining informed consent for the surgical procedure[1]. Addressing patient concerns and educating patients regarding this potential complication is a key factor in managing the situation[2].

The vast majority of patients who experience any degree of bleeding in the post-operative period seek medical attention. No consensus has been so far reached regarding the use of antibiotics as prophylaxis against post-tonsillectomy bleeding[2-5]. Of the four consultant-led firms in the ENT department, only one does not routinely prescribe antibiotics pre, peri and post-tonsillectomy.

The aim of this study was to establish the rate of post-tonsillectomy haemorrhage in the ENT department and compare it to established international standards. An effort was made to assess the characteristics of the problem regarding higher risk groups and seasonality, as well as to elucidate the role of antibiotics in relation to haemorrhage.

A preliminary four and a half year retrospective study (1464 patients) was concluded in 2003 and published in 2006[6]. The current study (2089 patients) includes a review up to December 2008. The results of both studies are combined in this review to achieve the 10 year conclusions. In November 2007, the ENT department moved from St Luke's Hospital to Mater Dei Hospital.

Three hundred sixty-eight tonsillectomies have been performed in Mater Dei Hospital up to December 2008. Of these, there were 23 patients who were readmitted with post-tonsillectomy haemorrhage (6.25% of all operations performed). Data was gathered regarding the operation details, patient demographics, methods of haemostasis during the original operation (and during the operation for those patients requiring surgery for post-operative haemostasis) as well as the use of antibiotics. All patients were operated under general anaesthesia, after routine pre-operative assessments by the house officer and the anaesthetic team were performed. The procedures were carried out by consultants, senior registrars and senior house officers.

The rate of post-tonsillectomy haemorrhage was determined by the rate of patients being readmitted to the ward. For these patients, the admission notes were reviewed and data regarding the findings on admission, blood investigation results, management and classification of severity was collected. The severity was classified as mild (conservative management), moderate (requiring operative intervention) and severe (operative intervention plus blood transfusion). The post-operative bleeding was classified as primary (within the first 24 hours post-operatively) and secondary (more than 24 hours post-operatively). A total of 3553 tonsillectomies were carried out during this study period of which 1833 were males (51.6%) and 1720 (48.4%) were females.

Patients ranged from 1 year up to 48 years of age. The number of patients was quite evenly distributed throughout the age groups; however the most common age group was 0-5 years, with 1705 (48%) patients.

Indication for tonsillectomy ranged from recurrent acute tonsillitis to removal for tumour suspicion. However for the purposes of this study, we excluded those for tumour suspicion.

One hundred forty-two patients were admitted with post-tonsillectomy haemorrhage which represents 3.99% of all patients undergoing tonsillectomy. Of these, 17 (12%) were classified as suffering from primary post-tonsillectomy bleeding, whereas 127 (88%) were classified with secondary bleeding. Of the 142 patients who were readmitted there was a slight male preponderance with 83 (58.5%) patients while there were 59 (41.5%) female patients.

The rates of post-tonsillectomy bleeds when compared to the total number of procedure performed. The actual percentage of post-tonsillectomy bleeding rates, when compared to the total number of procedures performed per age group, was significantly different. The highest percentage was found in the

20–29 year age group with up to 23% of patients operated being readmitted with bleeding. The lowest percentage was found in the 0–5 year age group with 1.34%. Bleeding occurred from day 1 up to day 34 post-operatively. It occurred most frequently around 6-8 days post-tonsillectomy.

The patients who were readmitted spent from 1 to 12 days in hospital with a mean of 1.6 days. The majority of patients were discharged after only one day of observation. Most patients were classified as suffering from mild bleeding. In fact 108 (78.8%) cases suffered only mild bleeding, 25 (18.2%) cases suffered from moderate bleeding and only 4 (2.9%) cases suffered serious bleeding.

78.9% of patients admitted had been receiving antibiotics post-tonsillectomy. Only 30 (21.1%) of patients had not received any antibiotics. This means that 2.81% (30 out of 1066) of all patients which were operated on and kept off antibiotics ended up being readmitted with post tonsillectomy haemorrhage. On the other hand, 4.50% (112 out of 2487) of all patients which were operated on and were given antibiotics were being readmitted with post tonsillectomy haemorrhage.

DISCUSSION

This study revealed a total post-tonsillectomy bleeding rate of 3.99% over a period of 10 years. This compares very well when compared to other studies. Blakely[7] reviewed the results of 4610 published papers found by carrying out a MEDLINE search, 63 of which reported post tonsillectomy bleeding rates. He suggests a maximum 'expected' sustained bleeding rate of 13.9%. The mean was of 4.5% with a maximum reported rate of 20% and a minimum of 0.6%.

The reported incidence of post-tonsillectomy haemorrhage proceeding to operation for haemostasis, ranges from 0.09 to 3%[8-11]. In our case the rate was as high as 20%. In part, this may be accounted for by the fact that most of the cases regarding post-tonsillectomy bleeding are dealt with by visiting senior registrars from the UK who spend a period of 6-12 months in our facility (they were responsible for 19 cases of this bleeding). In fact of the 29 cases where operative intervention was decided upon, it was only in 3 cases that this decision was taken by the resident UK trained senior. This is a rate of 2.13% which compares well to the published rates. Senior registrars from other countries took an additional 7 patients to theatre.

In keeping with published results[12,13], we found a higher rate of male patients being admitted suffering from post-tonsillectomy bleeding (58.5%). The most frequent prevalence was found in patients with an age group from 20-29 years.

12% of cases were classified with primary haemorrhage which compares well to other studies which however take into account *all* cases of post-tonsillectomy bleeding, including tumor suspicions[6,14]. With regards to the usage of antibiotics, our results between the consultant-led firm which used antibiotics compared to the three that did not show that they do not help in preventing bleeding post-tonsillectomy. This is in keeping with current trends[2,4,15]. As method of haemostasis during the original procedure itself, two methods were utilised – diathermy and ties. It is interesting to note that all patients who presented with bleeding post-tonsillectomy had had cautery during the tonsillectomy. It should be noted, however, that no data on how many ties were used in the original procedure has been recorded during the operations.

Overall, tonsillectomy is a relatively safe procedure. No deaths were identified during the past 10 years. This study shows that the overall rates of post-tonsillectomy bleeding in the ENT department of Mater Dei hospital is in keeping with the international published rates. There also seems to be no definite role for antibiotics.

REFERENCES CAN BE ACCESSED ON THESYNAPSE.NET

QUIZ

WHO IS SPONSORING THE VACCINES SECTION OF THE SYNAPSE APP?

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THE 5TH CORRECT ENTRY WILL WIN A MEDICAL LANGUAGE TRANSLATOR BOOK PUBLISHED BY MMSA.

QUIZ WINNER

WINNER OF THE MEDICAL LANGUAGE TRANSLATOR BOOK PUBLISHED BY MMSA

DR ALI ABDULNABI MD IS THE LUCKY WINNER OF THE MEDICAL LANGUAGE TRANSLATOR BOOK PUBLISHED BY MMSA. HE WAS THE 5TH PARTICIPANT WHO REPLIED CORRECTLY TO THE QUESTION, 'WHAT IS THE 4TH GENERATION TOPICAL FLUOROQUINOLONE INDICATED FOR BACTERIAL CONJUNCTIVITIS ADVERTISED IN VOLUME 1 ISSUE 01?'. THE CORRECT ANSWER WAS MOXIFLOXACIN.

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GLOBAL INITIATIVE TO REDUCE SALT INTAKE

CHARMAINE GAUCI

High levels of dietary sodium intake are associated with raised blood pressure and cardiovascular disease. Furthermore, a high salt diet may have direct harmful effects independent of its effect on blood pressure, for example, by increasing the risk of stroke, left ventricular hypertrophy and renal disease. Increasing evidence also suggests that salt intake is related to obesity, associated with renal stones and osteoporosis and is probably a major cause of stomach cancer.

Sodium intakes of different populations around the world were first brought to the attention of the research community through Louis Dahl's famous graph published in 1960, showing a positive linear relationship between prevalence of hypertension and mean sodium intake across five populations.[1] The review of salt intakes showed that sodium intakes around the world are well in excess of physiological need both in children and adults. In a recent study, it has been found that in European and Northern American countries, sodium intake is dominated by sodium added in manufactured foods (75% of intake).[2] Cereals and baked goods were the single largest contributor to dietary sodium intake in UK and US adults. On the other hand, in Japan and China, salt added at home (in cooking and at the table) and soy sauce were the largest sources.[2]

The WHO recommends no more than 2 grams of sodium (5 grams of salt) per day. Approximately 95% of sodium is consumed in the form of salt. According to Member States data collected for the survey,[2] the current daily salt consumption in most European countries is estimated or measured to range between 8-12 grams per day, with few Member States above and few below this intake level.

In Malta there is very limited data. *In fact the current salt intake in Malta is not known.* However, the 1986 Intersalt Study[3] found that Maltese men consumed 11g per day and women consumed 9g per day. The 2002 Health Interview Survey[4] conducted in Malta, showed that 47% of the participants added salt to their meals while cooking, whereas 23% added salt upon eating. In the Health Interview Survey of 2008[5], 22% of the population aged above 18 years self-reported hypertension. However the burden is much higher, especially in patients above 40s. In fact, the 2010 European Health Examination Survey[6] reports that 46% of patients aged 41-60 years were classified as having possible hypertension while 85.5% of patients aged 60 years have been classified as possibly hypertensive.

The impact of increased salt consumption has been defined as a critical issue by the WHO[7] and by the European Commission. All member states are encouraged to tackle this issue immediately as the current salt consumption patterns are leading to 80% of all deaths. Strazzullo et al,[8] and Taylor et al,[9] showed that a difference of 5g a day in habitual salt intake would result in a 23% decrease in stroke cases and 17% decrease in cardiovascular disease cases. A small reduction in blood pressure of 1-4 mmHg showed a reduction of cardiovascular deaths by 5 -20%.

A common EU framework for salt reduction[10] has been developed, describing a common vision for a general European approach towards salt reduction for better health. Several cost-effective analyses have been carried out to assess the health effects and financial cost of reducing population salt intake. Murray et al,[11] showed that non-personal health interventions, including government action, to stimulate a reduction in the salt content of processed foods, were cost-effective ways to limit CVD and could avert over 21 million DALYs (disability-adjusted life years) per year worldwide.

As part of the WHO Global Strategy on Diet, Physical Activity and Health and the Action Plan for Prevention and Control of Noncommunicable Diseases, three objectives have been set, namely to create enabling environments which facilitate consumer behavioural change regarding certain food choices, support the evaluation and monitoring of dietary salt intake, and facilitate the review of salt as a vehicle for fortification to prevent iodine deficiency disorders.

The actions to reduce salt consumption include:

1. Combined policy with industry to reduce the amount of salt
2. Clear labelling on food products
3. Increasing public awareness on effects of salt on health

Malta has joined the EU initiative to reduce salt in order to reduce the burden of illness. Various initiatives have already been initiated, targeting the general public to increase awareness on the effects of salt on health and to enhance skills in using alternative products in cooking. Work has also been initiated with industry to encourage the reduction of salt. However an information gap exists whereby the actual salt consumption of the Maltese population is not known. Furthermore we lack information on what the public is actually eating. Hence the Health Promotion and Disease Prevention Directorate is planning a Food consumption survey to be carried out in 2015. The aim is to provide the basis for public health initiatives in food and nutrition areas. One of the objectives is to identify the food groups that are the major salt contributors of the national diet in order to take actions to reduce sodium intakes and hence decrease the related burden of cardiovascular and other diseases.

REFERENCES CAN BE ACCESSED ON THESYNAPSE.NET

MMSA'S GOT TALENT

MARIKA AZZOPARDI INTERVIEWS TWO MEDICAL STUDENTS AND MEMBERS OF THE MALTA MEDICAL STUDENTS ASSOCIATION AND FINDS OUT ABOUT THE INTERESTING LIVES THEY LEAD

MARIKA AZZOPARDI

Matthew Baldacchino and Matthew Valentino are practically the same age, both medical students at the University of Malta and both members of the Malta Medical Students Association. As of October 2013 they are now both also representing Malta in the International Federation of Medical Students Association (IFMSA), in posts which help keep the Maltese medical students community in high profile.

Matthew Valentino who is a third year student, is the new Regional Assistant for Human Rights & Peace within the international association whilst Matthew Baldacchino who is a fourth year student is the new Regional Assistant for Public Health in Europe. Both roles have their own individual responsibilities. Both students explain more about these roles ...

Matthew V says, "We were both on the executive board of the MMSA up to last year and this enabled us to attend several different international meetings and conferences. It was a great way of learning more about the structure of the MMSA as well as the responsibilities linked to any one of the posts associated with it." Matthew B continues, "We started out as national officers within the local association and met each other via the MMSA. As things stand, our roles within the IFMSA will stretch on through to October 2014 when the new officers will get elected."

The international association is a great place wherein to share resources, access reports and research, and attend meetings online or in person. With an assured European-wide participation, each activity provides ample scope for communicating and socialising on a common front.

Matthew Valentino

Matthew Baldacchino

"As Regional Assistant for Human Rights & Peace, my post comes as the United Nations celebrates the 20 years anniversary of the founding of its Office of the High Commissioner for Human Rights. I have also been invited to specific high-profile events including two IFMSA General Assemblies, in March and in August. It is estimated that these conferences will attract some 800 students each from all over the world. The delegations are usually invited to participate in five-day sessions which focus on specific areas to share ideas and concepts."

> IT IS A HUGE SOCIAL LEARNING EXPERIENCE THAT INVOLVES CONSTANT OUTREACH. WE ACTUALLY HAVE SPECIFIC RESPONSIBILITIES TIED TO COMMUNITY NETWORKING LOCALLY AND OBVIOUSLY OUR FOREIGN EXPERIENCES HELP US IN THIS

On his part Matthew B has always been interested in public health and thus, his opportunity to experience that on an international level offers great scope for his career prospects. Whilst each student is still at a learning level, such experiences help shape their ideas and aspirations for the future.

Matthew V's direct superior within the IFMSA is from Slovakia, whilst Matthew B's head is Bulgarian. This also

means that both young men are strengthening their knowledge of working with people coming from diverse backgrounds, cultures and work ethics, yet sharing the very same common aim of improving health conditions, medical services, research options and more.

Matthew B confirms, "It is a huge social learning experience that involves constant outreach. We actually have specific responsibilities tied to community networking locally and obviously our foreign experiences help us in this." As he plans his first exchange abroad, Matthew B tells me more about how he represented Malta in Prague in 2012 at an international conference and also about conferences attended in Baltimore and Chile. On his part, Matthew V has already experienced a student exchange in the Netherlands. "It was an observatory experience rather than anything else. I observed some 35 surgeries which was great experience - of course I was not allowed to do anything else apart from observing. I also travelled to conferences via the MMSA, once to India, another time to Italy and a third time to Slovakia. The great thing is that the MMSA takes care of all the organisational part for students and also covers some travelling costs."

As these 21-year-olds explain, these opportunities as part and parcel of being an MMSA member. "Once you are a medical student, you automatically become an MMSA member. However many students take this for granted and are not at all aware of the great benefits an active membership can provide. Being pro-active leads to great opportunities - and they're all there for the taking, if students bother about it. We are certainly glad we did!"

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PRESENTATION: Onbrez Breezhaler 150mcg and 300mcg inhalation powder hard capsules containing indacaterol maleate, and separate Onbrez Breezhaler inhaler. **INDICATIONS:** For maintenance bronchodilator treatment of airflow obstruction in adult patients with chronic obstructive pulmonary disease (COPD). **DOSAGE AND ADMINISTRATION:** Recommended dose is the inhalation of the content of one 150mcg capsule once a day, administered at the same time of the day each day, using the Onbrez Breezhaler inhaler. Dose should only be increased on medical advice. The inhalation of the content of one 300mcg capsule once a day has been shown to provide additional clinical benefit with regard to breathlessness, particularly for patients with severe COPD. Maximum dose is 300mcg once daily. No dose adjustment required in elderly patients, for patients with mild and moderate hepatic impairment or for patients with renal impairment. No data available for use in patients with severe hepatic impairment. No relevant use in the paediatric population. If a dose is missed, the next dose should be taken at the usual time the next day. Onbrez Breezhaler capsules must not be swallowed. 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, to lactose or to any of the other excipients. **WARNINGS/PRECAUTIONS:** ***Asthma:*** Onbrez breezhaler is a long acting beta2-adrenergic agonist, which is only indicated for COPD and should not be used in asthma. 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.***Paradoxical bronchospasm:*** If paradoxical bronchospasm occurs Onbrez Breezhaler should be discontinued immediately and alternative therapy substituted. ***Deterioration of disease:*** Not indicated for treatment of acute episodes of bronchospasm, i.e. as rescue therapy. ***Systemic effects:*** Indacaterol should be used with caution in patients with cardiovascular disorders (coronary artery disease, acute myocardial infarction, cardiac arrhythmias, hypertension), in patients with convulsive disorders or thyrotoxicosis, and in patients who are unusually responsive to beta2-adrenergic agonists. ***Cardiovascular effects:*** Indacaterol may produce a clinically significant cardiovascular effect in some patients as measured by increases in pulse rate, blood pressure, and/or symptoms, ECG changes. In case such effects occur, treatment may need to be discontinued. ***Hypokalaemia:*** Beta2-adrenergic agonists may produce significant hypokalaemia in some patients, which has the potential to produce cardiovascular effects. In patients with severe COPD, hypokalaemia may be potentiated by hypoxia and concomitant treatment which may increase the susceptibility to cardiac arrhythmias. ***Hyperglycaemia:*** Inhalation of high doses of beta2-adrenergic agonists may produce increases in plasma glucose. Upon initiation of treatment with Onbrez Breezhaler plasma glucose should be monitored more closely in diabetic patients. During clinical studies, clinically notable changes in blood glucose were generally more frequent by 1 2% on Onbrez Breezhaler at the recommended doses than on placebo. Onbrez Breezhaler has not been investigated in patients with not well controlled diabetes mellitus. ***Pregnancy and Lactation:*** No data available from the use of indacaterol in pregnant women. Onbrez Breezhaler should only be used during pregnancy if the expected benefits outweigh the potential risks. Not known whether indacaterol / metabolites are excreted in human milk. A decision must be made whether to discontinue breast-feeding or discontinue Onbrez Breezhaler therapy, taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman. Immediate hypersensitivity reactions have been reported after administration of Onbrez Breezhaler. If signs suggesting allergic reactions (in particular, difficulties in breathing or swallowing, swelling of tongue, lips and face, urticaria, skin rash) occur, Onbrez Breezhaler should be discontinued immediately and alternative therapy instituted. **INTERACTIONS:** Concomitant administration of other sympathomimetic agents may potentiate the undesirable effects of Onbrez Breezhaler. Onbrez Breezhaler should not be used in conjunction with other long-acting beta2-adrenergic agonists or medicinal products containing long-acting beta2-adrenergic agonists.Concomitant hypokalaemic treatment with methylxanthine derivatives, steroids, or non-potassium-sparing diuretics may potentiate the possible hypokalaemic effect of beta2-adrenergic agonists, therefore use with caution. Indacaterol should not be given together with beta-adrenergic blockers (including eye drops) as these may weaken or antagonise the effect of beta2-adrenergic agonists. Where required, cardioselective beta-adrenergic blockers should be preferred, although they should be administered with caution. Inhibition of the key contributors of indacaterol clearance, CYP3A4 and P-gp, does not raise any safety concerns given the safety experience of treatment with Onbrez Breezhaler. Indacaterol has not been shown to cause interactions with co-medications. **ADVERSE REACTIONS:** The most common adverse reactions with Onbrez Breezhaler are: dizziness, nasopharyngitis, upper respiratory tract infection, sinusitis, , headache, , cough, , rhinorrhoea, respiratory tract congestion, muscle spasm, peripheral oedema. Common: Chest Pain, Oropharyngeal pain including throat irritation, Uncommon: Myalgia, Musculoskeletal pain, Pruritis/rash, Paradoxical bronchospasm, tachycardia, palpitations, hypersensitivity, diabetes mellitus and hyperglycaemia ,paraesthesia, atrial fibrillation and non-cardiac chest pain, ischaemic heart disease. Please refer to SmPC for a full list of adverse events for Onbrez Breezhaler. **LEGAL CATEGORY:** POM **PACK SIZES:** Onbrez Breezhaler 150mcg - carton containing 10 or 30 capsules and one Onbrez Breezhaler inhaler. Onbrez Breezhaler 300mcg - carton containing 30 capsules and one Onbrez Breezhaler inhaler **MARKETING AUTHORISATION HOLDER:** Novartis Europharm Limited, Wimblehurst Road, Horsham, West Sussex, RH12 5AB, United Kingdom. **MARKETING AUTHORISATION NUMBERS:** EU/1/09/593/001, 002, 007 **Please refer to Summary of Product Characteristics (SmPC) before prescribing.** Full prescribing information is available on request from Novartis Pharma Services Inc, Representative Office Malta P.O Box 4, Marsa, MRS 1000 Malta. Tel: +356 22983217/+35621222872 2014-MT-ONB-24-Mar-2014

References
1. Cazzola M, Matera MG. Novel long-acting bronchodilators for COPD and asthma. Br J Pharmacol. 2008;155(3):291-307.
2. Novartis Europharm Ltd. Onbrez Breezhaler. Summary of Product Characteristics.

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PIERRE VASSALLO

INFLAMMATORY BREAST CANCER

Inflammatory breast cancer (IBC) is a rare subtype of breast cancer that accounts for 2–5% of all breast cancers. It has a highly virulent course with a low 5-year survival rate of 25–50%. Standard treatment with preoperative chemotherapy, mastectomy, and radiation therapy has been shown to improve prognosis.

IBC usually presents with rapid onset of clinical signs that develop within 3 months which include breast erythema and edema, often with no palpable mass,and may involve one-third or more of the breast (Fig 1). Peau d'orange (french for "orange skin") may also be present where the skin is pitted and dimpled due to the presence of tumor emboli that obstruct the dermal lymphatics (Fig 2). The breast may be enlarged, warm, and tender. These symptoms may mimic inflammation, however there is no true inflammatory component to IBC. 20–40% of patients will already have distant metastases, which reflects the very aggressive nature of IBC.

The major differential diagnosis for IBC is breast infection (mastitis) with or without an abscess. Mastitis often manifests as cutaneous erythema, edema with skin thickening and fever. If a focal lump or skin fluctuance is seen, ultrasonography (US) will determine whether an abscess is present (Fig 3) and would also guide percutaneous drainage. Antibiotic treatment should result in complete resolution of the infection. If there is no response

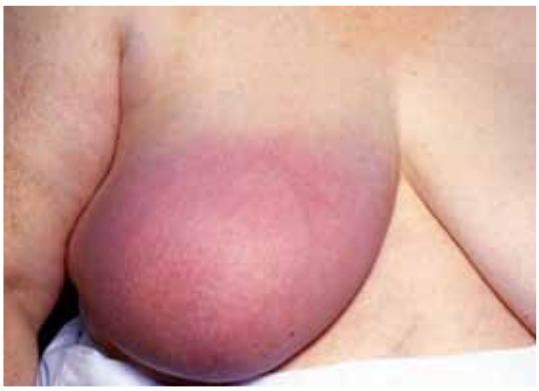

Figure 1: Breast erythema and oedema are seen in IBC, however there is no palpable mass

Figure 2: Peau d'orange appearance of the skin in IBC

IBC USUALLY PRESENTS WITH RAPID ONSET OF CLINICAL SIGNS THAT DEVELOP WITHIN 3 MONTHS WHICH INCLUDE BREAST ERYTHEMA AND EDEMA, OFTEN WITH NO PALPABLE MASS, AND MAY INVOLVE ONE-THIRD OR MORE OF THE BREAST

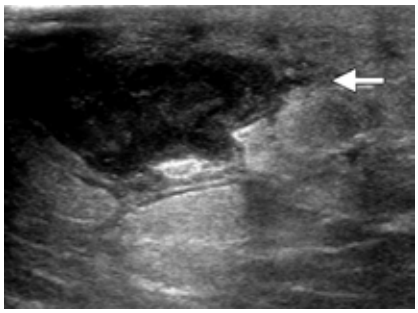

Figure 3: Breast abscess appearing as a hypoechoic area on ultrasound with ill-defined margins; needle aspiration obtained pus from this area, which helped diminish bacterial load and also provided a sample for bacterial culture and sensitivity studies

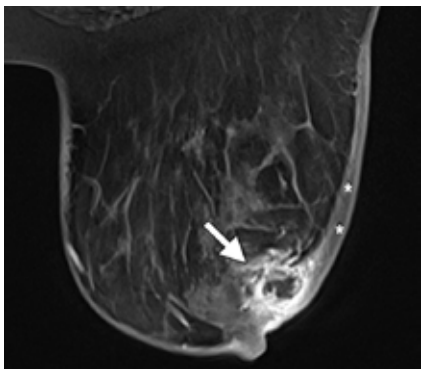

Figure 4: Breast MRI showing a breast abscess with rim enhancement (arrow) and adjacent skin thickening (*)

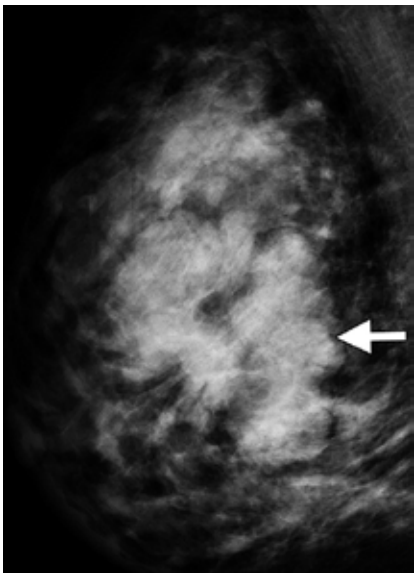

Figure 5: Mammogram showing a 7cm mass (arrow) in the upper inner breast

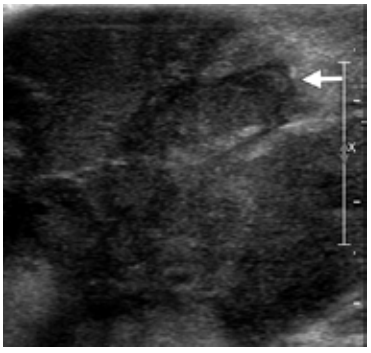

Figure 6: US image shows a 7cm hypoechoic mass which on US-guided core biopsy demonstrated high-grade invasive ductal carcinoma

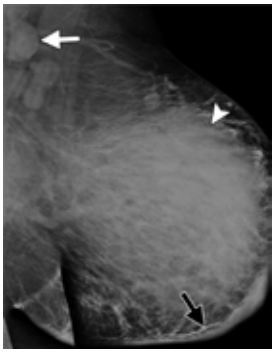

Figure 7: More common mammographic presentation of IBC with diffuse breast enlargement, diffuse increased density (arrowhead), skin thickening (black arrow), and enlarged axillary lymph nodes (white arrow)

or an incomplete response to antibiotic treatment within 1–2 weeks, malignancy such as IBC should be considered. Breast abscess formation presents as a ring enhancing lesion on MRI with adjacent skin thickening (Fig 4).

Locally advanced breast cancer (LABC) may also present with a similar clinical picture, however the onset of IBC occurs within a short period (usually 3 months) whereas that of LABC is more protracted. Erythema and skin induration (and peau d'orange) are less common, but may be present if skin infiltration by tumor cells occurs. Mammography of LABC will show a large mass (Fig 5) that may have been present clinically for a long time, while ultrasound shows a solid hypoechoic mass (Fig 6). Attempts at aspiration show no pus or fluid and histologic diagnosis is established by US-guided core biopsy. Skin punch biopsy is utilized to confirm cancerous infiltration of the skin, which is a feature of IBC.

LABC occurs in an older age group and has a better prognosis than IBC since it is less aggressive and grows more slowly. In LABC, the incidence of distant metastases is lower (10% in LABC vs 20-40% in IBC) and its genetic subtypes are more likely to respond to therapy; LABC is more likely to be oestrogen-receptor (ER) positive and less likely to be HER2 negative, while IBC has a high incidence of triple-negative cancers (50%) and is more frequently HER2 positive (40%). Functioning tumor suppressor gene (p53 gene) is lower in IBC and multiple genetic factors that stimulate tumor growth are more likely to be present.

In the imaging workup of IBC, mammography is usually the initial study that shows diffuse enlargement of the breast with diffusely increased density, skin thickening and possibly

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References: 1. Mancia G, Fagard R, Narkiewicz K et al. 2013 Practice guidelines for the management of arterial hypertension of the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC): ESH/ESC Task Force for the Management of Arterial Hypertension. J Hypertens. 2013; 31(10):1925-38. 2. Novartis Europharm Limited. Exforge HCT® Summary of Product Characteristics. 3. Calhoun DA, Lacourciere Y, Chiang YT, Glazer RD. Triple antihypertensive therapy with amlodipine, valsartan, and hydrochlorothiazide. A randomized clinical trial. Hypertension 2009;54:32–39

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Amlodipine dosage recommendations have not been established in patients with mild to moderate hepatic impairment. **CONTRAINDICATIONS:** Known hypersensitivity to the active substances, to other sulfonamides, to dihydropyridine derivatives, or to any of the excipients Second and third trimesters of pregnancyHepatic impairment, biliary cirrhosis or cholestasis Severe renal impairment (creatinine clearance < 30 mL/min) Anuria patients undergoing dialysis, Refractory hypokalaemia, Hyponatraemia, Hypercalcaemia Symptomatic hyperuricaemia. Exforge HCT is contraindicated in patients with severe renal impairment, diabetes, anuria or undergoing dialysis. Hydrochlorothiazide may raise the serum uric acid level due to reduced clearance of uric acid and may cause or exacerbate hyperuricaemia as well as precipitate gout in susceptible patients. Exforge HCT is contraindicated in patients with hypercalcaemia and should only be used after correction of any pre-existing hypercalcaemia. Exforge HCT should be discontinued if hypercalcaemia develops during treatment. Serum levels of calcium should be periodically monitored during treatment with thiazides. Severe hypotension, Shock (including cardiogenic shock), Obstruction of the outflow tract of the left ventricle (e.g. hypertrophic obstructive cardiomyopathy and high grade aortic stenosis), Haemodynamically unstable heart failure after acute myocardial infarction. Exforge HCT should not be used with angiotensin receptor antagonists (ARB) or ACE with aliskiren in patients with diabetes or renal impairment. **WARNINGS/PRECAUTIONS:** The safety and efficacy of amlodipine in hypertensive crisis have not been established. In sodium-depleted and/or volume-depleted patients, such as those receiving high doses of diuretics, symptomatic hypotension may occur after initiation of treatment with Exforge HCT. Exforge HCT should be used only after correction of any pre-existing sodium and/or volume depletion. Caution is advised when administering Exforge HCT to patients with renal impairment or systemic lupus erythematosus. Exforge HCT should be used with caution to treat hypertension in patients with unilateral or bilateral renal artery stenosis or stenosis to a solitary kidney since blood urea and serum creatinine may increase in such patients. Angioedema, including swelling of the larynx and glottis, causing airway obstruction and/or swelling of the face, lips, pharynx and/or tongue, has been reported in patients treated with valsartan. Some of these patients previously experienced angioedema with other medicinal products, including angiotensin-converting enzyme (ACE) inhibitors. Exforge should be discontinued immediately in patients who develop angioedema and should not be re-administered. Calcium channel blockers, including amlodipine, should be used with caution in patients with congestive heart failure, as they may increase the risk of future cardiovascular events and mortality. Disturbance of serum electrolyte balance (monitoring recommended), glucose tolerance and serum levels of cholesterol, tryglicerides and uric acid. Not recommended in patients below 18 years of age and in patients with primary hyperaldosteronism Beta-blocker withdrawal should be gradual. Caution in elderly and in patients with hepatic impairment or biliary obstructive disorders. Caution in patients with heart failure and coronary artery disease. As with all other vasodilators, special caution in patients suffering from aortic or mitral stenosis, significant aortic stenosis that is not high grade If a photosensitivity reaction occurs during treatment, it is recommended to stop the treatment. Not recommended during the first trimester of pregnancy. Avoid use in women planning to become pregnant and while breast-feeding. Caution when driving or using machinery. Patients taking Exforge and driving vehicles or operating machines I should be taken into account that dizziness or weariness may occasionally occur. Amlodipine can have mild or moderate influence on the ability to drive and use machines. If patients taking amlodipine suffer from dizziness, headache, fatigue or nausea the ability to react may be impaired. Treatment with Exforge HCT should only start after correction of hypokalaemia and any coexisting hypomagnesaemia. Thiazide diuretics can precipitate new onset hypokalaemia or exacerbate pre-existing hypokalaemia. Thiazide diuretics should be administered with caution in patients with conditions involving enhanced potassium loss, for example salt losing nephropathies and prerenal (cardiogenic) impairment of kidney function. If hypokalaemia develops during hydrochlorothiazide therapy, Exforge HCT should be discontinued until stable correction of the potassium balance. Thiazide diuretics can precipitate new onset hyponatraemia and hypochloraoemic alkalosis or exacerbate pre-existing hyponatraemia. Hyponatraemia, accompanied by neurological symptoms (nausea, progressive disorientation, apathy) has been observed. Treatment with hydrochlorothiazide should only be started after correction of pre-existing hyponatraemia. In case severe or rapid hyponatraemia develops during Exforge HCT therapy, the treatment should be discontinued until normalisation of natraemia. All patients receiving thiazide diuretics should be periodically monitored for imbalances in electrolytes, particularly potassium, sodium and magnesium. Thiazide diuretics may precipitate azotaemia in patients with chronic kidney disease. When Exforge HCT is used in patients with renal impairment, periodic monitoring of serum electrolytes (including potassium), creatinine and uric acid serum levels is recommended. Hydrochlorothiazide has been associated with an idiosyncratic reaction resulting in acute transient myopia and acute angle-closure glaucoma. Symptoms include acute onset of decreased visual acuity or ocular pain and typically occur within hours to a week of treatment initiation. Untreated acute-angle closure glaucoma can lead to permanent vision loss. The primary treatment is to discontinue hydrochlorothiazide as rapidly as possible. Prompt medical or surgical treatment may need to be considered if the intraocular pressure remains uncontrolled. Risk factors for developing acute angle closure glaucoma may include a history of sulphonamide or penicillin allergy. The safety of amlodipine in human pregnancy has not been established. Use in pregnancy is only recommended when there is no safer alternative and when the disease itself carries greater risk for the mother and foetus. Evaluation of patients with heart failure or post-myocardial infarction should always include assessment of renal function. Calcium channel blockers, including amlodipine, should be used with caution in patients with congestive heart failure, as they may increase the risk of future cardiovascular events and mortality. The concomitant use of ARBs with other agents acting on the RAAS is associated with increae in incidence of hypotension, hyperkalaemia, and changes in renal function. Therefore monitoring of blood pressure, renal function and electrolytes is recommended. **INTERACTIONS:** Monitoring recommended when used concomitantly with lithium. Reversible increases in serum lithium concentrations and toxicity have been reported during concomitant administration of lithium with ACE inhibitors, angiotensin II receptor antagonists including valsartan or thiazides. Since renal clearance of lithium is reduced by thiazides, the risk of lithium toxicity may presumably be increased further with Exforge HCT. Therefore careful monitoring of serum lithium concentrations is recommended during concomitant use. Caution when used concomitantly with drugs that may increase potassium levels. Caution If combined with other antihypertensives, curare derivatives, NSAIDs, corticosteroids, ACTH, amphotericin, carbenoxolone, Penicillin G, salicylic acid derivatives, digoxin, CYP3A4 inhibitors and inducers, antidiabetic agents, allopurinol, probenecid, sulfinpyrazone, pressor amines, amantadine, diazoxide, cytotoxic drugs, anticholinergic agents, methyldopa, cholestyramine, cholestipol resins, vitamin D, calcium salts, carbamazepine and ciclosporin, alcohol, anaesthetics and sedatives. Concomitant use of amlodipine with strong or moderate CYP3A4 inhibitors (protease inhibitors, azole antifungals, macrolides like erythromycin or clarithromycin, verapamil or diltiazem) may give rise to significant increase in amlodipine exposure. The clinical translation of these pharmacokinetic variations may be more pronounced in the elderly. Clinical monitoring and dose adjustment may thus be required. There is no data available regarding the effect of CYP3A4 inducers on amlodipine. The concomitant use of CYP3A4 inducers (e.g. rifampicin, Hypericum perforatum) may give a lower plasma concentration of amlodipine. Amlodipine should be used with caution together with CYP3A4 inducers. Co-administration of multiple doses of 10 mg amlodipine with 80 mg simvastatin resulted in a 77% increase in exposure to simvastatin compared to simvastatin alone. It is recommended to limit the dose of simvastatin to 20 mg daily in patients on amlodipine. Due to risk of hyperkalaemia, it is recommended that the co-administration of calcium channel blockers such as amlodipine should be avoided in patients susceptible to malignant hyperthermia and in the management of malignant hyperthermia. Co-administration of rifampicin, ciclosporin or ritonavir may increase the systemic exposure to valsartan. Concomitant administration of thiazide diuretics with substances that also have a blood pressure lowering effect may potentiate orthostatic hypotension. Cisapride may decrease the bioavailability of thiazide-type diuretic. Thiazides may alter glucose tolerance, dose adjustment of the antidiabetic medicinal product may be necessary. Absorption of hydrochlorothiazide is decreased by cholestyramine or colestipol. The hyponatraemic effect of diuretics may be intensified by concomitant administration of medicinal products such as antidepressants, antipsychotics, antiepileptics, etc. Caution is indicated in long-term administration of these medicinal products. Due to the risk of hypokalaemia, hydrochlorothiazide should be administered with caution when associated with medicinal products that could induce torsades de pointes, in particular Class Ia and Class III antiarrhythmics and some antipsychotics. Thiazides potentiate the antihypertensive action of other antihypertensive drugs (e.g. guanethidine, methyldopa, beta blockers, vasodilators, calcium channel blockers, ACE inhibitors, ARBs and Direct Renin Inhibitors. Hydrochlorothiazide may reduce the response to pressor amines such as noradrenaline. The clinical significance of this effect is uncertain and not sufficient to preclude their use. Concomitant use of thiazide type diuretics may lead to hypercalcaemia in patients pre-disposed for hypercalcaemia (e.g. hyperparathyroidism, malignancy or vitamin-D-mediated conditions) by increasing tubular calcium reabsorption. Administration of amlodipine with grapefruit or grapefruit juice is not recommended as bioavailability may be increased in some patients, resulting in increased blood pressure lowering effects. **ADVERSE REACTIONS:** Agranulocytosis, bone marrow depression, Decrease in haemoglobin and in haematocrit, Haemolytic anaemia, Leukopenia, Neutropenia, Thrombocytopenia, sometimes with purpura, Aplastic anaemia, Hypersensitivity, Anorexia, Hypercalcaemia, Hyperglycaemia, Hyperlipidaemia, Hyperuricaemia, Hypochloraemic alkalosis, Hypokalaemia, Hypomagnesaemia, Hyponatraemia, Worsening of diabetic metabolic state, Depression, Insomnia/sleep disturbances, Mood swings, confusion, Coordination abnormal, Dizziness, Dizziness postural, dizziness exertional, Dysgeusia, Extrapyramidal syndrome, Headache, Hypertonia, Lethargy, Paraesthesia, Peripheral neuropathy, neuropathy, Somnolence, Syncope, Tremor, Hypoaesthesia, Acute angle-closure glaucoma, visual disturbance, Visual impairment, Tinnitus, Vertigo, Palpitations, Tachycardia, Arrhythmias (including bradycardia, ventricular tachycardia, and atrial fibrillation), Myocardial infarction, Flushing, Hypotension, Orthostatic hypotension, Phlebitis, thrombophlebitis, Vasculitis, Cough, Dyspnoea, Respiratory distress, pulmonary oedema, pneumonitis, Rhinitis, Throat irritation, Abdominal discomfort, abdominal pain upper, Breath odour, Change of bowel habit, Constipation, Decreased appetite, Diarrhoea, Dry mouth, Dyspepsia, Gastritis, Gingival hyperplasia, Nausea, Pancreatitis, Vomiting, Hepatic enzyme elevation, including increase of serum bilirubin, Hepatitis, Intrahepatic cholestasis, jaundice, Alopecia, Angioderma, Cutaneous lupus erythematosus-like reactions, reactivation of cutaneous lupus erythematosus, Erythema multiforme, Exanthema, Hyperhidrosis, Photosensitivity reaction, Pruritus, Purpura, Rash, Skin discoloration, Urticaria and other forms of rash, Vasculitis necrotising and toxic epidermal necrolysis, Exfoliative dermatitis, Stevens-Johnson syndrome, Quincke oedema, Arthralgia, Back pain, Joint swelling, Muscle spasm, Muscular weakness, Myalgia, Pain in extremity, Ankle swelling, Elevation of serum creatinine, Micturition disorder, Nocturia, Pollakiuria, Renal dysfunction, Renal failure acute, Renal failure and impairment, Impotence, Gynaecomastia, Abasia, gait disturbance, Asthenia, Discomfort, malaise, Fatigue, Non cardiac chest pain, Oedema, Pain, Pyrexia, Lipids increased, Blood urea nitrogen increased, Blood uric acid increased, Glycosuria, Serum potassium decreased, Serum potassium increased, Weight increase, Weight decrease. **LEGAL CATEGORY:** POM **PACK SIZES:** Packs of 28 film-coated tablets **MARKETING AUTHORISATION HOLDER:** Novartis Europharm Limited, Wimblehurst Road, Horsham, West Sussex, RH12 5AB, United Kingdom. **MARKETING AUHORISATION NUMBER:** Exforge HCT 5 mg/160 mg/12.5 mg - EU/1/09/569/002 Exforge HCT 10 mg/160 mg/12.5 mg - EU/1/09/569/014 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
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enlarged lymph nodes (Fig 7). A less common mammographic presentation of IBC is that of multiple masses (Fig 8). US can help differentiate a benign cystic mass from a solid mass and can evaluate a solid mass according to its margins (smooth, irregular, or speculated), its size and extent (Fig 9).

If no mass lesion is detected on mammography or US, Magnetic Resonance Imaging (MRI) may be used to target biopsy as it has been shown to be the most accurate imaging technique for detection of the primary breast lesion in patients with IBC (Fig 10). The primary breast lesion is detected at mammography in 68–80% of cases, at US in 94–95% of cases, and at MRI imaging in 98–100% of cases. The more common appearance of IBC on MRI is however as a diffuse contrast enhancing area involving a large part of the breast, with skin thickening (Fig 11); presentation as a mass-lesion is less common on MRI. Involvement of the pectoralis major muscle and axillary, supraclavicular and internal mammary lymph nodes as well as the contra-lateral breast are common in IBC and are also best assessed with MRI. Evaluation for distant metastatic disease from IBC would require Computed Tomography (CT), MRI or [18F]-fluorodeoxyglucose (FDG) Positron Emission Tomography-Computed Tomography (FDG PET/CT).

Follow-up imaging during and after treatment may include mammography, US and MRI. Dynamic contrast-enhanced MRI kinetics are particularly useful for detecting tumor response (Fig 12).

Imaging is vital for the diagnosis and treatment planning for patients with IBC. The role of various imaging modalities in diagnosis, assessment of treatment response, and surveillance has been presented here.

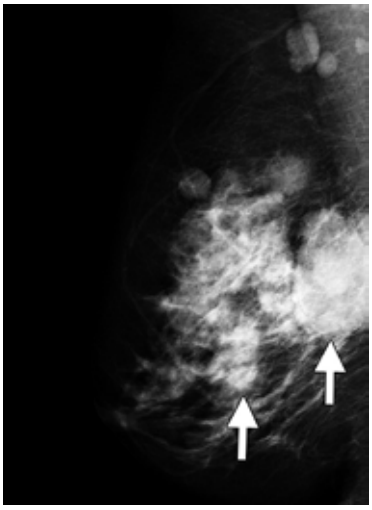

Figure 8: Less commonly IBC may present with multiple large masses (arrows) on mammography

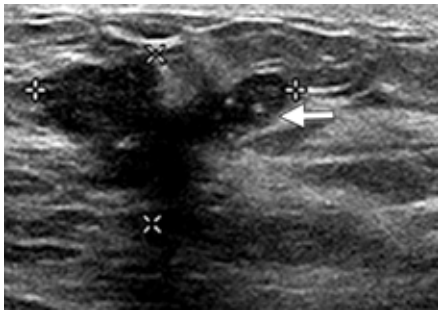

Figure 9: US image of IBC shows a 2.7cm, irregular, hypoechoic mass with posterior shadowing

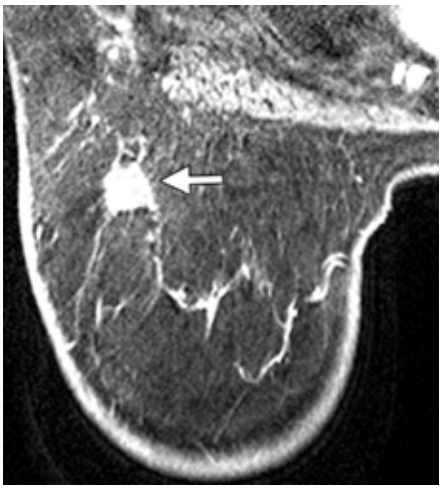

Figure 10: MR shows primary breast lesion in a patient with IBC, who had no detectible lesion on mammography and initial ultrasound

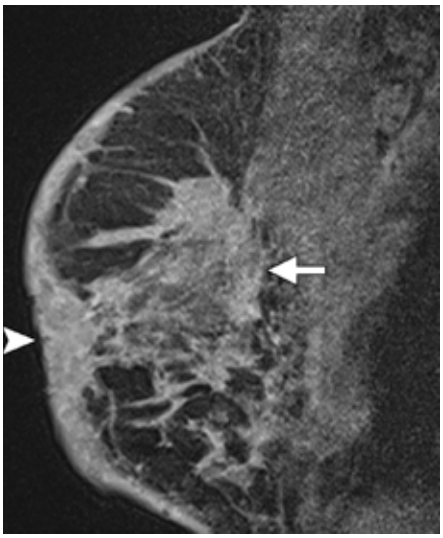

Figure 11: Most common MR presentation of IBC includes extensive non-mass-like enhancement (arrow) and skin thickening (arrowhead)

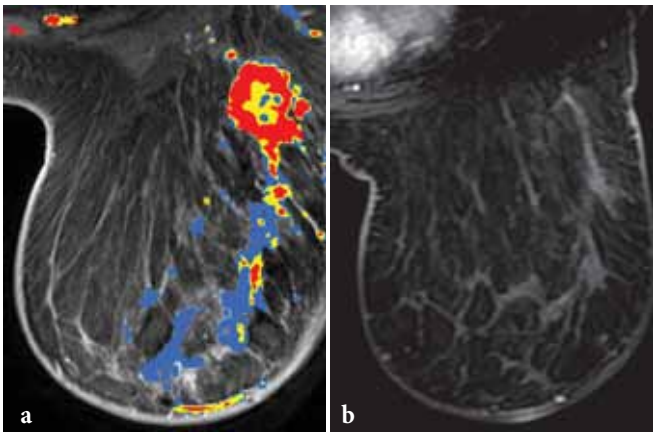

Figure 12: Dynamic contrast-enhanced MR kinetic studies: (a) Before treatment, areas of washout (red) and plateau or persistent enhancement (blue) are seen; washout kinetics are strongly indicative of cancer, while persistent or plateau kinetics are equivocal, (b) After treatment, there is no contrast enhancement, indicating complete response

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- ✔ No side effects
- ✔ > 10^9 bacteria per capsule
- ✔ Proven genetic stability (produced according to GMP)

Dosage

- ✔ 2 capsules per day the first month (preferably in the morning before breakfast)
- ✔ 1 capsule per day in the maintenance phase in the following months

Composition

- ✔ Lactobacillus rhamnosus Lcr35®
- ✔ Prebiotic excipients: Fructooligosaccharide, Lactose

Stability

- ✔ 2 Years at room temperature

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