Dermatology Practice Review™

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Welcome to the first issue of Dermatology Practice Review.

This new Review covers news and issues relevant to clinical practice in dermatology. It will bring you the latest updates, both locally and from around the globe, in relation to topics such as new and updated treatment guidelines, changes to medicines reimbursement and licensing, educational, medicolegal issues, professional body news and more.

In this inaugural issue, the TGA has issued a reminder to health professionals about the potential risks of psychiatric adverse effects associated with Roaccutane, while the *Journal of the American Academy of Dermatology* reports prescribing behaviour for oral antibiotics among United Kingdom GPs does not align with current acne guidelines, and exceeds recommended duration of therapy. A Danish study identified a significant association between patients who have rosacea and their risk of having certain GI diseases, including coeliac disease, Crohn's disease, ulcerative colitis, and irritable bowel syndrome. The Australian Institute of Health and Welfare's latest report on skin cancer shows that while Australia still has the second-highest rate of melanoma in the world, rates are dropping among younger people. Looking at etanercept biosimilars, Brenzys® has been listed for chronic plaque psoriasis and PBAC has recommended an Authority Required listing of ixekizumab for severe chronic plaque psoriasis that is refractory to treatment with non-biological DMARDs.

And finally on the back cover you will find a summary of upcoming local and international educational opportunities including workshops, webinars and conferences.

We hope you enjoy this new Research Review publication and look forward to hearing your comments and feedback.

Kind Regards,

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Clinical Practice

TGA safety update for Roaccutane

The TGA has issued a reminder to health professionals about the potential risks of psychiatric adverse effects associated with isotretinoin (Roaccutane) and the need for careful psychological assessment before and during the treatment.

The warning is based on a TGA evaluation of the findings of a UK Medicines and Healthcare Products Regulatory Agency report about the medicine and psychiatric adverse reactions.

It encourages health professionals to urge patients being treated with isotretinoin to read the CMI and take particular note of these potential adverse reactions, as well as the need to consult a doctor or pharmacist if they experience associated symptoms.

The Medicines and Healthcare Products Regulatory Agency (MHRA) public assessment report concluded that it is important to recognise that acne is associated with psychiatric disorders, regardless of whether or not isotretinoin is used.

Available data are insufficient to establish a causal association, the report says, but also could not rule out a link between this medicine and psychiatric disorders.

Read the advice here.

Prescribed oral antibiotics for acne among UK GPs does not align with guideline recommendations

Prescribing behaviour for oral antibiotics among United Kingdom general practitioners for treating acne did not align with current guidelines, and exceeded recommended duration of therapy, according to a study published in the *Journal of the American Academy of Dermatology.* Guidelines recommend limiting the duration of oral antibiotic therapy in acne to 3 to 6 months and prescribing concomitant topical retinoids for all patients.

Researchers conducted a retrospective cohort study of patients aged 12 to 22 years who were treated for acne and included in the Health Improvement Network database, a medical record database used by general practitioners in the UK to track patients' information.

There were 79,565 patients (55.2% male; median age, 16.8 years) who met criteria, with 104,914 antibiotic prescriptions. More than half of the antibiotic courses (56%) exceeded 3 months, 29% exceeded 6 months and 12% exceeded 1 year. In addition, 62% of the antibiotic courses were not associated with a topical retinoid. Lymecycline (39.4%), oxytetracycline (30%), minocycline (18.9%) and tetracycline (1.4%) were the most commonly prescribed antibiotics. Therapy had a mean duration of 175.1 days (95% CI, 174.0-176.2 days).

J Am Acad Dermatol. 2016;75(6):1142–1150.e1.

Download the abstract here.

Clinical Practice

Study identifies link between rosacea and several GI disorders

A Danish population-based cohort study identified a significant association between patients who have rosacea and their risk of having certain gastrointestinal (GI) diseases, including coeliac disease, Crohn's disease, ulcerative colitis, and irritable bowel syndrome.

The researchers conducted a nationwide cohort study of adults aged 18 years and older from national administrative registers, from January 1, 2008, to December 31, 2012. In total, 49,475 rosacea patients were included, with 4,312,213 individuals from the general population who were used as controls. The primary endpoints were any occurrences of coeliac disease, Crohn's disease, ulcerative colitis, and irritable bowel syndrome, *Helicobacter pylori* infection, and small intestinal bacterial overgrowth that occurred during the study period, conditions that were chosen due to their potential mechanistic and pathogenic overlap with rosacea.

At baseline, the prevalence of all six GI disorders was significantly higher among the patients with rosacea, compared with the controls. Adjusted hazard ratios showed a significant association between patients with rosacea and one of the following GI diagnoses: coeliac disease (HR 1.46), Crohn's disease (HR 1.45), ulcerative colitis (HR 1.19), and irritable bowel syndrome (HR 1.34). However, no significant association was found between rosacea and *Helicobacter pylori* infection or small intestinal bacterial overgrowth.

The findings from this study raise important questions about the pathogenic overlap between the studied GI disorders and rosacea. Most of the outcomes examined in the study carry several autoimmune characteristics and, although speculative, it is possible that shared autoimmune susceptibility may provide a link between rosacea and the examined GI disorders.

Br J Dermatol. 2016 Oct 31.

Download the abstract here.

Skin services review – Mohs surgery

On 4 May 2016, the Australia Department of Health informed stakeholders that the Government has agreed to implement the skin services review outcomes in full, commencing 1 November 2016.

The Department has since learned that there is some uncertainty regarding the effect of the changes on the items for Mohs surgery (MBS items 31000, 31001 and 31002). However, health care professionals can be assured that the Mohs surgery items have not been altered as a result of the skin services review. Flap and graft items as well as MBS item 31340 (removal of cartilage below skin) will still be permissible with these items. The Department will amend the proposed descriptors for the flap items to ensure the Mohs surgery items are referenced. It will be at the clinical practitioner's discretion to determine which service is required to close the defect created by the cancer.

Please note that there is a Dermatology, Allergy and Immunology Clinical Committee (DAICC) currently reviewing a suite of items, including the Mohs surgery items, on behalf of the MBS Reviews Taskforce.

Read more here.

Society and Professional Body News

AIHW: Skin cancer in Australia report

A report from the Australian Institute of Health and Welfare (AIHW), 'Skin cancer in Australia', provides comprehensive national information and statistics on skin cancer. It includes the latest available data and estimates to 2016, as well as trends over time.

The report shows the rate of skin cancers diagnosed in people under the age of 40 has decreased by more than 30% from 2002 to 2016. In 2002 there were 13 cases per 100,000 people, compared to nine cases per 100,000 people in 2016. According to the AIHW, long-running campaigns about the dangers of too much sun have had an impact and could be credited for the decrease.

But the report also found Australia has the second highest rate of melanoma in the world, with more than 13,000 new cases expected to be identified in 2016 alone. That amounts to 49 cases of melanoma per 100,000 people compared to 27 cases per 100,000 people in Australia in 1982. Nearly 1,800 people diagnosed with melanoma are expected to die this year. A person diagnosed with melanoma has a 90% chance of surviving at least five years – much higher than the survival rate of all cancers, at 67%.

While the total number of new cases of non-melanoma skin cancer (NMSC) was unknown, it was estimated to account for more cases diagnosed than all other cancers combined. In 2016, an estimated 560 people will die from NMSC, with a death rate of 1.9 deaths per 100,000 people.

Hospitalisations for all types of skin cancer have increased significantly over the past decade. In 2013-14, there were over 23,400 melanoma-related hospitalisations in Australia, a 63% rise from 2002-03. Over the same period, NMSC-related hospitalisations rose by 39%.

In 2014, 40,179 ($9.4 million) Medicare benefits claims were paid for melanoma and 959,243 ($127.6 million) for NMSC. In 2008-09, NMSC accounted for 8.1% of all health system spending on cancer in Australia (excluding cancer screening).

AIHW 2016. Skin cancer in Australia. Cat. no. CAN 96. Canberra: AIHW.

Download the full report here.

Product listing and reimbursement

Brenzys® biosimilar of etanercept registered

Brenzys®, a biosimilar of etanercept, has been registered in adults 18 years and older for the treatment of:

- Active, rheumatoid arthritis in patients who have had inadequate response to one or more disease-modifying anti-rheumatic drugs (DMARDs). Brenzys® can be used in combination with methotrexate.
- Severe, active rheumatoid arthritis to slow progression of disease-associated structural damage in patients at high risk of erosive disease.
- The signs and symptoms of active and progressive psoriatic arthritis, when the response to previous DMARDs has been inadequate.
- Patients with moderate to severe chronic plaque psoriasis, who are candidates for phototherapy or systemic therapy.
- The signs and symptoms of active ankylosing spondylitis.
- Patients with active* non-radiographic axial spondyloarthritis with objective signs of inflammation as indicated by elevated C-reactive protein and/or MRI change who have had an inadequate response to NSAIDs.
- *Active disease is defined as a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score of greater than or equal to 4.

PBAC recommended listing Brenzys®

The PBAC had earlier recommended the listing of Brenzys® as a biosimilar of etanercept (Enbrel®) on a cost minimisation basis with Enbrel® for all adult indications – rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and chronic plaque psoriasis. The PBAC considered that the evidence presented in the submission supported the claims of comparative safety and effectiveness of Brenzys® and Enbrel®.

The PBAC advised the Minister that it considered the Enbrel® and Brenzys® brands of etanercept could be marked as equivalent in the Schedule of Pharmaceutical Benefits ('a' flagged), for the purposes of substitution by the pharmacist at the point of dispensing for all the circumstances (restrictions) that both brands are listed against. The PBAC noted that the substitution process allows for patient and prescriber choice and is not automatic. For any individual prescription, a prescriber may choose to not permit brand substitution. If substitution has been permitted by the prescriber, the patient may choose which brand they wish to receive from the pharmacist.

In forming its view on brand substitution ('a' flagging), the PBAC considered a range of factors including:

- The evidence presented in the SB4-G31-RA trial in treatment-naïve patients initiating on either Enbrel® or Brenzys® supported a finding that Brenzys® has equivalent effectiveness and equivalent safety compared to Enbrel®.
- The key randomised clinical study in rheumatoid arthritis did not indicate differences in efficacy or safety of Brenzys® compared with Enbrel®.
- The clinical data provided in the submission did not suggest there were any identified populations where the risks of using the biosimilar product in place of the reference biologic were disproportionately high.
- In the SB4-G31-RA phase III extension study, which included 52 weeks of additional data, including from a one-way switch from Enbrel® to Brenzys®, the clinical evidence suggested no difference in efficacy, safety or immunogenicity between the biosimilar and the reference biologic.
- The drug, etanercept, is not immunogenic per se, and anti-drug antibodies are rare. Switching between brands of etanercept is unlikely to change this.
- The Advisory Committee on Prescription Medicines (ACPM) has declared Brenzys® a biosimilar for Enbrel®. The ACPM was satisfied of the similar safety and efficacy of Brenzys® and Enbrel® in rheumatoid arthritis, psoriatic arthritis, plaque psoriasis, ankylosing spondylitis and non-radiographic axial spondyloarthritis.

Read the TGA listing here.

Read the PBAC recommendation here.

PBAC recommends listing ixekizumab for plaque psoriasis

The PBAC recommended an Authority Required listing of ixekizumab for the treatment of severe chronic plaque psoriasis that is refractory to treatment with non-biological disease modifying anti-rheumatic drugs (DMARDs).

The PBAC accepted that the clinical place in therapy for treatment with ixekizumab would be as an alternative treatment option to the currently PBS listed biological DMARDs (bDMARDs). The PBAC noted the availability of five alternative bDMARDs listed on the PBS for the treatment of severe chronic plaque psoriasis and concluded that it was uncertain how ixekizumab addressed a clinical need that was not provided by another bDMARD.

The PBAC noted that in the sponsor's pre-PBAC response, the nominated comparator was changed (from ustekinumab in the submission) to secukinumab. The PBAC considered that any of the currently PBS listed bDMARDs could be an appropriate alternative therapy, and that in the absence of demonstrated superior comparative effectiveness or safety over the alternative therapies, ixekizumab should be cost-minimised to the least costly bDMARD.

The PBAC did not accept the submission's claim that ixekizumab was superior in comparative effectiveness and equivalent in comparative safety over ustekinumab and adalimumab. Noting potential exchangeability issues, and that only short-term comparative outcomes were available, the PBAC considered that there was no clear evidence that ixekizumab provided a significant improvement in efficacy or reduction of toxicity compared to the alternative bDMARDs.

Read more here.

Public Consultation on the draft Terms of Reference for the Post-market Review of biological DMARDs to treat severe chronic plaque psoriasis

The public consultation on the draft Terms of Reference for the Post-market Review of bDMARDs to treat severe chronic plaque psoriasis closed on 16 May 2016.

The draft Review Terms of Reference are:

1. Review current clinical guidelines for the treatment of severe chronic plaque psoriasis and compare to the PBS restrictions for use of bDMARDs in this indication.
2. Review and evaluate recent clinical evidence on the efficacy and safety of bDMARDs used in the treatment of severe chronic plaque psoriasis and compare to the evidence considered by PBAC in previous sponsor submissions.
3. Review the utilisation of PBS bDMARDs for the treatment of chronic plaque psoriasis and compare the patient response in practice to those observed in the clinical trial evidence considered by the PBAC. Compare the efficacy in practice among the listed bDMARDs in terms of time on treatment and discontinuations from treatment.
4. Subject to the findings from terms of reference 1, 2 and 3, review the cost effectiveness of bDMARDs for severe chronic plaque psoriasis.

All submissions to the Review can be viewed here.

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Medicolegal Issues

Private Health Facilities Amendment (Cosmetic Surgery) Regulation 2016

Following on from the recent public consultation by NSW Health on the regulation of the facilities carrying out cosmetic surgery, the Private Health Facilities Amendment (Cosmetic Surgery) Regulation 2016 (Amending Regulation) was made on 3 June 2016. Private health facilities are required to be licensed in NSW under the Private Health Facilities Act 2007 and Private Health Facilities Regulation 2010 and to comply with the standards in the Regulation.

A private health facility is a facility that carries out procedures falling in one of the classes of private health facilities set out in the Regulation, including the anaesthesia class and the surgical class.

The Amending Regulation amends the Private Health Facilities Regulation 2010 to create a new class of private health facilities, being the cosmetic surgery class. Under the changes, from **3 March 2017** any facility that carries out the following procedures (except for dental procedures) must be licensed under the cosmetic surgery class:

Cosmetic surgery means:

- any cosmetic surgical procedure that is intended to alter or modify a person's appearance or body and that involves anaesthesia (including a Biers Block), or
- any of the following surgical procedures (however described):
  - abdominoplasty (tummy tuck)
  - belt lipectomy
  - brachioplasty (armlift)
  - breast augmentation or reduction
  - buttock augmentation, reduction or lift
  - calf implants
  - facial implants that involve inserting an implant on the bone or surgical exposure to deep tissue
  - fat transfer that involves the transfer of more than 2.5 litres of lipoaspirate
  - liposuction that involves the removal of more than 2.5 litres of lipoaspirate
  - mastopexy or mastopexy augmentation
  - necklift
  - pectoral implants
  - penis augmentation
  - rhinoplasty
  - superficial musculoaponeurotic system facelift (SMAS facelift)
  - vaginoplasty or labiaplasty

Anaesthesia means:

- the administration of general, epidural or major regional anaesthetic or sedation resulting in more than conscious sedation, other than sedation provided in connection with dental procedures.

This means that the procedures listed in (b) above will be required to be carried out in a licensed facility regardless of the level of anaesthesia used. Whether a patient is admitted or not is also not relevant.

A copy of the Amending Regulation can be found here.

NEWS in brief

Cannabis trial for melanoma at University of Canberra

The University of Canberra has signed a $1 million collaboration with international pharmaceutical company Cann Pharmaceutical to commence a medical-grade cannabis therapy trial for melanoma patients. The two-year research project aims to produce a novel combination therapy treatment programme for some of the almost 50,000 Australians living with melanoma.

Read more here.

Direct-to-Consumer telemedicine websites and apps for skin disease

There are a plethora of self-diagnosis websites and apps with many more likely to appear in the future. A study reported in *Jama Dermatology* highlights the inaccuracy of many of the current ones with important diagnoses missed, incorrect treatment advice, lack of explanation about side effects and poor communication with the family doctor. A set of standards should be developed so patients are aware of the quality of these sites and choose an appropriate one.

JAMA Dermatol. 2016;152(7):768–75.

Read more here.

Conferences

27th Annual Cutaneous Malignancy Update

21-22 January 2017, Coronado, CA, USA

Details: http://tinyurl.com/hbbxvan

27th American Academy of Dermatology Annual Meeting

3-7 March 2017, Orlando, FL, USA

Details: https://www.aad.org/meetings/annual-meeting

12th International Congress on Systemic Lupus Erythematosus & the 7th Asian Congress on Autoimmunity

26-29 March 2017, Melbourne, VIC

Details: http://lupus2017.org/

Workshops, Webinars and CPD

18-19 February 2017, Melbourne, VIC

AND

1-2 April 2017, Adelaide, SA

Certificate in Primary Care Skin Cancer Medicine

Further information available here.

Certificate in Primary Care Skin Cancer Therapeutics

Further information available here.

Certificate in Primary Care Skin Cancer Surgery

Further information available here.

Research Review publications

Dermatology Research Review

with Dr Warren Weightman

http://tinyurl.com/gqez49g

Psoriasis Research Review

with Clinical Professor Kurt Gebauer

http://tinyurl.com/zcq897n

Educational Series - Natural vs Chemical

http://tinyurl.com/j2sw93a

Product Review - Daivobet Gel in Mild-to-Moderate Plaque Psoriasis

http://tinyurl.com/heqmns5

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