BEYOND THE SKIN

Managing eye disorders in severe atopic dermatitis

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DERMATOLOGY
ADVENT
ADVANCES IN
TYPE 2 INFLAMMATORY DISEASES

CHAIR

Dr Li-Chuen Wong

Paediatric & Adult Dermatologist
Head of Dermatology, Children's Hospital, Westmead

Dr Li-Chuen Wong is co-founder of Sydney Skin and is a consultant dermatologist specialising in both adult and paediatric dermatology. Dr Wong is a Visiting Medical Officer (VMO) and Head of the Dermatology department at the Children's Hospital, Westmead. She is also a Clinical Senior Lecturer at The University of Sydney, previous Director of Training NSW faculty and current Chair for the NSW faculty of the Australasian College of Dermatologists.

Dr John Hogden

Ophthalmologist, The Eye Health Centre, Brisbane

Dr Hogden is an ophthalmologist with sub-specialty training in corneal, external eye disease, cataract, anterior segment and refractive surgery. Dr Hogden trained at the Sydney Eye Hospital and then underwent further corneal fellowship training at the surgically renowned University of British Columbia (UBC) Vancouver Eye Care Centre, Canada. Dr Hogden is a member of the Royal Australian and New Zealand College of Ophthalmology, the American Academy of Ophthalmology and the American Society of Cataract and Refractive Surgery. He is a Visiting Medical Officer at the Royal Brisbane and

Women's Hospital where he is actively involved in ophthalmic education and clinical research. In January 2020 Dr Hogden opened his own Eye Health Centre practice in Aspley closely followed in May by his second Eye Health Centre practice in Wynnum.

Dr Yves Kerdraon

Ophthalmologist, Sydney Eye Hospital and Concord Repatriation General Hospital

Dr Yves Kerdraon completed his medical training at Sydney University in 1996, and ophthalmic training through the Sydney Eye Hospital in 2005. He later obtained sub-specialty training in diseases of the cornea and ocular surface disease in Bristol. He now performs corneal transplants and complex cataract surgery, working at Sydney Eye Hospital, Concord Repatriation General Hospital, and private rooms in Sydney city and Wollongong.

Through years of practice at Westmead and Concord, he has had considerable exposure to the cicatrising conjunctivitides, including the ocular sequelae of GVHD and SJS.

Dr Kerdraon has a keen involvement in the teaching of ophthalmic trainees and JMOs and is involved in various research projects involving keratoconus and Fuchs' corneal endothelial dystrophy.

A/Prof. Peter Foley

Director of Research at the Skin Health Institute and the Head of Dermatology Research at St Vincent's Hospital Melbourne

Peter Foley's interests include psoriasis, atopic dermatitis, hidradenitis suppurativa, photosensitivity disorders, and non-surgical management of nonmelanoma skin cancers.

Professor Foley is Australia's only councillor on the International Psoriasis Council, is co-convener of the Australasian Psoriasis Registry, is a former steering committee member of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis, and is a founding member of the Australasian Psoriasis Collaboration. He is participating in the NPS MedicineWise bDMARD program and is on the Board of the Photomedicine Society.

He has been an investigator in over 100 clinical trials and has over 100 published manuscripts

Prof. Connie Katelaris

Head of Unit, Immunology & Allergy Campbelltown Hospital and
Professor of Immunology & Allergy, Western Sydney University

Connie Katelaris is Head of Unit, Immunology and Allergy Campbelltown Hospital and Professor of Immunology & Allergy, Western Sydney University where she convenes the Masters course in Allergic Diseases. She also has a private practice in Westmead, Sydney.

Prof Katelaris and her team run both adult and paediatric clinics servicing a large number of children and adults with atopic dermatitis and they participate in atopic dermatitis research.

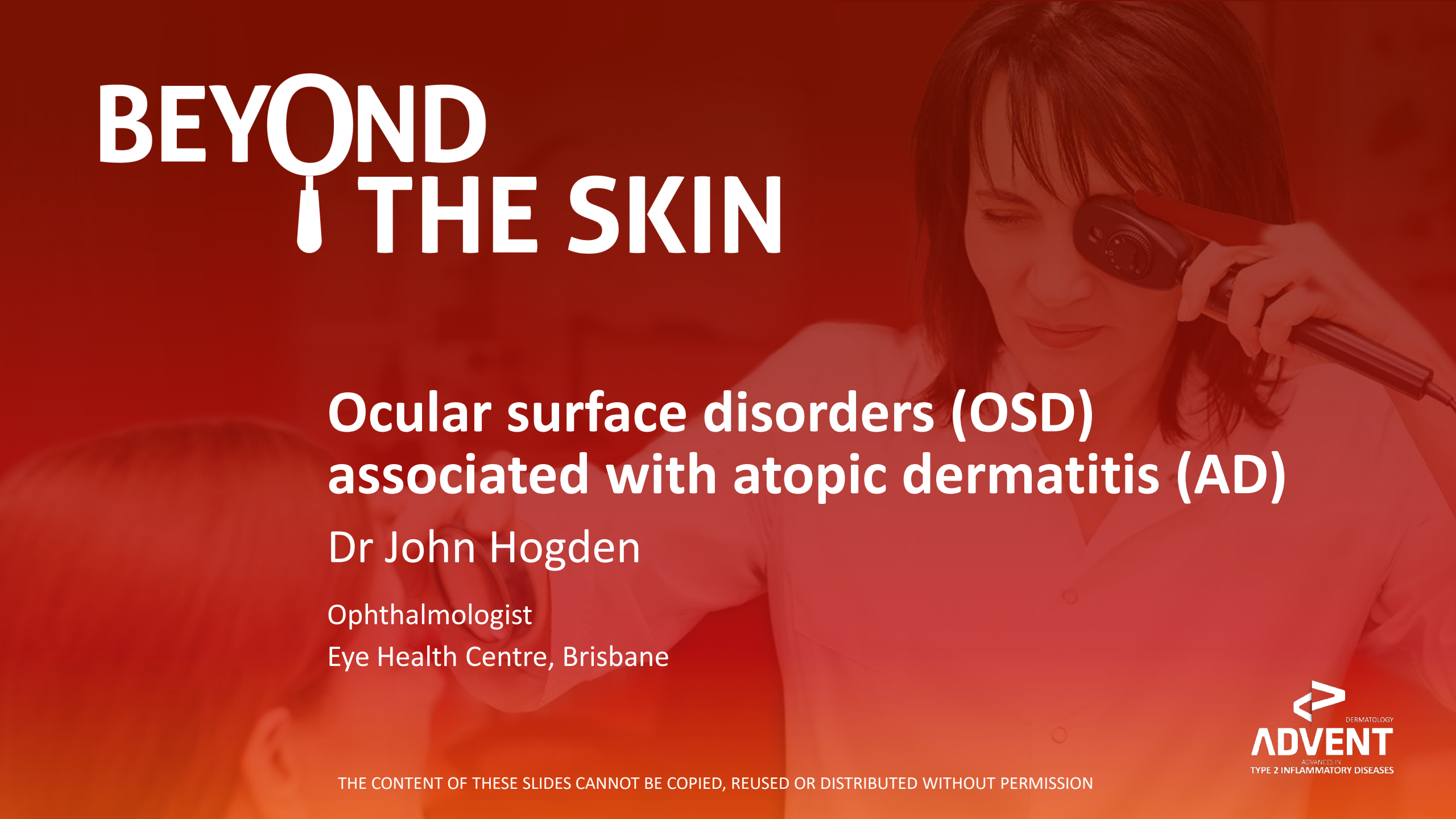
BEYOND THE SKIN

Ocular surface disorders (OSD) associated with atopic dermatitis (AD)

Dr John Hogden

Ophthalmologist

Eye Health Centre, Brisbane



DERMATOLOGY ADVENT ADVANCES IN TYPE 2 INFLAMMATORY DISEASES

Learning objectives

Ocular surface disorders (OSD) associated with atopic dermatitis (AD) and case study

At the conclusion of this part of the presentation, attendees should be able to:

- Understand that OSD often occur in patients with severe AD
- Recognise common presentations of OSD in patients with AD
- Understand how to assess patient risk factors, measure eye symptom severity, and identify any red flags (e.g., herpetic keratitis, bacterial keratitis, keratoconus); and
- Understand, from the case study, how to apply the recommendations in the Australian physician's algorithm[1] to the multidisciplinary management and treatment of OSD in a patient newly presenting with severe AD (before any advanced treatment is initiated)

AD, atopic dermatitis; **OSD**, ocular surface disorders

1. Foley P, et al. Australas J Dermatol. 2022;63:421–436.

Speaker disclosures

Dr. John Hogden has been a consultant, and/or scientific adviser, and/or investigator, and/or scientific officer, and/or speaker for Sanofi/Genzyme in 2020 and 2021

Adults with AD have a significant and disease severity-dependent increased risk of developing OSD[1]

- OSD, including allergic **conjunctivitis, blepharitis**, and **keratitis**, are common in patients with AD[1]
- OSD present in 32-56% of patients with severe AD[1]
- 'Red eye' is the most conspicuous clinical sign of acute conjunctivitis[2]

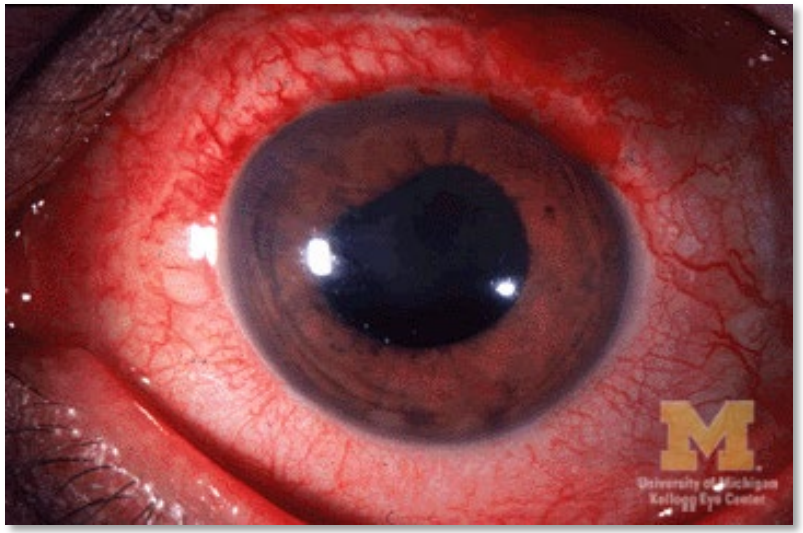


Image credit: https://commons.wikimedia.org/wiki/File:Anterior-uveitis.jpg

AD, atopic dermatitis, **OSD**, ocular surface disorders

1. Akinlade B, et al. Br J Dermatol. 2019;181:459–473. 2. Gooderham M, et al. J Cutan Med Surg. 2018;22:200–206.

Ocular co-morbidities of atopic dermatitis[1]

- Ocular diseases associated with AD include:
  - Eyelid dermatitis
  - Keratoconjunctivitis
  - Keratoconus
  - Cataract
  - Retinal detachment
- AD patients are also at higher risk for bacterial and viral ocular infections

Prevalence of eye disorders in patients with AD*

20–42% of AD patients have periocular AD

20–68% of AD patients have AKC

18–41% have keratoconus

Incidence of cataracts in AD is **5–38%**

Ocular HSV is **fourfold** higher in AD patients than in the general population

Retinal detachment is seen in up to **11.4%** of AD patients and is more likely to occur bilaterally (**19%** vs 7% in patients without AD)

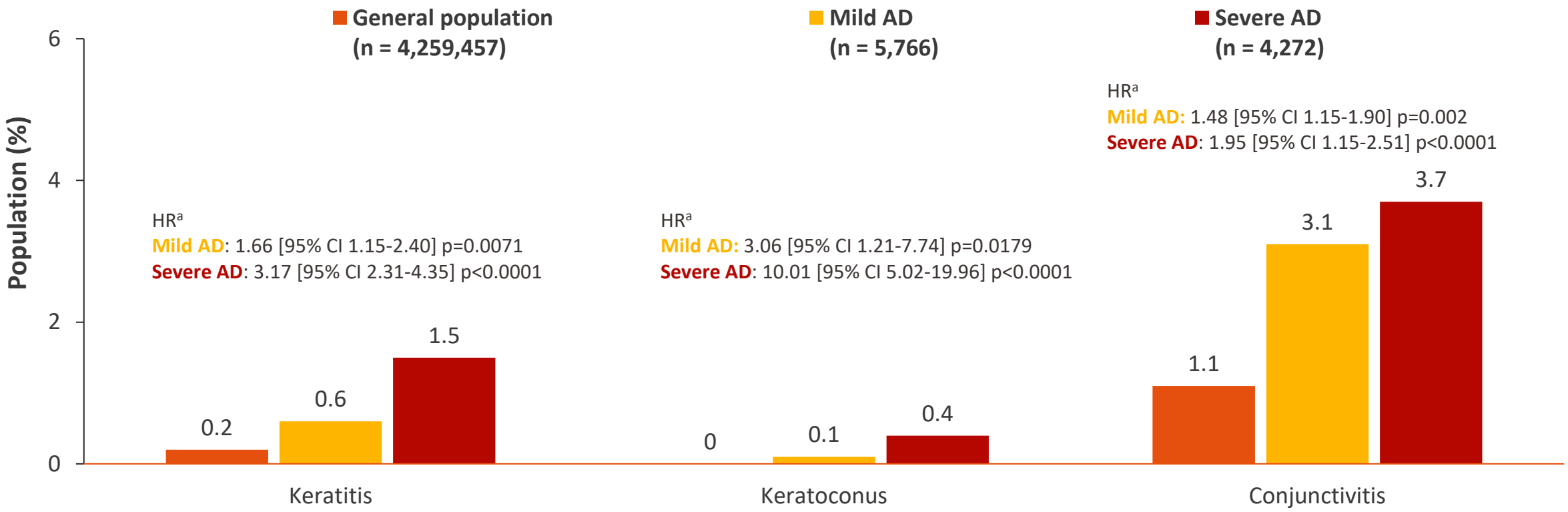
*All AD patients regardless of severity

AD, atopic dermatitis; **AKC**, atopic keratoconjunctivitis; **HSV**, herpes simplex virus

1. Beck KM, et al. Am J Clin Dermatol. 2019;20:797–805.

OSD increases with AD severity[1]

Prevalence of ocular disorders at baseline in a Danish epidemiological case–control retrospective study in patients with AD[1]



[a]HRs compared with general population; fully adjusted for age, sex, socioeconomic status, and healthcare consumption.

AD, atopic dermatitis; **HR,** hazard ratio

1. Thyssen JP, et al. J Am Acad Dermatol. 2017;77:280–286.e1.

Incidence of OSD in patients with moderate-to-severe AD[1]

Overall, **38.6%** of patients enrolled in the LIBERTY AD CHRONOS study (n=740) reported having at least one eye disorder in the past year at screening **before treatment initiation with dupilumab**

- Dry eye: 20.5%
- Perennial allergic conjunctivitis: 15.0%
- Atopic keratoconjunctivitis: 12.2%
- Ophthalmic herpes simplex: 4.2%
- Ophthalmological rosacea: 2.7%
- Keratoconus: 2.1%

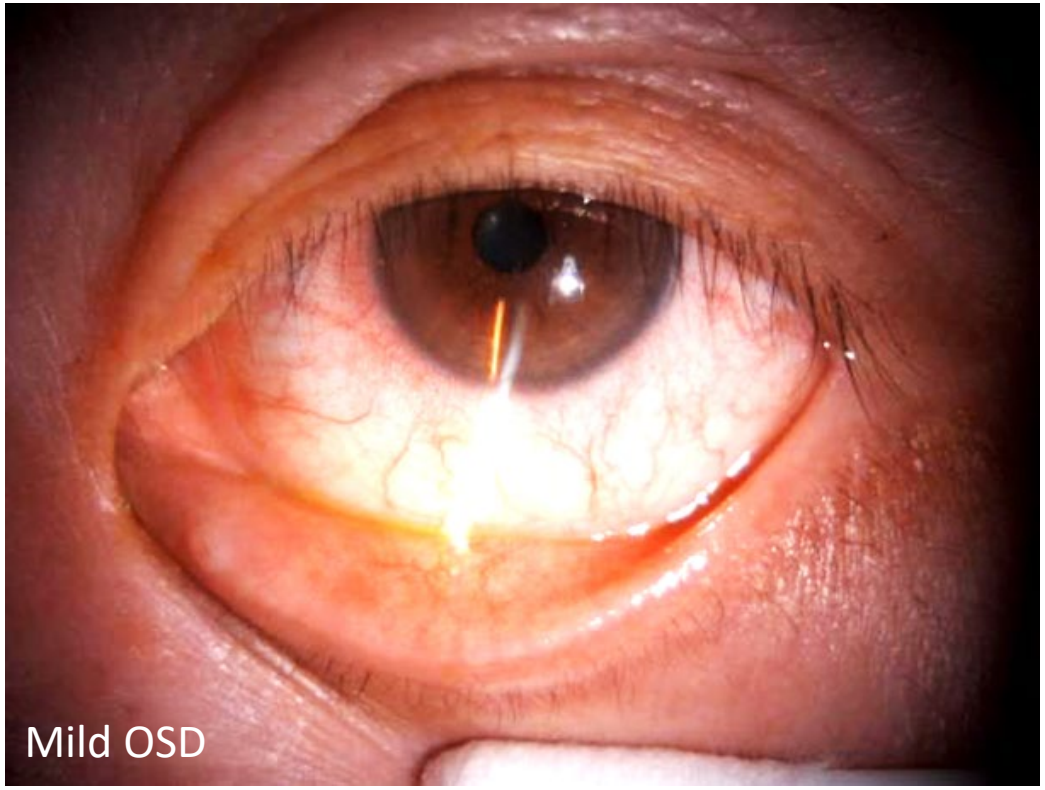


Image from clinical practice, used with permission. Not to be copied.

AD, atopic dermatitis; **OSD**, ocular surface disorder

1. Weyne J, et al. Dermatol Ther (Heidelb). 2020;10:1415–1421.

Risk of developing OSD in patients with AD

Adults with AD have a **significant** and **disease severity-dependent increased risk** of developing OSD, including conjunctivitis, keratitis and keratoconus, compared with the general population[1]

- Nearly half of patients with AD (32–56%) develop ocular surface disorders over the course of the disease[2]
- In AD, a higher risk of conjunctivitis is associated with:

- **Higher** baseline disease severity[1]
- **Longer** duration of AD[3]
- **Prior medical history** of conjunctivitis[2]
- **Higher** baseline levels of the serum biomarker TARC[2]
- **Higher** baseline IgE levels[3-5]
- **Higher** circulating eosinophil counts[2,3]

AD, atopic dermatitis; **IgE**, Immunoglobulin E; **OSD**, ocular surface disorders; **TARC**, thymus- and activation-regulated chemokine

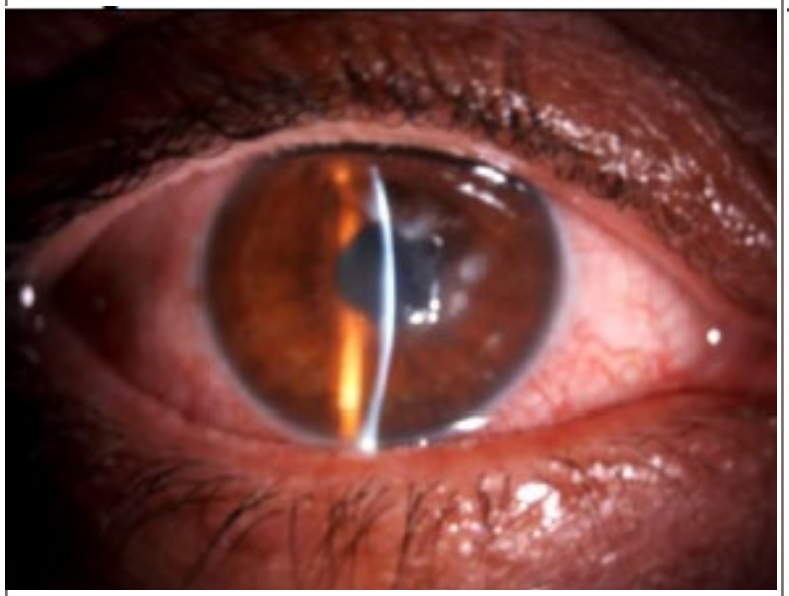
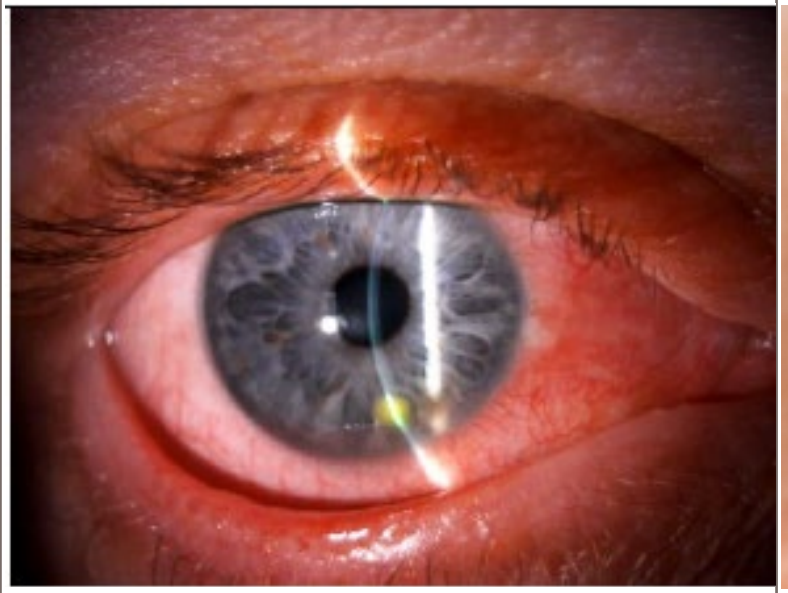
1. Thyssen JP, et al. J Am Acad Dermatol. 2017;77:280–286.e1. 2. Akinlade B, et al. Br J Dermatol. 2019;181:459–473. 3. Nettis E, et al. J Invest Allergol Clin Immunol. 2022;32:124–132. 4. Uchio E, et al. Br J Ophthalmol. 1998;82:82–87. 5. Bielory B, Bielory L. Immunol Allergy Clin North Am. 2010;30:323–336

Dermatologists and immunologists should proactively inquire about symptoms and risk factors for ocular disease, and, when appropriate, recommend evaluation by an ophthalmologist[1]

1. Beck KM, et al. Am J Clin Dermatol. 2019;20:797–805.

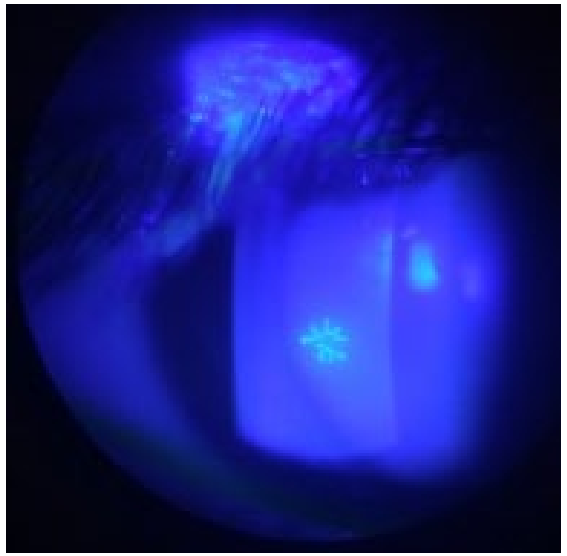
Red flags[1]

Ophthalmology referral for the following conditions

Herpetic Keratitis*	Bacterial Keratitis*	Keratoconus
		
Y Kerdraon	Y Kerdraon	Stock image

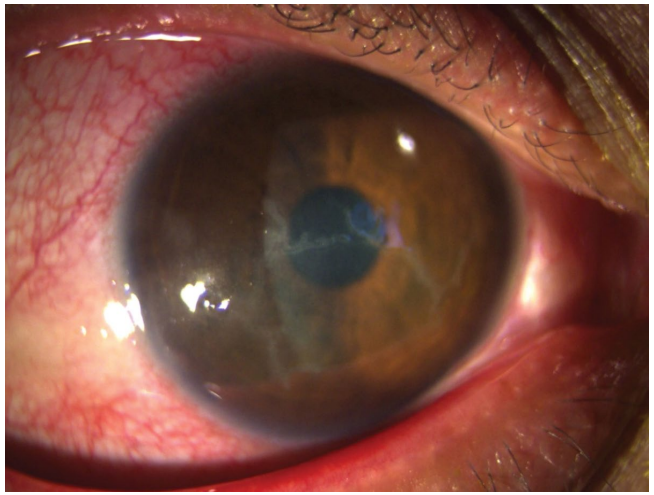
1. Foley P, et al. Australas J Dermatol. 2022;63:421–436.

Red flags: Herpetic (HSV) keratitis[1]



HSV dendrite with fluorescein

Image from:
https://eyewiki.aao.org/Herpes_Simplex_Epithelial_Keratitis



HSV dendrite without fluorescein

Image from: https://www.reviewofcontactlenses.com/article/herpes-simplex-keratitis-managing-the-masquerade

HSV stromal keratitis with scarring

Image from:
https://www.reviewofoptometry.com/article/ro0717-be-a-hero-to-your-hsvk-patients2

History: Prior history of herpetic eye disease

Symptoms: several days of blurred vision, mild pain and red eye

Signs: Any of eyelid vesicular rash, red eye, blurred vision, corneal ulcer (abnormal light reflex)

 | 1. Foley P, et al. Australas J Dermatol. 2022;63:421–436.

Red flags: Bacterial keratitis[1]

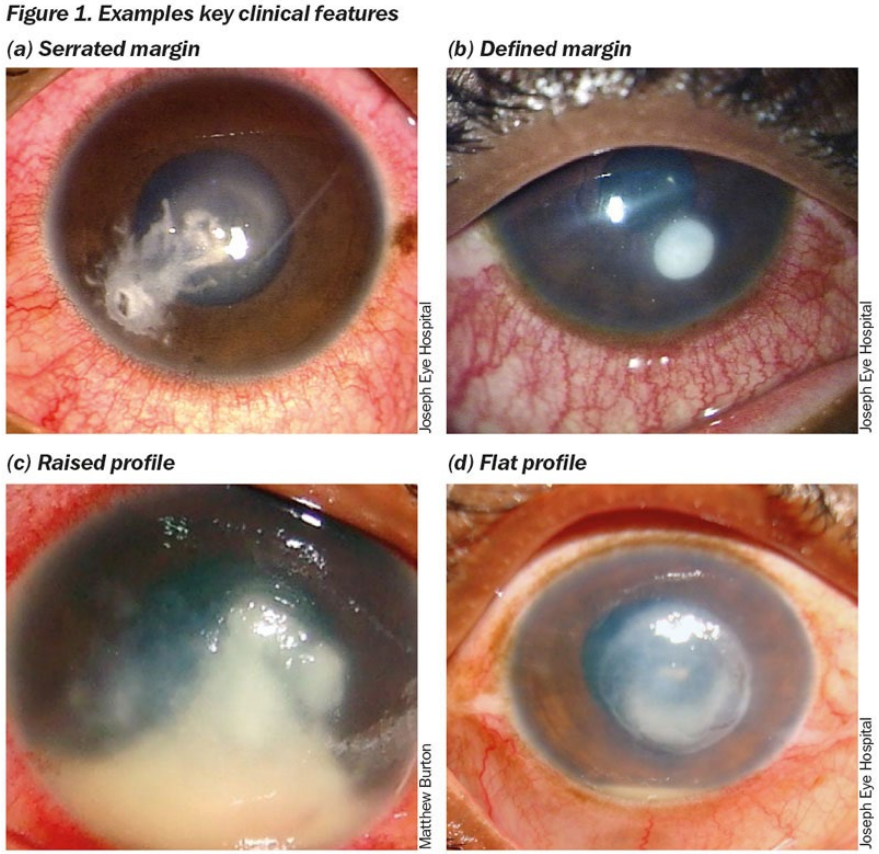


Image from: https://www.cehjournal.org/wp-content/uploads/figure1-Examples-key-clinical-features.jpg

Image from: https://www1.racgp.org.au/ajgp/2019/august/management-of-microbial-keratitis-in-general-pract

History: Contact lens wear
Symptoms: Rapid onset (1-3 days) of pain (often severe) and blurred vision
Signs: Any of red eye, blurred vision, corneal ulcer (abnormal light reflex), corneal white dot (infiltrate)

1. Foley P, et al. Australas J Dermatol. 2022;63:421–436.

Red flags: Keratoconus[1]

Stock image

History: Frequent/vigorous eye rubbing, younger age (<40 years), family history, frequent changes in spectacle prescription

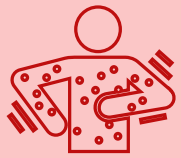
Symptoms: Decreased corneal sensation, reduced visual acuity, distorted vision, photophobia, with or without pain

Signs: Any of progressive corneal thinning and protrusion, irregular astigmatisim, impaired visual function

 | 1. Foley P, et al. Australas J Dermatol. 2022;63:421–436.

Assessment, outcome, and management[1]

An interdisciplinary decision framework for prescribers in the Australian setting



Risk factors

- Severe AD[a]
- Current/prior history of allergic conjunctivitis
- Current/prior history of herpetic eye disease
- Current use of contact lenses

→ **Prophylaxis**
Consider ophthalmology consultation

Red flags

- Herpetic keratitis
- Bacterial keratitis
- Keratoconus

→ **Refer to ophthalmologist**

Eye symptom severity
(DAOSD Activity Questionnaire)

Score = 0	**No eye management needed**
Score = 1–8	**Prescribing physician may manage**
Score = 9 or more	**Collaborative management with ophthalmologist**

[a]Severe AD defined as a baseline PGA score of 4 and baseline EASI score of ≥ 20.

AD, atopic dermatitis; **DAOSD,** dupilumab-associated ocular surface disorder; **EASI,** Eczema Area and Severity Index; **PGA,** physician global assessment

Figure adapted from: Foley P, et al. Australas J Dermatol. 2022;63:421–436. |

Eye-specific treatment[1]

An interdisciplinary decision framework for prescribers in the Australian setting*

High risk: Prophylaxis

Lubricating eye drops:

- Cellufresh, Bion-Tears, Systane (pf), Refresh (pf)
- Hyaluronic acid eye drops (Hylo-Fresh, Hylo-Forte)

Mild OSD: Prescribing physician may manage

Lubricating eye drops:

- Cellufresh, Bion-Tears, Systane (pf), Refresh (pf)
- Hyaluronic acid eye drops (Hylo-Fresh, Hylo-Forte)

Antihistamine eye drops:

- Azelastine 0.05%
- Livostin 0.05%

Mast cell stabiliser eye drops:

- Sodium cromoglycate 4% (Cromo-Fresh, Opticrom)

Combination antihistamine/mast cell stabiliser eye drops:

- Ketotifen (Zaditen)
- Olopatadine (Patanol)

Moderate-to-severe OSD: Collaborative management with ophthalmologist

Corticosteroid eye drops:

- Fluorometholone 0.1% eye drops (FML, Flarex)
- Prednisolone phosphate 0.5% (Prednisolone Minims)
- Prednisolone acetate 1% (Pred(nefrin) forte) drops
- Dexamethasone 0.1% eye drops (Maxidex)

Topical corticosteroids (eyelids)

- Hydrocortisone ointment (Hycor)

Inadequate response and/or side effects:

Calcineurin inhibitor eye drops:

- [off-label] Ciclosporin 0.05%, 0.1% (Ikervis, Restasis)
- Compounded tacrolimus ointment 0.03–0.1%

Anti-inflammatory eye drops:

- Lifitegrast

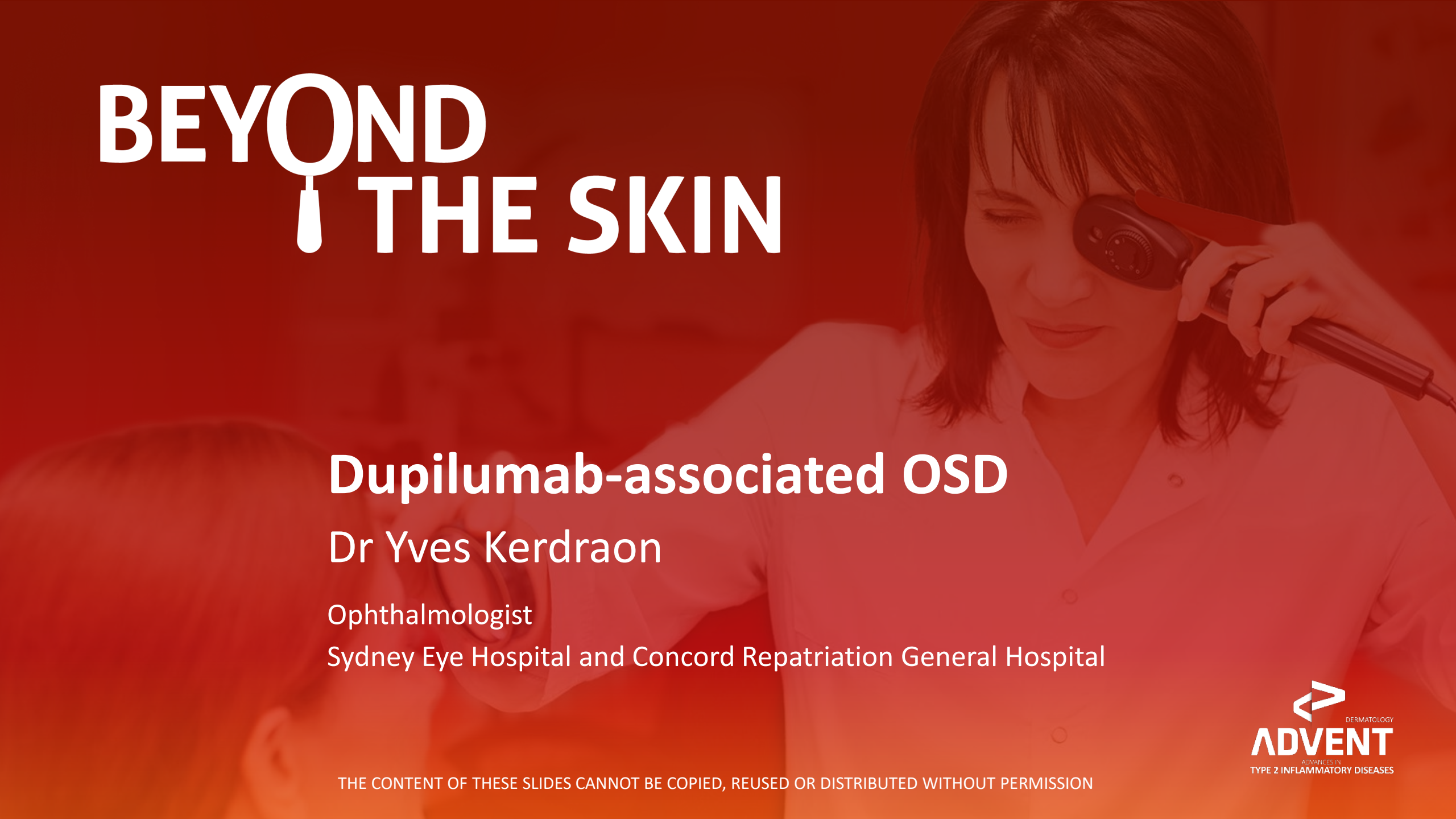
Maintenance therapy:

Combination topical corticosteroids and/or immunosuppressant

*Adapted from Foley et al, 2022

DAOSD, dupilumab-associated ocular surface disorder; **Pf,** preservative-free

1. Foley P, et al. Australas J Dermatol. 2022;63:421–436.



Dupilumab-associated OSD

Dr Yves Kerdraon

Ophthalmologist

Sydney Eye Hospital and Concord Repatriation General Hospital

DERMATOLOGY ADVENT ADVANCES IN TYPE 2 INFLAMMATORY DISEASES

Learning objectives

Managing dupilumab-associated ocular surface disorders (DAOSD) and case study

At the conclusion of this part of the presentation, attendees should be able to:

- Understand the incidence of DAOSD in clinical and real-world studies
- Understand the severity spectrum of DAOSD
- Recognise the risk factors associated with DAOSD
- Outline the various hypothesised mechanisms underpinning DAOSD; and
- Understand, from the case study, how to apply the recommendations in the Australian physician's algorithm[1] to the multidisciplinary management and treatment of DAOSD if it occurs during treatment with dupilumab

DAOSD, dupilumab-associated ocular surface disorders

1. Foley P, et al. Australas J Dermatol. 2022;63:421–436.

Speaker disclosures

Dr. Yves Kerdraon has been a speaker for Sanofi/Genzyme in 2020

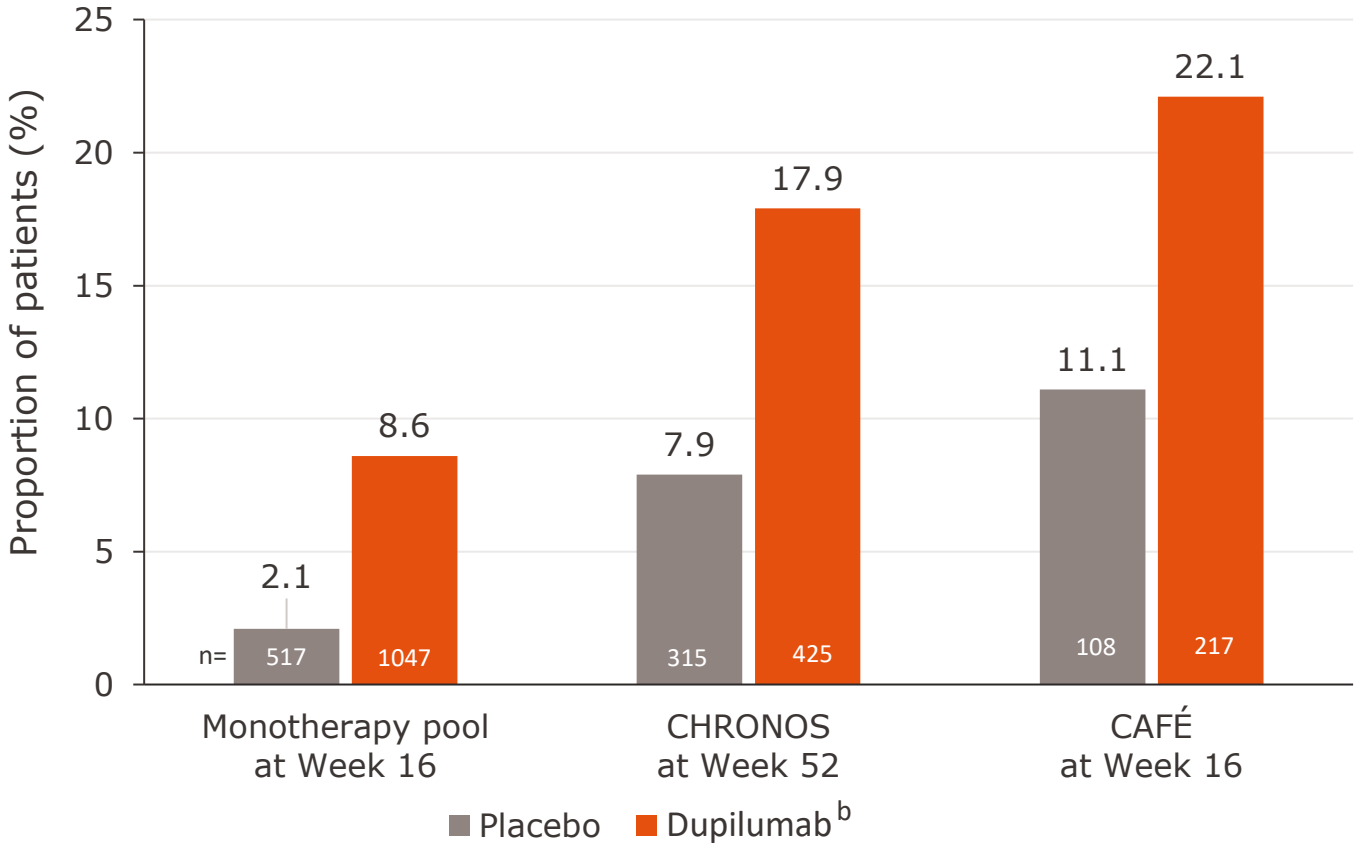
Dupilumab-associated ocular surface disorders (DAOSD)

What do you need to know?
How do you manage DAOSD?

DAOSD, dupilumab-associated ocular surface disorder

Conjunctivitis[a] in patients treated with dupilumab

The incidence of conjunctivitis in clinical studies ranged from 8.6% to 22.1% for patients treated with dupilumab[1–3]



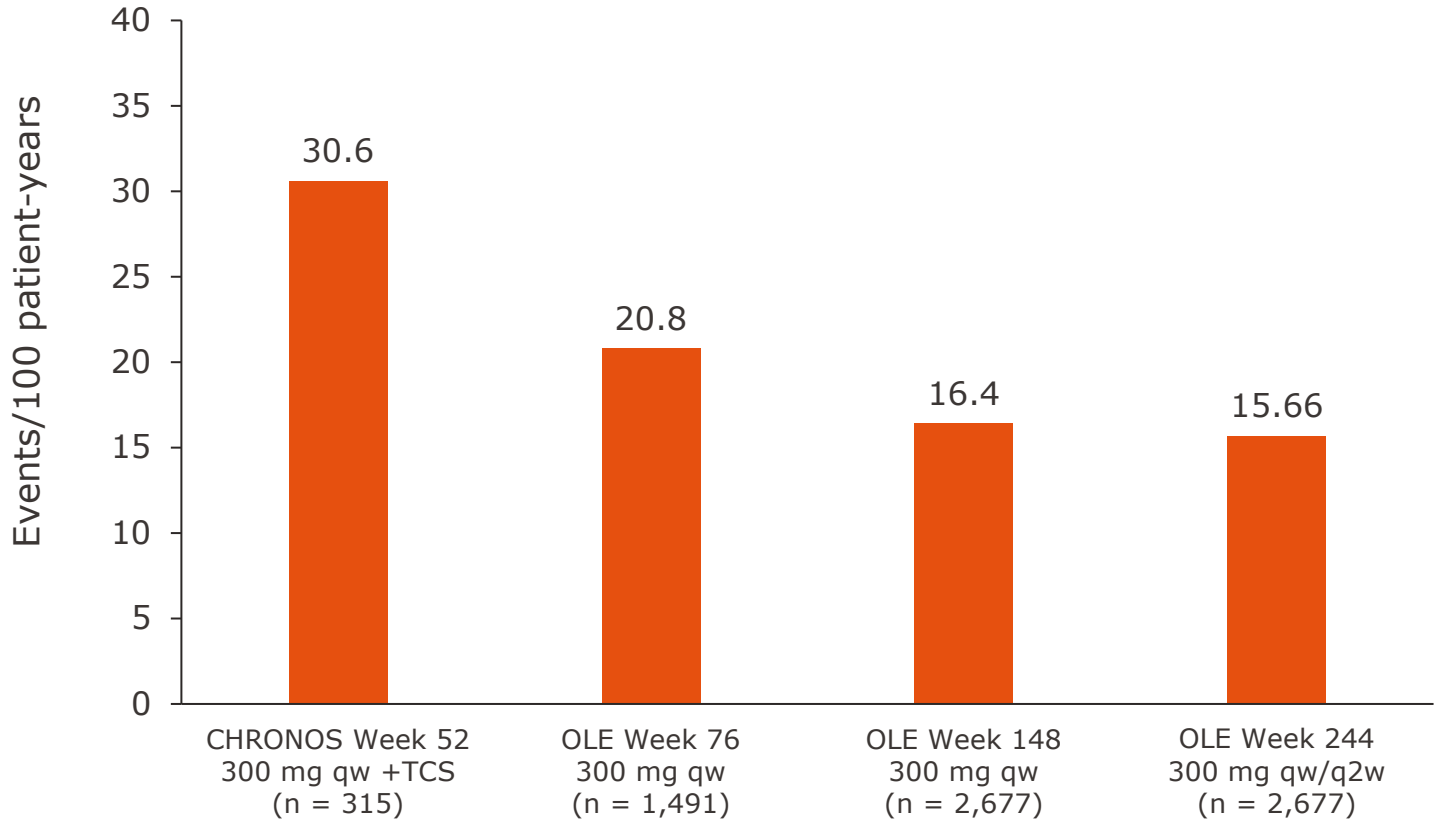
[a]Conjunctivitis refers to the group of adverse events coded as conjunctivitis, allergic conjunctivitis, bacterial conjunctivitis, viral conjunctivitis, adenoviral conjunctivitis, or atopic keratoconjunctivitis.
[b]Dupilumab 300 mg qw and 300 mg q2w arms combined. The approved dose in Australia for adults is 300 mg q2w.[4]

OSD, ocular surface disorder

1. Akinlade B, et al. Br J Dermatol. 2019;181:459–473. 2. Foley P, et al. Australas J Dermatol. 2022;63:421–436. 3. Beck LA, et al. Am J Clin Dermatol. 2022; 23:393–408. 4. Dupixent (Dupilumab) Australian Product Information. 2022. http://www.guildlink.com.au/gc/ws/sw/pi.cfm?product=swpdupix.

Conjunctivitis[a] rates decreased over time[1]

- 61% of conjunctivitis events occurred during the first year of dupilumab treatment[1]



LIBERTY AD OLE (NCT01949311) is an ongoing Phase 3 multicentre trial to assess the long-term safety and efficacy of dupilumab in adults with moderate-to-severe AD. Patients received 300 mg dupilumab qw, and in 2019 the protocol was amended to 300 mg q2w to align with the regimen approved by the regulatory agencies. The approved dose in Australia for adults is 300 mg q2w.[4]

[a]Conjunctivitis (reported as a narrow cluster of MedDRA Preferred Terms: conjunctivitis, conjunctivitis allergic, conjunctivitis bacterial, conjunctivitis viral, and atopic keratoconjunctivitis).
OLE, open-label extension; **q2w,** every 2 weeks; **qw,** once weekly; **TCS,** topical corticosteroid

1. Beck LA, et al. Am J Clin Dermatol. 2022;23:393–408; 2. Akinlade B, et al. Br J Dermatol. 2019;181:459–473. 3. Dupixent (Dupilumab) Australian Product Information. 2022. http://www.guildlink.com.au/gc/ws/sw/pi.cfm?product=swpdupix.

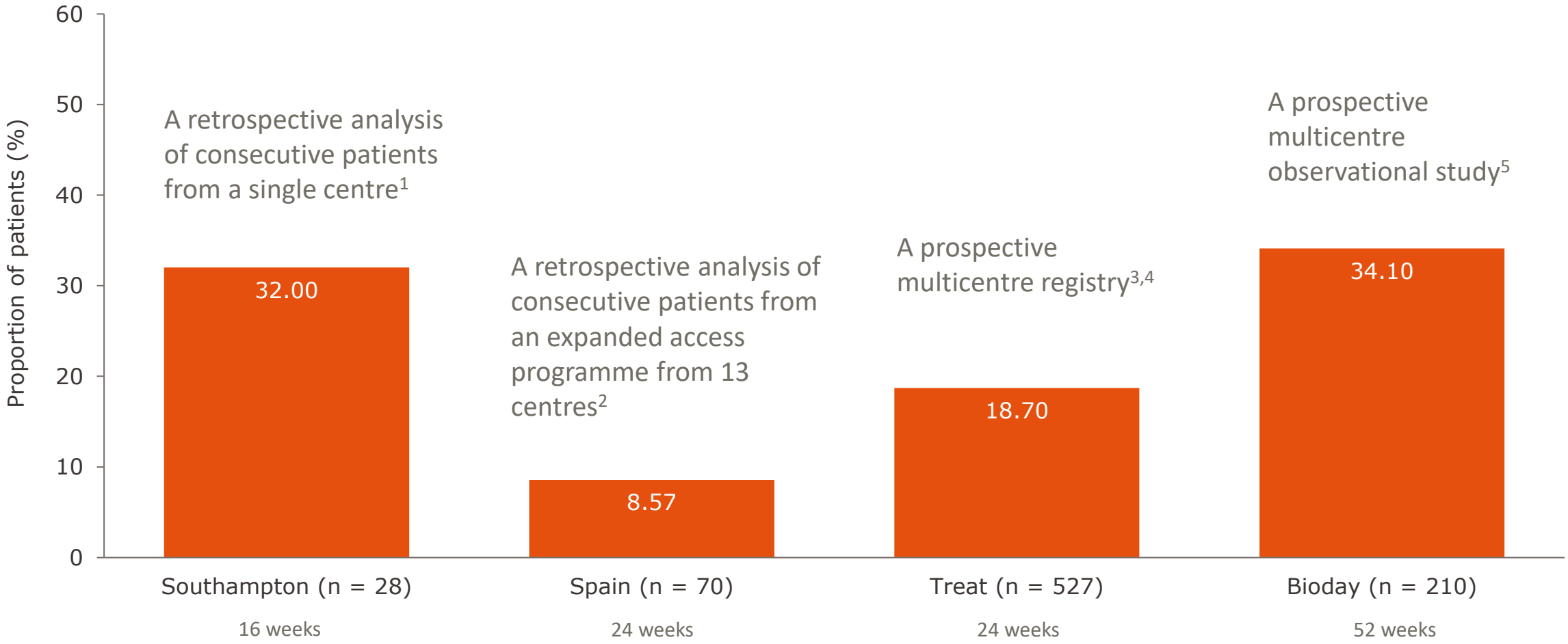
Natural history of DAOSD

- Most cases were **mild-to-moderate** in severity[1–2]
- Most cases resolved while continuing dupilumab[1,3]
- Of 1689 patients included in the clinical trials treated with dupilumab for AD:[2]
  - There were 214 cases of conjunctivitis **and 2 patients discontinued[2]**
    - One patient in monotherapy pool (300 mg qw group) permanently discontinued due to conjunctivitis[2]
    - One patient in the 300 mg qw + TCS group in CHRONOS discontinued due to allergic keratoconjunctivitis[2]
- Treatment discontinuation in open-label extension trials at 4 years was rare
  - **0.5%** of dupilumab-treated patients[1]

AD, atopic dermatitis; **DAOSD,** dupilumab-associated ocular surface disorder; **OLE,** open-label extension

1. Beck LA, et al. Am J Clin Dermatol. 2022;23:393–408. 2. Akinlade B, et al. Br J Dermatol. 2019;181:459–473. 3. Australian Approved Product Information for DUPIXENT (dupilumab). 29 June 2022.

Frequency of conjunctivitis reported in real-world studies[1–5]



1. Popiela M, et al. Eye. 2021;35:3277–3284. 2. Armario-Hita JC, et al. Br J Dermatol. 2019;181:1072–1074. 3. Siegels D, et al. Allergol Select. 2021;5:274-86. 4. Weidinger S. Presentation at 10. Münchner Dermatologisches Konsil, München, Sept 30, 2020. 5. Ariëns LF, et al. JAAD. 2021;84:1000–1009.

Paediatric clinical trials - atopic dermatitis

In children aged 6–11 years:

- Placebo (n=120) vs dupilumab (n=242): 4.2% vs 6.7–14.8%[1]
- There were two treatment discontinuations[1]

In adolescents aged 13–17 years:

- Reported events of conjunctivitis were mainly **mild** or **moderate**, and none were categorised as serious[2]
- Conjunctivitis rates were numerically higher in the treatment group
  - placebo 4.7%; n=85, dupilumab 10.8% (q4w, n=83) and 9.8% (q2w, n=82)[2]
- None of these events was serious or severe or led to treatment discontinuation[2]

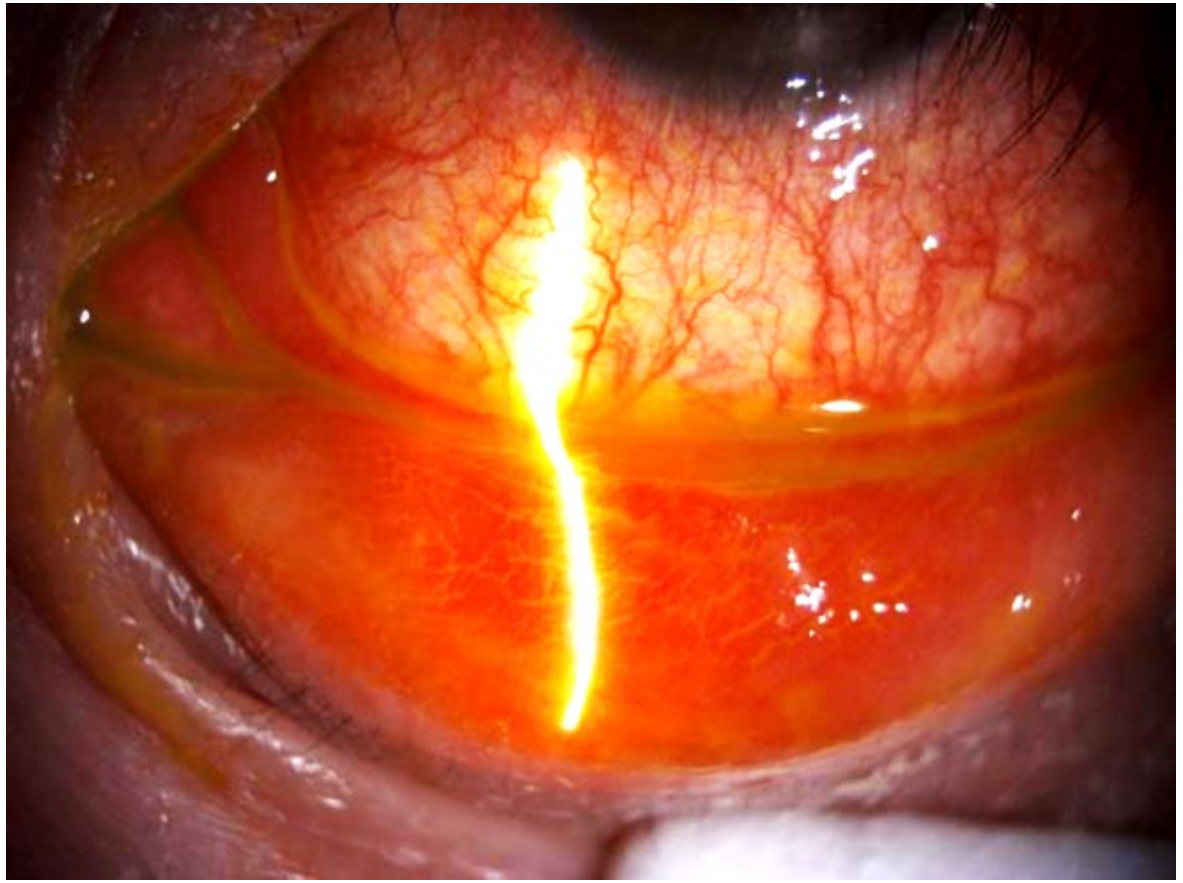
q2w, once every two weeks; **q4w**, once every four weeks

1. Paller AS, et al. J Am Acad Dermatol. 2020;83(5):1282-93. 2. Simpson EL, et al. JAMA Dermatol. 2020;156:44–56.

Incidence of DAOSD[1]

A retrospective analysis of the FDA Adverse Event Reporting System (FAERS) with 25,537 patients on dupilumab showed:

- Conjunctivitis: 4.96%
- Eye pruritus: 4.95%
- Ocular hyperaemia: 4.30%
- Dry eye: 3.87%
- Eye irritation: 3.06%
- Increased lacrimation: 2.15%



Moderate-to-severe DAOSD

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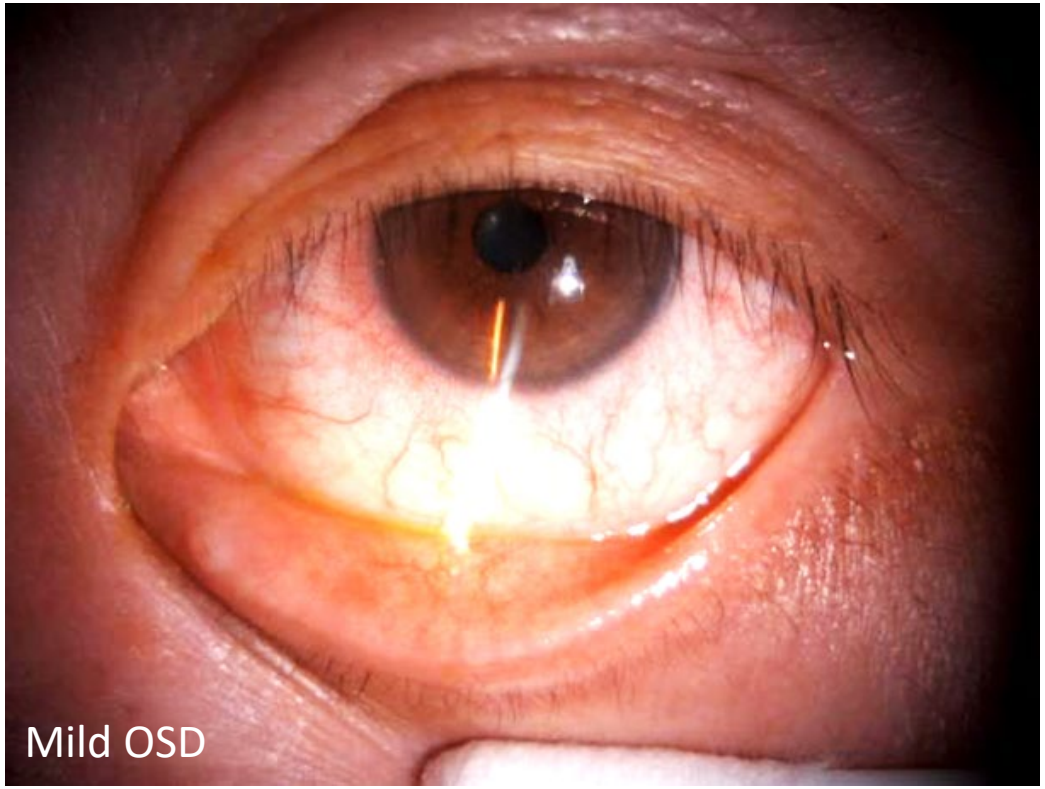
DAOSD, dupilumab-associated ocular surface disorder

1. Wang Y, Jorizzo JL. J Am Acad Dermatol. 2021;84:1010–1014.

What are the known risk factors for DAOSD?

- Prior history of ocular disease:[1,2]
  - Prior conjunctivitis; atopic keratoconjunctivitis; dry eye disease[1]
- Severe atopic dermatitis[1]
- Presence of facial or eyelid erythema[3,4]
- History of food allergy[3,4]
- Family history of atopy[3]
- Elevated levels of IgE, TARC, blood eosinophils[1,3]



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DAOSD, dupilumab-associated ocular surface disorder; **IgE,** immunoglobulin E; **TARC**, thymus- and activation-regulated chemokine

1. Akinlade B, et al. Br J Dermatol. 2019;181:459–473; 2. Ariëns LF, et al. JAAD. 2021;84:1000–1009; 3. Foley P, et al. Australas J Dermatol. 2022;63:421–436; 4. Achten RE, et al. Acta Derm Venereol. 2022;102:adv00666.

Pathogenesis of conjunctivitis observed during dupilumab treatment is unknown[1]

Multiple mechanisms likely play a role in the pathogenesis of conjunctivitis during dupilumab treatment

Loss of conjunctival goblet cells causing ocular surface disruption[2]

Increased OX40 ligand activity[3]

Disruption of an immune-mediated response of conjunctival-associated lymphoid tissue[4]

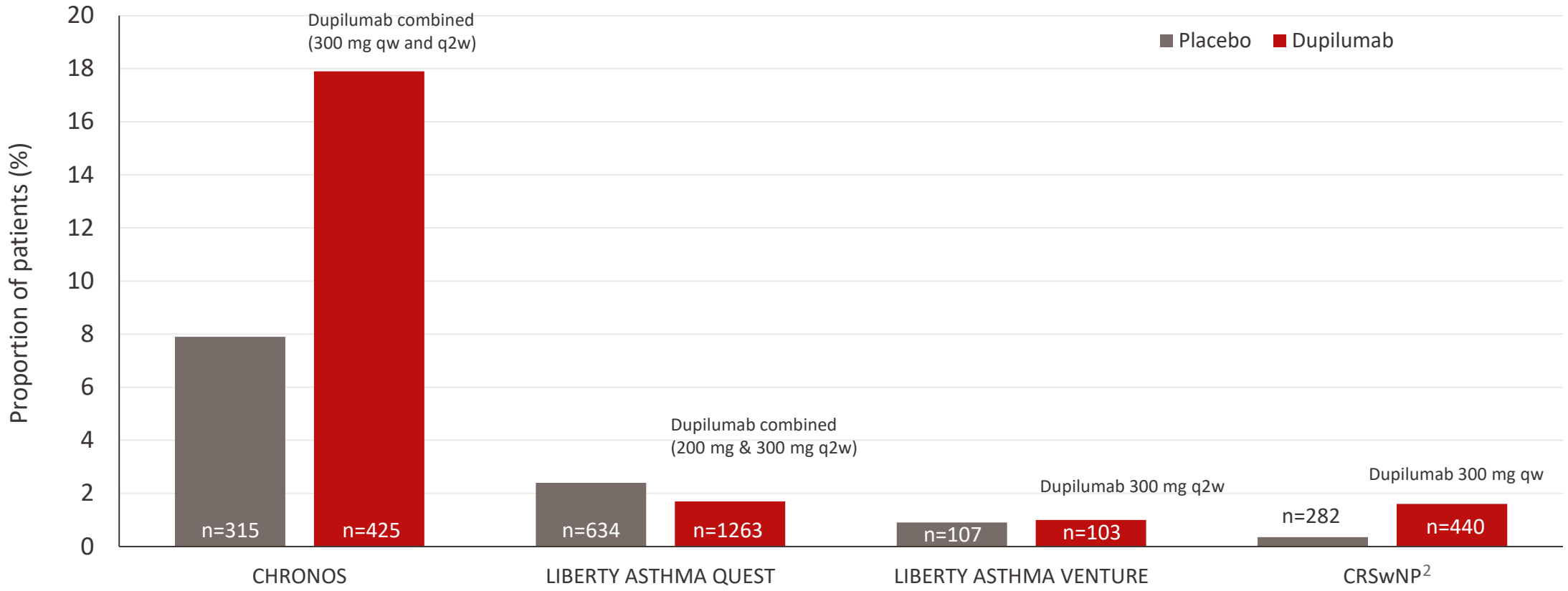
Eosinophils migrating into conjunctival epithelium[2]

Alterations in cytokine activity leading to increased *Demodex* mites[2,5]

IL, interleukin.

1. Akinlade B, et al. Br J Dermatol. 2019;181:459–473. 2. Bakker DS, et al. Br J Dermatol. 2019;180:1248–1249. 3. Mennini M, et al. N Engl J Med. 2017;376:1090. 4. Shen E, et al. Ocul Immunol Inflamm. 2018; 2019;27:1339–1341. 5. Thyssen JP. Br J Dermatol. 2018;178:1220.

Incidence of DAOSD in other indications[1,2]



[a]Conjunctivitis refers to the group of adverse events coded as conjunctivitis, allergic conjunctivitis, bacterial conjunctivitis, viral conjunctivitis, adenoviral conjunctivitis, or atopic keratoconjunctivitis.
CRSwNP, chronic rhinosinusitis with nasal polyps; **DAOSD,** dupilumab-associated ocular surface disorder. The approved dose in Australia for adults is 300 mg q2w.[3]

1. Akinlade B, et al. Br J Dermatol. 2019;181:459–473. 2. Bachert C et al. Lancet 2019. 394:1638-50. 3. Dupixent (Dupilumab) Australian Product Information. 2022.

Prior to starting dupilumab treatment

An interdisciplinary decision framework for prescribers in the Australian setting

Risk factors

- Severe AD[a]
- Current/prior history of allergic conjunctivitis
- Current/prior history of herpetic eye disease
- Current use of contact lenses

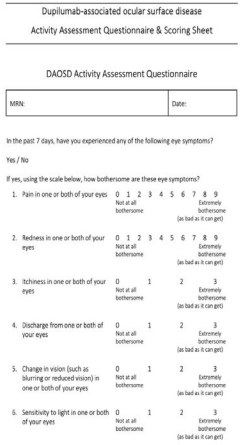
→ **Prophylaxis**
Consider ophthalmology consultation

Red flags

- Herpetic keratitis
- Bacterial keratitis
- Keratoconus

→ **Refer to ophthalmologist**

Eye symptom severity
(DAOSD Activity Questionnaire)



Dupilumab-associated ocular surface disease
Activity Assessment Questionnaire & Scoring Sheet

DAOSD Activity Assessment Questionnaire

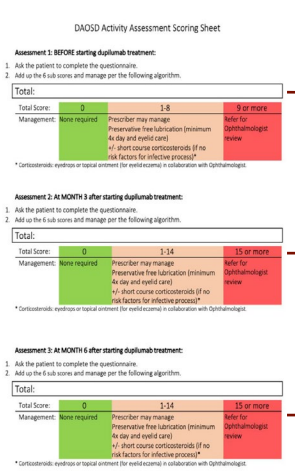
MRN: Date:

In the past 7 days, have you experienced any of the following eye symptoms?

Yes / No

If yes, using the scale below, how bothersome are these eye symptoms?

1. Pain in one or both of your eyes 0 1 2 3 4 5 6 7 8 9 (Not at all bothersome … Extremely bothersome (as bad as it can get))
2. Redness in one or both of your eyes 0 1 2 3 4 5 6 7 8 9 (Not at all bothersome … Extremely bothersome (as bad as it can get))
3. Itchiness in one or both of your eyes 0 1 2 3 (Not at all bothersome … Extremely bothersome (as bad as it can get))
4. Discharge from one or both of your eyes 0 1 2 3 (Not at all bothersome … Extremely bothersome (as bad as it can get))
5. Change in vision (such as blurring or reduced vision) in one or both of your eyes 0 1 2 3 (Not at all bothersome … Extremely bothersome (as bad as it can get))
6. Sensitivity to light in one or both of your eyes 0 1 2 3 (Not at all bothersome … Extremely bothersome (as bad as it can get))



DAOSD Activity Assessment Scoring Sheet

Assessment 1: BEFORE starting dupilumab treatment:
1. Ask the patient to complete the questionnaire.
2. Add up the 6 sub scores and manage per the following algorithm.

Total:

Total Score:	0	1-8	9 or more
Management:	None required	Prescriber may manage Preservative free lubrication (minimum 4x day and eyelid care) +/- short course corticosteroids (if no risk factors for infective process)*	Refer for Ophthalmologist review

* Corticosteroids: eyedrops or topical ointment (for eyelid eczema) in collaboration with Ophthalmologist.

Assessment 2: At MONTH 3 after starting dupilumab treatment:
1. Ask the patient to complete the questionnaire.
2. Add up the 6 sub scores and manage per the following algorithm.

Total:

Total Score:	0	1-14	15 or more
Management:	None required	Prescriber may manage Preservative free lubrication (minimum 4x day and eyelid care) +/- short course corticosteroids (if no risk factors for infective process)*	Refer for Ophthalmologist review

* Corticosteroids: eyedrops or topical ointment (for eyelid eczema) in collaboration with Ophthalmologist.

Assessment 3: At MONTH 6 after starting dupilumab treatment:
1. Ask the patient to complete the questionnaire.
2. Add up the 6 sub scores and manage per the following algorithm.

Total:

Total Score:	0	1-14	15 or more
Management:	None required	Prescriber may manage Preservative free lubrication (minimum 4x day and eyelid care) +/- short course corticosteroids (if no risk factors for infective process)*	Refer for Ophthalmologist review

* Corticosteroids: eyedrops or topical ointment (for eyelid eczema) in collaboration with Ophthalmologist.

Score = 0 → **No eye management needed**

Score = 1–8 → **Prescribing physician may manage**

Score = 9 or more → **Collaborative management with ophthalmologist**

[a]Severe AD defined as a baseline PGA score of 4 and baseline EASI score of ≥ 20.

AD, atopic dermatitis; **DAOSD,** dupilumab-associated ocular surface disorder; **EASI,** Eczema Area and Severity Index; **PGA,** physician global assessment

Figure adapted from: Foley P, et al. Australas J Dermatol. 2022;63:421–436. |

Managing DAOSD (month 3 and 6 of dupilumab treatment)

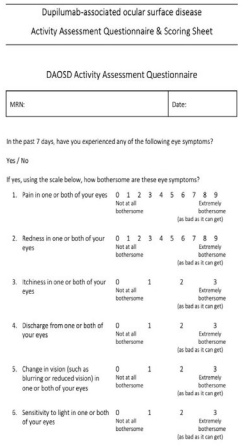
An interdisciplinary decision framework for prescribers in the Australian setting

Red flags

- Herpetic keratitis
- Bacterial keratitis
- Keratoconus

→ **Refer to ophthalmologist**

Eye symptom severity
(DAOSD Activity Questionnaire)


Dupilumab-associated ocular surface disease
Activity Assessment Questionnaire & Scoring Sheet

DAOSD Activity Assessment Questionnaire

MRN: Date:

In the past 7 days, have you experienced any of the following eye symptoms?

Yes / No

If yes, using the scale below, how bothersome are these eye symptoms?

1. Pain in one or both of your eyes 0 1 2 3 4 5 6 7 8 9 (Not at all bothersome … Extremely bothersome (as bad as it can get))
2. Redness in one or both of your eyes 0 1 2 3 4 5 6 7 8 9 (Not at all bothersome … Extremely bothersome (as bad as it can get))
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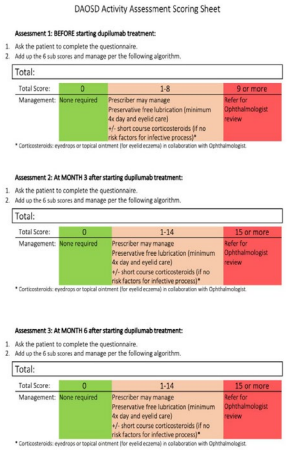
6. Sensitivity to light in one or both of your eyes 0 1 2 3 (Not at all bothersome … Extremely bothersome (as bad as it can get))


DAOSD Activity Assessment Scoring Sheet

Assessment 1: BEFORE starting dupilumab treatment:

1. Ask the patient to complete the questionnaire.
2. Add up the 6 sub scores and manage per the following algorithm.

Total:

Total Score:	0	1-8	9 or more
Management:	None required	Prescriber may manage Preservative free lubrication (minimum 4x day and eyelid care) +/- short course corticosteroids (if no risk factors for infective process)*	Refer for Ophthalmologist review

* Corticosteroids: eyedrops or topical ointment (for eyelid eczema) in collaboration with Ophthalmologist

Assessment 2: At MONTH 3 after starting dupilumab treatment:

1. Ask the patient to complete the questionnaire.
2. Add up the 6 sub scores and manage per the following algorithm.

Total:

Total Score:	0	1-14	15 or more
Management:	None required	Prescriber may manage Preservative free lubrication (minimum 4x day and eyelid care) +/- short course corticosteroids (if no risk factors for infective process)*	Refer for Ophthalmologist review

* Corticosteroids: eyedrops or topical ointment (for eyelid eczema) in collaboration with Ophthalmologist

Assessment 3: At MONTH 6 after starting dupilumab treatment:

1. Ask the patient to complete the questionnaire.
2. Add up the 6 sub scores and manage per the following algorithm.

Total:

Total Score:	0	1-14	15 or more
Management:	None required	Prescriber may manage Preservative free lubrication (minimum 4x day and eyelid care) +/- short course corticosteroids (if no risk factors for infective process)*	Refer for Ophthalmologist review

* Corticosteroids: eyedrops or topical ointment (for eyelid eczema) in collaboration with Ophthalmologist

→ Score = 0 → **No eye management needed**

→ Score = 1–14 → **Prescribing physician may manage**

→ Score = 15 or more → **Collaborative management with ophthalmologist**

DAOSD, dupilumab-associated ocular surface disorder

Figure adapted from: Foley P, et al. Australas J Dermatol. 2022;63:421–436. |

Eye-specific treatment for DAOSD[1]

An interdisciplinary decision framework for prescribers in the Australian setting

High risk: Prophylaxis[a]

Lubricating eye drops:

- Cellufresh, Bion-Tears, Systane (pf), Refresh (pf)
- Hyaluronic acid eye drops (Hylo-Fresh, Hylo-Forte)

Mild DAOSD: Prescribing physician may manage

Lubricating eye drops:

- Cellufresh, Bion-Tears, Systane (pf), Refresh (pf)
- Hyaluronic acid eye drops (Hylo-Fresh, Hylo-Forte)

Antihistamine eye drops:

- Azelastine 0.05%
- Livostin 0.05%

Mast cell stabiliser eye drops:

- Sodium chromoglycate 4% (Cromo-Fresh, Opticrom)

Combination antihistamine/mast cell stabiliser eye drops:

- Ketotifen (Zaditen)
- Olopatadine (Patanol)

Moderate-to-severe DAOSD: Collaborative management with ophthalmologist[b]

Corticosteroid eye drops:

- Fluorometholone 0.1% eye drops (FML, Flarex)
- Prednisolone phosphate 0.5% (Prednisolone Minims)
- Prednisolone acetate 1% (Pred(nefrin) forte) drops
- Dexamethasone 0.1% eye drops (Maxidex)

Topical corticosteroids (eyelids)

- Hydrocortisone ointment (Hycor)

Inadequate response and/or side effects:

Calcineurin inhibitor eye drops:

- [off-label] Ciclosporin 0.05%, 0.1% (Ikervis, Restasis)
- Compounded tacrolimus ointment 0.03–0.1%

Anti-inflammatory eye drops:

- Lifitegrast

Maintenance therapy:

Combination topical corticosteroids and/or immunosuppressant

[a]Prior to treatment with dupilumab. [b]If symptoms prevail despite optimal treatment, consider cessation of dupilumab.

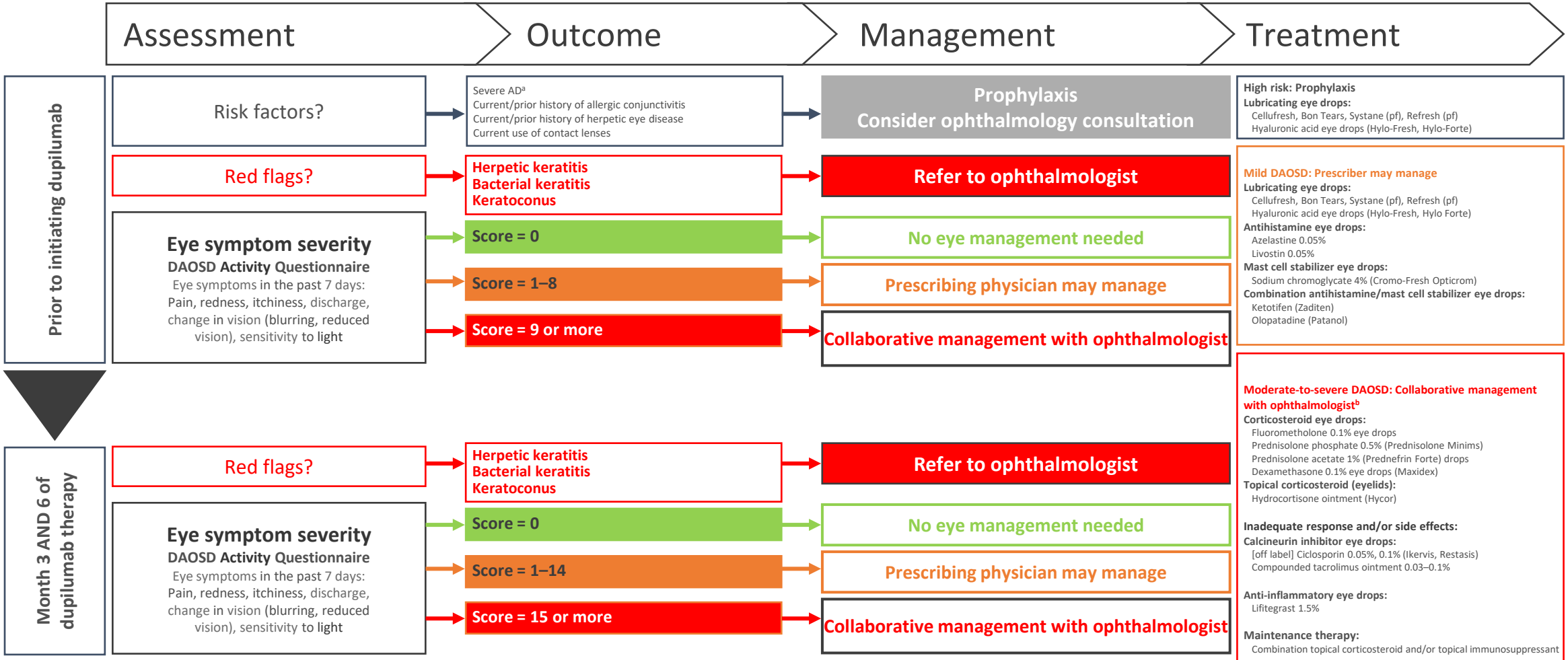
DAOSD, dupilumab-associated ocular surface disorder; **Pf,** preservative-free

1. Foley P, et al. Australas J Dermatol. 2022;63:421–436.

When should a dermatologist refer to an ophthalmologist?

- Pre-dupilumab risk stratification and symptom scoring
- Reassess: ongoing monitoring of signs and symptoms
- Patient monitoring
  - Ensure adequate access to prescriber or ophthalmologist
- Is dupilumab cessation an option?

An interdisciplinary decision framework for prescribers in the Australian setting



[a]Severe AD defined as a baseline PGA score of 4 and baseline EASI score of ≥ 20. [b]If symptoms prevail despite optimal treatment, consider cessation of dupilumab.

AD, atopic dermatitis; **DAOSD,** dupilumab-associated ocular surface disorder; **EASI,** Eczema Area and Severity Index; **pf,** preservative-free; **PGA,** Physician's Global Assessment

Foley P, et al. Australas J Dermatol. 2022;63:421–436. |

Infographic available for download

Infographic

Scan the QR code to download

Dupilumab-associated ocular surface disease:

An interdisciplinary decision framework for prescribers in the Australian setting

Adapted from: Peter Foley, Yves Kerdraon, John Hogden, Stephen Shumack, Lynda Spelman, Deshan Sebaratnam, Charles Su, Constance H Katelaris. Australas J Dermatol 2022 doi: 10.1111/ajd.13924

sanofi WILEY

Objectives

To provide guidance on dupilumab-associated ocular surface disease (DAOSD) assessment and management

The aim of these recommendations is to ensure patients are assessed and managed appropriately to reduce the impact of **DAOSD** and minimize disruption to dupilumab therapy.

Methods

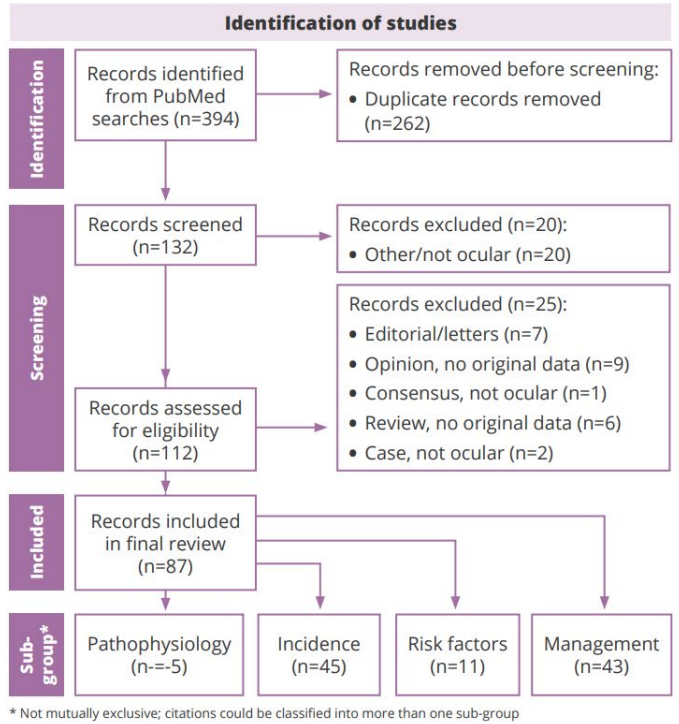
Systematic review of the literature undertaken to identify data on:

- Incidence
- Pathophysiology
- Risk factors
- Management

Critical review of the literature to inform:

- Decision framework for dupilumab prescribers
- Development of a graded severity scoring tool to guide appropriate management options

PRISMA flow diagram for identification of relevant publications.



* Not mutually exclusive; citations could be classified into more than one sub-group

DAOSD, dupilumab-associated ocular surface disorder

Foley P, et al. Australas J Dermatol. 2022;63:421–436. Infographic available from: https://onlinelibrary.wiley.com/pb-assets/assets/14400960/92235_Dupilumab-manuscript-infographic_Final-1670490944380.pdf Accessed April 2023.

Australian Product Information[1]

When treating patients with dupilumab…

Advise patients to report new onset or worsening eye symptoms to their healthcare provider.

Patients treated with dupilumab who develop conjunctivitis that does not resolve following standard treatment or signs and symptoms suggestive of keratitis should undergo ophthalmological examination, as appropriate.

1. Australian Approved Product Information for DUPIXENT (dupilumab). 29 June 2022.

DAOSD vs AKC - a different beast?

Clinically*:

- Commonly have conjunctival injection, subtarsal papillae, punctate epitheliopathy, blepharitis, itch, watering, photophobia
- Less commonly: subtarsal or limbal follicles, LSCF, conjunctival scarring, symblepharon

Pathologically (no comparative studies):

- Loss of goblet cells in DAOSD, whereas there is goblet cell hyperplasia in AKC and allergic conjunctivitis[1]
- Mixed immune cell infiltrate with CD4+, CD8+ T-cells, CD11c+ dendritic cells, CD14+ monocytes, and CD68+ macrophages[2]
- High expression of IFN-γ, TNF-α, IL-10, and IL-17A and co-expression of granzyme B[2]

***Personal communication Y. Kerdraon**

AKC, atopic keratoconjunctivitis; **DAOSD**, dupilumab-associated ocular surface disorder; **LSCF,** limbal stem cell deficiency; **IFN-γ**, interferon-gamma; **TNF-α**, tumour necrosis factor-alpha; **IL-10**, interleukin-10; **IL-17A**, interleukin-17A, **CD4+**, cluster of differentiation 4+, **CD8+**, cluster of differentiation 8+, **CD11c+**, cluster of differentiation 11c+, **CD14+**, cluster of differentiation 14+, **CD68+**, cluster of differentiation 68+.

1. Bakker DS, et al. Br J Dermatol. 2019;180(5):1248-1249; 2. Bakker DS et al. Allergy. 2021;76(12):3814-3817. |

Summary

- Patients with AD are at increased risk of OSD
- Most cases of DAOSD are mild-to-moderate
- DAOSD is manageable
- Most patients are able to remain on dupilumab

AD, atopic dermatitis; **OSD**, ocular surface disorder; **DAOSD**, dupilumab-associated ocular surface disorder

Learning objectives

As a result of attending this presentation, you should now be able to:

- Recognise common presentations of OSD in patients with AD
- Know how to assess patient risk factors, measure eye symptom severity, and identify any red flags (e.g. herpetic keratitis, bacterial keratitis, keratoconus)
- Recognise the risk factors associated with DAOSD
- Know how to apply the recommendations in the Australian physician's algorithm[1] to the multidisciplinary management and treatment of:
  - OSD in a patient newly presenting with severe AD (before any advanced treatment is initiated)
  - DAOSD if it occurs during treatment with dupilumab (including red flags, assessment of severity, management, and referral pathways)
- Recognise that DAOSD is usually mild-to-moderate in severity and rarely leads to treatment discontinuation

AD, atopic dermatitis; **DAOSD**, dupilumab-associated ocular surface disorder; **OSD**, ocular surface disorders

1. Foley P, et al. Australas J Dermatol. 2022;63:421–436.

Product Information

PBS Information: Refer to PBS schedule for full authority information. Authority required for patients aged ≥ 12 years with chronic severe atopic dermatitis and uncontrolled severe asthma. This product is not listed on the PBS for children 6 to 11 years of age with severe atopic dermatitis or moderate to severe asthma, or for patients with uncontrolled chronic rhinosinusitis with nasal polyps.

Please review full Product Information before prescribing. Full Product Information is available from sanofi-aventis australia pty ltd at http://www.guildlink.com.au/gc/ws/sw/pi.cfm?product=swpdupix or by contacting 1800 818 806.

Atopic dermatitis*:* **Adults and adolescents:** Treatment of moderate to severe atopic dermatitis in patients aged 12 years and older who are candidates for chronic systemic therapy. Not intended for episodic use. **Children 6 to 11 years of age:** Dupixent is indicated for the treatment of severe atopic dermatitis in patients aged 6 to 11 years old who are candidates for chronic systemic therapy. Dupixent is not intended for episodic use. **Asthma:** Add on maintenance treatment in patients aged 6 years and older with moderate to severe asthma with type 2 inflammation (elevated eosinophils or elevated FeNO) that is inadequately controlled despite therapy with other medicinal products for maintenance treatment. **Chronic rhinosinusitis with nasal polyposis (CRSwNP):** Dupixent is indicated as an add-on maintenance treatment in adult patients with inadequately controlled chronic rhinosinusitis with nasal polyposis (CRSwNP). **DOSAGE AND ADMINISTRATION: Atopic dermatitis – Adults:** Initial dose of 600 mg by subcutaneous injection (two 300 mg injections consecutively in different injection sites), followed by 300 mg given every other week. Refer to full PI for preparation, handling and administration. Treatment should be initiated and supervised by a dermatologist or immunologist **Atopic Dermatitis – Paediatric and Adolescent patients aged 6-17 years: Patients 15 kg to < 30 kg:** Initial dose of 600 mg (two 300 mg injections consecutively in different injection sites) followed by 300 mg every four weeks. **Patients 30 kg to < 60 kg:** Initial dose of 400 mg (two 200 mg injections consecutively in different injection sites) followed by 200 mg given every other week. **Patients ≥ 60 kg:** Initial dose of 600 mg by subcutaneous injection (two 300 mg injections consecutively in different injection sites) followed by 300 mg given every other week. **Asthma – Adults and adolescents:** Initial dose of 400 mg by subcutaneous injection (two 200 mg injections consecutively in different injection sites) followed by 200 mg given every other week. Refer to full PI for preparation, handling and administration. **Oral corticosteroid-dependent asthma or with co-morbid moderate-to-severe atopic dermatitis** or adults with co-morbid severe chronic rhinosinusitis with nasal polyposis: Initial dose of 600 mg by subcutaneous injection (two 300 mg injections consecutively in different injection sites) followed by 300 mg given every other week. **Asthma – Paediatric patients aged 6-11: Patients 15 kg to < 30 kg:** Initial dose of 100 mg followed by 100 mg given every other week, or an initial dose of 300 mg followed by 300 mg given every four weeks. **Patients 30 kg to < 60 kg:** Initial dose of 200 mg followed by 200 mg given every other week, or an initial dose of 300 mg followed by 300 mg given every four weeks. **Patients ≥ 60 kg:** Initial dose of 200 mg followed by 200 mg given every other week. **Chronic Rhinosinusitis with Nasal Polyposis:** The recommended dose of Dupixent for adult patients is an initial dose of 300 mg followed by 300 mg given every other week. Dupixent is intended for long-term treatment. Consideration should be given to discontinuing treatment in patients who have shown no response after 24 weeks of treatment for CRSwNP. Some patients with initial partial response may subsequently improve with continued treatment beyond 24 weeks. If after 24 weeks of treatment a patient's disease is stable, Dupixent may be given at a dose of 300 mg every four weeks in patients with CRSwNP who do not have comorbid asthma. **CONTRAINDICATIONS** Hypersensitivity to dupilumab or any of its excipients **PRECAUTIONS** Record the tradename and the batch number to improve traceability. Hypersensitivity, angioedema, helminth infections, conjunctivitis and keratitis, comorbid asthma, concomitant atopic conditions, eosinophilic conditions, acute asthma or deteriorating disease, gradual corticosteroid dose reduction. Refer to full PI. **INTERACTIONS** Live vaccines, No safety data on co-administration with other immunomodulators. Refer to full PI. **ADVERSE EFFECTS Atopic dermatitis:** Injection site reactions, conjunctivitis, conjunctivitis allergic, oral herpes, conjunctivitis bacterial, herpes simplex, eosinophilia, eye pruritus, blepharitis, dry eye, hypersensitivity – refer to full PI. **Asthma:** Injection site reactions, oropharyngeal pain, eosinophilia – refer to full PI. **Chronic Rhinosinusitis with Nasal Polyposis:** Injection site reactions, injection site swelling, conjunctivitis – refer to full PI. **Post marketing experience:** Angioedema, arthralgia, keratitis, ulcerative keratitis, facial rash. **NAME OF SPONSOR** sanofi-aventis australia pty ltd, 12-24 Talavera Road, Macquarie Park, NSW 2113. Based on Full Product Information with TGA date of approval of 29 June 2022 Date of Preparation: 30 June 2022

▼ This medicinal product is subject to additional monitoring in Australia. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at www.tga.gov.au/reporting-problems

BEYOND THE SKIN

Resources

Managing eye disorders in severe atopic dermatitis

DERMATOLOGY ADVENT ADVANCES IN TYPE 2 INFLAMMATORY DISEASES

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