Australian Government
Department of Health and Aged Care
Therapeutic Goods Administration

Australian Public Assessment Report for RANIVIZ

Active ingredient: ranibizumab

Sponsor: Actor Pharmaceuticals Pty Ltd

June 2024

About the Therapeutic Goods Administration (TGA)

- The Therapeutic Goods Administration (TGA) is part of the Australian Government Department of Health and Aged Care and is responsible for regulating therapeutic goods, including medicines, medical devices, and biologicals.
- The TGA administers the *Therapeutic Goods Act 1989* (the Act), applying a risk management approach designed to ensure therapeutic goods supplied in Australia meet acceptable standards of quality, safety, and efficacy.
- The work of the TGA is based on applying scientific and clinical expertise to decision-making, to ensure that the benefits to the Australian public outweigh any risks associated with the use of therapeutic goods.
- The TGA relies on the public, healthcare professionals and industry to report problems with therapeutic goods. The TGA investigates reports received to determine any necessary regulatory action.
- To report a problem with a therapeutic good, please see the information on the TGA website.

About AusPARs

- The Australian Public Assessment Report (AusPAR) provides information about the evaluation of a prescription medicine and the considerations that led the TGA to approve or not approve a prescription medicine submission. Further information can be found in Australian Public Assessment Report (AusPAR) guidance.
- AusPARs are prepared and published by the TGA.
- AusPARs are static documents that provide information that relates to a submission at a particular point in time. The publication of an AusPAR is an important part of the transparency of the TGA's decision-making process.
- A new AusPAR may be provided to reflect changes to indications or major variations to a prescription medicine subject to evaluation by the TGA.

Contents

List of abbreviations

Abbreviation	Meaning
ACM	Advisory Committee on Medicines
AE	Adverse Event
AMD	Age-related macular degeneration
ARTG	Australian Register of Therapeutic Goods
ASA	Australia-specific annex
BCVA	Best-corrected visual acuity
CMI	Consumer Medicines Information
CNV	Choroidal neovascularisation
COR	Comparable overseas regulator
DME	Diabetic macular oedema
DLP	Data lock point
EMA	European Medicines Agency
ETDRS	Early Treatment Diabetic Retinopathy Study
FAS_EU	Full analysis set for the EU
GMP	Good manufacturing practice
IVT	Intravitreal
nAMD	Neovascular (wet) AMD
PDR	Proliferative diabetic retinopathy
PI	Product Information
PM	Pathologic myopia
PSUR	Periodic safety update report
RMP	Risk management plan
RVO	Retinal vein occlusion
SAE	Serious adverse events
SOC	System organ class
TEAE	Treatment-Emergent Adverse Event
TGA	Therapeutic Goods Administration
TP	Tipping point
VA	Visual acuity
VEGF	Vascular Endothelial Growth Factor

Product submission

Submission details

Type of submission:	New biosimilar medicine
Product name:	RANIVIZ
Active ingredient:	Ranibizumab
Decision:	Approved
Date of decision:	12 December 2023
Date of entry onto ARTG:	20 December 2023
ARTG number:	400126
, *Black Triangle Scheme*	No
Sponsor's name and address:	Actor Pharmaceuticals Pty Ltd, Level 3 / 17 Randle Street, Surry Hills, NSW, 2010
Dose form:	Injection, solution
Strength:	10 mg / mL
Container:	Vial
Pack size:	1
Approved therapeutic use for the current submission:	RANIVIZ (ranibizumab) is indicated in adults for: • the treatment of neovascular (wet) age-related macular degeneration (AMD), • the treatment of visual impairment due to diabetic macular oedema (DME), • treatment of proliferative diabetic retinopathy (PDR), • the treatment of visual impairment due to choroidal neovascularisation, • the treatment of visual impairment due to choroidal neovascularisation (CNV) secondary to pathologic myopia (PM), • the treatment of visual impairment due to macular oedema secondary to retinal vein occlusion (RVO). Not recommended for use in preterm infants.
Route of administration:	Intravitreal-Within the Vitreous Cavity of The Eye
Dosage:	The recommended dose for RANIVIZ in adults is 0.5 mg given as a single intravitreal injection. This corresponds to an injection volume of 0.05 mL. The interval between two doses injected into the same eye should be at least four weeks. The recommended maximal dose (0.5 mg) should not be exceeded.
Pregnancy category:	D

Drugs which have caused, are suspected to have caused or may be expected to cause, an increased incidence of human fetal malformations or irreversible damage. These drugs may also have adverse pharmacological effects.

The use of any medicine during pregnancy requires careful consideration of both risks and benefits by the treating health professional. The pregnancy database must not be used as the sole basis of decision making in the use of medicines during pregnancy. The TGA does not provide advice on the use of medicines in pregnancy for specific cases. More information is available from obstetric drug information services in your state or territory.

Product background

This AusPAR describes the submission by Actor Pharmaceuticals Pty Ltd (the sponsor) to register RANIVIZ (ranibizumab) 10 mg / mL solution, injection, vial for the following proposed indications:

- the treatment of neovascular (wet) age-related macular degeneration,
- the treatment of visual impairment due to diabetic macular oedema,
- treatment of proliferative diabetic retinopathy,
- the treatment of visual impairment due to choroidal neovascularisation,
- the treatment of visual impairment due to choroidal neovascularisation secondary to pathologic myopia,
- the treatment of visual impairment due to macular oedema secondary to retinal vein occlusion.

The disease/condition

Age-related macular degeneration is the most common cause of legal blindness in the elderly population of the developed world. VEGF-A, known to promote both vascular growth and permeability, is considered to be responsible for the abnormal CNV. The most severe form of AMD is the wet form, characterised by abnormal CNV associated with vascular leak of lipids, fluid and blood leading to retinal oedema and retinal thickening. This cascade of events can profoundly impair visual acuity (VA) and ultimately produce a loss of vision. Besides neovascular (wet) AMD (nAMD), VEGF-A is thought to contribute to the pathophysiology of visual impairment due to CNV, DME and macular oedema secondary to retinal vein occlusion ([RVO], branch RVO or central RVO), proliferative diabetic retinopathy (PDR) in adults.

Current treatment options

The sponsor refers to the innovator LUCENTIS.

Thermal laser photocoagulation and photodynamic therapy are now only considered in rare cases or in a subset of AMD – polypoidal choroidal vasculopathy, where laser or photodynamic therapy is sometimes used when the neovascular lesion is well defined and extrafoveal.

Clinical rationale

RANIVIZ is developed to be a biosimilar to the biological reference product LUCENTIS, 10mg/ml solution for injection. Its active substance is ranibizumab, a recombinant, humanized antibody antigen-binding fragment (Fab) that binds selectively and with high affinity to vascular endothelial growth factor-A (VEGF-A). It belongs to the group of anti-neovascularization agents specifically developed for intraocular use. The binding prevents the interaction of VEGF-A with its receptors VEGFR-1 and VEGFR-2 on the surface of endothelial cells and thereby reduces neovascularization and vascular permeability as well as macular oedema and subsequent loss of vision.

Regulatory status

Australian regulatory status

This product is considered a new biosimilar medicine for Australian regulatory purposes.

Foreign regulatory status

This submission was submitted through the TGA's Comparable Overseas Regulator [B (COR-B)] process, using evaluation reports from European Medicines Agency (EMA). The full dossier was submitted to the TGA.

At the time the TGA considered this submission, a similar submission had been approved in EU (25 August 2022), UK (16 May 2022) and USA (02 August 2022). However, while all the PIs include the proposed indication of the treatment of visual impairment due to choroidal neovascularisation, all detail the treatment of visual impairment due to choroidal neovascularisation (CNV) secondary to pathologic myopia (PM) differently, which is included in the innovator (LUCENTIS) in Australia. Also, none approve use in pre-term infants.

Registration timeline

This submission was evaluated under the standard prescription medicines registration process.

Table 1 captures the key steps and dates for this submission.

Table 1: Timeline for Submission PM-2022-04707-1-5

Description	Date
Submission dossier accepted and first round evaluation commenced	3 January 2023
First round evaluation completed	21 April 2023
Sponsor provides responses on questions raised in first round evaluation	30 May 2023
Second round evaluation completed	3 July 2023
Sponsor's notification to the TGA of errors/omissions in evaluation reports	12 July 2023

Description	Date
Delegate's[1] Overall benefit-risk assessment	5 September 2023
Registration decision (Outcome)	12 December 2023
Administrative activities and registration in the ARTG completed	20 December 2023
Number of working days from submission dossier acceptance to registration decision*	134

*Statutory timeframe for standard submissions is 255 working days

* The COR-A process has a 120 working day evaluation and decision timeframe.

* The COR-B process has a 175 working day evaluation and decision timeframe.

Submission overview and risk/benefit assessment

Quality

The quality evaluator has confirmed that there are no objections on quality grounds to the approval of RANIVIZ.

The current application was submitted via the COR-B pathway. The quality evaluation report is based largely on the COR report from EMA and EMA's other evaluation reports provided in Module 1.11.4 via the COR-B process. Additional assessment on the Product Information, labels and stability were carried out to ensure the product meets Australian requirements.

Comprehensive characterisation studies support biosimilarity between RANIVIZ, EU LUCENTIS, US LUCENTIS and AU LUCENTIS with respect to structural, physicochemical, and biological properties.

Nonclinical

The non-clinical evaluation dossier was in accordance with the relevant EU guideline for similar monoclonal antibodies.1 The non-clinical evaluation dossier comprised a GLP compliant in vivo comparative single-dose toxicity study (including pharmacokinetics). This study was conducted using EU- and US-sourced LUCENTIS as the reference products. The non-clinical evaluation summary and conclusions are based on the EMA evaluation report.

The ability of the nonclinical studies to support comparability to RANIVIZ depends on the conclusion of the quality evaluator regarding the identity of ranibizumab-containing products across jurisdictions. Provided that EU– and US–sourced LUCENTIS are considered to be identical or highly comparable to the proposed Australian product, there are no nonclinical objections to the registration of RANIVIZ.

[1] In this report the 'Delegate' is the Delegate of the Secretary of the Department of Health and Aged Care who decided the submission under section 25 of the Act.

Clinical

The following clinical studies were undertaken:

Pharmacology

Pharmacokinetics (PK)

No PK studies in healthy volunteers were conducted for ethical and safety reasons (Intravitreal mode of application) and no pivotal PK study in the target population was performed. The comparative systemic exposure was to be shown as a safety endpoint in a subset of patients with neovascular AMD within the confirmatory comparative clinical safety and efficacy study FYB201-C2015- 01-P3. Overall, the total number of patients with positive ADAs in blood serum was low and comparable between treatment arms. This is considered acceptable.

Pharmacodynamics (PD)

From a PD perspective, the mechanism of action of ranibizumab is sufficiently described by the applicant and no concerns are raised given the absence of obvious PD biomarkers.

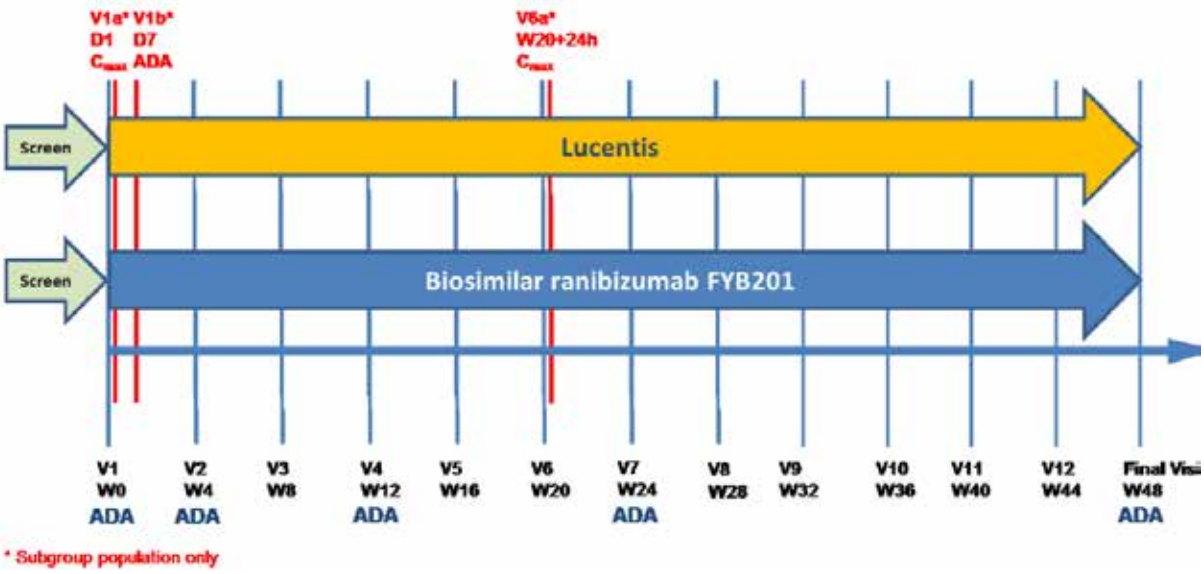
Efficacy

Test and reference product have the same qualitative and quantitative formulation and dose strength and use the same route of administration, dosage regimen and treatment duration based on the currently approved US Prescribing Information for LUCENTIS.

Study FYB201-C2015-01-P3 (COLUMBUS-AMD)

This was a 12-month (48-week), Phase III, randomised, active-controlled, evaluation-masked, parallel group, multicentre study to demonstrate clinical equivalence in terms of clinical pharmacology, efficacy and safety of RANIVIZ with US-LUCENTIS in the treatment of patients with sub foveal nAMD.

Figure 1: Schematic of study design



All patients received monthly IVT injections for a period of approximately 12 months (48 weeks). Patients were studied for approximately 5 months (20 Weeks) and received 6 IVT injections up to the main analysis, and for 12 months (48 Weeks) receiving 12 IVT injections up to the final analysis. All patients had a final follow-up visit at Week 48 (Month 12).

Analysis of study data was performed after 24 Weeks (main analysis) and 48 Weeks (final analysis). No formal interim analysis was planned or performed for this study.

The primary objective was to evaluate and compare functional changes in best corrected visual acuity (BCVA- by Early Treatment Diabetic Retinopathy Study (ETDRS)) letters after 2 months (8 weeks) of treatment with RANIVIZ or LUCENTIS, compared to baseline BCVA.

Two analyses were to be conducted:

A main analysis after all randomised patients have either completed the Week 24 assessments or have discontinued the study before 24 Weeks (database lock: 20-Apr-2018)

A final analysis after all randomised patients have either completed the Week 48 assessments or have discontinued the study (database lock: 01-Oct-2018).

Participant flow:

Table 2: Patients in each analysis set - All randomized patients

	FYB201 (N = 238)		Lucentis (N = 239)		Total (N = 477)	
Analysis Set	**n**	**%**	**n**	**%**	**n**	**%**
Safety Set (SAF)	238	100.0%	239	100.0%	477	100.0%
Full Analysis Set for EU (FAS_EU)	215	90.3%	214	89.5%	429	89.9%
Per Protocol Set for EU (PPS_EU)	200	84.0%	202	84.5%	402	84.3%
Pharmacokinetic Subgroup Analysis Set (PKS)	29	100.0%	30	96.8%	59	98.3%

N = total number of patients, n = number of patients in corresponding class, % = number of patients in corresponding class/ total number of patients x 100, SAF: Safety set, FAS_EU = Full analysis set for the EU; PPS_EU = Per protocol set for the EU Percentages are based on the number of patients randomized within each group, whereby the patients are tabulated according, to the planned treatment. Source: Table 28 CHMP assessment report day 210 page 111

Results for the primary efficacy outcome

The primary efficacy analysis for the change from BL in BCVA by ETDRS letters at Week 8 was based on the FAS_EU population. A mean change from baseline BCVA at Week 8 of 5.2 ETDRS letters (SD 7.75) was reached for RANIVIZ and of 6.0 ETDRS letters for LUCENTIS (SD 8.42).

Table 3: Absolute change from baseline in BCVA [ETDRS letters] at analysis visit V3/Week 8- FAS_EU

	FYB201 (N = 200)	Lucentis (N = 202)	Total (N = 402)
Absolute change from baseline in BCVA [ETDRS letters] at analysis visit V3/Week 8			
N*	200	202	402
n	200	202	402
Missing	0	0	0
Mean (SD)	5.3 (7.82)	6.2 (8.39)	5.8 (8.12)
Median	5.0	6.0	5.0
Interquartile range (Q1–Q3)	0.0–10.5	1.0–12.0	1.0–11.0
Range (min–max)	-16–30	-33–25	-33–30

BCVA = best-corrected visual acuity, ETDRS = Early Treatment Diabetic Retinopathy Study, FAS_EU = full analysis set for the EU, N = number of patients in corresponding class, N* = total number of patients still in the study for the respective analysis visit, n = number of patients with non-

missing assessment, Missing number of patients with missing assessment, Q1 = first quartile, Q3 = third quartile
Source Table 11-6 CSR

Table 4: ANCOVA for change from baseline in BCVA [ETDRS letters] at analysis visit V3/Week 8 - FAS_EU

	n	Missing	Arithmetic mean	LS mean[1]	SE LS mean	95% CI
FYB201	200	0	5.3	5.2	0.62	[4.0; 6.4]
Lucentis	202	0	6.2	6.0	0.62	[4.8; 7.2]
Difference						
FYB201 - Lucentis			-0.9	-0.8	0.82	[-2.4; 0.8]
CI contained in]-3.5; 3.5[[2]						**yes**

1 Estimates are adjusted for pooled country and baseline BCVA [letters).

2 If confidence interval for difference in LS means is completely contained in the interval]-3.5 letters, 3.5 letters[. FYB201 and LUCENTIS are considered equivalent.

ANCOVA = Analysis of Covariance, BCVA = best-corrected visual acuity, ETDRS = Early Treatment Diabetic Retinopathy Study, FAS_EU = full analysis set for the EU, n = number of patients with non-missing assessment at analysis visit V3/Week 8, Missing = number of patients with missing assessment at analysis vis it V3/Week 8, SE = standard error

Two-sided 95% confidence interval based on normal approximation.

Source: Table 11-7 CSR

Biosimilarity was shown by the LS means difference between both treatments of -0.7 ETDRS letters with a 95% CI of [-2.3; 0.9] ETDRS letters, which was completely contained within the pre-defined equivalence margin of ± 3.5 letters.

The sensitivity analysis using the PP population was supportive, as was an MMRM using data from all patients in the FAS_EU population.

The sponsor provided tipping point (TP) analysis where several scenarios were considered for shift parameter θ for missing observations estimated by MI method. The results all implied that the main conclusion is robust to all sensible deviations from MAR.

No subgroup analyses had been performed for the primary endpoint. Upon request, the Applicant provided additional subgroup analyses by pooled country, total lesion area, and loss in vision acuity at baseline.

Overall, biosimilarity was supported in almost all subgroups and no systematic problems were identified.

Several functional and anatomical parameters were assessed as secondary efficacy endpoints, in order to support demonstration of similar efficacy between RANIVIZ and LUCENTIS.

Safety

Study FYB201-C2015-01-P3 (COLUMBUS-AMD)

Study duration was 12 months, with 12 monthly injections. A study duration of 12 months is considered a relevant time period to assess safety and immunogenicity in a biosimilarity exercise. Per treatment arm, 238 (RANIVIZ) and 239 (US-LUCENTIS) patients were included, respectively.

A total of 321 patients (67.3%) reported 1106 TEAEs at any time after the first dose of the study drug until the End of Study (EOS). The incidence and severity of the reported TEAEs were generally comparable between the RANIVIZ and US-LUCENTIS treatment arms.

The most commonly affected preferred terms (PTs) in the SOC eye disorders were neovascular age-related macular degeneration (RANIVIZ: n = 19 [8.0%]; US-LUCENTIS: n = 22 [9.2%]), Conjunctival haemorrhage (RANIVIZ: n = 14 [5.9%]; US-LUCENTIS: n = 19 [7.9%]), and Punctate keratitis (RANIVIZ: n = 8 [3.4%]; US-LUCENTIS: n = 12 [5.0%]).

Based on these analyses, no distinct differences between treatment arms can be detected with regard to incidences of ocular TEAEs, related ocular TEAEs, severe ocular TEAEs, related severe TEAEs, serious ocular TEAEs and related serious ocular TEAEs, neither in the study eye nor in the fellow eye.

Most TEAEs were of mild or moderate intensity: few TEAEs were severe (19 TEAEs in 11 patients in the RANIVIZ arm and 32 TEAEs in 22 patients in the US-LUCENTIS arm). Severe TEAEs were recorded in twice as many patients in the LUCENTIS arm, but without clinically relevant differences or increased frequency in particular SOCs.

No distinct differences between treatment arms can be detected with regard to incidences of ocular TEAEs, related ocular TEAEs, severe ocular TEAEs, related severe TEAEs, serious ocular TEAEs and related serious ocular TEAEs, neither in the study eye nor in the fellow eye.

Frequency and type of "local" (study eye or both eyes) TEAEs were overall comparable between both treatment groups, and no clinically relevant differences were identified.

Ocular adverse events that were expected to occur (very) commonly (according to the LUCENTIS SmPC) were overall comparable between treatment arms in the present study, although it is notable that some AEs occurred at lower-than-expected rates (such as IOP increased, conjunctival haemorrhage).

Treatment related adverse events (adverse drug reactions)

A total of 45 patients experienced treatment related[5] TEAEs (FYB201: 20 patients; 8.4% and LUCENTIS: 25 patients; 10.5%). TEAEs related to study drug were most frequently recorded in SOC Eye disorders (28 patients; 5.9%) with PTs: Cataract (5 patients; 1.0%), Retinal pigment epithelial tear (4 patients; 0.8%), Visual acuity reduced (3 patients; 0.6%), and Punctate keratitis and Vitreous haemorrhage (2 patients each; 0.4%), other PTs were recorded in single patients.

AEs related to intravitreal (IVT) injection procedure

IVT procedure related TEAEs occurred in 21.4% of patients in the RANIVIZ group (n = 51) and in 27.6% of the patients in the LUCENTIS group (n = 66). Frequent PTs for IVT procedure related TEAEs were reported in SOC Eye disorders for PTs Conjunctival haemorrhage (RANIVIZ: n = 13 [5.5%]; US-LUCENTIS: n = 19 [7.9%]) and Punctate keratitis (RANIVIZ: n = 6 [2.5%]; US-LUCENTIS: n = 11 [4.6%]) and in SOC Investigations for PT Intraocular pressure increased (RANIVIZ: n = 8 [3.4%], US-LUCENTIS: n = 9 [3.8%]). Overall, TEAEs related to study drug as well as to the IVT injection procedure were observed at numerically higher frequencies in the US-LUCENTIS group than for RANIVIZ. The same holds true for severe TEAE, which were recorded in twice as many patients in the LUCENTIS arm.

Serious adverse events

30 SAEs were reported for 19 patients (8.0%) in the RANIVIZ arm, whereas 45 events were reported for 32 patients (13.4%) in the US-LUCENTIS arm.

Ocular (Study eye) SAEs6

2 patients in the RANIVIZ experienced endophthalmitis and iridocyclitis, and 3 patients in the US-LUCENTIS arm experienced cataract (1 patient) and endophthalmitis (2 patients). One endophthalmitis case was judged as related to study drug and to IVT procedure, the other 2 cases were judged as related to the IVT procedure only. The case of cataract was related to the IVT procedure and the iridocyclitis case was related to both study drug and IVT procedure. Only for 1 patient in the LUCENTIS arm did the endophthalmitis lead to interruption of study drug administration. All patients recovered from the local SAEs.

Systemic SAEs

The frequency of systemic SAEs was somewhat higher in the LUCENTIS group with 29 patients (12.1%) compared to 17 patients (7.1%) in the RANIVIZ group. Overall, 6 of the serious TEAEs reported in 6 patients were judged as related to study medication. Among these were 4 systemic related SAEs, two in the RANIVIZ group (myocardial infarction and transient ischaemic shock) and two in the LUCENTIS group (cerebrovascular accident and circulatory collapse).

Deaths

Three patients died during the study; 2 patients in the RANIVIZ group (PTs: chronic obstructive pulmonary disease and cardiopulmonary failure) and 1 patient (PT: respiratory failure) in the LUCENTIS group. All were unlikely related to study drug or to the IVT procedure.

Risk management plan

The summary of safety concerns and their associated risk monitoring and mitigation strategies are presented in Table 5. The TGA may request an updated RMP at any stage of a product's life-cycle, during both the pre-approval and post-approval phases.

Actor Pharmaceuticals Pty Ltd has submitted EU-RMP version 1.0 (date 8 June 2022; DLP 14 June 2021) and ASA version 0.1 (date 9 November 2022) in support of this application. At round 2, the sponsor has provided ASA version 0.2 (date 12 May 2023) in association with previously submitted EU-RMP version 1.0 (date 8 June 2022; DLP 14 June 2021).

The proposed summary of safety concerns and their associated risk monitoring and mitigation strategies are summarised below:

Table 5: Summary of safety concerns

Summary of safety concerns		Pharmacovigilance		Risk minimisation	
		Routine	Additional	Routine	Additional
Important identified risks	Infectious endophthalmitis	P	-	P	P
	Intraocular inflammation	P	-	P	P
	Retinal detachment and retinal tear	P	-	P	P
	Intraocular pressure	P	-	P	P
Important potential risks	None	-	-	-	-

Summary of safety concerns		Pharmacovigilance		Risk minimisation	
		Routine	Additional	Routine	Additional
Missing information	None	-	-	-	-

The proposed summary of safety concerns aligns with the safety concerns in the EU RMP for RANIVIZ and other biosimilar's with the same indications. The safety concerns relating to the ROP indication for pre-term infants in the reference product's RMP has been removed. The safety specifications, this is considered acceptable from an RMP perspective.

The proposed pharmacovigilance plan and the proposed risk minimisation is acceptable from an RMP perspective.

The RMP evaluated recommended the following wording for conditions of registration, relating to the versions of the risk management plan:

The RANIVIZ EU-Risk Management Plan (RMP) (version 1.0, dated 8 June 2022, data lock point 14 June 2021), with Australian Specific Annex (version 0.2, dated 12 May 2023), included with submission PM-2022-04707-1-5, and any subsequent revisions, as agreed with the TGA will be implemented in Australia.

Risk-benefit analysis

Delegate's considerations

Quality:

The Module 3 evaluator concluded that there were no objections on quality grounds to the approval of RANIVIZ.

The current application was submitted via the COR-B pathway. The quality evaluation report is based largely on the COR and other reports from the EMA. Additional assessment on the Product Information, labels and stability were carried out to ensure the product meets Australian requirements.

Comprehensive characterisation studies support biosimilarity between RANIVIZ, EU LUCENTIS, US LUCENTIS and AU LUCENTIS with respect to structural, physicochemical, and biological properties.

Efficacy:

In the pivotal comparative efficacy study COLUMBUS-AMD in nAMD patients, equivalence between RANIVIZ and US-LUCENTIS was demonstrated for the primary efficacy endpoint, both in the FAS and in the PP population. This was supported by sensitivity analyses. Several functional and anatomical parameters were assessed as secondary efficacy endpoints, to support demonstration of similar efficacy between RANIVIZ and LUCENTIS.

Overall, comparability of RANIVIZ to LUCENTIS was demonstrated for all efficacy endpoints.

The sponsor provided scientific justification for the inclusion of the indication, "Treatment of visual impairment due to choroidal neovascularisation (CNV) secondary to pathologic myopia".

The justification for extrapolation is based on:

- The mechanism(s) of action in each condition of use for which marketing authorization is sought.

- The evaluation of differences in expected toxicities in each condition of use and patient population.

This is considered acceptable.

Safety:

The exposure to study drug was overall comparable. Per treatment arm, 238 (RANIVIZ) and 239 (US-LUCENTIS) patients were included, respectively. The present sample size is sufficiently large to conclude on comparability in terms of common or very common adverse effects.

The number of patients who discontinued treatment was similar in both treatment arms (n = 16 in each arm). The overall number and percentage of TEAEs was comparable between the two treatment groups. Overall, the SOC Eye disorders was the most commonly affected SOC for both treatment arms in the SAF. Severe TEAEs were recorded in twice as many patients in the LUCENTIS arm, but without clinically relevant differences or increased frequency in particular SOCs. No distinct differences between treatment arms can be detected with regard to incidences of ocular TEAEs, related ocular TEAEs, severe ocular TEAEs, related severe TEAEs, serious ocular TEAEs and related serious ocular TEAEs, neither in the study eye nor in the fellow eye. In summary, the safety evidence is compatible with biosimilarity.

Proposed action

Biosimilarity of RANIVIZ to LUCENTIS has been satisfactorily demonstrated, supporting a favourable benefit-risk for RANIVIZ in the proposed indications. There are no objections on quality grounds to the approval of RANIVIZ. There are no outstanding clinical issues requiring advice from ACM.

Outcome

Based on a review of quality, safety, and efficacy, the TGA decided to register RANIVIZ (ranibizumab) 10 mg / mL, solution for injection, vial, is indicated in adults for:

- the treatment of neovascular (wet) age-related macular degeneration (AMD),
- the treatment of visual impairment due to diabetic macular oedema (DME),
- treatment of proliferative diabetic retinopathy (PDR),
- the treatment of visual impairment due to choroidal neovascularisation,
- the treatment of visual impairment due to choroidal neovascularisation (CNV) secondary to pathologic myopia (PM),
- the treatment of visual impairment due to macular oedema secondary to retinal vein occlusion (RVO).

Not recommended for use in preterm infants.

Attachment 1. Product Information

The Product Information (PI) approved with the submission for [Tradename] which is described in this AusPAR can be found as Attachment 1. It may have been superseded. For the most recent PI and Consumer Medicines Information (CMI), please refer to the TGA PI/CMI search facility.

Therapeutic Goods Administration

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Reference/Publication #