Australian Government
Department of Health, Disability and Ageing
Therapeutic Goods Administration

Australian Public Assessment Report for Andriga

Active ingredients: abiraterone, prednisolone

Sponsor: Actor Pharmaceuticals Pty Ltd

March 2026

About the Therapeutic Goods Administration (TGA)

- The Therapeutic Goods Administration (TGA) is part of the Australian Government Department of Health, Disability and Ageing 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
ADT	Androgen deprivation therapy
ARTG	Australian Register of Therapeutic Goods
$AUC_{(0-t)}$	Area under the plasma concentration-time curve from the first time point [t=0] to the time point of the last measured concentration [t(last)]
$AUC_{(0-\infty)}$	Area under the plasma concentration-time curve from the first time point [t=0] to infinity [∞]
$AUC_{(t-\infty)}$	Residual area, extrapolated area expressed as fraction of $AUC_{(0-\infty)}$
C_{max}	Maximum plasma concentration
CMI	Consumer Medicines Information
CSPC	metastatic castration sensitive disease
mCRPC	castration resistant prostate cancer
mHSPC	Hormone sensitive prostate cancer
NMT	No more than
PI	Product Information
PSA	PSA
PSUR	Periodic safety update report
RMP	Risk management plan
TGA	Therapeutic Goods Administration
T_{max}	Time of maximum plasma concentration
λz	Elimination rate constant

Product submission

Submission details

Type of submission:	New combination (of previously approved active ingredients)
Product names:	Andriga-5, Andriga-10
Active ingredient:	Abiraterone acetate and prednisolone
Decision:	Approved
Date of decision:	29 January 2025
Approved therapeutic use for the current submission:	Andriga-5 is indicated for the treatment of newly diagnosed high-risk metastatic hormone sensitive prostate cancer (mHSPC) in combination with androgen deprivation therapy (ADT). Andriga-10 is indicated for the treatment of: • patients with metastatic advanced prostate cancer (castration resistant prostate cancer, mCRPC) who are asymptomatic or mildly symptomatic after failure of androgen deprivation therapy (ADT) or • patients with mCRPC who have received prior chemotherapy containing a taxane.
Date of entry onto ARTG:	7 July 2025
ARTG numbers:	Andriga-5 (437512) Andriga-10 (437511)
▼*Black Triangle Scheme*	No
Sponsor's name and address:	Actor Pharmaceuticals Pty Ltd, Level 6, 50 Berry Street, North Sydney NSW 2060, Australia
Dose form:	Abiraterone: Tablet, film coated Prednisolone: Tablet
Strength:	Each abiraterone film-coated tablet contains 500 mg abiraterone acetate. Each prednisolone tablet contains 5 mg prednisolone
Container:	Andriga-5 and Andriga-10 are supplied in a polyvinyl chloride/polyvinylidene chloride -aluminium combination blister packed in a carton.
Pack size:	Andriga-5 is a composite blister pack containing 2 medicinal products: • abiraterone acetate 1000 mg (as two 500 mg film-coated tablets) and prednisolone 5 mg (as one 5 mg tablet). Andriga-10 is a composite blister pack containing 2 medicinal products:

	• abiraterone acetate 1000 mg (as two 500 mg film-coated tablets) and prednisolone 10 mg (as two 5 mg tablets).
Route of administration:	Oral
Dosage:	For information regarding dosage, refer to the Product Information.
Pregnancy category:	**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. Accompanying texts should be consulted for further details. 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 Andriga-5 (generic abiraterone acetate 1000 mg and generic prednisolone 5 mg) and Andriga-10 (generic abiraterone acetate 1000 mg and generic prednisolone 10 mg). The reference medicine for the abiraterone acetate 500 mg film-coated tablet is Zytiga 500 mg film-coated tablets (ARTG no. 275372), currently registered by Janssen-Cilag Pty Ltd. The prednisolone 5 mg tablets are proposed as a generic to the reference medicine, Panafcortelone 5 mg tablets (ARTG no. 27962) currently registered by Aspen Pharmacare Australia Pty Ltd. The proposed indications are:[1]

> *Andriga-5 is indicated for the treatment of newly diagnosed high-risk metastatic hormone sensitive prostate cancer (mHSPC) in combination with androgen deprivation therapy (ADT).*
>
> *Andriga-10 is indicated for the treatment of:*
>
> *-patients with metastatic advanced prostate cancer (castration resistant prostate cancer, mCRPC) who are asymptomatic or mildly symptomatic after failure of androgen deprivation therapy (ADT) or*
>
> *-patients with mCRPC who have received prior chemotherapy containing a taxane.*

[1] This is the original indication proposed by the sponsor when the TGA commenced the evaluation of this submission. It may differ to the final indication approved by the TGA and registered in the Australian Register of Therapeutic Goods.

Disease or condition

Epidemiology

Prostate cancer is the commonest cancer in males worldwide. It is estimated that there are 1.6 million cases of prostate cancer and 366,000 deaths per year.[2]

Prostate cancer is the third most common cause of cancer death in Australia. In Australia, around 24,000 new cases are diagnosed per year, constituting around 27% of all cancers in males. Around 3500 people die from prostate cancer per year, constituting around 13% of cancer deaths in males.

The overall prevalence of prostate cancer in Australia is around 20,000.[3] The standardised incidence rate is around 150 cases per 100,000 males per year.[4] The age standardised mortality is 22 cases per 100,000 men per year.[5] Approximately 12.8% of men will be diagnosed with prostate cancer during their lifetime.[6]

Contemporary diagnosis and treatment have significantly improved the outlook for patients with prostate cancer. The 5-year survival from prostate cancer increase from 63% (1989-1993) to 97.5% (2014-2020).[7]

Prostate cancer is frequently asymptomatic at presentation. The commonest method of early detection is via an elevated prostate specific antigen (PSA) level in the blood. Normal range for PSA varies with age and is affected by confounding factors such as perineal trauma, intercurrent prostatitis or certain medications. Digital rectal examination alone (DRE) fails to detect a significant number of cancers. The decision to undertake biopsy depends on PSA, DRE, imaging results (MRI or PET scan) and expected life span.[8]

At the time of diagnosis, 79.5% of patients have localised cancer, 15% have regional lymph node involvement and 10.8% have distant metastases.[9]

Diagnosis – non metastatic disease

The diagnosis of non-metastatic prostate cancer requires histologic examination of tissue obtained on prostate biopsy.

Histology

Ninety-five percent of prostate cancers are adenocarcinomas. The Gleason grade is based solely on the architectural features of prostate cancer cells and closely correlates with clinical behaviour. A higher score indicates a higher likelihood of non-organ confined disease, and worse outcomes after treatment. The Gleason score is derived by adding together the Gleason grade for the two most prominent architectures. Pathologists will not diagnose prostate cancer on tissue from needle biopsy where the Gleason *score* is 2-5. Hence the Gleason score range for prostate

[2] Global Burden of Disease Cancer Collaboration; Global, Regional, and National Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life-years for 32 Cancer Groups, 1990 to 2015: A Systematic Analysis for the Global Burden of Disease Study. JAMA Oncol. 2017 Apr 1;3(4):524-548. doi: 10.1001/jamaoncol.2016.5688. Erratum in: JAMA Oncol. 2017 Mar 1;3(3):418. doi: 10.1001/jamaoncol.2017.0098. PMID: 27918777; PMCID: PMC6103527.

[3] *Cancer Australia*, 'Prostate cancer in Australia statistics' updated 18 December 2025.

[4] *National Cancer Control Indicators.* Prostate Cancer Incidence.

[5] *National Cancer Control Indicators.* Prostate Cancer Mortality.

[6] National Cancer Institute. Surveillance, Epidemiology and End Results Program (SEER) Cancer Stat Facts: Prostate Cancer.

[7] *National Cancer Control Indicators.* 5-year relative survival from diagnosis

[8] Mary-Ellen Taplin, MD, Joseph A Smith, MD. Clinical presentation and diagnosis of prostate cancer. *UptoDate.com.* Updated Feb 11, 2026.

[9] National Cancer Institute. Surveillance, Epidemiology and End Results Program (SEER). Cancer Statistics Explorer Network.

cancer is 6-10. The Gleason score is combined with the Tumour Node Metastasis (TNM) score to derive a histological grade group and predict prognosis.[10]

In a validation study of the histological grade grouping the following increasing mortality was observed:[11]

- Grade group 1: Gleason score ≤6
- Grade group 2: Gleason score 3+4 = 7 (hazard ratio [HR] for death 2.8 relative to grade group 1)
- Grade group 3: Gleason score 4+3 = 7 (HR 6.0 relative to grade group 1)
- Grade group 4: Gleason score = 8 (including 4+4 = 8, 3+5 = 8, or 5+3 = 8; HR 7.1 relative to grade group 1)
- Grade group 5: Gleason scores 9 to 10 (4+5, 5+4, or 5+5; HR 12.7 relative to grade group 1)

The five-year recurrence-free survival rates were 95, 83, 65, 63, and 35 percent, respectively, for grade group 1, 2, 3, 4, and 5.[12]

Clinically insignificant prostate cancer

Autopsy studies initially noted that there was a disproportionate number of prostate cancers that never caused any symptoms, and subsequent randomized trials confirmed that a great proportion of cancers diagnosed through prostate-specific antigen (PSA) screening were "clinically insignificant" (i.e., very low risk) … The identification of those males who have clinically insignificant prostate cancer has been the centre of prostate cancer research for decades.

Although debated, current definitions of insignificant cancer based on pathologic findings at needle biopsy include grade group 1 cancer, <3 cores with cancer, and ≤50 percent of core involved by cancer. These patients can choose to be followed on an active surveillance program, although significant percentages of cases will progress to higher-grade and higher-volume tumour if not treated; the latent period of progression is uncertain. Because of this, close follow-up with serum PSA, repeat biopsy, and/or magnetic resonance imaging is necessary to detect early progression…Grade group 1 prostatic adenocarcinoma of a small volume can thus be considered an early phase of prostate cancer, which can be clinically insignificant.[13]

Perineural invasion and extraprostatic extension

Perineural invasion (PNI) in a core biopsy is an important predictor of pathologic stage, with most, but not all studies finding a correlation between PNI on biopsy and extraprostatic extension at the time of prostatectomy. Extraprostatic extension is usually documented only at the time of radical prostatectomy, but direct extension of tumour cells beyond the confines of

[10] van Leenders GJLH, van der Kwast TH, Grignon DJ, Evans AJ, Kristiansen G, Kweldam CF, Litjens G, McKenney JK, Melamed J, Mottet N, Paner GP, Samaratunga H, Schoots IG, Simko JP, Tsuzuki T, Varma M, Warren AY, Wheeler TM, Williamson SR, Iczkowski KA; ISUP Grading Workshop Panel Members. The 2019 International Society of Urological Pathology (ISUP) Consensus Conference on Grading of Prostatic Carcinoma. Am J Surg Pathol. 2020 Aug;44(8):e87-e99. doi: 10.1097/PAS.0000000000001497. PMID: 32459716; PMCID: PMC7382533

[11] Berney DM, Beltran L, Fisher G, North BV, Greenberg D, Møller H, Soosay G, Scardino P, Cuzick J. Validation of a contemporary prostate cancer grading system using prostate cancer death as outcome. Br J Cancer. 2016 May 10;114(10):1078-83. doi: 10.1038/bjc.2016.86. Epub 2016 Apr 21. PMID: 27100731; PMCID: PMC4865975

[12] Carter HB, Partin AW, Walsh PC, Trock BJ, Veltri RW, Nelson WG, Coffey DS, Singer EA, Epstein JI. Gleason score 6 adenocarcinoma: should it be labeled as cancer? J Clin Oncol. 2012 Dec 10;30(35):4294-6. doi: 10.1200/JCO.2012.44.0586. Epub 2012 Oct 1. PMID: 23032616; PMCID: PMC3515766

[13] Ximing J Yang. Interpretation of prostate biopsy. UptoDate.com

the prostatic capsule into periprostatic adipose tissue can occasionally be observed in needle biopsy specimens. The presence of extraprostatic extension is clinically significant because it changes the tumour stage to a clinical T3 lesion, which constitutes locally advanced disease.'[13]

Diagnosis – metastatic disease

'Individuals who present with symptomatic metastatic disease with a metastatic pattern typical for prostate cancer (i.e., bone metastases) and an elevated PSA usually do not need a prostate biopsy. For patients presenting with de novo metastatic disease, if confirmation of the diagnosis is clinically indicated, this can generally be obtained from histologic examination of a biopsy specimen from a metastatic focus, which is less invasive than a prostate biopsy.'

Germline testing

According to the National Comprehensive Cancer Network guidelines, germline testing for alterations in homologous recombination DNA repair genes (e.g., *BRCA1*, *BRCA2*, *ATM*, *CHEK2*) is suggested for males with very low-risk, low-risk, and intermediate-risk disease if family history is positive for an inherited cancer predisposition syndrome or if the prostate tumour shows intraductal histology. Intraductal histology is enriched for mutations in homologous recombination DNA repair genes (e.g., *BRCA2*). Genetic results may influence the management of males with early-stage prostate cancer:

- Germline mutations in *BRCA1, BRCA2, ATM* and *CHEK2* have been associated with lethal prostate cancer.
- Males found to have *BRCA* or *ATM* mutations have a higher risk of grade reclassification among males undergoing active surveillance'

Clinical versus pathologic staging

For patients who undergo radical prostatectomy, additional information about the extent of disease is obtained from the surgical specimen, and this forms the basis for pathologic staging. When this reveals poor prognostic features (Gleason grade higher than the original biopsy, extraprostatic extension, seminal vesicle involvement, or lymph node involvement), additional therapy may be recommended following prostatectomy.

Current treatment options

Localised disease

The choice of treatment for an individual patient with a non-high-grade localized prostatic adenocarcinoma are external beam radiation therapy (RT) with or without brachytherapy, brachytherapy alone, radical prostatectomy, or active surveillance.

Recurrent or metastatic prostate cancer

The role of androgens in stimulating prostate cancer was identified more than 60 years ago.[14] These findings led to the development of ADT as a treatment for patients with advanced prostate cancer. Although ADT is palliative, it can normalize serum levels of prostate-specific antigen (PSA) in over 90 percent of patients and can produce objective tumour responses in 80 to 90 percent. This antitumor activity can improve quality of life by reducing bone pain as well as the

[14] Huggins C, Hodges CV Studies on prostatic cancer: I. The effects of castration, of estrogen, and of androgen injection on serum phosphatases in metastatic carcinoma of the prostate. Cancer Res. 1941; 1:293

rates of complications (e.g., pathologic fracture, spinal cord compression, ureteral obstruction).[15]

Some males with advanced prostate cancer have evidence of metastatic disease at presentation, while others develop metastatic disease after definitive treatment of localized disease; in some cases, this may be manifested only by an elevation in the serum level of PSA, termed an isolated biochemical recurrence. The majority of males in all three groups have not been receiving long-term ADT, and serum testosterone levels are typically >50 ng/dL. These males are considered to have castration-sensitive prostate cancer (CSPC).

By contrast, males who relapse or recur while receiving ADT are considered to have castration-resistant prostate cancer (CRPC), although they may still respond to some forms of hormone therapy.

Contemporary research has led to the development of multiple combined modality approaches for males with advanced CSPC that are associated with better outcomes than can be achieved with ADT alone. The goals of systemic therapy are to prolong survival, minimize complications, and maintain quality of life. In addition to systemic therapy, there are some patients who might benefit from local therapy to the prostate or to individual metastases to prolong survival.

Combination therapy with androgen deprivation therapy

- ADT plus abiraterone/prednisone
  - abiraterone blocks intracellular conversion of androgen precursors
  - Initially shown to prolong survival in castration resistant disease (CRPC)
  - Randomised controlled trials (RCT) show prolonged survival in patients with high risk localized disease and metastatic castration sensitive disease (CSPC) compared to ADT alone.
- ADT plus enzalutamide or apalutamide
  - Binds to androgen binding site on androgen receptor and act as inhibitor
  - 3 RCT show benefit over ADT alone for CSPC.
- ADT plus docetaxel
  - Docetaxel prolongs survival in mCRPC.
  - Combination with ADT provides further survival benefit.
- Triplet therapy
  - Docetaxel plus ADT plus third systemic agent e.g. abiraterone
  - Improves survival over ADT plus docetaxel.

If doublet therapy is chosen, there are only limited clinical trial data comparing the combination of ADT plus abiraterone versus ADT plus docetaxel, and there are no data comparing either of these approaches with ADT plus either apalutamide or enzalutamide.

Given the lack of comparative data supporting one approach over any other, the choice of the specific regimen is usually based on disease extent, and a discussion with the patient about

[15] Dawson NA, Overview of systemic treatment for recurrent or metastatic castration-sensitive prostate cancer. UpToDate.com

potential toxicities associated with abiraterone, docetaxel, apalutamide, and enzalutamide, as well as the expected duration and cost of treatment.

Clinical rationale

The use of abiraterone for the treatment of mCRPC and mHSPC is recommended worldwide in combination with a glucocorticoid (such as prednisolone). This is based on the clinical action of abiraterone, which leads to unacceptable adverse events in most patients when given alone. Since the demonstration that addition of glucocorticoids mitigate the adverse effects of abiraterone, this combination therapy of abiraterone plus glucocorticoid was established as the treatment of first choice for the treatment of mCRPC and mHSPC.

Glucocorticoids also show an additive decreasing effect on testosterone levels when added to abiraterone monotherapy, leading to a higher efficacy of the combination when compared to abiraterone alone. Prednisolone causes fewer adverse metabolic effects and is the glucocorticoid of choice in this combination product.

An additional advantage of the combination package is the increased likelihood of compliance by patients. In this case, a combination medicinal product is not possible, therefore, a combination blister package was the optimal means by which to increase compliance and patient convenience.

Regulatory status

Australian regulatory status

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

International regulatory status

At the time the TGA considered this submission, a similar submission had been approved in Germany. The sponsor had submitted an application with Germany acting as the Reference Member State (RMS) leading the Decentralised Procedure. The drug is only approved in Germany and not in any specific Concerned Member States.

Registration timeline

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

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

Table 1. Timeline for Andriga (abiraterone and prednisolone), Submission PM-2024-00131-1-4

Description	Date
Submission dossier accepted and first round evaluation commenced	29 February 2024
Evaluation completed	11 November 2024
Registration decision (Outcome)	29 January 2025
Registration in the ARTG completed	7 July 2025

Description	Date
Number of working days from submission dossier acceptance to registration decision*	151

*Statutory timeframe for standard submissions is 255 working days

Assessment overview

A summary of the TGA's assessment for this submission is provided below.

Quality evaluation summary

Abiraterone drug substance is sourced from Aurisco Pharmaceutical Co., Ltd in China and is supported by an acceptable Active Substance Master File/Drug Master File. The default Australian standard is the USP monograph. The drug substance was shown to be consistently manufactured as polymorphic Form A (the most stable crystalline form of abiraterone acetate), with acceptable control of impurities, residual solvents and particle size distribution. Minor issues were noted during assessment, but none were considered to have an impact on drug substance quality. Overall, the abiraterone acetate drug substance was considered acceptable at the time of review.

Prednisolone drug substance is sourced from Tianjin Tianyao Pharmaceuticals Co., Ltd and is supported by a Certificate of Suitability issued by the European Directorate for the Quality of Medicines & HealthCare. The Ph. Eur. monograph applies as the default Australian standard. The overall quality of the prednisolone drug substance was considered acceptable with some minor issues identified. Consequently, revised specifications were submitted and accepted, including changes to impurity controls and updates reflecting an improved manufacturing process that mitigates nitrosamine risk. Particle size distribution limits were removed based on prednisolone's BCS Class I classification and evidence that PSD does not impact dissolution or bioavailability.

The abiraterone acetate 500 mg tablets are manufactured as conventional wet-granulated, film-coated tablets by Haupt Pharma Münster GmbH in Germany. The formulation is closely aligned with that of the Zytiga reference product. A pivotal fasted bioequivalence study comparing the test product to EU-sourced Zytiga demonstrated bioequivalence, with C_{max} and AUC values falling within the accepted 80–125% range.

The abiraterone acetate drug product is supported by validated in house analytical methods for assay and related substances, which differ from the USP monograph methods but were shown to be robust, specific, and capable of resolving all relevant impurities. Forced degradation and mass balance data were assessed, with no further action required despite a noted mass balance discrepancy under heat stress conditions. Process validation commitments were provided, including validation for the first three batches of any new batch size. Stability data support a 36 month shelf life, with no significant increase in water content observed, and water content is not included in the finished product specification, consistent with the USP monograph.

The prednisolone 5 mg tablets are immediate-release tablets that differ in excipient composition from the Australian reference product. A biowaiver based on the Biopharmaceutics Classification System was requested and accepted, as prednisolone was demonstrated to be a BCS Class I drug substance with high solubility and high permeability, and comparative dissolution studies showed equivalent release profiles.

For the prednisolone 5 mg tablets, the sponsor proposed to increase the shelf life acceptance limit for "Impurity 1" from NMT 0.5% to NMT 1.0%, aligning with a pending EU variation. The sponsor subsequently supplied an EU report in which the limit for Impurity 1 at NMT 1.0% was considered acceptable and approved. Based on the TGA toxicology Section advise that a positive recommendation by the EU can be appropriate grounds to accept the higher limit (NMT 1.0%), the TGA accepted the revised limit (NMT 1.0% for Impurity 1).

Comprehensive nitrosamine risk assessments were submitted for both drug substances and the combination product, taking into account ICH, EMA, and FDA guidance. Multiple batches were tested, with nitrosamines reported as below the limit of detection. No significant nitrosamine risk was identified.

The combination product consists solely of co-packaging the abiraterone acetate and prednisolone tablets into PVC/PVdC-aluminium blister packs. The packaging materials and container closure systems were considered acceptable. However, the shelf life of the combination product is limited by the component with the shortest supported shelf life. As a result, the recommended shelf life for the combination product is 24 months when stored below 25°C.

Evaluations covering sterility, endotoxin, viral safety, and container safety identified no outstanding issues.

There are no objections on quality grounds to the approval of Andriga-5 and Andriga-10.

Nonclinical evaluation summary

No new nonclinical data or further nonclinical evaluation were required for this submission. The TGA considers that previously submitted and evaluated data satisfactorily address nonclinical aspects of safety/efficacy relating to this submission.[16,17]

Clinical evaluation summary

One clinical study report was submitted (Study 051B18). The purpose of this study was to compare bioequivalence of abiraterone after single dose administration (fasting conditions) of Abiraterone acetate 500 mg film-coated tablets – test product - (Alfred E. Tiefenbacher (GmbH & Co. KG)) with Zytiga® 500 mg Filmtabletten – reference product (Janssen-Cilag International NV) in 58 healthy subjects.

The study design was single dose, randomised, open label, two-treatment, four-period, two-sequence, crossover, replicate for test and reference product at one study site. The subjects were 58 healthy male Caucasians age 18-55 years, BMI 18.5 – 30.0 kg/m^2.

After an overnight fasting of about 10 hours the subjects were administered 500 mg abiraterone acetate starting at 8:00 (time 0; administration time was staggered beginning at 8:00 for the first group of subjects) in sitting position on Day 1.

Eighteen blood samples were drawn for pharmacokinetic analysis at the prescribed times (pre-dose (within 60 min) and 0.33, 0.67, 1.00, 1.33, 1.67, 2.00, 2.33, 2.67, 3.00, 3.50, 4.00, 6.00, 8.00, 12.00, 24.00, 36.00 and 48.00 hours after drug administration).

- Samples per subject per period: 18

[16] AusPAR for abiraterone

[17] AusPAR for prednisolone

- Samples per subject in the study: 72
- Total number of samples per period: 1044 (planned)
- Total number of samples in the study: 4176 (planned)
- Measured samples: 4201 (including drop-outs
- Primary pharmacokinetic parameters assessed: $AUC_{(0-t)}$, C_{max} , $AUC_{(0-\infty)}$, $AUC_{(t-\infty)}$, T_{max}, $t½$ and λz.
- Safety evaluation:
  - general medical examination
  - heart rate and blood pressure (in sitting position; after 5 minutes rest)
  - 12-lead ECG (at baseline and at the end of the study)
  - documentation of adverse events

The results (Table 2) of the study show that for the extent of absorption (AUC) the 90 %confidence intervals are within the acceptance range of 80.00 % - 125.00 %. For the *rate* of absorption (C_{max}) the 90 %-confidence intervals are within the acceptance range of 70.92 % - 141.01 % as well as within the 'conventional' acceptance range of 80.00 % - 125.00 %.

Table 2. Relative bioavailability and pharmacokinetic parameters (Geometric mean values; N = 116)

Parameter	Abiraterone	
Mean relative bioavailability (ratio) (%)	T/R	105.86
$AUC_{(0-t)}$ (ng/mL·h)	T	380.388
	R	358.122
$AUC_{(0-\infty)}$ (ng/mL·h)	T	399.305
	R	377.188
C_{max} (ng/mL)	T	80.321
	R	78.348

T: Test product

R: Reference product

There were 21 adverse events observed in 12 subjects. These were headache (3 with test product, 9 with reference product), nausea (2 with test product), abdominal pain (1 with test product), soft defecation (1 with reference product), burning with urination (1 with test product), burning urination (1 with test product), dysuria (1 with test product), throat ache (1 with reference product) and weakness (1 with test product).

All observed adverse events were non-serious and all of mild or moderate intensity (11 adverse events were classified as mild, 10 adverse events were classified as moderate). All observed adverse events were considered possibly related to investigational products. Ten adverse events were observed with test product in 6 subjects and 11 adverse events were observed with reference product in 8 subjects. Four subjects needed therapy for adverse event. All subjects recovered fully.

In summary it was concluded that, for the extent of absorption (AUC), and the rate of absorption (C_{max}), bioequivalence is acceptable for Abiraterone acetate 500 mg film-coated tablets – test product - (Alfred E. Tiefenbacher (GmbH & Co. KG)) compared with Zytiga 500 mg Filmtabletten – reference product (Janssen-Cilag International NV).

Risk management plan

The sponsor received notification from the TGA on 28 Sep 2023 that no RMP would be needed.

With respect to pharmacovigilance, the Sponsor undertakes to appropriately handle reports of adverse events originating in Australia in accordance with both local and global Standard Operating Procedures (SOPs), and with the Australian Requirements and Recommendations for Pharmacovigilance Responsibilities of Sponsors of Medicines version 3.0.

Risk-benefit analysis

The approved therapeutic indication for the reference abiraterone product, Zytiga, requires co-administration with prednisolone to improve safety. The proposed doses and indications for Andriga are identical to Zytiga. Hence, the efficacy and safety have been established for abiraterone + prednisolone at the proposed doses and for the proposed indications in people with mHSPC or mCRPC.

The sponsor notes that a combination medicinal product was not possible due to the nature of the pharmaceutical ingredients, and therefore they have proposed a composite blister pack instead. The sponsor proposes that this composite pack has the potential to assist with medication adherence and convenience for patients.

The clinical rationale for the proposed product is based on valid therapeutic principles and relevant established evidence. The rationale is aligned with the potential benefits listed in the TGA Guidance for fixed combination prescription medicines[18], namely:

- the simplification of therapy (leading to improved medical compliance)
- one active substance counteracting an adverse reaction produced by another active substance within that combination medicine.

The efficacy and safety of abiraterone + prednisolone have already been established for:

- newly diagnosed high-risk mHSPC in combination with ADT
- patients with mCRPC who are asymptomatic or mildly symptomatic after failure of ADT or
- patients with mCRPC who have received prior chemotherapy containing a taxane

The manufacturing and quality control, including bioavailability equivalence for the drug preparations related to this submission have been demonstrated. The potential benefit of combination-packaging of these agents is real with little or no apparent risk. It is possible that combined packaging may increase efficacy through improved compliance and enhance safety through reduced dosing errors.

[18] Therapeutic Goods Administration. Fixed combination prescription medicines. Last updated 26 May 2014

Assessment outcome

Based on a review of quality, safety, and efficacy, the TGA decided to register Andriga (abiraterone and prednisolone), for the following indications:

> *Andriga-5 is indicated for the treatment of:*
>
> *newly diagnosed high-risk metastatic hormone sensitive prostate cancer (mHSPC) in combination with androgen deprivation therapy (ADT).*
>
> *Andriga-10 is indicated for the treatment of:*
>
> *-patients with metastatic advanced prostate cancer (castration resistant prostate cancer, mCRPC) who are asymptomatic or mildly symptomatic after failure of androgen deprivation therapy (ADT) or*
>
> *-patients with mCRPC who have received prior chemotherapy containing a taxane.*

Product Information and Consumer Medicine Information

For the most recent Product Information (PI) and Consumer Medicine Information (CMI), please refer to the TGA PI/CMI search facility.

Therapeutic Goods Administration

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https://www.tga.gov.au