AS SOON AS YOU SEE
A RAPIDLY RISING PSA
IN PATIENTS RECEIVING ADT...

For Healthcare Professionals only

# PUSH BACK ON DISEASE PROGRESSION*

For HCPs

# AN EARLY LEAD IN THE FIGHT AGAINST PROSTATE CANCER†

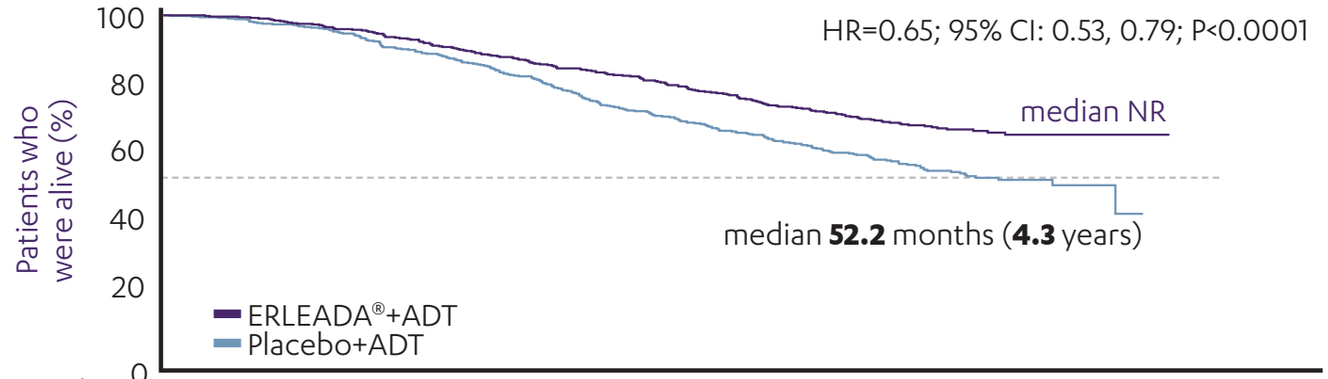
*More information is available upon request
†As indicated by the TITAN (mCSPC) and SPARTAN (nmCRPC) studies

Erleada® (apalutamide) tablets

# TITAN study[1]

TITAN was a phase 3, randomized, double-blind, placebo-controlled, multicenter study designed to evaluate the efficacy and safety of ERLEADA® compared to placebo in patients with metastatic castration-sensitive prostate cancer (mCSPC; N=1052).[1] Patients were randomised (1:1) to receive either ERLEADA® orally at a dose of 240 mg once daily (N = 525) or placebo once daily (N = 527).[2] All patients in the TITAN trial received concomitant GnRH analog or had prior bilateral orchiectomy.[2]

Overall Survival[1]




| Months: | 0 | 6 | 12 | 18 | 24 | 30 | 36 | 42 | 48 | 54 | 60 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Patients at Risk: | | | | | | | | | | | |
| ERLEADA®+ADT | 525 | 513 | 489 | 452 | 425 | 394 | 362 | 227 | 52 | 3 | 0 |
| Placebo+ADT | 527 | 510 | 474 | 436 | 374 | 339 | 301 | 181 | 43 | 0 | 0 |

*Graph is adapted from Chi KN, et al. *JCO* 2021;39:2294-2303.

**mCSPC** **metastatic** castration-**sensitive** prostate cancer

**35%**[1]
Reduced risk of death†

Additional information:

**52%**[3]
Reduced risk of radiographic progression or death‡

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) include apalutamide (ERLEADA®) with androgen deprivation therapy as a **Category 1 preferred** treatment option for patients with mCSPC.[4]

**ADT:** androgen deprivation therapy; **CI:** confidence interval; **HR:** hazard ratio; **NR:** not reached; **TITAN:** A Study of Apalutamide (JNJ-56021927, ARN-509) Plus Androgen Deprivation Therapy (ADT) Versus ADT in Participants With mHSPC (NCT02489318)
† HR (95% CI): 0.65 (0.53, 0.79), P<0.0001; ‡ HR (95% CI): 0.48 (0.39, 0.60), P<0.001

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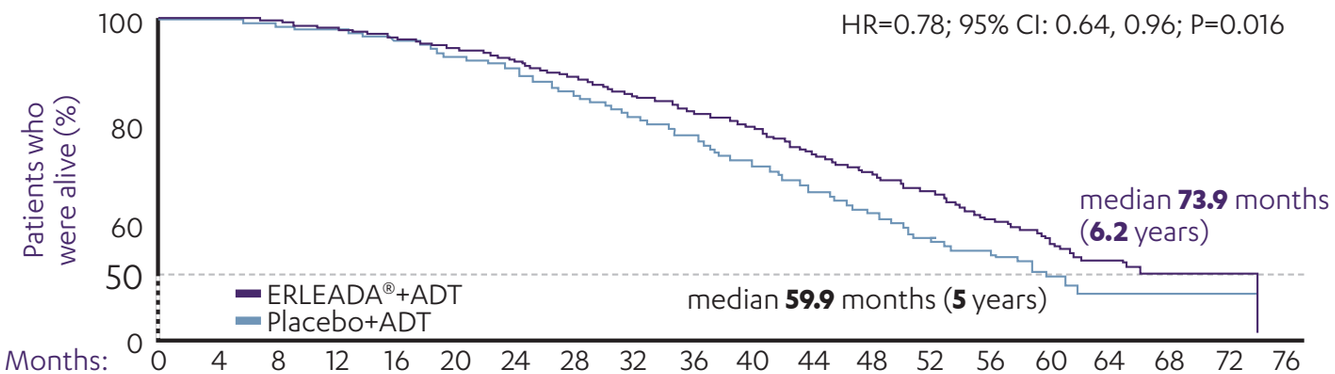
# SPARTAN study[5]

SPARTAN was a phase 3, randomized, double-blind, placebo-controlled, multicenter study designed to evaluate the efficacy and safety of ERLEADA® compared to placebo in patients with high-risk nonmetastatic castration-resistant prostate cancer (nmCRPC; N=1207).[5] Patients were randomised (2:1) to receive either ERLEADA® orally at a dose of 240 mg once daily in combination with androgen deprivation therapy (ADT) (medical castration or prior surgical castration) or placebo with ADT.[2]

Overall Survival[5]




*Graph is adapted from Smith MR, et al. *Eur Urol* 2021;79:150-158.

**nmCRPC** **nonmetastatic** castration-**resistant** prostate cancer

Additional information:

**72%**[6] Reduction in the risk of distant metastasis or death†

**+2 years**[6] Metastasis-free survival‡

The NCCN Guidelines® include apalutamide (ERLEADA®) with continued androgen deprivation therapy as a **Category 1 preferred** treatment option for patients with nmCRPC and a PSA doubling time ≤10 months.[4]

**ADT**: androgen deprivation therapy; **HR**: hazard ratio; **CI**: confidence interval; **NE**: not estimable
† HR (95% CI): 0.28 (0.23, 0.35), P<0.001; ‡ Median, months: 40.5 (3.4 years) vs 16.2 (1.4 years)

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## Summary of the safety profile[2]

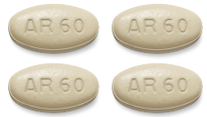
| Adverse Reactions | Percentage (%) |
|---|---|
| Fatigue | 26 |
| **Skin rash** | **26 (of any grade) and 6 (Grade 3 or 4)** |
| Hypertension | 22 |
| Hot flush | 18 |
| Arthralgia | 17 |
| Diarrhoea | 16 |
| Fall | 13 |
| Weight decreased | 13 |
| Fractures | 11 |
| Hypothyroidism | 8 |

Symptoms of rash are **highly treatable** using the following[2]:

- **Topical steroid cream**
- **Oral antihistamines**
- **Oral steroids**

## Recommended dose[2]

**Four**
60 mg tablets once daily

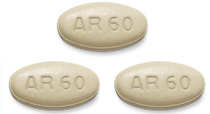



240 mg

Tablets shown are not actual size.

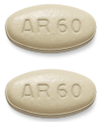
## Dose modifications[2]

**Three**
60 mg tablets once daily




180 mg

**Two**
60 mg tablets once daily




120 mg

If a ≥Grade 3 toxicity or an intolerable adverse reaction is experienced by the patient, dosing should be held rather than permanently discontinuing treatment until symptoms improve to ≤Grade 1 or original grade, then should be resumed at the same dose or a reduced dose (180 mg or 120 mg), if warranted.[2]

If the toxicity recurs at Grade 3 or higher, then the dose of apalutamide should be reduced to the next lower dose level (from 240 mg to 180 mg, and from 180 mg to 120 mg).[2] A maximum of 2 dose level reductions (to 120 mg) is allowed.[2] If further dose reductions are needed, apalutamide should be discontinued.[2]

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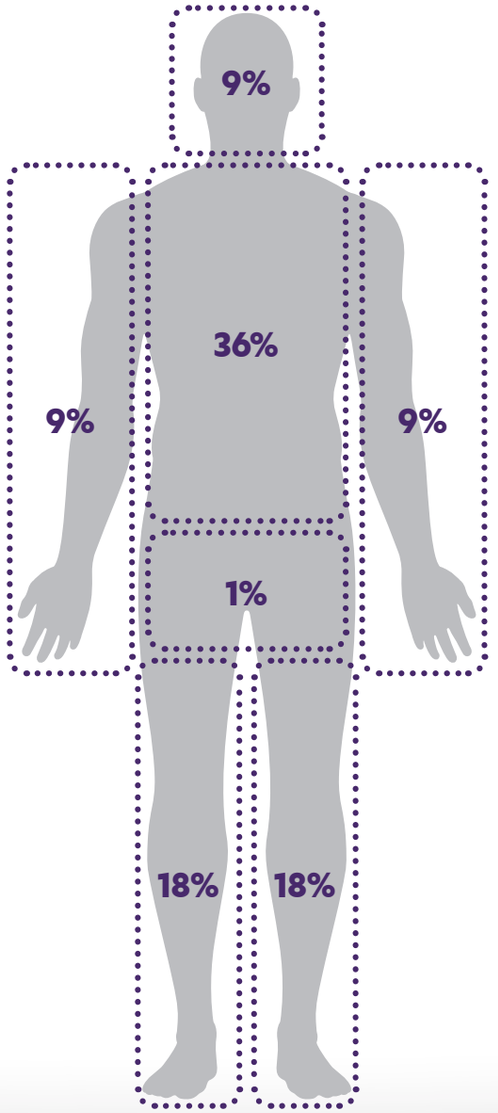
# Body surface area (BSA) estimation for rash

| Body area[7] | BSA involvement[7] |
|---|---|
| **Head** | **9%** |
| Anterior | 4.5% |
| Posterior | 4.5% |
| **Trunk** | **36%** |
| Anterior | 18% |
| Chest | 9% |
| Abdomen | 9% |
| Posterior | 18% |
| **Upper extremities** | **18%** |
| Right upper extremity | 9% |
| Anterior | 4.5% |
| Posterior | 4.5% |
| Left upper extremity | 9% |
| Anterior | 4.5% |
| Posterior | 4.5% |
| **Lower extremities** | **36%** |
| Right lower extremity | 18% |
| Anterior | 9% |
| Posterior | 9% |
| Left lower extremity | 18% |
| Anterior | 9% |
| Posterior | 9% |
| **Groin** | **1%** |




**Rule of Nines**
(also known as the Wallace Rule of Nines)

**Quick and easy tool**
also used in trauma and emergency medicine[8]

**Assigned percentages**
to different areas of the body are in **multiples of 9**[7]

**Simply add up**
the assigned percentages of affected parts of the body[7] to find the estimated **total BSA for rash grading**

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# Brief overview: Clinical characteristics and management of rash

## GRADE 1

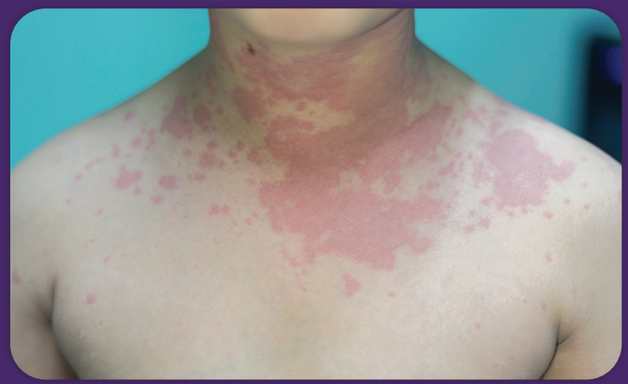

Photo shown is for illustration purposes only and does not represent patients who are taking Erleada®

**Characteristics[9]**

Macules/papules covering <10% BSA with or without symptoms (eg, pruritus, burning, stinging)

**< 10% BSA** + **Pruritus** / **Burning** / **Stinging**

**Management strategy[7]**

**Topical steroid cream**
**AND**
**Oral antihistamines**

**Continue** apalutamide at current dose

## GRADE 2

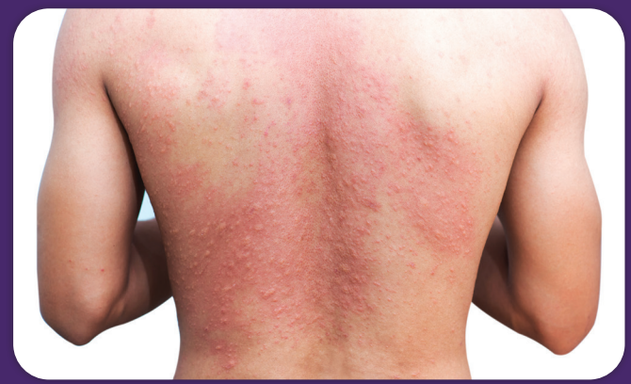

Photo shown is for illustration purposes only and does not represent patients who are taking Erleada®

**Characteristics[9]**

Macules/papules covering 10–30% BSA with or without symptoms; limiting instrumental activities of daily living (ADL)

**10–30% BSA** [ADL affected] + **Pruritus** / **Burning** / **Stinging**

**Management strategy[7]**

**Topical steroid cream**
**AND**
**Oral antihistamines**

- **Hold** apalutamide for ≤28 days
- **Monitor** if symptoms improve
- **Reinitiate** when rash is grade ≤1

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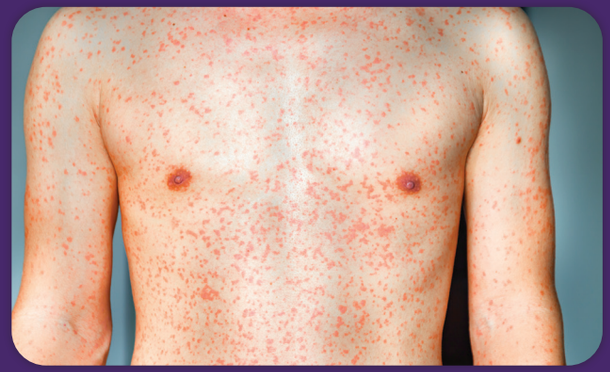
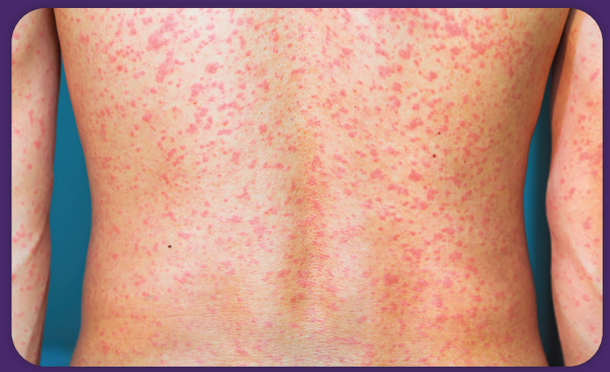
# Brief overview: Clinical characteristics and management of rash

## GRADE 3





Photos shown are for illustration purposes only and do not represent patients who are taking Erleada®

**Characteristic**[9]

Macules/papules covering >30% BSA with or without associated symptoms; limiting self-care ADL

**> 30% BSA**
[ADL affected]

- **Pruritus**
- **Burning**
- **Stinging**

**Management strategy**[7]

**Topical steroid cream**

**AND**

**Oral antihistamines**

**AND**

Consider short course of **oral steroids**

- **Hold** apalutamide for ≤28 days
- **Reassess** after 2 weeks

*If rash grade reduces to ≤1:*

- **Reinitiate** apalutamide and consider dose reduction

*If no improvement or worsened:*

- **Initiate** oral steroids (if not already done) and refer to a dermatologist
- If after 28 days and rash grade is still >1, consider discontinuation of apalutamide

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Creation date: August 2021
Creation Number: CP-236561

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**References: 1.** Chi KN, et al. *JCO* 2021;39:2294–2303. **2.** ERLEADA®_Approved Prescribing Information_Malaysia_EU SmPC vNov2020 + TITAN AI. **3.** Chi KN, et al. *NEJM* 2019;381:13–24. **4.** NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) – Prostate Cancer (Version 2.2021). National Comprehensive Cancer Network. Available at: https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. **5.** Smith MR, et al. *Eur Urol* 2021;79:150–158. **6.** Smith MR, et al. *NEJM* 2018;378:1408–1418. **7.** ERLEADA® (apalutamide)– Rash. Janssen Scientific Affairs. Available at: https://www.janssenmd.com/erleada/safety/rash/rash. **8.** Moore RA, et al. NCBI Bookshelf 2020. Available at: https://www.ncbi.nlm.nih.gov/books/NBK513287/. **9.** Common Terminology Criteria for Adverse Events (CTCAE 4.03). National Cancer Institute. Available at: https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_4.03.xlsx. **10.** Erleada® Consumer Medication Information Leaflet (RiMUP) dated 08 July 2020. **11.** Hormone Therapy for Prostate Cancer. American Cancer Society. Available at: https://www.cancer.org/cancer/prostate-cancer/treating/hormone-therapy.html. **12.** ASCO Answers - Rash. American Society of Clinical Oncology. Available at: https://www.cancer.net/sites/cancer.net/files/asco_answers_rash.pdf.

**ERLEADA® (Apalutamide) Film-Coated Tablets – Abbreviated Prescribing Information. Active Ingredient:** Apalutamide. **Indication:** In adult men for the treatment of non metastatic castration resistant prostate cancer (nmCRPC) who are at high risk of developing metastatic disease; in adult men for the treatment of metastatic hormone-sensitive prostate cancer (mHSPC) in combination with androgen deprivation therapy (ADT). **Posology:** The recommended dose is 240 mg (four 60 mg tablets) as an oral single daily dose. It should be swallowed whole and can be taken with or without food. Medical castration with gonadotropin releasing hormone analogue (GnRHa) should be continued during treatment in patients not surgically castrated. If a ≥ Grade 3 toxicity or an intolerable adverse reaction is experienced by the patient, dosing should be held rather than permanently discontinuing treatment until symptoms improve to ≤ Grade 1 or original grade, then should be resumed at the same dose or a reduced dose (180 mg or 120 mg), if warranted. If the toxicity recurs at Grade 3 or higher, then the dose of apalutamide should be reduced to the next lower dose level (from 240 mg to 180 mg, and from 180 mg to 120 mg). A maximum of 2 dose level reductions (to 120 mg) is allowed. If further dose reductions are needed, apalutamide should be discontinued. Permanently discontinue ERLEADA® in patients who develop a seizure during treatment. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients listed; women who are or may become pregnant. **Warnings and Precautions**: ERLEADA® is not recommended in patients with a history of seizures or other predisposing factors e.g. underlying brain injury, recent stroke (within one year), primary brain tumours or brain metastases. If a seizure develops during treatment with ERLEADA®, treatment should be discontinued permanently. Patients should be evaluated for fracture and fall risk before starting ERLEADA®, monitored and managed according to established treatment guidelines and use of bone-targeted agents should be considered. Monitor for signs and symptoms of ischemic heart disease and management of cardiovascular risk factors should be optimised. Co administration with warfarin and coumarin-like anticoagulants should be avoided. If co-administered, additional International Normalised Ratio (INR) monitoring should be conducted. Monitor for risk factors e.g. hypercholesterolaemia, hypertriglyceridaemia, or other cardio-metabolic disorders since the safety has not been established in patients with clinically significant recent cardiovascular disease. Consider discontinuation of ERLEADA® for Grade 3 and 4 events. In patients with a history of or risk factors for QT prolongation, physicians should assess the benefit-risk ratio including the potential for Torsade de pointes prior to initiating ERLEADA®. **Interactions:** No initial dose adjustment is necessary when ERLEADA® is co administered with a strong inhibitor of CYP2C8 (e.g. gemfibrozil, clopidogrel) and CYP3A4 (e.g. ketoconazole, ritonavir, clarithromycin). However, a reduction of the ERLEADA® dose based on tolerability should be considered. CYP2C8 and CYP3A4 inducers are not expected to have clinically relevant effects. Concomitant use of ERLEADA® with medicinal products that are primarily metabolised by CYP3A4 (e.g. darunavir, felodipine, midazolam, simvastatin), CYP2C19 (e.g. diazepam, omeprazole), CYP2C9 (e.g. warfarin, phenytoin), substrates of P gp (e.g. colchicine, dabigatran etexilate, digoxin), BCRP or OATP1B1 (e.g. lapatinib, methotrexate, rosuvastatin, repaglinide) can result in lower exposure of these medicinal products. Caution is advised when prescribing ERLEADA® with medicinal products known to prolong QT interval or able to induce Torsade de pointes e.g. class IA (quinidine, disopyramide) or class III (amiodarone, sotalol, dofetilide, ibutilide) antiarrhythmic medicinal products, methadone, moxifloxacin, antipyschotics (e.g. haloperidol). **Adverse Reactions:** Decreased appetite, hot flush, hypertension, diarrhoea, skin rash, fracture, arthralgia, fatigue, decreased weight and fall. **Pharmaceutical Form:** Film-coated tablet. **Pack Size:** Bottle of 120's. Please refer to the full prescribing information before prescribing. Full prescribing information is available upon request. [EU SmPC vNov2020 + TITAN AI].

Please consult your physician on medical related matters pertaining to Erleada®.

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