Cutterguide: **N/A** Printing Process: **Offset**
GD: **NB 31098**

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AVODART ABRIDGED PRESCRIBING INFORMATION: *Please refer to full Summary of Product Characteristics (SPC) before prescribing.*
ACTIVE INGREDIENT: Dutasteride 0.5 mg. **PHARMACEUTICAL FORM:** Soft capsules. **INDICATIONS:** For the treatment of moderate to severe symptoms of benign prostatic hyperplasia (BPH) and the reduction of the risk of acute urinary retention (AUR) and surgery in patients with moderate to severe symptoms of BPH. **POSOLOGY:** Avodart can be administered alone or in combination with the alpha-blocker tamsulosin (0.4 mg). The recommended dose of Avodart is one capsule (0.5 mg) taken orally once a day. The capsules should be swallowed whole, with or without food. Improvement may be observed at an early stage, it can take up to 6 months before a response to the treatment can be achieved. No dose adjustment is necessary in the elderly. **CONTRAINDICATIONS:** Women, severe hepatic impairment, hypersensitivity to the active substance or excipient/s. **PRECAUTIONS FOR USE:** Cardiac failure; Effects on prostate specific antigen (PSA) and prostate cancer detection (digital rectal examination, as well as other evaluations for prostate cancer, must be performed on patients). Serum prostate-specific antigen (PSA) concentration is an important component in the detection of prostate cancer. Avodart causes a decrease in mean serum PSA levels by approximately 50%, after 6 months of treatment; Leaking capsules (Dutasteride is absorbed through the skin, therefore, women, children and adolescents must avoid contact); Caution should be used in the administration of dutasteride to patients with mild to moderate hepatic impairment; Breast neoplasia (Physicians should instruct their patients to promptly report any changes in their breast tissue such as lumps or nipple discharge). **DRUG INTERACTIONS:** Long-term combination of dutasteride with drugs that are potent inhibitors of the enzyme CYP3A4 (e.g. ritonavir, indinavir, nefazodone, itraconazole, ketoconazole administered orally) may increase serum concentrations of dutasteride. Dutasteride has no effect on the pharmacokinetics of warfarin or digoxin. This indicates that dutasteride does not inhibit/induce CYP2C9 or the transporter P-glycoprotein. **PREGNANCY & LACTATION:** Avodart is contraindicated for use by women. **EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:** Not expected to interfere with the ability to drive or operate machinery. **UNDESIRABLE EFFECTS:** Impotence, altered (decreased) libido, ejaculation disorders, breast disorders (includes breast enlargement and/or breast tenderness), allergic reactions including rash, pruritus, urticaria, localised oedema, and angioedema. Kindly refer to full SPC for full list. **OVERSDOSE:** There is no specific antidote for Avodart, therefore, in suspected overdosage symptomatic and supportive treatment should be given as appropriate. **LEGAL CATEGORY:** POM. **LOCAL PRESENTATION:** Avodart 0.5 mg X 30 soft capsules. **MARKETING AUTHORISATION HOLDER:** GlaxoSmithKline UK Ltd. **MARKETING AUTHORISATION NUMBER:** MA 300/00301. **DATE OF PREPARATION:** January 2014.

COMBODART ABRIDGED PRESCRIBING INFORMATION: *Please refer to full Summary of Product Characteristics (SPC) before prescribing.*
ACTIVE INGREDIENTS: 0.5 mg dutasteride and 0.4 mg tamsulosin hydrochloride. **PHARMACEUTICAL FORM:** Hard capsule. **THERAPEUTIC INDICATIONS:** Treatment of moderate to severe symptoms of benign prostatic hyperplasia (BPH). Reduction in the risk of acute urinary retention (AUR) and surgery in patients with moderate to severe-symptoms of BPH. **DOSAGE AND METHOD OF USE:** One capsule (0.5 mg/0.4 mg) taken orally approximately 30 minutes after the same meal each day. **CONTRAINDICATIONS:** Women, children and adolescents; patients with hypersensitivity to dutasteride, other 5-alpha reductase inhibitors, tamsulosin (including tamsulosin-induced angioedema) soya, peanuts or any of the other excipients. **PRECAUTIONS:** Prescribe after careful benefit risk assessment due to the potential increased risk of adverse events (including cardiac failure) and after consideration of alternative treatment options including monotherapies. Digital rectal examination, as well as other evaluations for prostate cancer or other conditions which can cause the same symptoms as BPH, must be performed on patients prior to initiating therapy with Combodart and periodically thereafter. Patients receiving Combodart should have a new PSA baseline established after 6 months of treatment. It is recommended to monitor PSA values regularly thereafter. **DRUG INTERACTIONS:** *Dutasteride:* with drugs that are potent inhibitors of the enzyme CYP3A4 may increase serum concentrations of dutasteride. Dutasteride has no effect on the pharmacokinetics of warfarin or digoxin. *Tamsulosin:* Concomitant administration of tamsulosin hydrochloride with drugs which can reduce blood pressure could lead to enhanced hypotensive effects. Dutasteride-tamsulosin should not be used in combination with other alpha-1 adrenergic blockers. Caution should be exercised with concomitant administration of warfarin and tamsulosin hydrochloride. Diclofenac may increase the elimination rate of tamsulosin. **PREGNANCY AND LACTATION:** Combodart is contraindicated for use by women. **ABILITY TO DRIVE AND USE MACHINES:** Possible occurrence of symptoms related to orthostatic hypotension such as dizziness when taking Combodart. **ADVERSE EVENTS:** *Common:* Dizziness, sexual side effects. *Please refer to full SPC for further information on adverse events.* **PRESENTATIONS:** Available in packs of 30 capsules. **LEGAL CATEGORY:** POM. **MAH:** GlaxoSmithKline UK Ltd. **MA NUMBER:** MA 300/00401. **Date of preparation:** November 2013.

In order to ensure that this product information reflects the most up-to-date clinical and post-marketing surveillance data, please always refer to the latest Summary of Product Characteristics (SPC) which is available from GlaxoSmithKline (Malta) Ltd (Tel: +356 21238131)

REPORTING ADVERSE EVENTS (AEs):
Malta & Gibraltar: **If you become aware of any AEs, medication errors and/or use during pregnancy in association with GSK products, please report the event promptly to:** GSK (Malta) Limited, 1, De la Cruz Avenue, Qormi QRM 2458, Malta (Tel: +356 21238131)

Malta: **alternatively, any suspected AEs and medication errors can also be reported via the national Adverse Drug Reactions (ADRs) reporting system:**

Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and posted to the Malta Medicines Authority, Post-licensing Directorate, 203, Level 3, Rue D'Argens, Gżira GŻR 1368, MALTA, or sent by email to postlicensing.medicinesauthority@gov.mt

Gibraltar: **alternatively, any suspected AEs and medication errors can also be reported via the UK regulatory authority (MHRA):** https://yellowcard.mhra.gov.uk/

References:
1. Roehrborn CG. Int J Impot Res 2008; 20: s19–26.
2. Green KL, J Urol 2009; 182: 2232-2241.
3. Marks LS *et al.* J Urol 2006; 176: 868–874.
4. Andriole G *et al.* Urology 1998; 52: 195–202.
5. Thompson I *et al.* N Engl J Med 2003; 349; 215–224.
6. Etzioni R *et al.* J Urol 2005; 174: 877–881.
7. Marberger M *et al.* BJU Int. 2012; 109: 1162-1169.
8. Duodart European Summary of Product Characteristics, February 2012.
9. Avodart European Summary of Product Characteristics, February 2012.

Job code: MLT_GIB/DUTT/0001/14
Date of preparation: January 2014

Updated approach for monitoring PSA in patients receiving dutasteride

Prescribing information can be found on pages 4.

GSKEDC-ADI-2014-2861-PSA-LP_D2.indd 1-2

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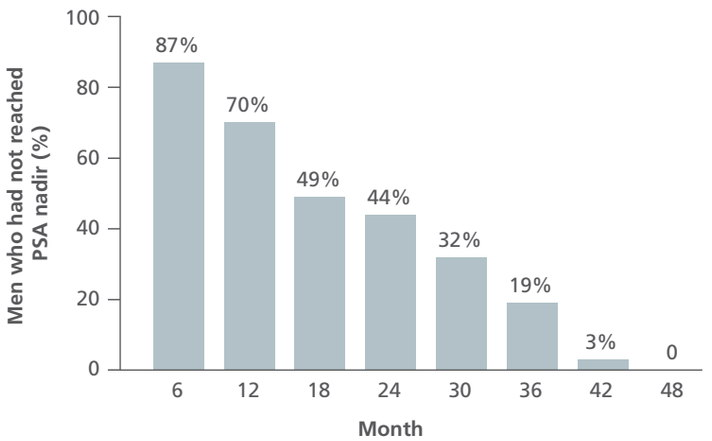
Historical background

- PSA, measured during the assessment of a man with presumed BPH / LUTS, is a powerful predictor of potential disease progression[1]
- Assessment of serum PSA plays important roles in the detection and assessment of prostate cancer[2]
- 5ARIs decrease serum PSA, the magnitude of which increases with the duration of therapy[3]
- The "doubling rule" has been suggested as a way to preserve the utility of PSA in men treated with a 5-ARI[4]
  - However, due to continued PSA decrease over time, the "doubling rule":
    - by the end of Year 3 it has to be changed to x 2.3[5]
    - by 7 years, it is predicted that it should be x 2.5[6]

PSA findings from the REDUCE study[7]

- A continued decrease in PSA beyond 2 years was observed in men treated with dutasteride

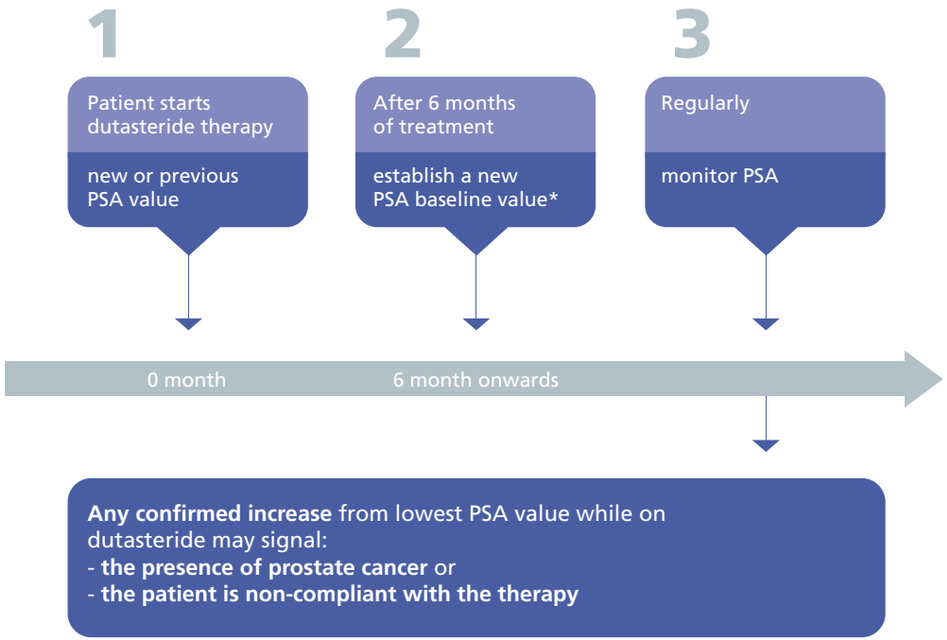
PSA level in men treated with dutasteride continues to decline over time



Adapted from Marberger M *et al.* BJU Int. 2012; 109: 1162-1169.

Updated recommendations

3 steps to monitor and assess PSA in patients receiving dutasteride[8,9]



- The PSA increase from lowest value appears to be a more accurate cancer indicator than a doubled value in some patients[3]
- Using the new PSA monitoring recommendations in men taking dutasteride, maintains the sensitivity of PSA as a marker to detect prostate cancer in general male population[7]

*PSA baseline value = lowPSA value = nadir