SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Sidopros 8D Capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains: Silodosin 8 mg/Capsule and Dutasteride USP 0.5 mg.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Hard gelatin capsule.

Blue/White coloured size-0 hard gelatin capsule containing white to off-white coloured granular powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

The product is indicated for the treatment of the signs and symptoms of BPH (Benign Prostatic Hyperplasia) in men with an enlarged prostate. It is not intended for use as an antihypertensive drug and is not approved for the prevention of prostate cancer.

4.2 Posology and method of administration

For oral administration: One capsule shall be taken once a day after a meal, or as directed by the physician. The capsules shall be taken as whole.

4.3 Contraindications

Silodosin is contraindicated for use in the following:

- Severe renal impairment (CCr <30 mL/min).
- Severe hepatic impairment (Child-Pugh score ≥10).
- Concomitant administration with strong Cytochrome P450 3A4 (CYP3A4) inhibitors (e.g. ketoconazole, clarithromycin, itraconazole, ritonavir).
- Patients with a history of hypersensitivity to silodosin or any of the excipients.

Dutasteride is contraindicated for use in the following:

- Pregnancy: In animal reproduction and developmental toxicity studies, dutasteride inhibited development of the external genitalia of the male foetus. Therefore, dutasteride may cause foetal harm when administered to a pregnant woman. If dutasteride is used during pregnancy or if the patient becomes pregnant while taking dutasteride, the patient should be apprised of the potential hazard to the foetus.
- Women of childbearing potential.
- Paediatric patients.
- Patients with previously demonstrated clinically significant hypersensitivity (e.g. serious skin reactions, angio-oedema) to dutasteride or other 5 alpha-reductase inhibitors.

4.4 Special warnings and precautions for use

Silodosin

Orthostatic effects: Postural hypotension, with or without symptoms (e.g. dizziness), may develop when beginning silodosin treatment.

Carcinoma of the prostate: Carcinoma of the prostate and BPH cause many of the same symptoms. These two diseases frequently co-exist. Therefore, patients thought to have BPH should be examined prior to starting therapy with silodosin to rule out the presence of carcinoma of the prostate.

Renal impairment: In a clinical pharmacology study, plasma concentrations (AUC and Cmax) of silodosin were approximately three times higher in subjects with moderate renal impairment compared with subjects with normal renal function, while half-lives of silodosin doubled in duration. The dose of silodosin should be reduced to 4 mg in patients with moderate renal impairment. Exercise caution and monitor such patients for adverse events. Silodosin is contraindicated in patients with severe renal impairment.

Hepatic impairment: Silodosin has not been tested in patients with severe hepatic impairment and therefore should not be prescribed to such patients.

Intraoperative floppy iris syndrome: This has been observed during cataract surgery in some patients on alpha1-blockers or previously treated with alpha1-blockers. This variant of small pupil syndrome is characterised by a flaccid iris that billows in response to intraoperative irrigation currents, progressive intraoperative miosis despite pre-

operative dilation with standard mydriatic drugs, and potential prolapse of the iris toward the phacoemulsification incisions. Patients planning cataract surgery should be advised to inform their ophthalmologist that they are taking silodosin.

Dutasteride

Effects on Prostate-Specific Antigen (PSA) and the use of PSA in prostate cancer detection: In clinical studies, dutasteride reduced serum PSA concentration by approximately 50% within 3 to 6 months of treatment. This decrease was predictable over the entire range of PSA values in patients with symptomatic BPH, although it may vary in individuals. Dutasteride may also cause decreases in serum PSA in the presence of prostate cancer. A new PSA baseline should be established at least 3 months after starting treatment and PSA monitored periodically thereafter. Any confirmed increase from the lowest PSA value while on dutasteride may signal the presence of prostate cancer and should be evaluated, even if PSA levels are still within the normal range for men not taking a 5 alpha-reductase inhibitor. Noncompliance with dutasteride may also affect PSA test results.

To interpret an isolated PSA value in a man treated with dutasteride for 3 months or more, the PSA value should be doubled for comparison with normal values in untreated men. The free-to-total PSA ratio (percent free PSA) remains constant, even under the influence of dutasteride, and no adjustment to its value appears necessary if used as an aid in prostate cancer detection.

Increased risk of high-grade prostate cancer: In men aged 50 to 75 years with a prior negative biopsy for prostate cancer and a baseline PSA between 2.5 ng/mL and 10.0 ng/mL, who were taking dutasteride for prevention of prostate cancer in a 4-year trial, there was an increased incidence of Gleason score 8-10 prostate cancer compared with men taking placebo (dutasteride 1.0% versus placebo 0.5%). Similar results were observed in a 7-year placebo-controlled trial with finasteride 5 mg (1.8% versus 1.1%). 5 alpha-reductase inhibitors may increase the risk of development of high-grade prostate cancer; whether this is due to their effect on prostate volume or trial-related factors has not been established.

Evaluation for other urological diseases: Lower urinary tract symptoms of BPH can be indicative of other urological diseases, including prostate cancer. Patients should be assessed to rule out prostate cancer and other

urological diseases prior to treatment with dutasteride and periodically thereafter.

Exposure of women — risk to the male foetus: Dutasteride should not be handled by a woman who is pregnant or who could become pregnant. Dutasteride is absorbed through the skin and could result in unintended foetal exposure. If contact occurs, the contact area should be washed immediately with soap and water.

Blood donation: Men being treated with dutasteride should not donate blood until at least 6 months have passed following their last dose, to prevent administration of dutasteride to a pregnant female transfusion recipient.

4.5 Interaction with other medicinal products and other forms of interaction

Silodosin

Moderate and strong CYP3A4 inhibitors: Use of strong CYP3A4 inhibitors such as itraconazole or ritonavir may cause plasma concentrations of silodosin to increase. Concomitant administration of strong CYP3A4 inhibitors and silodosin is contraindicated.

Strong P-glycoprotein (P-gp) inhibitors: Silodosin is not recommended in patients taking strong P-gp inhibitors such as cyclosporine.

Alpha-blockers: The pharmacodynamic interactions between silodosin and other alpha-blockers have not been determined; however, interactions may be expected and silodosin should not be used in combination with other alpha-blockers.

Antihypertensives: Caution should be exercised during concomitant use with antihypertensives, and patients should be monitored for possible adverse events.

Food interactions: The effect of a moderate-fat, moderate-calorie meal on silodosin pharmacokinetics was variable, decreasing Cmax by approximately 18-43% and AUC by 4-49% across different studies. Safety and efficacy clinical trials for silodosin were always conducted with food intake, and patients should be instructed to take silodosin with a meal to reduce risk of adverse events.

Dutasteride

Cytochrome P450 3A inhibitors: Because of the potential for drug-drug interactions, use caution when prescribing dutasteride to patients taking potent, chronic CYP3A4 enzyme inhibitors (e.g. ritonavir).

4.6 Fertility, pregnancy and lactation

Fertility

Silodosin: Possible effects on male fertility could be observed based on findings in rats at exposures at least two times higher than the maximum recommended human dose (MRHD, based on AUC). These findings may be reversible, and the clinical relevance is unknown.

Dutasteride: The clinical significance of dutasteride's effect on semen characteristics for an individual patient's fertility is not known.

Pregnancy

Silodosin is not indicated for use in women. Dutasteride is contraindicated for use in women of childbearing potential and during pregnancy.

Lactation

The product is contraindicated for use in women of childbearing potential, including nursing women. It is not known whether dutasteride is excreted in human milk.

4.7 Effects on ability to drive and use machines

Postural hypotension, with or without symptoms (e.g. dizziness), may develop with silodosin and dutasteride therapy. Patients should be cautioned about driving, operating machinery, or performing hazardous tasks when initiating therapy.

4.8 Undesirable effects

Silodosin

The incidence of treatment-emergent adverse reactions listed below were derived from two 12-week, multicentre, double-blind, placebo-controlled clinical studies of silodosin 8 mg daily in BPH patients. Adverse reactions that occurred in at least 2% of patients treated with silodosin and more frequently than with placebo are shown below.

Adverse Reaction	Silodosin N=466, n (%)	Placebo N=457, n (%)
Retrograde ejaculation	131 (28.1)	4 (0.9)
Dizziness	15 (3.2)	5 (1.1)

Diarrhoea	12 (2.6)	6 (1.3)
Orthostatic hypotension	12 (2.6)	7 (1.5)
Headache	11 (2.4)	4 (0.9)
Nasopharyngitis	11 (2.4)	10 (2.2)
Nasal congestion	10 (2.1)	1 (0.2)

In the above clinical trials, the following adverse events were also reported by between 1% and 2% of patients receiving silodosin and occurred more frequently than with placebo: insomnia, PSA increased, sinusitis, abdominal pain, asthenia and rhinorrhoea. One case of syncope in a patient taking prazosin concomitantly and one case of priapism were reported in the silodosin treatment group. In a 9-month open-label safety study of silodosin, one case of intraoperative floppy iris syndrome was reported.

Postmarketing experience: The following adverse reactions have been identified during post-approval use of silodosin. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Skin and subcutaneous tissue disorders: Toxic skin eruption, purpura, skin rash, pruritus and urticaria.

Hepatobiliary disorders: Jaundice, impaired hepatic function associated with increased transaminase values.

Immune system disorders: Allergic-type reactions, not limited to skin reactions, including swollen tongue and pharyngeal oedema, resulting in serious outcomes.

Dutasteride

Clinical trials experience: The most common adverse reactions reported in subjects receiving dutasteride were impotence, decreased libido, breast disorders (including breast enlargement and tenderness), and ejaculation disorders. Study withdrawal due to adverse reactions occurred in 4% of subjects receiving dutasteride, most commonly due to impotence (1%).

Monotherapy: Clinical adverse reactions reported in at least 1% of subjects receiving dutasteride and at a higher incidence than placebo, by time of onset:

Adverse reaction / arm	Months 0-6	Months 7-12	Months 13-18	Months 19-24
Impotence – Dutasteride	4.7%	1.4%	1.0%	0.8%
Impotence – Placebo	1.7%	1.5%	0.5%	0.9%
Decreased libido – Dutasteride	3.0%	0.7%	0.3%	0.3%
Decreased libido – Placebo	1.4%	0.6%	0.2%	0.1%
Ejaculation disorders – Dutasteride	1.4%	0.5%	0.5%	0.1%
Ejaculation disorders – Placebo	0.5%	0.3%	0.1%	0.0%
Breast disorders – Dutasteride	0.5%	0.8%	1.1%	0.6%
Breast disorders – Placebo	0.2%	0.3%	0.3%	0.1%

Sample sizes for dutasteride/placebo arms were approximately n=2,167/2,158 (months 0-6), n=1,901/1,922 (months 7-12), n=1,725/1,714 (months 13-18), and n=1,605/1,555 (months 19-24). Sexual adverse reactions are associated with dutasteride treatment (including monotherapy and combination with tamsulosin) and may persist after treatment discontinuation; the role of dutasteride in this persistence is unknown. Breast disorders include breast tenderness and breast enlargement.

Combination with alpha-blocker therapy: The most common adverse reactions reported in ≥1% of subjects receiving combination therapy (dutasteride plus tamsulosin) were impotence, decreased libido, breast disorders (including breast enlargement and tenderness), ejaculation disorders, and dizziness. Ejaculation disorders occurred significantly more often in subjects receiving combination therapy (11%) compared with dutasteride (2%) or tamsulosin (4%) monotherapy.

Post-marketing experience: The following adverse reactions have been identified during post-approval use of dutasteride.

Immune system disorders: Hypersensitivity reactions, including rash, pruritus, urticaria, localized oedema, serious skin reactions, and angio-oedema.

Neoplasms: Male breast cancer.

Psychiatric disorders: Depressed mood.

Reproductive system and breast disorders: Testicular pain and testicular swelling.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are requested to report any suspected adverse reactions via the Pharmacy and Poisons Board, Pharmacovigilance Electronic Reporting System (PvERS):

https://pv.pharmacyboardkenya.org

4.9 Overdose

Silodosin: Should overdose of silodosin lead to hypotension, support of the cardiovascular system is of first importance. Restoration of blood pressure and normalization of heart rate may be accomplished by maintaining the patient in the supine position. If this measure is inadequate, administration of intravenous fluid should be considered. If necessary, vasopressors could be used, and renal function should be monitored and supported as needed. Dialysis is unlikely to be of significant benefit since silodosin is highly (97%) protein-bound.

Dutasteride: There is no specific antidote for dutasteride. Therefore, in cases of suspected overdosage, symptomatic and supportive treatment should be given as appropriate, taking the long half-life of dutasteride into consideration.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

The symptoms associated with benign prostatic hyperplasia (BPH) are related to bladder outlet obstruction, comprised of a static component (related to an increase in prostate size caused by proliferation of smooth muscle cells in the prostatic stroma) and a dynamic component (an

increase in smooth muscle tone in the prostate and bladder neck, leading to constriction of the bladder outlet).

Silodosin

Silodosin is a selective antagonist of post-synaptic alpha1-adrenoreceptors located in the human prostate, bladder base, bladder neck, prostatic capsule and prostatic urethra. Blockade of these receptors relaxes smooth muscle in these tissues, improving urine flow and reducing BPH symptoms. An in vitro study of binding affinity to the three alpha1-adrenoreceptor subtypes (alpha1A, alpha1B, alpha1D) demonstrated that silodosin binds with high affinity to the alpha1A subtype.

Dutasteride

Dutasteride inhibits the conversion of testosterone to DHT (dihydrotestosterone), the androgen primarily responsible for the initial development and subsequent enlargement of the prostate gland. Testosterone is converted to DHT by 5 alpha-reductase, which exists as type 1 and type 2 isoforms; type 2 is primarily active in reproductive tissues, while type 1 is also responsible for testosterone conversion in the skin and liver. Dutasteride is a competitive and specific inhibitor of both isoenzymes, forming a stable enzyme complex from which dissociation is extremely slow. Dutasteride does not bind to the human androgen receptor.

5.2 Pharmacokinetic properties

Silodosin

Absorption: The pharmacokinetics of silodosin are linear across doses of 0.1 mg to 24 mg per day. The absolute bioavailability is approximately 32%.

Food effect: The effect of a moderate-fat, moderate-calorie meal was variable, decreasing Cmax by approximately 18-43% and AUC by 4-49% across different studies.

Distribution: Silodosin has an apparent volume of distribution of 49.5 L and is approximately 97% protein-bound.

Metabolism: Silodosin undergoes extensive metabolism through glucuronidation, alcohol and aldehyde dehydrogenase, and CYP3A4 pathways. Its main metabolite is a glucuronide conjugate (KMD-3213G), formed by UGT2B7, which is active, has an extended half-life (~24 hours)

and reaches plasma exposure approximately four times greater than silodosin. Co-administration with UGT2B7 inhibitors (e.g. probenecid, valproic acid, fluconazole) may increase silodosin exposure. The second major metabolite (KMD-3293) is not expected to contribute significantly to overall pharmacologic activity.

Excretion: Following oral administration of 14C-labelled silodosin, radioactivity recovery after 10 days was approximately 33.5% in urine and 54.9% in faeces. Plasma clearance after intravenous administration was approximately 10 L/hour.

Special populations: No dose adjustment based on race or geriatric status is required. Silodosin has not been evaluated in patients under 18 years. Orthostatic hypotension and dizziness incidence was greater in subjects with moderate renal impairment. No dosing adjustment is required in mild or moderate hepatic impairment; pharmacokinetics in severe hepatic impairment have not been studied.

Dutasteride

Absorption: Time to peak serum concentration (Tmax) occurs within 2 to 3 hours after a single 0.5 mg dose. Absolute bioavailability is approximately 60% (range 40-94%). Food reduces Cmax by 10-15%, which is not clinically significant.

Distribution: Dutasteride has a large volume of distribution (300-500 L) and is highly bound to plasma albumin (99.0%) and alpha1-acid glycoprotein (96.6%). At 12 months of dosing, semen dutasteride concentrations averaged 3.4 ng/mL, with about 11.5% of serum concentration partitioning into semen.

Metabolism: Dutasteride is extensively metabolised by CYP3A4 and CYP3A5, producing 4′-hydroxydutasteride, 6-hydroxydutasteride, 6,4′-dihydroxydutasteride and (via CYP3A4) 15-hydroxydutasteride metabolites. It is not metabolised in vitro by CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, or CYP2E1.

Excretion: Dutasteride and its metabolites are excreted mainly in faeces (~5% unchanged, ~40% as metabolites); only trace amounts of unchanged drug appear in urine. The terminal elimination half-life is approximately 5 weeks at steady state. Serum concentrations remain detectable for up to 4-6 months after discontinuation of treatment.

Special populations: Pharmacokinetics have not been investigated in patients under 18 years. No dose adjustment is necessary in the elderly.

Dutasteride is contraindicated in pregnancy and women of childbearing potential. Effects of race, renal impairment, and hepatic impairment on pharmacokinetics have not been specifically studied; no renal dose adjustment is anticipated, but exposure could be higher in hepatically impaired patients due to extensive metabolism.

5.3 Preclinical safety data

Silodosin

In a 2-year oral carcinogenicity study in rats, an increase in thyroid follicular cell tumour incidence was seen in male rats at high doses, believed to result from TSH stimulation secondary to altered thyroxine metabolism; this was not observed in clinical trials, and relevance to human risk is unknown. In a 2-year carcinogenicity study in mice, female mice at high doses showed increased incidence of mammary gland adenoacanthomas and adenocarcinomas, considered secondary to silodosin-induced hyperprolactinemia not observed in clinical trials. Silodosin showed no evidence of mutagenic or genotoxic potential in the Ames assay, mouse lymphoma assay, unscheduled DNA synthesis assay, and in vivo mouse micronucleus assay, with a weakly positive response in Chinese Hamster Lung chromosomal aberration assays at high, cytotoxic concentrations. Fertility studies in male and female rats showed dose-dependent, largely reversible effects at high doses; clinical relevance is unknown.

Dutasteride

Carcinogenicity studies in mice showed increased benign hepatocellular adenomas in female mice at high doses. In rats, an increase in Leydig cell adenomas and hyperplasia was observed at high multiples of the maximum recommended human dose (MRHD), consistent with an effect on the hypothalamic-pituitary-testicular axis following 5 alpha-reductase inhibition. Dutasteride showed no genotoxic potential in bacterial mutagenesis, chromosomal aberration, and micronucleus assays. Fertility studies in male rats showed dose- and time-dependent decreases in fertility, largely reversible on recovery; studies in female rats showed reduced litter size and feminization of male foetuses at exposures 2 to 10 times the MRHD, in the presence of maternal toxicity. Non-specific, reversible, centrally-mediated toxicity was observed in rats and dogs at very high exposure multiples. Dermal absorption studies in rabbits showed substantial systemic absorption of dutasteride under occluded and prolonged contact conditions.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Lactose Monohydrate BP
- Microcrystalline Cellulose (PH-102) USP
- Polystardone XL-10 IH
- Isopropyl Alcohol BP
- Dichloromethane (Methylene Dichloride) BP
- Magnesium Stearate BP
- Mannitol BP
- Pregelatinized Starch USP
- Sodium Lauryl Sulphate BP
- E.H.G Capsule Blue/White Size "0" IH

6.2 Incompatibilities

None known.

6.3 Shelf life

24 months from the date of manufacture (2 years).

6.4 Special precautions for storage

Do not store above 30°C. Protect from direct sunlight. Keep all medicines out of reach of children.

6.5 Nature and contents of container

Blister pack of 3 x 10's in a unit box along with a literature insert.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing Authorization Holder / Registrant

Dawa Limited,

Plot No. 7879/8, Baba Dogo Road, Ruaraka,

P.O. Box 16633-00620, Nairobi, Kenya.

8. Manufacturer

Corona Remedies Private Limited,

Village: Jatoli, P.O: Oachghat, Tehsil Solan,

Dist: Solan (H.P) – 173223, India.

E-mail: info@coronaremedies.com

9. Date of First Registration/Renewal of Registration

10. Date of revision of the text

October 2025