NAPP

A member of the Mundipharma network of associated companies

Integrated data from the CANVAS Program and CREDENCE trials:

canagliflozin and cardiorenal outcomes across the spectrum of composite cardiorenal outcomes

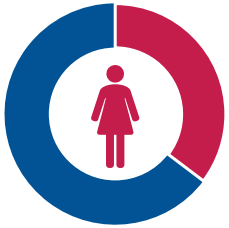
Neuen BL *et al.* Presented at the American Society of Nephrology Kidney Week, 22–25 October 2020, virtual meeting

Invokana® canagliflozin tablets

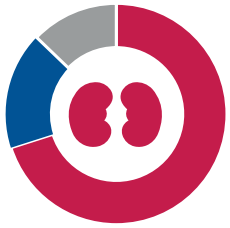
Baseline characteristics of patients who had T2DM with high cardiovascular risk or established CVD/CKD[a,b,1]

Mean age **63.2 years** (SD 8.5 years)

35.3% of patients were **female**



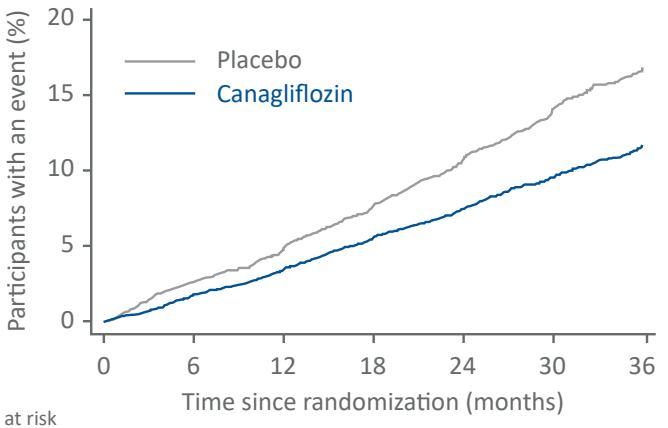
70% of patients had an **eGFR >60 mL/min/1.73m²**



Almost half of patients had a **UACR <30 mg/g**

Effect of canagliflozin on the primary cardiorenal outcome[1]

The endpoint comprised **HHF, non-fatal MI, non-fatal stroke, doubling of serum creatinine, kidney failure, CV or kidney death**



No. at risk							
Placebo	6546	6340	6153	5925	4452	2583	1763
Canagliflozin	7997	7813	7629	7396	5936	4048	3116

23% RRR

HR (95% CI)[c]
0.77 (0.70–0.84)
p <0.001

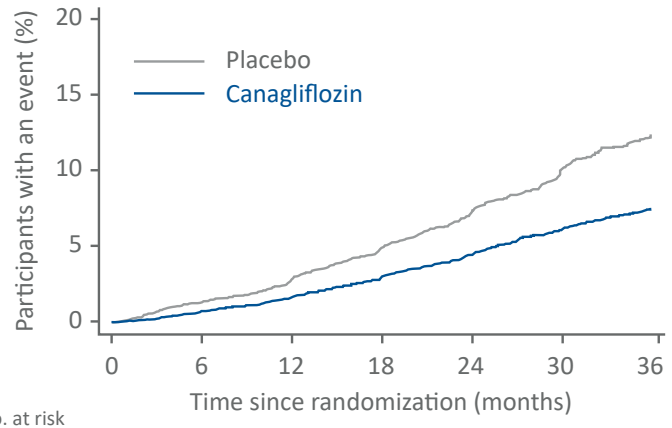
ARR per 1000 pts treated for 2.5 years (95% CI)[d]
−41 (−51 to −31)

Proportion of events (%)
Canagliflozin vs placebo
12.9% vs 15.5%

Click here to view results stratified by renal function

Effect of canagliflozin on the secondary heart failure renal outcome[1]

The endpoint comprised **HHF, doubling of serum creatinine, kidney failure, CV or kidney death**



No. at risk							
Placebo	6546	6424	6284	6099	4622	2690	1848
Canagliflozin	7997	7899	7775	7597	6125	4196	3263

28% RRR

HR (95% CI)[c]
0.72 (0.65–0.80)
p <0.001

ARR per 1000 pts treated for 2.5 years (95% CI)[d]
−34 (−42 to −26)

Proportion of events (%)
Canagliflozin vs placebo
8.3% vs 10.9%

Click here to view results stratified by renal function

[a]eGFR calculated according to the CKD-EPI equation and albuminuria quantified using the UACR at baseline; [b]combined data from both trials; [c]Cox regression stratified by trial with treatment by subgroup interaction terms to tests for trend with no adjustment for multiplicity; [d]estimated using Poisson regression

Abbreviations: ARR: Absolute Risk reduction; CI: Confidence Interval; CV: Cardiovascular; CVD: Cardiovascular Disease; CKD: Chronic Kidney disease; eGFR: estimated Glomerular Filtration Rate; HHF: Hospitalization for Heart Failure; HR: Hazard Ratio; MI: Myocardial Infarction; pts: Patients; RRR: Relative Risk Reduction; SD: Standard Deviation; T2DM: Type 2 Diabetes Mellitus; UACR: Urine Albumin to Creatinine Ratio.

Reference: 1. Neuen BL, et al. Canagliflozin and Cardiorenal outcomes across the spectrum of kidney function and albuminuria: Integrated data from the CANVAS program and CREDENCE trials. Presented at: The American Society of Nephrology (ASN) Kidney Week 2020 Reimagined: A fully digital meeting; October 22-25, 2020. PO2630.

CANVAS CREDENCE

Job code: UK-INV-2100150 Prepared: May 2021

NAPP

A member of the Mundipharma network of associated companies

Integrated data from the CANVAS Program and CREDENCE trials:

canagliflozin and cardiorenal outcomes across the spectrum of composite cardiorenal outcomes

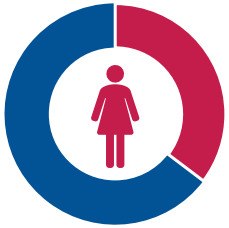
Neuen BL *et al.* Presented at the American Society of Nephrology Kidney Week, 22–25 October 2020, virtual meeting

Invokana® canagliflozin tablets

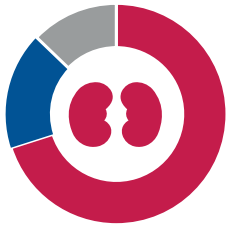
Baseline characteristics of patients who had T2DM with high cardiovascular risk or established CVD/CKD[a,b,1]

Mean age **63.2 years** (SD 8.5 years)

35.3% of patients were **female**



70% of patients had an **eGFR >60 mL/min/1.73m²**



Almost half of patients had a **UACR <30 mg/g**

Effect of canagliflozin on the primary outcome stratified by renal function[1]

eGFR (mL/min/1.73m²)	Canagliflozin (n/N)	Placebo (n/N)	HR (95% CI)[c]
≥90	172/2062	112/1545	0.97 (0.76–1.23)
75 to <90	217/1897	177/1440	0.81 (0.66–0.99)
60 to <75	237/1783	212/1458	0.81 (0.67–0.98)
45 to <60	204/1310	240/1182	0.71 (0.59–0.86)
<45	205/943	275/920	0.66 (0.55–0.79)
UACR (mg/g)			
<30	380/4028	292/3010	0.81 (0.69–0.94)
30 to 300	210/1573	149/1189	0.92 (0.74–1.13)
>300 to 2200	294/1882	361/1799	0.72 (0.62–0.84)
>2200	145/459	211/494	0.69 (0.56–0.86)

***p*-trends[d]**
eGFR: 0.0067 | UACR: 0.057

Click here to view overall results

Effect of canagliflozin on the secondary outcome stratified by renal function[1]

eGFR (mL/min/1.73m²)	Canagliflozin (n/N)	Placebo (n/N)	HR (95% CI)[c]
≥90	73/2062	61/1545	0.74 (0.53–1.05)
75 to <90	123/1897	98/1440	0.84 (0.64–1.10)
60 to <75	141/1783	146/1458	0.71 (0.56–0.89)
45 to <60	151/1310	186/1182	0.69 (0.55–0.86)
<45	176/943	227/920	0.70 (0.58–0.86)
UACR (mg/g)			
<30	185/4028	142/3010	0.79 (0.63–0.99)
30 to 300	129/1573	92/1189	0.91 (0.69–1.19)
>300 to 2200	217/1882	287/1799	0.66 (0.56–0.79)
>2200	131/459	196/494	0.67 (0.54–0.84)

***p*-trends[d]**
eGFR: 0.41 | UACR: 0.056

Click here to view overall results

[a]eGFR calculated according to the CKD-EPI equation and albuminuria quantified using the UACR at baseline; [b]combined data from both trials; [c]Cox regression stratified by trial with treatment by subgroup interaction terms to tests for trend with no adjustment for multiplicity; [d]estimated using Poisson regression

Abbreviations: ARR: Absolute Risk reduction; CI: Confidence Interval; CV: Cardiovascular; CVD: Cardiovascular Disease; CKD: Chronic Kidney disease; eGFR: estimated Glomerular Filtration Rate; HHF: Hospitalization for Heart Failure; HR: Hazard Ratio; MI: Myocardial Infarction; pts: Patients; RRR: Relative Risk Reduction; SD: Standard Deviation; T2DM: Type 2 Diabetes Mellitus; UACR: Urine Albumin to Creatinine Ratio.

Reference: 1. Neuen BL, et al. Canagliflozin and Cardiorenal outcomes across the spectrum of kidney function and albuminuria: Integrated data from the CANVAS program and CREDENCE trials. Presented at: The American Society of Nephrology (ASN) Kidney Week 2020 Reimagined: A fully digital meeting; October 22-25, 2020. PO2630.

CANVAS CREDENCE

Job code: UK-INV-2100150 Prepared: May 2021

NAPP

A member of the Mundipharma network of associated companies

Invokana®
canagliflozin tablets

Invokana now includes evidence for the protection against diabetic kidney disease progression.[1]

Invokana is indicated for the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise:

- **as monotherapy when metformin is considered inappropriate due to intolerance or contraindications**
- **in addition to other medicinal products for the treatment of diabetes**

For study results with respect to combination of therapies, effects on glycaemic control, cardiovascular and renal events, and the populations studied, see sections 4.4, 4.5 and 5.1 of the SmPC.[1]

Overall safety profile of Invokana

The safety profile of Invokana has been evaluated in over 22,500 patients with T2DM, including 13,278 patients treated with canagliflozin in 15 double-blind, controlled phase 3 and phase 4 clinical studies.[1]

Adverse reactions from placebo- and active-controlled studies and post-marketing experience[1]	
Very Common (≥1/10)	• Vulvovaginal candidiasis • Hypoglycaemia in combination with insulin or sulphonylurea
Common (≥1/100 to <1/10)	• Balanitis or balanoposthitis, Urinary tract infection (pyelonephritis and urosepsis have been reported postmarketing) • Constipation, Thirst, Nausea • Polyuria or Pollakiuria • Dyslipidaemia, Haematocrit increased
Uncommon (≥1/1,000 to <1/100)	• Dehydration • Dizziness postural, Syncope • Hypotension, Orthostatic hypotension • Photosensitivity, Rash, Urticaria • Bone fracture • Renal failure (mainly in context of volume depletion) • Blood creatinine increased, Blood urea increased, Blood potassium increased, Blood phosphate increased • Lower limit amputations (mainly toe and midfoot) especially in patients at high risk for heart disease
Rare (≥1/10,000 to <1/1,000)	• Anaphylactic reaction • Diabetic ketoacidosis • Angioedema
Not Known	• Necrotising fasciitis of the perineum (Foumier's gangrene)

Genital mycotic infections have been reported as a common adverse effect of all SGLT2is and urinary tract infections are also frequently reported.[1-4]
Diabetic ketoacidosis is a rare adverse reaction (affecting up to 1/1,000 patients) that can occur with the use of any SGLT2i.[1-4]

Adverse events should be reported. Reporting forms and information can be found at **www.mhra.gov.uk/yellowcard** .
Adverse events should also be reported to Napp Pharmaceuticals at **drugsafetyuk@napp.co.uk**.

Abbreviations: SGLT2i: Sodium-Glucose Cotransporter 2 inhibitor; SmPC: Summary of Product Characteristics; T2DM: Type 2 Diabetes Mellitus.

References: 1. Invokana Summary of Product Characteristics. 2020. **2.** Dapagliflozin Summary of Product Characteristics. AstraZeneca. 2021. **3.** Empagliflozin Summary of Product Characteristics. Boehringer Ingelheim. 2020. **4.** Ertugliflozin Summary of Product Characteristics. Merck Sharp & Dohme Ltd. 2021.

CANVAS CREDENCE

Job code: UK-INV-2100150 Prepared: May 2021

NAPP

A member of the Mundipharma network of associated companies

INVOKANA® (canagliflozin) 100 mg & 300 mg film-coated tablets.

Prescribing information
UNITED KINGDOM

Invokana® canagliflozin tablets

Please refer to the Summary of Product Characteristics (SmPC) before prescribing.

INDICATIONS: The treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise as monotherapy when metformin is considered inappropriate due to intolerance or contraindications, or in addition to other medicinal products for the treatment of diabetes.

DOSAGE & ADMINISTRATION: Adults: recommended starting dose: 100 mg once daily. In patients tolerating this dose and with eGFR ≥ 60 mL/min/1.73 m^2 needing tighter glycaemic control, dose can be increased to 300 mg once daily. For oral use, swallow whole. Caution increasing dose in patients ≥ 75 years old, with known cardiovascular disease or for whom initial canagliflozin-induced diuresis is a risk. Correct volume depletion prior to initiation. When add-on, consider lower dose of insulin or insulin secretagogue to reduce risk of hypoglycaemia. **Children:** no data available. **Elderly:** consider renal function and risk of volume depletion. **Renal impairment:** for the treatment of diabetic kidney disease (DKD) as add on to standard of care (SOC) (ACE inhibitors or ARBs), initiate with 100 mg dose. The glycaemic lowering efficacy of canagliflozin is reduced in patients with moderate renal impairment and likely absent in severe renal impairment. If eGFR falls below 60 mL/min/1.73 m^2 during treatment, adjust or maintain dose at 100 mg once daily.

eGFR (mL/min/1.73m^2) or CrCl (mL/min)	Total daily dose of canagliflozin
≥ 60	Initiate with 100 mg If tolerating 100 mg and needing additional glycaemic control, increase dose to 300 mg
45 to < 60[a]	Initiate with 100 mg If already taking ***Invokana*** – continue 100 mg
30 to < 45[a, b]	Initiate with 100 mg If already taking ***Invokana*** – continue 100 mg
< 30[a, b]	Do not initiate If already taking ***Invokana*** – continue 100 mg[c]

a Consider addition of other anti-hyperglycaemic agents if further glycaemic control is needed

b With urinary albumin/creatinine ratio > 300 mg/g [c] Continue until dialysis or renal transplantation

Hepatic impairment: mild or moderate; no dose adjustment. Severe; not studied, not recommended.

CONTRAINDICATIONS: Hypersensitivity to active substance or any excipient.

SPECIAL WARNINGS & PRECAUTIONS: Not for use in type 1 diabetes. **Renal impairment:** regardless of pretreatment, patients on canagliflozin had an initial fall in eGFR that attenuated over time. eGFR < 60 mL/min/1.73 m^2: higher incidence of adverse reactions associated with volume depletion particularly with 300 mg dose; more events of elevated potassium; greater increases in serum creatinine and blood urea nitrogen (BUN); limit dose to 100 mg once daily. Not studied in severe renal impairment. Monitor renal function prior to initiation and at least annually. **Volume depletion:** caution in patients for whom a canagliflozin-induced drop in blood pressure is a risk (e.g. known cardiovascular disease, eGFR < 60 mL/min/1.73 m^2, anti-hypertensive therapy with history of hypotension, on diuretics or elderly). Not recommended with loop diuretics or in volume depleted patients. Monitor volume status and serum electrolytes. **Diabetic ketoacidosis (DKA):** rare DKA cases reported, including life-threatening and fatal. Presentation may be atypical (blood glucose <14mmol/L). Risk appears higher in patients with moderate to severe decrease in renal function who require insulin. Consider DKA in event of non-specific symptoms. If DKA is suspected or diagnosed, discontinue ***Invokana*** treatment immediately. Interrupt treatment in patients who are undergoing major surgical procedures or have acute serious medical illnesses. Monitoring of (preferably blood) ketone levels is recommended in these patients. Consider risk factors for development of DKA before initiating ***Invokana*** treatment. **Elevated haematocrit:** careful monitoring if already elevated. **Genital mycotic infections:** risk in male and female patients, particularly in those with a history of GMI. **Lower limb amputation:** consider risk factors before initiating. Monitor patients with a higher risk of amputation events, counsel on routine preventative foot care and adequate hydration. Consider discontinuing ***Invokana*** when events preceding amputation occur (e.g. lower-extremity skin ulcer, infection, osteomyelitis or gangrene). **Necrotising fasciitis of the perineum (Fournier's gangrene):** post-marketing cases reported with SGLT2 inhibitors. Rare but serious, patients should seek medical attention if experiencing symptoms including pain, tenderness, erythema, genital/perineal swelling, fever, malaise. If Fournier's gangrene suspected, ***Invokana*** should be discontinued, and prompt treatment instituted. **Urine laboratory assessment:** glucose in urine due to mechanism of action. **Lactose intolerance:** do not use in patients with galactose intolerance, total lactase deficiency or glucose-galactose malabsorption. **Sodium:** essentially "sodium-free".

CANVAS CREDENCE

Job code: UK-INV-2100150 Prepared: May 2021

NAPP

A member of the Mundipharma network of associated companies

INVOKANA® (canagliflozin) 100 mg & 300 mg film-coated tablets.

Prescribing information

UNITED KINGDOM

Invokana® canagliflozin tablets

INTERACTIONS: Diuretics: may increase risk of dehydration and hypotension. **Insulin and insulin secretagogues:** risk of hypoglycaemia; consider lower dose of insulin or insulin secretagogue. **Effects of other medicines on *Invokana:*** enzyme inducers (e.g. St. John's wort, rifampicin, barbiturates, phenytoin, carbamazepine, ritonavir, efavirenz) may decrease exposure of canagliflozin; monitor glycaemic control. Consider dose increase to 300 mg if administered with UGT enzyme inducer. Cholestyramine may reduce canagliflozin exposure; take canagliflozin at least 1 hour before or 4-6 hours after a bile acid sequestrant. **Effects of *Invokana* on other medicines:** monitor patients on digoxin, other cardiac glycosides, dabigatran. Inhibition of Breast Cancer Resistance Protein cannot be excluded; possible increased exposure of drugs transported by BCRP (e.g. rosuvastatin and some anti-cancer agents).

PREGNANCY: No human data. Not recommended.

LACTATION: Unknown if excreted in human milk. Should not be used during breast-feeding.

SIDE EFFECTS: Very common (≥1/10): vulvovaginal candidiasis, hypoglycaemia in combination with insulin or sulphonylurea. **Common (≥1/100 to <1/10):** balanitis or balanoposthitis, urinary tract infection (including pyelonephritis and urosepsis), constipation, thirst, nausea, polyuria or pollakiuria, dyslipidemia, haematocrit increased. **Uncommon (<1/100) but potentially serious:** necrotising fasciitis of the perineum (Fournier's gangrene) (frequency not known), anaphylactic reaction, diabetic ketoacidosis, syncope, hypotension, orthostatic hypotension, urticaria, angioedema, bone fracture, renal failure (mainly in the context of volume depletion), lower limb amputations (mainly of the toe and midfoot). **Refer to SmPC for details and other side effects.**

LEGAL CATEGORY: POM

PACK SIZES, MARKETING AUTHORISATION NUMBER(S) & BASIC NHS COSTS Invokana 100 mg film coated tablets: 30 tablets; EU/1/13/884/002; £39.20. ***Invokana* 300 mg film coated tablets:** 30 tablets; EU/1/13/884/006; £39.20.

MARKETING AUTHORISATION HOLDER: Janssen-Cilag International NV, Turnhoutseweg 30, B-2340 Beerse, Belgium.

® INVOKANA is a registered trade mark of Janssen-Cilag International NV and is used under licence.

Adverse events should be reported. Reporting forms and information can be found at **www.mhra.gov.uk/yellowcard** . Adverse events should also be reported to Napp Pharmaceuticals at **drugsafetyuk@napp.co.uk**.

FURTHER INFORMATION IS AVAILABLE FROM: Napp Pharmaceuticals Ltd. Cambridge Science Park Milton Road, Cambridge, CB4 0AB, UK. For medical information enquiries, please contact medicalinformationuk@napp.co.uk.

UK/INV-18164(3) **Date of Preparation** July 2020

CANVAS CREDENCE

Job code: UK-INV-2100150 Prepared: May 2021

NAPP

A member of the Mundipharma network of associated companies

INVOKANA® (canagliflozin) 100 mg & 300 mg film-coated tablets.

Prescribing information

NORTHERN IRELAND AND REPUBLIC OF IRELAND.

Invokana® canagliflozin tablets

Please refer to the Summary of Product Characteristics (SmPC) before prescribing.

INDICATIONS: The treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise as monotherapy when metformin is considered inappropriate due to intolerance or contraindications, or in addition to other medicinal products for the treatment of diabetes.

DOSAGE & ADMINISTRATION: Adults: recommended starting dose: 100 mg once daily. In patients tolerating this dose and with eGFR ≥ 60 mL/min/1.73 m^2 needing tighter glycaemic control, dose can be increased to 300 mg once daily. For oral use, swallow whole. Caution increasing dose in patients ≥ 75 years old, with known cardiovascular disease or for whom initial canagliflozin-induced diuresis is a risk. Correct volume depletion prior to initiation. When add-on, consider lower dose of insulin or insulin secretagogue to reduce risk of hypoglycaemia. **Children:** no data available. **Elderly:** consider renal function and risk of volume depletion. **Renal impairment:** for the treatment of diabetic kidney disease (DKD) as add on to standard of care (SOC) (e.g. ACE inhibitors or ARBs), initiate with 100 mg dose. The glycaemic lowering efficacy of canagliflozin is reduced in patients with moderate renal impairment and likely absent in severe renal impairment. If eGFR falls below 60 mL/min/1.73 m^2 during treatment, adjust or maintain dose at 100 mg once daily.

eGFR (mL/min/1.73m^2) or CrCl (mL/min)	Total daily dose of canagliflozin
≥ 60	Initiate with 100 mg If tolerating 100 mg and needing additional glycaemic control, increase dose to 300 mg
45 to < 60[a]	Initiate with 100 mg If already taking ***Invokana*** – continue 100 mg
30 to < 45[a, b]	Initiate with 100 mg If already taking ***Invokana*** – continue 100 mg
< 30[a, b]	Do not initiate If already taking ***Invokana*** – continue 100 mg[c]

a Consider addition of other anti-hyperglycaemic agents if further glycaemic control is needed

b With urinary albumin/creatinine ratio > 300 mg/g [c] Continue until dialysis or renal transplantation

Hepatic impairment: mild or moderate; no dose adjustment. Severe; not studied, not recommended.

CONTRAINDICATIONS: Hypersensitivity to active substance or any excipient.

SPECIAL WARNINGS & PRECAUTIONS: Not for use in type 1 diabetes. **Renal impairment:** regardless of pretreatment, patients on canagliflozin had an initial fall in eGFR that attenuated over time. eGFR < 60 mL/min/1.73 m^2: higher incidence of adverse reactions associated with volume depletion particularly with 300 mg dose; more events of elevated potassium; greater increases in serum creatinine and blood urea nitrogen (BUN); limit dose to 100 mg once daily. Not studied in severe renal impairment. Monitor renal function prior to initiation and at least annually. **Volume depletion:** caution in patients for whom a canagliflozin- induced drop in blood pressure is a risk (e.g. known cardiovascular disease, eGFR < 60 mL/min/1.73 m^2, anti-hypertensive therapy with history of hypotension, on diuretics or elderly). Not recommended with loop diuretics or in volume depleted patients. Monitor volume status and serum electrolytes. **Diabetic ketoacidosis (DKA):** rare DKA cases reported, including life-threatening and fatal. Presentation may be atypical (blood glucose <14mmol/L). Risk appears higher in patients with moderate to severe decrease in renal function who require insulin. Consider DKA in event of non-specific symptoms. If DKA is suspected or diagnosed, discontinue ***Invokana*** treatment immediately. Interrupt treatment in patients who are undergoing major surgical procedures or have acute serious medical illnesses. Monitoring of (preferably blood) ketone levels is recommended in these patients. Consider risk factors for development of DKA before initiating ***Invokana*** treatment. **Elevated haematocrit:** careful monitoring if already elevated. **Genital mycotic infections:** risk in male and female patients, particularly in those with a history of GMI. **Urinary tract infections:** post-marketing cases of complicated UTIs including pyelonephritis and urosepsis frequently leading to treatment interruption. **Lower limb amputation:** Consider risk factors before initiating. Monitor patients with a higher risk of amputation events, counsel on routine preventative foot care and adequate hydration. Consider discontinuing ***Invokana*** when events preceding amputation occur (e.g. lower-extremity skin ulcer, infection, osteomyelitis or gangrene). **Necrotising fasciitis of the perineum (Fournier's gangrene):** post-marketing cases reported with SGLT2 inhibitors. Rare but serious, patients should seek medical attention if experiencing symptoms including pain, tenderness, erythema, genital/perineal swelling, fever, malaise. If Fournier's gangrene suspected, ***Invokana*** should be discontinued, and prompt treatment instituted. **Urine laboratory assessment:** glucose in urine due to mechanism of action.

CANVAS CREDENCE

Job code: UK-INV-2100150 Prepared: May 2021

NAPP

A member of the Mundipharma network of associated companies

INVOKANA® (canagliflozin) 100 mg & 300 mg film-coated tablets.

Prescribing information

NORTHERN IRELAND AND REPUBLIC OF IRELAND.

Invokana® canagliflozin tablets

Lactose intolerance: do not use in patients with galactose intolerance, total lactase deficiency or glucose-galactose malabsorption. **Sodium:** essentially "sodium-free".

INTERACTIONS: Diuretics: may increase risk of dehydration and hypotension. **Insulin and insulin secretagogues:** risk of hypoglycaemia; consider lower dose of insulin or insulin secretagogue. **Effects of other medicines on *Invokana:*** enzyme inducers (e.g. St. John's wort, rifampicin, barbiturates, phenytoin, carbamazepine, ritonavir, efavirenz) may decrease exposure of canagliflozin; monitor glycaemic control. Consider dose increase to 300 mg if administered with UGT enzyme inducer. Cholestyramine may reduce canagliflozin exposure; take canagliflozin at least 1 hour before or 4-6 hours after a bile acid sequestrant. Effects of Invokana on other medicines: monitor patients on digoxin, other cardiac glycosides, dabigatran. Inhibition of Breast Cancer Resistance Protein cannot be excluded; possible increased exposure of drugs transported by BCRP (e.g. rosuvastatin and some anti-cancer agents).

PREGNANCY: No human data. Not recommended.

LACTATION: Unknown if excreted in human milk. Should not be used during breast-feeding.

SIDE EFFECTS: Very common (≥1/10): vulvovaginal candidiasis, hypoglycaemia in combination with insulin or sulphonylurea. **Common (≥1/100 to <1/10):** balanitis or balanoposthitis, urinary tract infection (including pyelonephritis and urosepsis), constipation, thirst, nausea, polyuria or pollakiuria, dyslipidemia, haematocrit increased. **Uncommon (<1/100) but potentially serious:** necrotising fasciitis of the perineum (Fournier's gangrene) (frequency not known), anaphylactic reaction, diabetic ketoacidosis, syncope, hypotension, orthostatic hypotension, urticaria, angioedema, bone fracture, renal failure (mainly in the context of volume depletion), lower limb amputations (mainly of the toe and midfoot). **Refer to SmPC for details and other side effects.**

LEGAL CATEGORY: POM

PACK SIZES, MARKETING AUTHORISATION NUMBER(S) & BASIC NHS COSTS Invokana 100 mg film coated tablets: 30 tablets; EU/1/13/884/002; £39.20. ***Invokana* 300 mg film coated tablets:** 30 tablets; EU/1/13/884/006; £39.20.

MARKETING AUTHORISATION HOLDER: Janssen-Cilag International NV, Turnhoutseweg 30, B-2340 Beerse, Belgium.

® INVOKANA is a registered trade mark of Janssen-Cilag International NV and is used under licence.

Adverse events should be reported. Reporting forms and information can be found at **www.mhra.gov.uk/yellowcard** . Adverse events should also be reported to Napp Pharmaceuticals at **drugsafetyuk@napp.co.uk**.

FURTHER INFORMATION IS AVAILABLE FROM: Napp Pharmaceuticals Ltd. Cambridge Science Park Milton Road, Cambridge, CB4 0AB, UK. For medical information enquiries, please contact medicalinformationuk@napp.co.uk.

IE-INV-2100004 **Date of Preparation** April 2021

CANVAS CREDENCE

Job code: UK-INV-2100150 Prepared: May 2021