TUKYSA® ▼ (tucatinib) film-coated tablets Prescribing Information for Great Britain (GB) and Northern Ireland (NI)

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. Refer to section 4.8 of the SPC for how to report adverse reactions.

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

Presentation: Film-coated tablets each containing 50 mg or 150 mg of tucatinib.

Indication: TUKYSA is indicated in combination with trastuzumab and capecitabine for the treatment of adult patients with HER2-positive locally advanced or metastatic breast cancer who have received at least 2 prior anti-HER2 treatment regimens.

Dosage and Administration: Treatment should be initiated and supervised by a physician experienced in the administration of anti-cancer therapies. The recommended dose is 300 mg tucatinib orally twice daily (bd), with or without a meal, continuously in combination with trastuzumab (given intravenously (IV) as an initial 8 mg/kg dose followed by 6 mg/kg IV every 21 days, or subcutaneously at 600 mg every 21 days) and capecitabine (1000 mg/m^2 orally twice daily on days 1 to 14 every 21 days). *Refer to the SmPC for co-administered trastuzumab and capecitabine for additional information*. The treatment components can be administered in any order. Treatment with TUKYSA should be continued until disease progression or unacceptable toxicity. *Missed dose:* the patient should take their next dose at the regularly scheduled time. *Dose modification:* Consult the SmPCs for tucatinib, trastuzumab and capecitabine for dose modification guidance for toxicities suspected to be caused by those therapies. Dose of tucatinib may be reduced from 300mg bd to 250mg bd (first reduction), 200mg bd (second reduction) and 150mg bd (third reduction). Permanently discontinue treatment in patients unable to tolerate 150mg bd. Avoid concomitant use with strong CYP2C8 inhibitors. If this cannot be avoided, see SmPC for dose modification guidance. *Elderly:* No dose adjustment is required in patients aged ≥ 65 years. Tucatinib has not been investigated in patients above the age of 80 years. *Renal impairment:* No dose adjustment is required for mild, moderate or severe renal impairment. *Hepatic impairment:* No dose adjustment is required in patients with mild or moderate hepatic impairment. For patients with severe hepatic impairment (Child-Pugh C), a reduced starting dose of 200 mg bd is recommended. *Paediatric population:* The safety and efficacy of TUKYSA in paediatric patients have not been established.

Contraindications: Hypersensitivity to the active substance or to any of the excipients.

Special warnings and precautions: I*ncreased ALT, AST and total bilirubin* (monitor these every three weeks or as clinically indicated); *increased creatinine without impaired renal function* (use alternative markers such as BUN, cystatin C or calculated GFR to determine whether renal function is impaired); *diarrhoea* (severe events such as dehydration, hypotension, acute kidney injury and death have been reported – see SmPC for details on prompt medical management and tucatinib dose modification); *embryo- foetal toxicity* (foetal abnormalities occurred in rabbits at maternal exposures similar to clinical exposures at the recommended dose – see below for contraception guidance); *sensitive CYP3A substrates* (check the concomitant medicine SmPC because tucatinib is a strong CYP3A inhibitor which could increase the plasma concentration of the CYP3A substrate and lead to life-threatening toxicities); *PgP substrates* (check the concomitant medicine SmPC because tucatinib may increase the plasma concentration of the PgP substrate which could lead to toxicities); *a strong CYP3A inducer/moderate CYP2C8 inducer* (avoid concomitant use as these medicines decreased tucatinib concentration and may reduce its activity); strong/moderate CYP2C8 inhibitor (avoid concomitant use with strong CYP2C8 inhibitors which will increase tucatinib concentrations and risk of toxicity. No clinical data for use with moderate CYP2C8 inhibitors, so increase monitoring for tucatinib toxicity if co-administering); *tucatinib contains 55.3mg sodium per 300mg dose and 60.6mg potassium per 300mg dose* (relevant for patients with kidney impairment or on a controlled potassium diet).

Fertility, contraception, pregnancy and lactation: Tucatinib may cause harmful pharmacological effects when administered to women during pregnancy and/or on the foetus/newborn child. Women of childbearing potential should be advised to avoid becoming pregnant and to use effective contraception during and up to at least 1 week after treatment. Male patients with female partners of childbearing potential should also be advised to use effective contraception during and up to at least 1 week after treatment. It is unknown whether tucatinib/metabolites are excreted in human milk. Breast feeding should be discontinued during and up to 1 week after treatment. Tucatinib may impair fertility in females of reproductive potential.

Driving and operating machinery: Tucatinib has no or negligible influence on the ability to drive and use machines. Consider patients' clinical status when assessing ability to perform tasks that require judgement, motor or cognitive skills.

Undesirable effects: Across two studies involving 431 patients who received tucatinib in combination with trastuzumab and capecitabine, *very common (incidence ≥ 1/10)* adverse reactions observed were epistaxis, diarrhoea, nausea, vomiting, stomatitis*, rash*, arthralgia, AST increase, ALT increase, blood bilirubin increased (also includes hyperbilirubinaemia), and weight decrease. Stomatitis* includes stomatitis, oropharyngeal pain, mouth ulceration, oral pain, lip ulceration, glossodynia, tongue blistering, lip blister, oral dysaesthesia, tongue ulceration and aphthous ulcer. Rash* includes rash maculo-papular, rash, dermatitis acneiform, erythema, rash macular, rash papular, rash pustular, rash pruritic, rash erythematous, skin exfoliation, urticaria, dermatitis allergic, palmar erythema, plantar erythema and skin toxicity. Serious adverse reactions occurred in 29% of patients treated with tucatinib and include diarrhoea (4%), vomiting (3%) and nausea (2%). Please refer to the *TUKYSA SmPC for information on other adverse effects*.

Overdose: In the event of an overdose, treatment with tucatinib should be withheld and general supportive measures should be applied.

Price: TUKYSA 50 mg film-coated tablets, carton of 88 tablets: £1,968.42
TUKYSA 150 mg film-coated tablets, carton of 84 tablets: £5,636.84

Legal category: POM

Marketing authorisation number: GB: PLGB 00057/1728 (50mg), PLGB 00057/1729 (150mg); NI: EU/1/20/1526/001 (50 mg), EU/1/20/1526/002 (150 mg)

Marketing authorisation holder: GB: Pfizer Limited, Ramsgate Road, Sandwich, Kent, CT13 9NJ; NI: Pfizer Europe MA EEIG, Boulevard de la Plaine 17, 1050 Bruxelles, Belgium

Adverse events should be reported.
Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.
Adverse events should also be reported to Pfizer Medical Information on 01304 616161.

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