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| **Indication** | Monotherapy treatment of unresectable locally advanced or metastatic cholangiocarcinoma which has a fibroblast growth factor receptor 2 (FGFR2) gene fusion/rearrangement in patients with disease progression during or after previous systemic therapy.<br><br>NB the patient must have not received any specifically FGFR2-targeted therapy unless they received futibatinib via a company early access scheme or pemigatinib monotherapy had to be stopped within 3 months of its start solely as a consequence of dose-limiting toxicity and in the clear absence of progressive disease. |
| **Treatment Intent** | Palliative |
| **Frequency and number of cycles** | Repeat every 28 days, continuously.<br><br>Continue until disease progression, unacceptable toxicity or patient's choice to stop treatment.<br><br>A formal medical review as to whether treatment with futibatinib should continue or not should be scheduled to occur r at least by the end of the first 8 weeks of treatment. |
| **Monitoring Parameters pre-treatment** | • **Virology screening:** All new patients referred for systemic anti-cancer treatment should be screened for hepatitis B and C and the result reviewed prior to the start of treatment. Patients not previously tested who are starting a new line of treatment, should also be screened for hepatitis B and C. Further virology screening will be performed following individual risk assessment and clinician discretion.<br>• FBC, U&Es (including $Ca^{2+}$ and $PO_4^{3-)}$ and LFTs baseline, weekly during cycle 1 and then at every cycle thereafter.<br>• If neuts >/=1 and PLT >/=75 continue with treatment, if PLTS 50-74 discuss with consultant, otherwise delay.<br>• If a patient develops hyperphosphatemia (>ULN) during cycle 1 bloods should be checked at day 8 of cycle 2 onwards until phosphate is </=7 mg/dL (<2.26mmol/L), for 2 consecutive cycles on a stable dose of phosphate binders.<br>• Patients should be counselled prior to treatment on the importance of following a low phosphate diet.<br>• **Ophthalmological examination:** Futibatinib can cause serous retinal detachment. Ophthalmological examination should be performed prior to initiation of therapy, 6 weeks thereafter, and urgently at any time for visual symptoms. Results of ophthalmology assessment to be reviewed as part of the pre-treatment assessment.<br>• Patients that have clinically significant medical eye disorders, such as retinal disorders, including but not limited to, central serous retinopathy, macular/retinal degeneration, diabetic retinopathy, and previous retinal detachment should be treated with caution at clinician's discretion.<br>• The patient should not have untreated or symptomatic brain metastases prior to starting treatment.<br>• **Hepatic impairment:** No dose adjustment required in mild, moderate or severe impairment. No safety data in severe hepatic impairment.<br>• **Renal impairment:** Dose adjustment is not required for patients with mild to moderate renal impairment, CrCL 30 to 89 mL/min. There are no data in patients with severe renal impairment (CrCl < 30 mL/min) or for patients with end-stage renal disease receiving intermittent haemodialysis use with caution.<br>• **Management of adverse reactions and dose adjustments:**<br>  ○ **Hyperphosphatemia:** Increases in phosphate levels can occur whilst taking futibatinib. Monitor for hyperphosphatemia throughout treatment. Initiate a low phosphate diet and phosphate lowering therapy when serum phosphate level is >/=5.5 mg/dL (>/=1.77mmol/L). For serum phosphate levels >7 mg/dL (>2.26mmol/L), initiate or intensify phosphate lowering therapy and dose reduce, withhold, or permanently discontinue futibatinib based on duration |

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| | and severity of hyperphosphatemia (see table 1). If treatment is stopped or serum phosphate level falls below normal range, phosphate-lowering therapy and diet should be discontinued. For guidance on phosphate lowering therapy see EKHUFT guidance: *Management of Chronic Kidney Disease Mineral Bone Disorder*<br>○ **Serous retinal detachment:** Futibatinib can cause serous retinal detachment, which may present with symptoms such as blurred vision, visual floaters, or photopsia. Patients should be advised to report any changes in vision during treatment, including blurred vision, flashes of light, or seeing black spots. For serous retinal detachment reactions, dose modification or interruption maybe required see table 1.<br>• **Dose Modification:** Co-administration of futibatinib with strong CYP3A4/P-gp inhibitors, such as itraconazole, should be avoided, but if this is not possible, based on careful monitoring of tolerability, a futibatinib dose reduction to the next lower level should be considered. Co-administration of futibatinib with strong or moderate CYP3A4/P-gp inducers, such as rifampicin, should be avoided, but if this is not possible, gradually increasing the futibatinib dose based on careful monitoring of tolerability should be considered.<br>If a dose reduction is required the first dose reduction should be to 16mg OD, second dose reduction to 12mg OD. If a dose of 12mg OD cannot be tolerated futibatinib should be discontinued. See table 1 for dose modification guidance.<br>• **Common drug interactions (for comprehensive list refer to BNF/SPC):**<br>○ Concomitant use with strong P-gp and CYP3A inhibitors (e.g. grapefruit/grapefruit juice, itraconazole, ketoconazole) should be avoided. If unavoidable see dose modification section above.<br>○ Avoid concomitant use with strong P-gp and CYP3A inducers (e.g. carbamazepine, phenytoin, phenobarbital, rifampicin) or moderate P-gp and CYP3A inducers (e.g., bosentan, efavirenz, etravirine, phenobarbital, primidone) if unavoidable see dose modification section above.<br>○ Futibatinib is an inhibitor of P-gp and BCRP. Consider more frequent monitoring for adverse reactions associated with concomitantly administered drugs that are sensitive substrates of P-gp (e.g., digoxin, dabigatran, colchicine) or BCRP (e.g. rosuvastatin) and reduce the dose of these drugs if necessary.<br>○ Futibatinib may increase exposure of drugs that are substrates of P-gp or BCRP.<br>○ Futibatinib has the potential to induce CYP1A2. Coadministration of futibatinib with CYP1A2 sensitive substrates (e.g. olanzapine, theophylline) may decrease their exposure and therefore may affect their activity.<br>○ Patients should not drink grapefruit juice or eat grapefruit whilst taking futibatinib.<br>• **Missed dose**: If a dose is missed by more than 12 hours or vomiting occurs after taking a dose, an additional dose should not be taken, and treatment should be resumed with the next scheduled dose**.**<br>• **Contraception:** An effective method of contraception should be used in women of childbearing potential and in men with women partners of childbearing potential during treatment and for 1 week following completion of therapy.<br>• **Driving and machinery:** Patients should be advised to be cautious when driving or operating machines in case they experience fatigue or visual disturbances during the treatment.<br>• **For oral self-administration**: refer to local Trust policy on oral anti-cancer medicines and supply Patient Information Leaflet. |
| **References** | CDF list V1.355 accessed online 25.03.2025 Blueteq form accessed online 25.03.2025 EMC accessed online 25.03.2025 letter to healthcare professionals only. LYTGOBI SPC supplied from Taiho Oncology Europe GmbH 31.04.2025. SPC accessed online 27.10.2025 |

NB For funding information, refer to CDF and NICE Drugs Funding List

**Table 1 Recommended Dosage Modifications for Adverse Reactions**

| Adverse Reaction | Severity | Dose modification |
|---|---|---|
| Retinal Pigment Epithelial Detachment (RPED) | Asymptomatic | Continue futibatinib at current dose. Monitoring should be performed. |
| | Moderate decrease in visual acuity (best corrected visual acuity 20/40 or better or </= 3 lines of decreased vision from baseline); limiting instrumental activities of daily living | Withhold. If improved on subsequent examination, futibatinib should be resumed at the next lower dose level.<br><br>If symptoms recur, persist or examination does not improve, permanent discontinuation of futibatinib should be considered based on clinical status. |
| | Marked decrease in visual acuity (best corrected visual acuity worse than 20/40 or >3 lines decreased vision from baseline up to 20/200); limiting activities of daily living | Withhold until resolution. If improved on subsequent examination, futibatinib may be resumed at 2 dose levels lower. If symptoms recur, persist or examination does not improve, permanent discontinuation of futibatinib should be considered based on clinical status. |
| | Visual acuity worse than 20/200 in affected eye; limiting activities of daily living | Permanent discontinuation of futibatinib should be considered based on clinical status |
| Hyperphosphatemia | Serum phosphate >/=5.5 - </=7 mg/dL (>/=1.77mmol/L -2.26mmol/L) | Continue at the current dose and initiate phosphate lowering therapy.<br>Monitor serum phosphate weekly. |
| | Serum phosphate >7 - </=10 mg/dL (>2.26mmol/L - </=3.23mmol/L) | Initiate or adjust phosphate lowering therapy.<br>Monitor serum phosphate weekly and dose reduce to next lower dose<br>– If the serum phosphate resolves to </=7 mg/dL (2.26mmol/L) within 2 weeks after dose reduction, continue at this reduced dose.<br>– If serum phosphate is not </=7 mg/dL (2.26mmol/L) within 2 weeks, further reduce to the next lower dose.<br>– If serum phosphate is not </=7 mg/dL (2.26mmol/L) within 2 weeks after the second dose reduction, withhold until serum phosphate is </=7 mg/dL and resume at the dose prior to suspending. |
| | Serum phosphate >10 mg/dL (</=3.23mmol/L) | Initiate or intensify phosphate lowering therapy and monitor serum phosphate weekly and<br>Withhold until phosphate is </=7 mg/dL (2.26mmol/L) and resume at the next lower dose.<br>Permanently discontinue I if serum phosphate is not </=7 mg/dL (2.26mmol/L) within 2 weeks following 2 dose reductions. |
| Other Adverse Reactions | Grade 3[a] | Withhold until toxicity resolves to Grade 1 or baseline, then resume futibatinib:<br>– for haematological toxicities resolving within 1 week, at the dose prior to withholding.<br>– for other adverse reactions, at next lower dose. |
| | Grade 4[a] | Permanently discontinue. |
| a Severity as defined by National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE version 4.03). | | |

**Repeat every 28 days**

| TTO | Drug | Dose | Route | Directions |
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| Day 1 | **FUTIBATINIB** | **20mg*** | PO | OD continuously at the same time each day.<br>Swallow whole, do not chew crush or dissolve tablets.<br><br>Available as 4mg tablets. |
| | Hypromellose | 0.3% | topical | One drop each eye QDS.<br>Dispense on cycle 1 only, then only if required. |
| | Metoclopramide | 10mg | PO | 10mg up to three times a day PRN.<br>Do not take for more than 5 days continuously.<br><br>Dispense on Cycle 1 only, then only if required |
| | Loperamide | 2mg | PO | Take two capsules (4mg) after first loose stool, then one capsule (2mg) after each loose stool when required. (Maximum 16mg per day).<br><br>Dispense on Cycle 1 only, then only if required. |
| | * see dose modifications if concurrent CYP3A4/P-gp inhibitors or inducers | | | |
| | NB where phosphate lowing therapy is indicated (see protocol) consider calcium carbonate. If calcium carbonate is not indicated (because of hypercalcaemia or low serum parathyroid hormone levels) or not tolerated consider sevelamer carbonate. | | | |