TRIFLURIDINE-TIPIRACIL (Lonsurf)

INDICATION (ICD10) C16, C18, C20

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (N/A) (TR12)

1. Trifluridine–tipiracil for previously treated metastatic colorectal cancer, unsuitable for other available therapies, who have failed at least two prior regimens (fluoropyrimidine, oxaliplatin or irinotecan-based chemotherapies, anti-vascular endothelial growth factor (VEGF) agents and anti-epidermal growth factor receptor (EGFR) agents) for advanced/metastatic disease (those patients relapsing during or within 6 months of completing adjuvant chemotherapy can count the adjuvant line as one line of therapy for advanced/metastatic disease). PS 0 or 1. (TA405)
2. Trifluridine plus tipiracil monotherapy for the third or more line of systemic therapy for locally advanced or metastatic adenocarcinoma of the stomach or gastro-oesophageal junction. PS 0 or 1.

REGIMEN

Days 1 to 5 and 8 to 12
TRIFLURIDINE-TIPIRACIL 35mg/m^2/dose (maximum 80mg/dose) twice daily orally

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 28 days until disease progression (formal medical review by end of 2nd cycle)

ADMINISTRATION

One tablet contains Trifluridine 15mg + Tipiracil 6.14mg or Trifluridine 20mg +Tipiracil 8.19mg
Tablets should be taken 12 hours apart.
Swallowed with water within 1 hour after completion of the morning and evening meals.

ANTI-EMETICS

Low risk days 1 to 12

CONCURRENT MEDICATION REQUIRED

Trifluridine-tipiracil	-

EXTRAVASATION AND TYPE OF LINE / FILTERS

Not applicable

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E and LFTs every day 1
Neutrophils x 10^9/L ≥1.5 day 1 (and see dose modifications)
Platelets x 10^9/L ≥100 day 1 (and see dose modifications)
Serum creatinine - GFR each cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Trifluridine-tipiracil	Bone marrow suppression Diarrhoea Renal and hepatic impairment Stomatitis

DOSE MODIFICATIONS

Level 1 dose reduction: From 35mg/m^2 to 30mg/m^2
Level 2 dose reduction: From 30mg/m^2 to 25mg/m^2
Level 3 dose reduction: From 25mg/m^2 to 20mg/m^2
A maximum of 3 dose reductions are permitted to a minimum dose of 20mg/m^2 twice daily.
Dose escalation is not permitted after it has been reduced.

Haematological Neutrophils <0.5×10^9/L	interrupt treatment, resume once ≥1.5×10^9/L
Platelets <50×10^9/L	interrupt treatment, resume once ≥75×10^9/L
Febrile neutropenia	• Interrupt dosing until toxicity resolves to grade 1 or baseline. • When resuming dosing, decrease the dose level by 5mg/m^2/dose from the previous dose level. • Dose reductions are permitted to a minimum dose of 20mg/m^2/dose twice daily (or 15mg/m^2/dose twice daily in severe renal impairment). • Do not increase dose after it has been reduced.
CTCAE grade 4 neutropenia (<0.5x10^9/L) or thrombocytopenia (<25×10^9/L) that results in more than 1 week's delay in start of next cycle	• Interrupt dosing until toxicity resolves to grade 1 or baseline. • When resuming dosing, decrease the dose level by 5mg/m^2/dose from the previous dose level. • Dose reductions are permitted to a minimum dose of 20mg/m^2/dose twice daily (or 15mg/m^2/dose twice daily in severe renal impairment). • Do not increase dose after it has been reduced.

Non-haematological

CTCAE non-haematologic grade 3 or grade 4 adverse reaction; except for grade 3 nausea and/or vomiting controlled by antiemetic therapy or diarrhoea responsive to antidiarrhoeal medicinal products	• Interrupt dosing until toxicity resolves to grade 1 or baseline. • When resuming dosing, decrease the dose level by 5mg/m^2/dose from the previous dose level. • Dose reductions are permitted to a minimum dose of 20mg/m^2/dose twice daily (or 15mg/m^2/dose twice daily in severe renal impairment). • Do not increase dose after it has been reduced.

Hepatic impairment

Bilirubin of >1.5xULN	Not recommended

Renal impairment

CrCl >30ml/min	give 100% dose
CrCl 15-29ml/min	Starting dose of 20mg/m^2 twice daily is recommended. One dose reduction to a minimum dose of 15mg/m^2 twice daily is permitted based on individual safety and tolerability. Dose escalation is not permitted after it has been reduced.

REFERENCES

1. SPC