TRASTUZUMAB DERUXTECAN (Enhertu)

INDICATION (ICD10) C50

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (TRAD1) (TRAD2)

1. Trastuzumab deruxtecan for treating over- expressed HER2 positive (HER2 3+) unresectable locally advanced or metastatic breast cancer (without untreated or symptomatic brain metastases) after 2 or more anti-HER2 therapies, which must have included trastuzumab and trastuzumab emtansine. PS 0 or 1.
2. For treating over-expressed HER2 positive (HER2 3+) unresectable locally advanced or metastatic breast cancer in patients who have received 1 or more anti-HER2 therapies (at least trastuzumab and a taxane for advanced / metastatic breast cancer or developed disease recurrence during or within 6 months of completing an adjuvant or neoadjuvant treatment regimen which contained at least trastuzumab and a taxane or adjuvant treatment with trastuzumab emtansine) and who are treatment-naïve for trastuzumab emtansine in the advanced/metastatic disease with a baseline left ventricular ejection fraction (LVEF) of at least 50%. PS 0 or 1.

REGIMEN

Day 1 TRASTUZUMAB DERUXTECAN 5.4mg/kg in #ml glucose 5% IV infusion over 90 minutes

diluent volume for dose prescribed as per national standardised product specification

If the prior infusion was well tolerated subsequent infusions may be administered over 30 minutes

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 21 days until disease progression or unacceptable toxicity

ANTI-EMETICS

High risk day 1

CONCURRENT MEDICATION REQUIRED

None required

EXTRAVASATION AND TYPE OF LINE / FILTERS

Trastuzumab deruxtecan – not known consider non-vesicant

Administer via administration set with polyethersulfone (PES) ≤0.22micron inline filter
Peripheral or central line

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E and LFTs every cycle
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
Baseline weight and every cycle
Monitor cardiac function as per network guidelines. Prior to consideration of treatment with trastuzumab deruxtecan the patient has a baseline left ventricular ejection fraction (LVEF) of at least 50%.
Chest CT (high resolution if available) imaging at regular intervals (6 weekly initially for 6 months then 3 monthly) to monitor for signs of pneumonitis (as per local practice).

MAIN TOXICITES AND ADVERSE REACTIONS

Trastuzumab deruxtecan	GI disorders Interstitial lung disease / pneumonitis Neutropenia, anaemia Left ventricular ejection fraction (LVEF) decreased

DOSE MODIFICATIONS

Trastuzumab deruxtecan

Dose reduction schedule

Starting dose is 5.4mg/kg	Dose to be administered
First dose reduction	4.4mg/kg
Second dose reduction	3.2mg/kg
Requirement for further dose reduction	Discontinue treatment

Haematological

Trastuzumab deruxtecan

Neutropenia grade 3 (less than 1.0-0.5x10^9/L)	• Interrupt until resolved to grade 2 or less, then maintain dose.
Neutropenia grade 4 (less than 0.5x10^9/L)	• Interrupt until resolved to grade 2 or less. • Reduce dose by one level.
Febrile neutropenia Absolute neutrophil count of less than 1.0x10^9/L and temperature greater than 38.3°C or a sustained temperature of 38°C or greater for more than one hour.	• Interrupt until resolved. • Reduce dose by one level.

Non-haematological

Trastuzumab deruxtecan

Interstitial lung disease (ILD) / pneumonitis Asymptomatic ILD/pneumonitis (grade 1)	Interrupt trastuzumab deruxtecan until resolved to grade 0, then: • if resolved in 28 days or less from date of onset, maintain dose. • if resolved in greater than 28 days from date of onset, reduce dose one level. • consider corticosteroid treatment as soon as ILD/pneumonitis is suspected
Interstitial lung disease (ILD) / pneumonitis Symptomatic ILD/pneumonitis (grade 2 or greater)	• Permanently discontinue. • Promptly initiate corticosteroid treatment as soon as ILD/pneumonitis is suspected.
Left ventricular ejection fraction (LVEF) decreased LVEF greater than 45% and absolute decrease from baseline is 10% to 20%	• Continue treatment.
Left ventricular ejection fraction (LVEF) decreased LVEF 40% to 45% And absolute decrease from baseline is less than 10%	• Continue treatment. • Repeat LVEF assessment within 3 weeks.
Left ventricular ejection fraction (LVEF) decreased LVEF 40% to 45% And absolute decrease from baseline is 10% to 20%	• Interrupt treatment • Repeat LVEF assessment within 3 weeks. • If LVEF has not recovered to within 10% from baseline, permanently discontinue treatment • If LVEF recovers to within 10% from baseline, resume treatment at the same dose.
Left ventricular ejection fraction (LVEF) decreased LVEF less than 40% or absolute decrease from baseline is greater than 20%	• Interrupt treatment • Repeat LVEF assessment within 3 weeks. • If LVEF of less than 40% or absolute decrease from baseline of greater than 20% is confirmed, permanently discontinue treatment.
Left ventricular ejection fraction (LVEF) decreased Symptomatic congestive heart failure (CHF)	• Permanently discontinue treatment.

Hepatic impairment

Trastuzumab deruxtecan

Total bilirubin ≤1.5xULN, irrespective of AST	No dose adjustment required
Total bilirubin >1.5xULN, irrespective of AST	Insufficient data. Monitor carefully

Renal Impairment

Trastuzumab deruxtecan

CrCl ≥30ml/min	No dose adjustment. Monitor carefully. A higher incidence of grade 1 and 2 ILD has been observed in patients with moderate renal impairment (CrCl ≥30 to <60ml/min).
CrCl <30ml/min	Limited data and so no dose recommendations can be made.

REFERENCES

1. SPC March 2