Management of symptomatic adverse reactions to trastuzumab emtansine (Kadcyla®)

Table 1: Dose modification guidelines for increased transaminases (AST/ALT)

Grade 2 **(> 2.5 to ≤ 5 × the ULN)**	**Grade 3** **(> 5 to ≤ 20 × the ULN)**	**Grade 4** **(> 20 × the ULN)**
No dose modification is required.	Do not administer trastuzumab emtansine until AST/ALT recovers to Grade ≤ 2 (>2.5 to ≤5 x ULN), and then dose reduce (see notes).	Discontinue trastuzumab emtansine

Table 2: Dose modification guidelines for hyperbilirubinemia

Grade 2 **(> 1.5 to ≤ 3 × the ULN)**	**Grade 3** **(> 3 to ≤ 10 × the ULN)**	**Grade 4** **(> 10 × the ULN)**
Do not administer trastuzumab emtansine until total bilirubin recovers to Grade ≤ 1 (>ULN to 1.5x ULN). No dose modification is required.	Do not administer trastuzumab emtansine until total bilirubin recovers to Grade ≤ 1 (>ULN to 1.5x ULN), and then dose reduce (see notes).	Discontinue trastuzumab emtansine.

Treatment should be discontinued in patients with serum transaminases >3 x ULN and bilirubin >2 x ULN

Table 3: Dose modification guidelines for thrombocytopenia

Grade 3 **(Platelets: 25 x10^9/l to < 50 x 10^9/l)**	**Grade 4** **(Platelets: < 25 x 10^9 /l)**
Do not administer trastuzumab emtansine until platelet count recovers to ≤ Grade 1 (i.e. platelets ≥ 75 x10^9/l). No dose modification is required.	Do not administer trastuzumab emtansine until platelet count recovers to ≤ Grade 1 (i.e. platelets ≥ 75 x 10^9/l), and then dose reduce (see notes).

Table 4: Dose modifications for left ventricular dysfunction

LVEF < 40%	**LVEF > 45%**	**LVEF 40% to ≤45% and decrease is < 10% points from baseline**	**LVEF 40% to ≤45% and decrease is ≥ 10% points from baseline**	**Symptomatic CHF**
Do not administer trastuzumab emtansine. Repeat LVEF assessment within 3 weeks. If LVEF < 40% is confirmed, discontinue trastuzumab emtansine.	Continue treatment with trastuzumab emtansine.	Continue treatment with trastuzumab emtansine. Repeat LVEF assessment within 3 weeks.	Do not administer trastuzumab emtansine. Repeat LVEF assessment within 3 weeks. If the LVEF has not recovered to within 10% points from baseline, discontinue trastuzumab emtansine.	Discontinue trastuzumab emtansine.

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Version 1 (07/09/2016)
N.B. Version numbers re-started from 1 when adverse reaction information separated from proforma