Panel member request: Reevaluate the data regarding the use of ECF (epirubicin, cisplatin, and fluorouracil) and ECF modifications (epirubicin, oxaliplatin or cisplatin, and fluorouracil or capecitabine) as perioperative chemotherapy options for adenocarcinoma in medically fit patients.

Panel member request: Consider adding fluoropyrimidine and oxaliplatin as a perioperative chemotherapy option.

Internal request: Consider adding regimens for “Postoperative Chemotherapy”.

Institutional review request: Reevaluate the epirubicin containing regimens for First-Line Therapy for metastatic or locally advanced cancer.

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<td><strong>ESOPH-F 2 of 12</strong></td>
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| Panel member request:     | Based on a review of the data, the panel discussed the Categories of Evidence for ECF (epirubicin, cisplatin, and fluorouracil) and ECF modifications (epirubicin, oxaliplatin or cisplatin, and fluorouracil or capecitabine) and their use as options for perioperative chemotherapy. Based on the voting results, the panel consensus supported making the following changes:  
  - ECF (epirubicin, cisplatin and fluorouracil) was changed from category 3 to category 2B recommendation  
  - All ECF modifications (epirubicin, oxaliplatin or cisplatin, and fluorouracil or capecitabine) were changed from category 3 to category 2B recommendations. | YES NO ABSTAIN ABSENT |
|                           |                             | 13 9 2 4 |

| **ESOPH-F 3 of 12**       |                             |      |
| Internal request:         | Based on a review of the data, clinical experience, and discussion the panel supported adding “capecitabine and oxaliplatin” as a category 2A recommendation for postoperative chemotherapy with a footnote stating that “cisplatin may not be used interchangeably with oxaliplatin in this setting”:  
|                           |                             | 17 2 3 6 |

| **ESOPH-F 3 of 12**       | Based on a review of the data, the panel supported making the following changes for First-Line Therapy (Other Regimens):  
  - Changed ECF was changed from category 1 to category 2B  
  - All ECF modifications changed from category 1 to category 2B recommendation. | YES NO ABSTAIN ABSENT |
|                           |                             | 13 9 3 3 |
## ESOPH-F 3 of 12

**Institutional review request:** Under Second-Line Therapy; Other Regimens, re-evaluate the data for “Fluoropyrimidine (fluorouracil and capecitabine) and irinotecan” and consider making “fluorouracil and irinotecan” a preferred regimen for unresectable, locally advanced or metastatic cancer.

Based on a review of the data and discussion, the panel supported making the following changes for unresectable, locally advanced or metastatic cancer:

- **First-Line therapy**
  - “Fluorouracil and irinotecan” changed from category 1 to category 2A recommendation.

- **Second-Line Therapy**
  - “Fluorouracil and irinotecan” moved from “Other Regimens” to “Preferred Regimens”
  - “Fluorouracil and irinotecan” changed from category 2B to category 2A recommendation
  - “Capecitabine and irinotecan” was removed from the list of “Other regimens”

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<td>YES</td>
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<tr>
<td>Institutional review request: Under Second-Line Therapy; Other Regimens, re-evaluate the data for “Fluoropyrimidine (fluorouracil and capecitabine) and irinotecan” and consider making “fluorouracil and irinotecan” a preferred regimen for unresectable, locally advanced or metastatic cancer.</td>
<td>Based on a review of the data and discussion, the panel supported making the following changes for unresectable, locally advanced or metastatic cancer: First-Line therapy  • “Fluorouracil and irinotecan” changed from category 1 to category 2A recommendation. Second-Line Therapy  • “Fluorouracil and irinotecan” moved from “Other Regimens” to “Preferred Regimens”  • “Fluorouracil and irinotecan” changed from category 2B to category 2A recommendation  • “Capecitabine and irinotecan” was removed from the list of “Other regimens”</td>
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<td>Submission from Wellstat Therapeutics Corporation: Review the data and consider including uridine triacetate in the Guidelines for emergency use when indicated for overdose or early onset of severe toxicity in conjunction with 5-FU and/or capecitabine.</td>
<td>Based on a review of the data and discussion, the panel agreed not to include uridine triacetate in the following settings:  • As a bullet in the Principles of Systemic Therapy (ESOPH-F) under “Infusional fluorouracil or capecitabine”  • As a footnote to treatments featuring fluorouracil, capecitabine, fluoropyrimidine in the Principles of Systemic Therapy (ESOPH-F)  • Evidence Blocks version of the NCCN Guidelines for Esophageal and Esophagogastric Cancer  • Discussion section  o Under “Chemotherapy for Locally Advanced or Metastatic Cancer (MS-26)  o Add a subheading “Fluorouracil Toxicity” (MS-35)  • Chemotherapy Order Templates to fluorouracil (or capecitabine) as appropriate</td>
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