Supplementary Information

Title: Characterization of serous retinopathy associated with cobimetinib: Integrated safety analysis of four studies.

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Table S1. Preferred terms used to identify SR/RPED

| MedDRA Search Terms                                                                 | Additional Preferred Terms                  |
|-------------------------------------------------------------------------------------|--------------------------------------------|
| Chorioretinal disorder                                                             | Foveal degeneration                        |
| Chorioretinopathy                                                                   | Macular detachment                         |
| Detachment of macular retinal pigment epithelium                                   | Retinal edema                              |
| Detachment of retinal pigment epithelium                                             | Serous retinal detachment                   |
| Macular fibrosis                                                                    | Serous retinopathy                         |
| Macular edema                                                                       |                                            |
| MEK inhibitor-associated serous retinopathy                                         |                                            |
| Retinal detachment                                                                  |                                            |
| Retinal disorder                                                                    |                                            |
| Retinal pigment epithelial tear                                                     |                                            |
| Retinal tear                                                                        |                                            |
| Retinopathy                                                                         |                                            |
| Scleral buckling surgery                                                             |                                            |
| Sub-retinal fluid                                                                   |                                            |

MedDRA Medical Dictionary for Regulatory Activities; RPED retinal pigment epithelial detachment; SR serous retinopathy.
Table S2. Risk factors for SR/RPED and ocular confounders

| Risk factors identified from literature review | Concomitant ocular confounders                                    |
|-----------------------------------------------|------------------------------------------------------------------|
| Hypertension                                  | Maculopathy                                                      |
| Previous psychopharmacological medical use    | Retinal depigmentation                                            |
|                                               | Macular fibrosis                                                  |
| Antihistamine use                             | Age-related macular degeneration                                  |
| Alcohol use                                   | Ocular vascular disorder                                         |
| Male sex                                      | Retinal vascular occlusion                                        |
| Sleeping disturbances                         | Retinal degeneration                                              |
| Gastroesophageal reflux disease               | Retinal detachment                                                |
| Use of antacids or anti-reflux agents         | Vision blurred                                                   |
| Age ≥ 50 years                                | Chorioretinal disorder                                           |
| Autoimmune disease                           | Retinal disorder                                                  |
| Peptic ulcer                                  | Visual acuity reduced                                             |
| Psychological stress                          | Scleral buckling surgery                                          |
| Obesity                                       | Macular degeneration                                              |
|                                               | Retinopathy hypertensive                                          |

RPED retinal pigment epithelial detachment; SR serous retinopathy.
Table S3. Optical coherence tomography in patients with ≥ 1 occurrence of SR in study CO39721

| OCT Findings, eyes (%) | Eyes with SR |
|------------------------|--------------|
|                        | Baseline     | First SR Onset | First SR Resolution | Last SR Resolution | Last Available Visit |
|                        | n = 35       |               |                    |                   |                      |
| Any abnormal OCT finding | 8 (22.9)     | 34 (97.1)     | 2 (5.7)            | 3 (8.6)            | 10 (28.6)            |
| Subretinal fluid       | –            | 32 (91.4)     | 2 (1.8)            | 1 (2.9)            | 4 (11.4)             |
| Focal subretinal fluid | –            | 22 (62.9)     | 2 (1.8)            | –                  | 4 (11.4)             |
| Subfoveal              | –            | 21 (60.0)     | 2 (1.8)            | –                  | 4 (11.4)             |
| Extrafoveal            | –            | 1 (2.9)       | –                  | –                  | –                    |
| Multifocal subretinal fluid | –        | 9 (25.7)     | –                  | 1 (0.9)            | –                    |
| Subfoveal              | –            | 2 (5.7)       | –                  | 1 (0.9)            | –                    |
| Extrafoveal            | –            | 1 (2.9)       | –                  | –                  | –                    |
| Both subfoveal and extrafoveal | –        | 6 (17.1)     | –                  | –                  | –                    |
| Normal                 | 26 (74.3)    | 1 (2.9)       | 22 (62.9)          | 10 (54.3)          | 23 (65.7)            |
| Missing                | 1 (2.9)      | 0             | 11 (31.4)          | 13 (37.1)          | 2 (5.7)              |

OCT optical coherence tomography; SR serous retinopathy.