

## Summary of Investigation Results

### Cladribine

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| Non-proprietary name<br>Brand name                   | Non-proprietary name                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | Brand name<br>(marketing authorization holder) |
|                                                      | Cladribine                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | LEUSTATIN Injection 8 mg<br>(Clinigen K.K)     |
| Japanese market launch                               | June 2002                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                |
| Indications                                          | <ul style="list-style-type: none"> <li>○ Hairy cell leukemia</li> <li>○ The following relapsed, recurrent, or refractory diseases: <ul style="list-style-type: none"> <li>• Indolent or follicular B-cell non-Hodgkin lymphoma</li> <li>• Mantle cell lymphoma</li> </ul> </li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                |
| Summary of revisions                                 | <p>The statement in 9.6 Breast-feeding Women section under 9 PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS should be revised from “Breast-feeding is not recommended” to “Breast-feeding should be avoided,” and the period during which breast-feeding should be avoided should be added.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                |
| Investigation results and background of the revision | <p>Cladribine has been shown to be excreted into human breast milk. Given that cladribine is a genotoxic agent with the potential to adversely affect a breast-fed infants through exposure via human breast milk, it was considered appropriate to revise the precaution for breast-feeding to state that breast-feeding should be avoided. In addition, taking into account the elimination half-life of the drug, it was considered appropriate to specify a period of 7 days during which breast-feeding should be avoided. Of note, opinions regarding the impact of revising the precaution for breast-feeding to state that breast-feeding should be avoided, were sought from relevant academic societies, and no specific major problems were confirmed.</p> |                                                |