Daratumumab (Darzalex®) in a new pharmaceutical form associated with a new strength and a new route of administration for the treatment of multiple myeloma

### General information

**Drug description**

Human IgGκ CD38-targeting monoclonal antibody

**Indication**

New pharmaceutical form, new strength and new route of administration of daratumumab

### Current pharmaceutical form/strength/route of administration [1]

**DARZALEX**® 20 mg/ml concentrate for solution for infusion.

- Each 5 ml vial contains 100 mg of daratumumab (20 mg daratumumab per ml).
- Each 20 ml vial contains 400 mg of daratumumab (20 mg daratumumab per ml).

### Regulatory status

|---------|---------|

**Approval status for this indication**: On 30 April 2020, the CHMP recommended the addition of a new pharmaceutical form (solution for injection) of daratumumab, associated with a new strength (1800 mg in 15-ml vial) and a new route of administration (subcutaneous injection into the abdomen).

**Indications**: The new formulation can be used for all the authorised indications of Darzalex®, as follows:

- in combination with lenalidomide and dexamethasone or with bortezomib, melphalan and prednisone for the treatment of adult patients with newly diagnosed multiple myeloma (MM) who are ineligible for autologous stem cell transplant (ASCT)
- in combination with bortezomib, thalidomide and dexamethasone for the treatment of adult patients with newly diagnosed MM who are eligible for ASCT
- in combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of adult patients with MM who have received at least one prior therapy
- as monotherapy for the treatment of adult patients with relapsed and refractory MM, whose prior therapy included a proteasome inhibitor (PI) and an immunomodulatory agent and who have demonstrated disease progression on the last therapy.

- Orphan status
- Medicine under additional monitoring
- Accelerated assessment

**Costs**

Darzalex® solution for injection 1800 mg = € 6,288.00 (ex-factory price) [4]

COLUMBA trial patients received daratumumab once weekly (cycles 1 and 2), every 2 weeks (cycles 3–6), and then every 4 weeks (28-day cycles) until progressive disease or toxicity. Patients received a median of six cycles per group.

### Study characteristics

<table>
<thead>
<tr>
<th>Trial name</th>
<th>n</th>
<th>Intervention (I)</th>
<th>Comparator (C)</th>
<th>PEs (co-primary)</th>
<th>Characteristics</th>
<th>Biomarker</th>
<th>Funding</th>
<th>Publication(s)</th>
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1. This medicine had an accelerated assessment, meaning that it is a medicine of major interest for public health, so its timeframe for review was 150 evaluation days rather than 210.
**COLUMBA**

NCT03277105

**MMY3012**

1800 mg of subcutaneous daratumumab co-formulated with rHuPH20 2000 U/mL

16 mg/kg of intravenous daratumumab

- overall response (partial response or better)
- maximum trough concentration ($C_{\text{trough}}$)

ongoing$, multicentre, open-label, non-inferiority, randomized phase 3 trial

- Janssen Research & Development

**Efficacy (I vs. C)**

| Overall response | 41% vs. 37% (relative risk 1.11, 95% CI 0.89–1.37) |
| CR or better | 1.9% vs. 2.7% |
| Very good partial response | 17.3% vs. 14.3% |
| Partial response | 22.1% vs. 20.1% |

$C_{\text{trough}}$: the geometric means ratio for $C_{\text{trough}}$ was 107.93% (90% CI 95.74–121.67), and the maximum $C_{\text{trough}}$ was 593 μg/ml (SD 306) in the subcutaneous group and 522 μg/ml (226) in the intravenous group.

Rate of infusion-related reaction: 12.7% vs. 34.5%

Median PFS: 5.99 months vs. 6.08 months, HR 0.99 (95% CI 0.78-1.26)

**ESMO-MCBS version 1.1**

Not applicable

<table>
<thead>
<tr>
<th>Risk of bias (study level)</th>
<th>Risk of bias</th>
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</thead>
<tbody>
<tr>
<td>Adequate generation of randomisation sequence</td>
<td>yes</td>
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<tr>
<td>Adequate allocation concealment</td>
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<tr>
<td>Blinding</td>
<td>open-label</td>
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<td>Selective outcome reporting unlikely</td>
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<tr>
<td>Other aspects which increase the risk of bias</td>
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<tr>
<td>First published: 04/2020</td>
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<td>Last updated: 07/2020</td>
<td></td>
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Abbreviations: AE=adverse event, ASCT=autologous stem cell transplant, CHMP=Committee for Medicinal Products for Human Use, CI=confidence interval, CR=complete response, CTSQ=Cancer Therapy Satisfaction Questionnaire, $C_{\text{trough}}$=maximum trough concentration, EMA=European Medicines Agency, ESMO-MCBS=European Society of Medical Oncology – Magnitude of Clinical Benefit Scale, FDA=Food and Drug Administration, HR=hazard ratio, MM=multiple myeloma, n=number, SAE=serious adverse event, OS=overall survival, PE=primary endpoint, PFS=progression-free survival, PI=proteasome inhibitor, QoL=quality of life

**Safety (I vs. C)**

| Grade 3 treatment-emergent AEs: n=119/260 (46%) vs. n=126/258 (49%) |
| SAEs: n=68/260 (26%) vs. n=76/258 (29%) |
| Death: n=1/260 (0.4%) vs. and n=4/258 (1.6%) |
| Discontinuation due to AEs: n=18/260 (7%) vs. n=21 (8%) |

**References:**

4. Apotheker-Verlag Ö. Warenverzeichnis online [Available from: https://warenverzeichnis.apoverlaq.at/].

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$^2$ COLUMBA trial is ongoing until 12/2023

$^3$ Death judged to be treatment-related

$^4$ COLUMBA trial is currently ongoing

$^5$ Industry-funded; trial was designed by the study sponsor