SECTION 1: Identification of the substance/mixture and of the company/undertaking

1.1. Product identifier
Product name ROACCUTANE Capsules 10 mg
Product code SAP-10112031

1.2. Relevant identified uses of the substance or mixture and uses advised against
Use - oral treatment of severe acne, resistant against other therapies

1.3. Details of the supplier of the safety data sheet
Company information
Enquiries: Roche Products Pty Limited
P.O. Box 255
Dee Why, N.S.W. 2099
AUS-Australia
Australia
Phone 0061-2-9454-9624
Fax 0061-2-9971-7401
E-Mail info.sds@roche.com

Local representation:

1.4. Emergency telephone number
Emergency telephone number
Phone 0061-2-9454-9624

SECTION 2: Hazards identification

2.1. / 2.2. Classification of the substance or mixture / Label elements
GHS Classification
Health Hazards:
3.7 D Reproductive toxicity (Category 1A)
H360D May damage the unborn child.

Signalword: Danger
Label:

Precautionary statements:
- P201 Obtain special instructions before use.
- P273 Avoid release to the environment.
Australian Remark - HAZARDOUS SUBSTANCE. DANGEROUS GOODS.
- Listed on the Australian Inventory of Chemical Substances (AICS) *1
- Poisons Schedule - Schedule 4 *1

Classification and labelling according to EU directive 67/548/EEC

<table>
<thead>
<tr>
<th>R51/53</th>
<th>Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.</th>
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</thead>
<tbody>
<tr>
<td>R61</td>
<td>May cause harm to the unborn child.</td>
</tr>
<tr>
<td>S45</td>
<td>In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible).</td>
</tr>
<tr>
<td>S53</td>
<td>Avoid exposure --- obtain special instructions before use.</td>
</tr>
<tr>
<td>S61</td>
<td>Avoid release to the environment. Refer to special instructions/Safety data sheets.</td>
</tr>
</tbody>
</table>

2.3. Other hazards

Note - Women of childbearing potential must not be engaged in any work where dust exposure might occur. In case of doubt a risk assessment is advised.
- Women of childbearing potential have to avoid any overexposure (limit values see chapter 8)

*1 referring to: Isotretinoin

**SECTION 3: Composition/information on ingredients**

<table>
<thead>
<tr>
<th>Characterization</th>
<th>consisting of 3.6% Isotretinoin, with the remainder consisting of excipients that are not classified as hazardous</th>
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</table>
| Synonyms         | - ROACCUTANE Capsules (soft) 10 mg  
- Isotretinoin capsules |
| UN number        | 3077                                                                                                          |
| Ingredient       | Concentration   | EU-Classification  |
| Isotretinoin     | 3.6 %            | (pure ingredient)  |
SECTION 4: First aid measures

4.1. Description of first aid measures

Eye contact - rinse immediately with tap water for 10 minutes - open eyelids forcibly - consult a physician

Skin contact - remove immediately contaminated clothes, wash affected skin with water and soap - do not use any solvents

Inhalation - remove the casualty to fresh air and keep him/her calm - in the event of symptoms get medical treatment

Ingestion - summon a physician immediately

4.2. Most important symptoms and effects, both acute and delayed

Note - no information available

4.3. Indication of any immediate medical attention and special treatment needed

Note to physician - treat symptomatically

SECTION 5: Firefighting measures

5.1. Extinguishing media

Suitable extinguishing media - adapt extinguishing media to surrounding fire conditions

5.2. Special hazards arising from the substance or mixture

Specific hazards - substance is hazardous for water: contain fire-fighting wastewater

5.3. Advice for firefighters

Special method of fire-fighting - for reasons of environmental protection hold the extinguishing agent back

SECTION 6: Accidental release measures

6.1. Personal precautions, protective equipment and emergency procedures

Personal precautions - ensure adequate ventilation

6.2. Environmental precautions

Environmental protection - do not allow to enter drains or waterways - if the substance reaches waters or the sewer system, inform the competent authority
6.3. Methods and material for containment and cleaning up

Methods for cleaning up
- collect spilled material (avoid dust formation) and hand over to waste removal in sealed containers

SECTION 7: Handling and storage

7.1. Precautions for safe handling

Technical measures
- processing in closed systems, if possible superposed by inert gas (e.g. nitrogen)
- provide suitable exhaust ventilation at the processing machines
- take precautionary measures against electrostatic charging
- avoid formation and deposition of dust

7.2. Conditions for safe storage, including any incompatibilities

Storage conditions
- below 25 °C
- protected from light

Validity
- see "best use before" date stated on the label

SECTION 8: Exposure controls/personal protection

8.1. Control parameters

Threshold value (Roche) air
- IOEL (Internal Occupational Exposure Limit): 0.002 mg/m³ *1

8.2. Exposure controls

General protective and hygiene measures
- instruction of employees mandatory
- shower after work recommended

Respiratory protection
- in case of open handling or accidental release: particle mask or respirator with independent air supply

Hand protection
- protective gloves (e.g. made of neoprene, nitrile or butyl rubber)

Eye protection
- safety glasses

Analytics
- sampling on glassfiber filter and chemical determination of the active compound (e.g. HPLC) *1

*1 referring to: Isotretinoin

SECTION 9: Physical and chemical properties

9.1. Information on basic physical and chemical properties

Colour
- brownish-red
ROACCUTANE Capsules 10 mg

Form: gelatin capsule soft

Solubility:
- < 100 mg/l, water (25 °C) *1
- 3'000 mg/l, peanut oil (25 °C) *1
- 12'000 mg/l, ethanol (25 °C) *1
- 15'000 mg/l, n-octanol (25 °C) *1
- 24'000 mg/l, acetone (25 °C) *1

Partition coefficient: log P_{ow} 6.6 (octanol/water°C) *1

9.2. Other information

Note: no information available

*1 referring to: Isotretinoin

SECTION 10: Stability and reactivity

10.1. Reactivity

Note: no information available

10.2. Chemical stability

Note: no information available

10.3. Possibility of hazardous reactions

Note: no information available

10.4. Conditions to avoid

Conditions to avoid:
- light (gradual decomposition) *1
- warming (gradual decomposition) *1

10.5. Incompatible materials

Note: no information available

10.6. Hazardous decomposition products

Note: no information available

*1 referring to: Isotretinoin
**SECTION 11: Toxicological information**

### 11.1. Information on toxicological effects

<table>
<thead>
<tr>
<th>Effect</th>
<th>Details</th>
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<tbody>
<tr>
<td>Acute toxicity</td>
<td>LD$_{50}$ &gt; 4’000 mg/kg (oral, rat)</td>
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<tr>
<td>Mutagenicity</td>
<td>not mutagenic (various test systems)</td>
</tr>
<tr>
<td>Carcinogenicity</td>
<td>not cancerogenic</td>
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<tr>
<td>Reproductive toxicity</td>
<td>teratogenic (human and animal)</td>
</tr>
<tr>
<td>Note</td>
<td>dosage: daily 0.5 - 1.0 mg/kg (oral)</td>
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<tr>
<td></td>
<td>half-life of elimination: between 7 - 39 hours (average approx. 20 hours)</td>
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<tr>
<td></td>
<td>systemic symptoms: signs of vitamin A hypervitaminosis (dryness of mucous membranes, exanthems, pruritus; high doses: signs of intracranial pressure like headache, vomiting, etc.)</td>
</tr>
</tbody>
</table>

*1 referring to: Isotretinoin

**SECTION 12: Ecological information**

### 12.1. Toxicity

<table>
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<th>Ecotoxicity</th>
<th>Details</th>
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<tr>
<td>Ecotoxicity</td>
<td>strongly toxic for planktonic crustaceans (Daphnia magna)</td>
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<tr>
<td></td>
<td>EC$_{50}$ (48 h) 2.06 mg/l (FDA Technical Assistance Document No. 4.08)</td>
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<td></td>
<td>highly toxic for fish (rainbow trout)</td>
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<tr>
<td></td>
<td>LC$_{100}$ (96 h) 0.61 mg/l</td>
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<tr>
<td></td>
<td>LC$_{50}$ (96 h) 0.52 mg/l</td>
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<td>LC$_0$ (96 h) 0.45 mg/l</td>
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<td>NOEC (96 h) 0.05 mg/l</td>
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<td>(OECD No. 203)</td>
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<td></td>
<td>barely toxic for microorganisms (activated sludge)</td>
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<td>LC$_{50}$ (3 h) &gt; 100 mg/l</td>
</tr>
<tr>
<td></td>
<td>(Activated Sludge Respir. Inhib. Test, OECD No. 209)</td>
</tr>
</tbody>
</table>

### 12.2. Persistence and degradability

| Inherent biodegradability | inherently biodegradable 59 %, 28 days (MITI Test II, OECD No. 302 C) |

### 12.3. Bioaccumulative potential

Note - no information available

### 12.4. Mobility in soil

Note - no information available
12.5. Results of PBT and vPvB assessment

Note - no information available

12.6. Other adverse effects

Note - the substance shows a potential of bioaccumulation *1

*1 referring to: Isotretinoin

SECTION 13: Disposal considerations

13.1. Waste treatment methods

Waste from residues - incinerate in qualified installation with flue gas scrubbing
- observe local/national regulations regarding waste disposal
- medicines should not be disposed of via wastewater
- return to supplier or hand over to authorised disposal company

Contaminated packaging - incinerate contaminated packaging material in qualified installation with flue gas scrubbing

SECTION 14: Transport information

<table>
<thead>
<tr>
<th>IATA</th>
<th>Class</th>
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<th>PI</th>
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<td>3077</td>
<td>III</td>
<td>F-A S-F</td>
<td>P002/IBC08</td>
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<td>marine pollutant</td>
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<td>M7</td>
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</table>

Proper shipping name ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S.

Technical name Isotretinoin mixture
SECTION 15: Regulatory information

15.1. Safety, health and environmental regulations/legislation specific for the substance or mixture

Water hazard class (Germany) 3: strongly hazardous for water (according to annex 4 of directive VwVwS of 17.05.1999)

Regulatory status (Australia) - This product has been approved by the Therapeutic Goods Administration (TGA); AUST R 50840

SECTION 16: Other information

Safety-lab number - BS-2435 *1
- BS-7164 *1
- BS-9093 *1

R phrases (chapter 3 ingredients)
- R36/37/38 Irritating to eyes, respiratory system and skin.
- R50/53 Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
- R61 May cause harm to the unborn child.

Edition documentation - changes from previous version in sections 3, 16

*1 referring to: Isotretinoin

The information in this safety data sheet is based on current scientific knowledge. It should not be taken as expressing or implying any warranty concerning product characteristics.
SECTION 1: Identification of the substance/mixture and of the company/undertaking

1.1. Product identifier

Product name: ROACCUTANE Capsules 20 mg
Product code: SAP-10111991

1.2. Relevant identified uses of the substance or mixture and uses advised against

Use: - oral treatment of severe acne, resistant against other therapies

1.3. Details of the supplier of the safety data sheet

Company information:
Enquiries:
Roche Products Pty Limited
P.O. Box 255
Dee Why, N.S.W. 2099
AUS-Australia
Australia

Phone: 0061-2-9454-9624
Fax: 0061-2-9971-7401
E-Mail: info.sds@roche.com

1.4. Emergency telephone number

Emergency telephone number:
Phone: 0061-2-9454-9624

SECTION 2: Hazards identification

2.1. / 2.2. Classification of the substance or mixture / Label elements

GHS Classification:
Health Hazards:
3.7 D Reproductive toxicity (Category 1A)
H360D May damage the unborn child.

Signalword: Danger
Label:

Precautionary statements:
- P201 Obtain special instructions before use.
- P273 Avoid release to the environment.
ROACCUTANE Capsules 20 mg

Australian Remark
- HAZARDOUS SUBSTANCE. DANGEROUS GOODS.
- Listed on the Australian Inventory of Chemical Substances (AICS) *1
- Poisons Schedule - Schedule 4 *1

Classification and labelling according to EU directive 67/548/EEC

![Skull and Crossbones](image1)
![Warning Symbol](image2)

R51/53 Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
R61 May cause harm to the unborn child.
S45 In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible).
S53 Avoid exposure --- obtain special instructions before use.
S61 Avoid release to the environment. Refer to special instructions/Safety data sheets.

2.3. Other hazards

Note
- Women of childbearing potential must not be engaged in any work where dust exposure might occur. In case of doubt a risk assessment is advised.
- Women of childbearing potential have to avoid any overexposure (limit values see chapter 8)

*1 referring to: Isotretinoin

SECTION 3: Composition/information on ingredients

Characterization
consisting of 4% Isotretinoin, with the remainder consisting of excipients that are not classified as hazardous

Synonyms
- ROACCUTANE Capsules (soft) 20 mg
- Isotretinoin capsules

UN number
3077

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Concentration (pure ingredient)</th>
<th>EU-Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isotretinoin</td>
<td>3.9 %</td>
<td>T, N R36/37/38, R50/53, R61 S36/37, S45, S53, S60, S61</td>
</tr>
</tbody>
</table>

CAS: 4759-48-2
SECTION 4: First aid measures

4.1. Description of first aid measures

- **Eye contact**
  - rinse immediately with tap water for 10 minutes
  - open eyelids forcibly
  - consult a physician

- **Skin contact**
  - remove immediately contaminated clothes, wash affected skin with water and soap
  - do not use any solvents

- **Inhalation**
  - remove the casualty to fresh air and keep him/her calm
  - in the event of symptoms get medical treatment

- **Ingestion**
  - summon a physician immediately

4.2. Most important symptoms and effects, both acute and delayed

**Note**
- no information available

4.3. Indication of any immediate medical attention and special treatment needed

**Note to physician**
- treat symptomatically

SECTION 5: Firefighting measures

5.1. Extinguishing media

**Suitable extinguishing media**
- adapt extinguishing media to surrounding fire conditions

5.2. Special hazards arising from the substance or mixture

**Specific hazards**
- substance is hazardous for water: contain fire-fighting wastewater

5.3. Advice for firefighters

**Special method of fire-fighting**
- for reasons of environmental protection hold the extinguishing agent back

SECTION 6: Accidental release measures

6.1. Personal precautions, protective equipment and emergency procedures

**Personal precautions**
- ensure adequate ventilation

6.2. Environmental precautions

**Environmental protection**
- do not allow to enter drains or waterways
- if the substance reaches waters or the sewer system, inform the competent authority
6.3. Methods and material for containment and cleaning up

Methods for cleaning up
- collect spilled material (avoid dust formation) and hand over to waste removal in sealed containers

SECTION 7: Handling and storage

7.1. Precautions for safe handling

Technical measures
- processing in closed systems, if possible superposed by inert gas (e.g. nitrogen)
- provide suitable exhaust ventilation at the processing machines
- take precautionary measures against electrostatic charging
- avoid formation and deposition of dust

7.2. Conditions for safe storage, including any incompatibilities

Storage conditions
- below 25 °C
- protected from light

Validity
- see "best use before" date stated on the label

SECTION 8: Exposure controls/personal protection

8.1. Control parameters

Threshold value (Roche) air
- IOEL (Internal Occupational Exposure Limit): 0.002 mg/m³ *1

8.2. Exposure controls

General protective and hygiene measures
- instruction of employees mandatory
- shower after work recommended

Respiratory protection
- in case of open handling or accidental release:
  particle mask or respirator with independent air supply

Hand protection
- protective gloves (eg made of neoprene, nitrile or butyl rubber)

Eye protection
- safety glasses

Analytics
- sampling on glassfiber filter and chemical determination of the active compound (eg HPLC) *1

*1 referring to: Isotretinoin

SECTION 9: Physical and chemical properties

9.1. Information on basic physical and chemical properties

Colour
half brown-red, half opaque white
ROACCUTANE Capsules 20 mg

country-specific

Form
gelatin capsule soft

Solubility

< 100 mg/l, water (25 °C)  *1
3'000 mg/l, peanut oil (25 °C)  *1
12'000 mg/l, ethanol (25 °C)  *1
15'000 mg/l, n-octanol (25 °C)  *1
24'000 mg/l, acetone (25 °C)  *1

Partition coefficient
log P_{ow} 6.6 (octanol/water°C)  *1

9.2. Other information

Note - no information available

*1 referring to: Isotretinoin

SECTION 10: Stability and reactivity

10.1. Reactivity

Note - no information available

10.2. Chemical stability

Note - no information available

10.3. Possibility of hazardous reactions

Note - no information available

10.4. Conditions to avoid

Conditions to avoid - light (gradual decomposition)  *1
- warming (gradual decomposition)  *1

10.5. Incompatible materials

Note - no information available

10.6. Hazardous decomposition products

Note - no information available

*1 referring to: Isotretinoin
SECTION 11: Toxicological information

11.1. Information on toxicological effects

Acute toxicity - \( \text{LD}_{50} > 4'000 \text{ mg/kg} \) (oral, rat) *1

Mutagenicity - not mutagenic (various test systems) *1

Carcinogenicity - not cancerogenic *1

Reproductive toxicity - teratogenic (human and animal) *1

Note - dosage: daily 0.5 - 1.0 mg/kg (oral) *1

- half-life of elimination: between 7 - 39 hours (average approx. 20 hours) *1

- systemic symptoms: signs of vitamin A hypervitaminosis (dryness of mucous membranes, exanthems, pruritus; high doses: signs of intracranial pressure like headache, vomiting, etc.) *1

*1 referring to: Isotretinoin

SECTION 12: Ecological information

12.1. Toxicity

Ecotoxicity - strongly toxic for planktonic crustaceans (Daphnia magna)
\( \text{EC}_{50} (48 \text{ h}) = 2.06 \text{ mg/l} \)
(FDA Technical Assistance Document No. 4.08) *1

- highly toxic for fish (rainbow trout)
\( \text{LC}_{190} (96 \text{ h}) = 0.61 \text{ mg/l} \)
\( \text{LC}_{50} (96 \text{ h}) = 0.52 \text{ mg/l} \)
\( \text{LC}_{50} (96 \text{ h}) = 0.45 \text{ mg/l} \)
\( \text{NOEC} (96 \text{ h}) = 0.05 \text{ mg/l} \)
(OECD No. 203) *1

- barely toxic for microorganisms (activated sludge)
\( \text{LC}_{50} (3 \text{ h}) > 100 \text{ mg/l} \)
(Activated Sludge Respir. Inhib. Test, OECD No. 209) *1

12.2. Persistence and degradability

Inherent biodegradability - inherently biodegradable
59 %, 28 days
(MITI Test II, OECD No. 302 C) *1

12.3. Bioaccumulative potential

Note - no information available

12.4. Mobility in soil

Note - no information available
### 12.5. Results of PBT and vPvB assessment

Note - no information available

### 12.6. Other adverse effects

Note - the substance shows a potential of bioaccumulation *1

*1 referring to: Isotretinoin

### SECTION 13: Disposal considerations

#### 13.1. Waste treatment methods

- incinerate in qualified installation with flue gas scrubbing
- observe local/national regulations regarding waste disposal
- medicines should not be disposed of via wastewater
- return to supplier or hand over to authorised disposal company

Contaminated packaging - incinerate contaminated packaging material in qualified installation with flue gas scrubbing

### SECTION 14: Transport information

#### IATA

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Proper shipping name: ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S.

Technical name: Isotretinoin mixture
SECTION 15: Regulatory information

15.1. Safety, health and environmental regulations/legislation specific for the substance or mixture

Water hazard class (Germany) 3: strongly hazardous for water (according to annex 4 of directive VwVwS of 17.05.1999)

Regulatory status (Australia) - This product has been approved by the Therapeutic Goods Administration (TGA); AUST R 50839

SECTION 16: Other information

Safety-lab number - BS-2435 *1
- BS-7164 *1
- BS-9093 *1

R phrases (chapter 3 ingredients)
R36/37/38 Irritating to eyes, respiratory system and skin.
R50/53 Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
R61 May cause harm to the unborn child.

Edition documentation - changes from previous version in sections 3, 16

*1 referring to: Isotretinoin

The information in this safety data sheet is based on current scientific knowledge. It should not be taken as expressing or implying any warranty concerning product characteristics.