SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Rapifen™ solution for injection or infusion

2. Qualitative and Quantitative Composition

Each ml of Rapifen contains alfentanil hydrochloride 544 micrograms, equivalent to 500 micrograms alfentanil base.

For excipients, see section 6.1.

3. Pharmaceutical Form

Solution for injection or infusion.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

In adults, as an opioid analgesic supplement for use before and during anaesthesia.

It is indicated for:

- Short procedures and outpatient surgery.
- Procedures of medium and long duration when given as a bolus followed by supplemental doses or by continuous infusion.

At very high doses, Rapifen may be used in adults as an anaesthetic induction agent in ventilated patients.

Rapifen is indicated for use in neonates, infants children and adolescents as:

- an opioid analgesic in association with a hypnotic to induce anaesthesia
- an opioid analgesic in association with general anaesthesia and for both short and long surgical procedures

4.2 Posology and method of administration

For intravenous administration.
Rapifen by the intravenous route can be administered to both adults and children. Rapifen should be used as bolus injections (short procedures) or bolus supplemented by increments or by infusion (long painful surgical procedures).

The dosage of Rapifen should be individualised according to age, bodyweight, physical status, underlying pathological condition, use of other drugs and type of surgery and anaesthesia.

**Adults patients**

The usual recommended dosage regimen is as follows:

<table>
<thead>
<tr>
<th>Adults</th>
<th>Initial</th>
<th>Supplemental</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous respiration</td>
<td>500 mcg (1 ml)</td>
<td>250 mcg (0.5 ml)</td>
</tr>
<tr>
<td>Assisted ventilation</td>
<td>30-50 mcg/kg</td>
<td>15 mcg/kg</td>
</tr>
</tbody>
</table>

If desired, Rapifen can be mixed with sodium chloride injection BP, dextrose injection BP or compound sodium lactate injection BP (Hartmann’s solution). Such dilutions are compatible with plastic bags and giving sets. These dilutions should be used within 24 hours of preparation.

In spontaneously breathing patients, the initial bolus dose should be given slowly over about 30 seconds (dilution may be helpful).

After intravenous administration in unpremedicated adult patients, 1 ml Rapifen may be expected to have a peak effect in 90 seconds and to provide analgesia for 5-10 minutes. Periods of more painful stimuli may be overcome by the use of small increments of Rapifen. For procedures of longer duration, additional increments will be required.

In ventilated patients, the last dose of Rapifen should not be given later than about 10 minutes before the end of surgery to avoid the continuation of respiratory depression after surgery is complete.

In ventilated patients undergoing longer procedures, Rapifen may be infused at a rate of 0.5-1 microgram/kg/minute. Adequate plasma concentrations of alfentanil will only be achieved rapidly if this infusion is preceded by a loading dose of 50-100 microgram/kg given as a bolus or fast infusion over 10 minutes.

Lower doses may be adequate, for example where anaesthesia is being supplemented by other agents.

The infusion should be discontinued up to 30 minutes before the anticipated end of surgery.

Increasing the infusion rate may prolong recovery. Supplementation of the anaesthetic, if required, for periods of painful stimuli, is best managed by extra bolus doses of Rapifen (1-2 ml) or low concentrations of a volatile agent for brief periods.

Patients with severe burns presenting for dressing, etc, have received a loading dose of 18-28 mcg/kg/min for up to 30 minutes without requiring mechanical ventilation. In heart surgery, when used as a sole anaesthetic, doses in the range of 12-50 mg/hour have been used.

**Paediatric patients**

Assisted ventilation equipment should be available for use in children of all ages, even for short procedures in spontaneously breathing children.
Data in children, particularly those aged 1 month to 1 year are limited (see section 5.2).

- **Neonates (0 to 27 days):** The pharmacokinetics are very variable in neonates, particularly in those born preterm. Clearance and protein binding are lower, and a lower dose of Rapifen may be required. Neonates should be closely monitored and the dose of Rapifen titrated according to the response.

- **Infants and toddlers (28 days to 23 months):** Clearance may be higher in infants and toddlers compared to that in adults. For maintenance of analgesia, the rate of infusion of Rapifen may need to be increased.

- **Children (2 to 11 years):** Clearance may be slightly higher in children and the rate of infusion may need to be increased.

- **Adolescents:** The pharmacokinetics of alfentanil in adolescents are similar to those in adults and no specific dosing recommendations are required.

**Dosing recommendations for paediatric patients**

The wide variability in response to Rapifen makes it difficult to provide dosing recommendations for younger children. For older children a bolus dose of 10 to 20 mcg/kg Rapifen for induction of anaesthesia (i.e. to supplement propofol or inhalation anaesthesia) or as an analgesic is considered appropriate. Supplemental boluses of 5 to 10 mcg/kg Rapifen at appropriate intervals can be administered.

To maintain analgesia in children during surgery, a Rapifen infusion rate of 0.5 to 2 mcg/kg/min may be administered. The dose must be titrated up or down according to the needs of the individual patient. When combined with an intravenous anaesthetic agent the recommended dose is approximately 1 mcg/kg/min.

There may be a higher risk of respiratory complications and muscle rigidity when Rapifen is administered to neonates and very young children. Necessary precautions are detailed in section 4.4.

**Elderly and debilitated patients**

Elderly (>65 years of age) and debilitated patients may require lower or less frequent dosing owing to a longer half-life of Rapifen in this age group (dilution may be helpful).

### 4.3 Contraindications

Obstructive airways disease or respiratory depression if not ventilating.

Concurrent administration with monoamine oxidase inhibitors or within 2 weeks of their discontinuation.

Administration in labour or before clamping of the cord during caesarean section due to the possibility of respiratory depression in the newborn infant.

Patients with a known intolerance to alfentanil and other morphinomimetics.
4.4 Special warnings and precautions for use

**Warnings:**

Following administration of Rapifen, a fall in blood pressure may occur. The magnitude of this effect may be exaggerated in the hypovolaemic patient or in the presence of concomitant sedative medication. Appropriate measures to maintain a stable arterial pressure should be taken.

Significant respiratory depression and loss of consciousness will occur following administration of Rapifen in doses in excess of 1 mg and is dose-related. This and the other pharmacological effects of Rapifen are usually of short duration and can be reversed by the specific opioid antagonists (e.g. naloxone). Additional doses of the antagonists may be necessary because the respiratory depression may last longer than the duration of action of the opioid antagonist.

Like other opioids, alfentanil may cause bradycardia, an effect that may be marked and rapid in onset but which can be antagonised by atropine. Particular care must be taken following treatment with drugs which may depress the heart or increase vagal tone, such as anaesthetic agents or beta-blockers, since they may predispose to bradycardia or hypotension. Heart rate and blood pressure should therefore be monitored carefully. If hypotension or bradycardia occur, appropriate measures should be instituted.

Cardiac arrest following bradycardia has been reported on very rare occasions in non-atropinised patients. Therefore it is advisable to be prepared to administer an anticholinergic drug.

**Precautions:**

It is wise to reduce the dosage in the elderly and debilitated patients. In hypothyroidism, pulmonary disease, decreased respiratory reserve, alcoholism and liver or renal impairment the dosage should be titrated with care and prolonged monitoring may be required.

Patients on chronic opioid therapy or with a history of opioid abuse may require higher doses.

Rapifen may induce muscle rigidity during induction. Rigidity, which may also involve the thoracic muscles, can be avoided by the following measures:

- Slow IV injection (usually sufficient for lower doses);
- Premedication with a benzodiazepine;
- Administration of a muscle relaxant just prior to administration of Rapifen.

Non-epileptic (myo)clonic movements can occur.

As with all potent opioids, profound analgesia is accompanied by marked respiratory depression, which may persist into or recur in the early postoperative period. Care should be taken after infusions or large doses of Rapifen to ensure that adequate spontaneous breathing has been established and maintained in the absence of stimulation before discharging the patient from the recovery area. Resuscitation equipment and narcotic antagonists should be readily available. Hyperventilation during anaesthesia may alter the patient’s response to CO₂, thus affecting respiration postoperatively.

The use of rapid bolus injections of opioids should be avoided in patients with compromised intracerebral compliance; in such patients a transient decrease in the
mean arterial pressure has occasionally been accompanied by a transient reduction of the cerebral perfusion pressure.

This medicinal product contains less than 1 mmol sodium (23 mg) per 5 mg dose, i.e. essentially ‘sodium-free’.

**Paediatric population**

There may be a higher risk of respiratory complications when Rapifen is administered to neonates and very young children than when it is used in older children and adults. For this reason, young paediatric subjects should be monitored immediately after administration of Rapifen is commenced. Assisted ventilation equipment should be available for use in children of all ages, even for short procedures in spontaneously breathing children.

If Rapifen is used in neonates and young infants, the simultaneous use of a muscle relaxant should be considered because of the risk of muscle rigidity. All children should be monitored for a sufficient period of time following cessation of treatment with Rapifen to ensure the return of spontaneous respiration has been achieved.

Due to variable pharmacokinetics in neonates a lower dose of Rapifen may be required. Neonates should be closely monitored and the dose of Rapifen titrated according to the response. (See section 4.2)

### 4.5 Interaction with other medicinal products and other forms of interaction

**Drugs modifying the effect of alfentanil**

**Central Nervous System (CNS) depressants**

Drugs such as barbiturates, benzodiazepines, neuroleptics, general anaesthetics and other non-selective CNS depressants (e.g. alcohol) may enhance or prolong the respiratory depressant effects of opioids. If other narcotic or CNS depressant drugs are used concurrently with alfentanil, the effects of the drugs can be expected to be additive. When patients have received such drugs, the dose of alfentanil required will be less than usual. Concomitant use with Rapifen in spontaneously breathing patients may increase the risk of respiratory depression, profound sedation, coma, and death.

**Effect of Rapifen on other drugs**

Following the administration of Rapifen, the dose of other CNS-depressant drugs should be reduced. This is particularly important after surgery, because profound analgesia is accompanied by marked respiratory depression, which can persist or recur in the postoperative period. Administration of a CNS depressant, such as a benzodiazepine, during this period may disproportionally increase the risk for respiratory depression.

In combination with alfentanil, the blood concentrations of propofol are 17% higher than in the absence of alfentanil. The concomitant use of alfentanil and propofol may require a lower dose of Rapifen.

**Cytochrome P450 3A4 (CYP3A4) inhibitors**

Alfentanil is metabolised mainly via the human cytochrome P450 3A4 enzyme. *In vitro* data suggest that potent cytochrome P450 3A4 enzyme inhibitors (e.g., ketoconazole, itraconazole, ritonavir) may inhibit the metabolism of alfentanil. Available human pharmacokinetic data indicate that the metabolism of alfentanil is
inhibited by fluconazole, voriconazole, erythromycin, diltiazem and cimetidine (known cytochrome P450 3A4 enzyme inhibitors). This could increase the risk of prolonged or delayed respiratory depression. The concomitant use of such drugs requires special patient care and observation; in particular, it may be necessary to lower the dose of Rapifen.

Treatment with drugs which may depress the heart or increase vagal tone, such as beta-blockers and anaesthetic agents, may predispose to bradycardia or hypotension. Bradycardia and possibly cardiac arrest can occur when Rapifen is combined with non-vagolytic muscle relaxants.

**Monoamine Oxidase Inhibitors (MAOI)**

It is usually recommended to discontinue MAO-inhibitors 2 weeks prior to any surgical or anaesthetic procedure.

**Serotonergic drugs**

Coadministration of alfentanil with a serotonergic agent, such as Selective Serotonin Reuptake Inhibitors (SSRIs), Serotonin Norepinephrine Reuptake Inhibitors (SNRIs), or Monoamine Oxidase Inhibitors (MAOIs), may increase the risk of serotonin syndrome, a potentially life-threatening condition.

### 4.6 Fertility, pregnancy and lactation

**Pregnancy**

Although no teratogenic or acute embryotoxic effects have been observed in animal experiments, insufficient data are available to evaluate any harmful effects in man. Consequently, it is necessary to consider possible risks and potential advantages before administering this drug to pregnant patients.

Intravenous administration during childbirth (including caesarian section) is not recommended because alfentanil crosses the placenta and may suppress spontaneous respiration in the newborn period. If Rapifen is administered nevertheless, assisted ventilation equipment must be immediately available for use if required for the mother and infant. An opioid antagonist for the child must always be available. The half-life of the opioid antagonist may be shorter than the half-life of alfentanil, therefore, repeated administration of the opioid antagonist may be necessary.

**Breast-feeding**

Alfentanil may enter the maternal milk. Therefore, breast-feeding or use of expressed breast milk is not recommended for 24 hours following the administration of Rapifen.

### 4.7 Effects on ability to drive and use machines

Where early discharge is envisaged, patients should be advised not to drive or operate machinery for at least 24 hours following administration.

This medicine can impair cognitive function and can affect a patient’s ability to drive safely. This class of medicine is in the list of drugs included in regulations under 5a of the Road Traffic Act 1988. When prescribing this medicine, patients should be told:
• The medicine is likely to affect your ability to drive
• Do not drive until you know how the medicine affects you
• It is an offence to drive while under the influence of this medicine
• However, you would not be committing an offence (called ‘statutory defence’) if:
  o The medicine has been prescribed to treat a medical or dental problem and
  o You have taken it according to the instructions given by the prescriber and in the information provided with the medicine and
  o It was not affecting your ability to drive safely.

4.8 Undesirable effects

Adverse Reactions

The most frequently reported Adverse reactions (incidence ≥10%) are: nausea and vomiting. Undesirable effects listed below in Table 1 have been reported in clinical trials (1157 subjects) and/or from spontaneous reports from post-marketing experience. The following terms and frequencies are applied:

Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); and not known (cannot be estimated from the available clinical trial data).

Adverse reactions from spontaneous reports during worldwide postmarketing experience with alfentanil that met threshold criteria are included. Unlike for clinical trials, precise frequencies cannot be provided for spontaneous reports. The frequency for these reports is therefore classified as ‘not known’.

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>Adverse Reactions reported in clinical trials and/or postmarketing</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Frequency Category</td>
</tr>
<tr>
<td></td>
<td>Very Common (≥1/10)</td>
</tr>
<tr>
<td>Immune System Disorders</td>
<td>Hypersensitivity (including anaphylactic reaction, anaphylactoid reaction and urticaria)</td>
</tr>
<tr>
<td>Psychiatric Disorders</td>
<td>Euphoric Mood</td>
</tr>
<tr>
<td>Nervous System Disorders</td>
<td>Movement Disorder; Dizziness; Sedation;</td>
</tr>
<tr>
<td>Eye Disorders</td>
<td>Dyskinesia</td>
</tr>
<tr>
<td>------------------------</td>
<td>------------</td>
</tr>
<tr>
<td>Cardiac Disorders</td>
<td>Visual Disturbance</td>
</tr>
<tr>
<td>Vascular Disorders</td>
<td>Bradycardia; Tachycardia</td>
</tr>
<tr>
<td></td>
<td>Hypotension; Hypertension; Blood Pressure Decreased; Blood Pressure Increased</td>
</tr>
<tr>
<td>Respiratory, Thoracic and Mediastinal Disorders</td>
<td>Apnoea</td>
</tr>
<tr>
<td></td>
<td>Hiccups; Hypercapnia; Laryngospasm; Respiratory Depression (including fatal outcome)</td>
</tr>
<tr>
<td>Gastrointestinal Disorders</td>
<td>Nausea; Vomiting</td>
</tr>
<tr>
<td>Skin and Subcutaneous Tissue Disorders</td>
<td>Dermatitis Allergic; Hyperhidrosis</td>
</tr>
<tr>
<td>Musculoskeletal and Connective Tissue Disorders</td>
<td>Muscle Rigidity</td>
</tr>
<tr>
<td>General Disorders and Administration Site Conditions</td>
<td>Chills; Injection Site Pain; Fatigue</td>
</tr>
<tr>
<td>Injury, Poisoning and Procedural Complications</td>
<td>Procedural Pain</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Paediatric population**

Frequency, type and severity of adverse reactions in children are expected to be the same as in adults, with the exception of the following:

Mild to moderate muscle rigidity has been seen frequently in neonates, although the number of neonates included in clinical studies was small. Severe rigidity and jerking
can occur less commonly and may be accompanied by transient impaired ventilation, especially with high doses of Rapifen or with a rapid rate of intravenous injection.

**Reporting of suspected adverse reactions**

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

### 4.9 Overdose

The manifestations of alfentanil overdose are generally an extension of its pharmacological action, which include the following:

<table>
<thead>
<tr>
<th>Action</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bradycardia</td>
<td>Anticholinergics such as atropine or glycopyrrolate.</td>
</tr>
<tr>
<td>Hypoventilation or apnoea</td>
<td>O₂ administration, assisted or controlled respiration and an opioid antagonist may be required.</td>
</tr>
<tr>
<td>Muscle rigidity</td>
<td>Intravenous neuromuscular blocking agent may be given.</td>
</tr>
</tbody>
</table>

If hypotension is severe or persists, the possibility of hypovolaemia should be considered and controlled with appropriate parenteral fluid administration.

The suggested treatments given above do not preclude the use of other clinically indicated counter measures.

Body temperature and adequate fluid intake should be maintained and the patient observed for 24 hours. A specific opioid antagonist (e.g., naloxone) should be available to treat respiratory depression.

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: opioid anesthetics, ATC code: N01AH02

The analgesic potency of Rapifen is one quarter that of fentanyl. The duration of action of Rapifen is one third that on an equianalgesic dose of fentanyl and is clearly dose-related. Its depressant effects on respiratory rate and alveolar ventilation are also of shorter duration than those of fentanyl.

The onset of action of Rapifen is four times more rapid than that of an equianalgesic dose of fentanyl. The peak analgesic and respiratory depressant effects occur within 90 seconds.
In man, alfentanil at therapeutic doses had no detrimental effects on myocardial performance. The cardiovascular stability is remarkable both in healthy and poor-risk patients. The only changes seen in blood pressure and heart rate are transient, slight decreases occurring immediately after induction. The incidence and degree of respiratory depression is less and of shorter duration after alfentanil than with fentanyl. Like other opioid analgesics, alfentanil increases the amplitude of the EEG and reduces its frequency. Alfentanil reduces intraocular pressure by about 45%. It blocks increases in plasma cortisol and in plasma antidiuretic and growth hormones throughout surgery and prevents increases in plasma catecholamines up to but not during or after cardiopulmonary bypass in patients undergoing open heart surgery.

5.2 Pharmacokinetic properties

Alfentanil is a synthetic opioid with μ-agonist pharmacological effects.

After bolus injections ranging from 2.4 to 125 mcg/kg, plasma levels in man decay triexponentially with a terminal half life of approximately 90 minutes. Total distribution volume varies from 0.4 to 1.0 L/kg, indicating a limited distribution of alfentanil to the tissues. Plasma clearance, varying from 3.3 to 8.3 ml/kg/min represents approximately one third of liver plasma flow indicating that elimination of alfentanil is not flow dependent. Since only 0.4% of the dose is excreted with the urine as unchanged drug, elimination of alfentanil occurs mainly by metabolism.

These main parameters in patients undergoing surgery are similar to those in healthy volunteers. Only when the drug was given as the sole anaesthetic in a continuous high infusion over about 5 hours was the clearance of alfentanil reduced resulting in a plasma half-life of about 200 minutes, the distribution volume not being markedly changed.

Plasma protein binding of alfentanil is 92%, mainly due to a strong binding to the ‘acute phase’ α1 acid-glycoprotein. It is not bound to the blood cells. Pharmacokinetics were comparable in rats, dogs and man. The elderly show a longer half-life for Rapifen after IV bolus doses.

Special Populations

Paediatric patients

The data in children are limited. The values for the pharmacokinetic parameters are shown in the table below.
## Pharmacokinetic Parameters of Alfentanil in Paediatric Subjects

<table>
<thead>
<tr>
<th></th>
<th>$t_{1/2\beta}$ (hr)</th>
<th>CL (mL/kg/min)</th>
<th>Vdss (L/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preterm Neonates (0-27 days) Gestational age 25-40 weeks; $n=68$</td>
<td>0.7-8.8</td>
<td>0.9-8.4</td>
<td>0.3-1.2</td>
</tr>
<tr>
<td>Term Neonates (0-27 days) Gestational age: 35-41 weeks; $n=18$</td>
<td>4.1-5.5</td>
<td>1.7-3.2</td>
<td>0.5-0.8</td>
</tr>
<tr>
<td>Infants &amp; Toddlers 28 days - 23 months; $n=34$</td>
<td>0.9-1.2</td>
<td>7.7-13.1</td>
<td>0.4-1.1</td>
</tr>
<tr>
<td>Children 2-11 years; $n=32$</td>
<td>0.7-1.3</td>
<td>4.7-10.2</td>
<td>0.2-1.0</td>
</tr>
<tr>
<td>Adolescents 12-14 years; $n=3$</td>
<td>1.1-1.9</td>
<td>5.5-7.4</td>
<td>0.3-0.6</td>
</tr>
</tbody>
</table>

Note: Data for neonates, infants & toddlers, and children are given as range of mean values.

CL = clearance, Vdss = volume of distribution at steady state, $t_{1/2\beta}$ = half-life in the elimination phase.

Protein binding in newborns is 75% and increases in children to 85%.

Pharmacokinetic information on the use of alfentanil in children is limited. Alfentanil is metabolised by CYP3A4. CYP3A4 activity is low in neonates and increases after birth to reach 30 to 40% of adult levels at 1 month of age. Activity of CYP3A4 increases further to 45% at 6 months, 80% at 12 months.

**Hepatic Impairment**

After administration of a single intravenous dose of 50 mcg/kg, the terminal half-life in cirrhotic patients is significantly longer than in controls. The volume of distribution remains unchanged. The free fraction of alfentanil increases in cirrhotic patients to 18.5% compared with 11.5% in controls. This increase in free fraction together with a reduction in clearance from 3.06 mL/min/kg in controls to 1.60 mL/min/kg in cirrhotic patients will result in a more prolonged and pronounced effect (see Section 4.4.).

**Renal Impairment**

The volume of distribution and clearance of the free fraction is similar in renal failure patients and healthy controls. The free fraction of alfentanil in patients with renal failure is increased to 12.4 to 19% compared with 10.3 to 11% in controls. This may result in an increase in clinical effects of alfentanil (see Section 4.4.).

### 5.3 Preclinical safety data

Preclinical effects observed were only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use.

### 6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Sodium chloride
Water for injection

6.2 Incompatibilities
See ‘Dosage and dosage schedules’.

6.3 Shelf Life
5 years.

6.4 Special precautions for storage
Store in a controlled drug store. This medicinal product does not require any special storage conditions.

6.5 Nature and Contents of Container
Colourless glass one-point-cut ampoules (PhEur, Type I).
Pack size: packs of 10 x 2 ml ampoules; packs of 5 and 10* x 10 ml ampoules.
*Not all pack sizes maybe marketed.

6.6 Special precautions for disposal and other handling
For single use only. Discard any unused contents.
Wear gloves while opening ampoule.
Accidental dermal exposure should be treated by rinsing the affected area with water.
Avoid usage of soap, alcohol, and other cleaning materials that may cause chemical or physical abrasions to the skin.

7 MARKETING AUTHORISATION HOLDER
Janssen-Cilag Limited
50-100 Holmers Farm Way
High Wycombe
Buckinghamshire
8 MARKETING AUTHORISATION NUMBER(S)

PL 00242/0091

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

28/09/2005

10 DATE OF REVISION OF THE TEXT

02/05/2017